
Janssen Research & Development*

Investigator's Brochure

JNJ-64007957 (teclistamab)

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SUMMARY OF CHANGES FROM PREVIOUS EDITION

The following summarizes only the major changes to the previous edition (Edition 9) of this Investigator's Brochure (IB). New or updated safety and/or efficacy information is not detailed in this table but can be found in the IB.

Section	Summary of Change
General	All changes made to the sections noted have been incorporated into the Summary Section as appropriate. The IB Edition History has been removed as part of a template update.
Section 1, Introduction	No new information available.
Section 2, Physical, Chemical, and Pharmaceutical Properties and Formulations	Section 2.3: updated formulation components of the drug product to remove one component no longer being used.
Section 3, Nonclinical Studies	Section 3.1.2.3: condensed BCMA target expression text and updated with 1 new study on co-expression of BCMA and GPRC5D in human lymphoid and gastrointestinal tract tissues (PATHLJ23-007).
Section 4, Effects in Humans	Section 4.1.1: summary table of teclistamab monotherapy and combination studies moved to Appendix 2. Section 4.3.1.1: added efficacy data from TriMM-2 study (MMY1002) as of 31 January 2024 (primary analysis) and 30 April 2025 (final analysis), TriMM-3 study (MMY1005) as of 22 May 2025, and RedirecTT-1 study (MMY1003) as of 18 March 2025. Section 4.3.2: added/updated safety data for TriMM-2 as of 30 April 2025 (final analysis), and updated safety data for TriMM-3 as of 22 May 2025, RedirecTT-1 RP2R as of 18 March 2025, MajesTEC-4 study (EMN30/MMY3003) as of 03 March 2025, and MajesTEC-5 study (GMMG-HD10/DSMM-XX/MMY2003) Arms A, A1, B, and C as of 22 August 2025. Added safety data for MajesTEC-5 Arm D as of 10 July 2025. Streamlined safety data for MajesTEC-7 study (MMY3005). Section 4.4.1: new location for pharmacodynamics data. Added pharmacodynamics data from TriMM-2 as of 31 January 2024, RedirecTT-1 as of 18 March 2025, and MajesTEC-2 (MMY1004) as of 22 August 2024. Section 4.5: updated immunogenicity data for TriMM-2, TriMM-3, RedirecTT-1, and MajesTEC-2. Section 4.6: updated estimated exposure to teclistamab since launch. Added statement regarding the safety profile in the post-marketing setting.

Section	Summary of Change
Section 5 , Summary of Data and Guidance for Investigators	Updates made to PK and immunogenicity data for combination therapy in Section 4 have been incorporated into Section 5. Section 5.16: ADR table updated to reflect recent data cuts. No new ADRs were added.
Section 6 , Reference Safety Information	Added TAURUS study (EMN33/54767414MMY2089) to list of studies included in the RSI table. Added justification for life-threatening SARs. RSI table updated to reflect recent data cuts. Added new SARs considered expected by the Sponsor for the purposes of expedited reporting of SUSARs: metapneumovirus pneumonia, cellulitis, neutropenic sepsis, pneumonia klebsiella, and viral upper respiratory tract infection.
Appendices	Appendix 1.1: added study PATHLJ23-007. Appendix 1.4: added compliance table for GLP safety studies. Appendix 2: new location for summary table of teclistamab monotherapy and combination studies. Updated the number of patients for each study as of 22 August 2025.

TABLE OF CONTENTS

SUMMARY OF CHANGES FROM PREVIOUS EDITION	2
TABLE OF CONTENTS	4
LIST OF IN-TEXT TABLES AND FIGURES	7
LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS	8
SUMMARY.....	11
1. INTRODUCTION.....	14
1.1. Multiple Myeloma	14
1.2. B cell Maturation Antigen	15
1.3. Teclistamab.....	15
2. PHYSICAL, CHEMICAL, AND PHARMACEUTICAL PROPERTIES AND FORMULATIONS	16
2.1. Product Identification.....	16
2.2. Physical and Chemical Characteristics	16
2.3. Formulation Information	16
2.4. Other Pertinent Information.....	17
3. NONCLINICAL STUDIES.....	17
3.1. Nonclinical Pharmacology.....	17
3.1.1. Identification of a Toxicology Species for Teclistamab.....	17
3.1.2. Primary Pharmacodynamics.....	17
3.1.2.1. Teclistamab In Vitro and In Vivo Pharmacology.....	17
3.1.2.2. BCMA Expression on Hematological Tissues	17
3.1.2.3. BCMA Expression on Normal Tissues	18
3.1.2.4. Effect of Teclistamab on BCMA Signaling and Ligand Binding.....	18
3.1.2.5. Teclistamab-mediated T Cell-dependent Cytotoxicity of Multiple Myeloma Cell Lines.....	18
3.1.2.6. Teclistamab-mediated T Cell-dependent Cytotoxicity of Multiple Myeloma Cell Line in Healthy Whole Blood Assay	19
3.1.2.7. Teclistamab Binding, Cytotoxicity and T Cell Activation Assays Using Patient-derived CD138 ⁺ Multiple Myeloma Bone Marrow Cells	20
3.1.2.8. Teclistamab Cytotoxicity Assays Using Autologous CD138 ⁺ Multiple Myeloma Bone Marrow Cells.....	22
3.1.2.9. Effect of Teclistamab in Murine T Cell Redirection Tumor Models	22
3.1.3. Secondary Pharmacodynamics.....	23
3.1.4. Safety Pharmacology.....	23
3.2. Pharmacokinetics and Metabolism in Animals	24
3.2.1. Methods of Analysis.....	24
3.2.2. Absorption and Pharmacokinetics	24
3.2.2.1. Pharmacokinetics, Toxicokinetics, and Immunogenicity in Monkeys.....	24
3.2.2.2. Single-dose Subcutaneous Pharmacokinetics in Gottingen Minipigs	25
3.2.3. Distribution	25
3.2.4. Metabolism and Excretion	25
3.2.5. Pharmacokinetic Drug Interactions.....	25
3.3. Toxicology	26
3.3.1. Single-Dose Toxicity	26
3.3.2. Repeat-Dose Toxicity	27
3.3.3. Genotoxicity and Carcinogenicity	27
3.3.4. Reproduction and Developmental Studies	27
3.3.5. Local Tolerance	27
3.3.6. Other Toxicity Studies.....	28
3.4. Conclusions for Nonclinical Studies.....	28

4. EFFECTS IN HUMANS	28
4.1. Overview	28
4.1.1. Ongoing and Completed Clinical Studies	29
4.2. Pharmacokinetics and Product Metabolism	30
4.2.1. Teclistamab Monotherapy Pharmacokinetics	30
4.2.2. Teclistamab Pharmacokinetics in Combination Therapy Studies	32
4.3. Safety and Efficacy	32
4.3.1. Efficacy	32
4.3.1.1. MajesTEC-1 Study (MMY1001)	32
4.3.1.2. TriMM-2 Study (MMY1002)	33
4.3.1.3. TriMM-3 Study (MMY1005)	34
4.3.1.4. RedirecTT-1 Study (MMY1003)	34
4.3.2. Safety and Tolerability	35
4.3.2.1. Teclistamab Safety in Monotherapy Studies	36
4.3.2.1.1. MajesTEC-1 Study (MMY1001)	36
4.3.2.1.1.1. Primary Analysis in Participants Treated at the Recommended Dose	36
4.3.2.1.1.2. Follow-up Analysis in Participants Treated at the Recommended Dose	38
4.3.2.1.1.3. China Cohort Participants Treated at the Recommended Dose	39
4.3.2.1.1.4. Safety Data for Other Notable MajesTEC-1 Treatment Regimens	39
4.3.2.1.2. Study MMY1002 (Japan)	40
4.3.2.2. Teclistamab Safety in Combination Therapy Studies	41
4.3.2.2.1. TriMM-2 Study (MMY1002)	41
4.3.2.2.2. TriMM-3 Study (MMY1005)	44
4.3.2.2.3. RedirecTT-1 Study (MMY1003)	44
4.3.2.2.4. MajesTEC-2 Study (MMY1004)	46
4.3.2.2.5. MajesTEC-4 Study (EMN30/MMY3003)	49
4.3.2.2.5.1. Safety Run-in 1: Teclistamab 1.5 mg/kg SC + Lenalidomide	49
4.3.2.2.5.2. Safety Run-in 2	49
4.3.2.2.6. MajesTEC-5 Study (GMMG-HD10/DSMM-XX/MMY2003)	51
4.3.2.2.7. MajesTEC-7 Study (MMY3005)	54
4.3.2.2.7.1. Safety Run-in 1 (Tec-DR)	54
4.3.2.2.7.2. Safety Run-in 2 (Tec-DR)	55
4.4. Biomarker Evaluations	55
4.4.1. Pharmacodynamics	55
4.5. Immunogenicity (Anti-drug Antibodies)	57
4.6. Marketing Experience	57
5. SUMMARY OF DATA AND GUIDANCE FOR INVESTIGATORS	58
5.1. Description of Teclistamab	58
5.2. Clinical Pharmacokinetics	58
5.3. Pharmacodynamics	59
5.4. Indications and Use	59
5.5. Contraindications	59
5.6. Precautions and Warnings	59
5.7. Drug Interactions	62
5.8. Carcinogenicity, Mutagenicity, and Impairment of Fertility	62
5.9. Pregnancy and Breastfeeding	62
5.10. Immunogenicity (Anti-drug Antibodies)	63
5.11. Use in Specific Populations (Geriatric and Pediatric)	63
5.12. Use in Renal/Hepatic Dysfunction/Failure	63
5.13. Effects on Ability to Drive and Use Machines	63
5.14. Overdosage and Abuse Potential	63
5.15. How Supplied	64
5.16. Adverse Drug Reactions	64
6. REFERENCE SAFETY INFORMATION	70
7. REFERENCES	73

APPENDIX 1:	OVERVIEW OF NONCLINICAL STUDIES OF TECLISTAMAB	75
APPENDIX 2:	SUMMARY OF TECLISTAMAB MONOTHERAPY AND COMBINATION STUDIES.....	81
APPENDIX 3:	CLINICAL TABLES AND FIGURES FOR STUDY MAJESTEC-1 (64007957MMY1001)	93

LIST OF IN-TEXT TABLES AND FIGURES

TABLES

Table 1:	Adverse Drug Reactions Associated with Teclistamab; All Treated Analysis Set (Study 64007957MMY1001)	65
Table 2:	Serious Adverse Reactions for Teclistamab Considered Expected for Safety Reporting Purposes; All Treated Analysis Set (Study 54767414MMY2089, 64007957MMY1001, 64007957MMY1002, 64007957MMY1003, 64007957MMY1004, 64007957MMY2003, 64007957MMY3003, 64007957MMY3005, 64407564MMY1002, & 64407564MMY1005).....	71

FIGURES

Figure 1:	Schematic Overview of the Mode-of-Action of Teclistamab	16
Figure 2:	T Cell-mediated Teclistamab Antibody-dependent Cytotoxicity of Multiple Myeloma Cell Lines	19
Figure 3:	Dose Response Curve of H929 Cell Cytotoxicity in Whole Blood After 48-hour Incubation with Teclistamab	20
Figure 4:	Cytotoxic Potency of Teclistamab Antibody Against Human Primary Multiple Myeloma Plasma Cells	21
Figure 5:	Teclistamab-mediated Cytotoxicity of BCMA ⁺ Multiple Myeloma Tumors in Murine Models	23
Figure 6:	Mean (SD) Serum Concentration-time Profiles of Teclistamab After SC Administration of Teclistamab at 0.06/0.3 then 1.5 mg/kg Weekly (RP2D) in Subjects with Multiple Myeloma (Phase 1); Pharmacokinetics Analysis Set (64007957MMY1001; Pivotal RP2D [Phase 1 only])	31

LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviations

ADA	anti-drug antibody
ADR	adverse drug reactions
AE(s)	adverse event(s)
APRIL	A proliferation-inducing ligand
ASCT	autologous stem cell transplant
ASTCT	American Society for Transplantation and Cellular Therapy
BAFF	B cell activating factor
B cell(s)	B lymphocyte(s)
BCMA	B cell maturation antigen
BSA	bovine serum albumin
CA	California
CAR	chimeric antigen receptor
cBCMA	cynomolgus B cell maturation antigen
cCD3	cynomolgus cluster of differentiation 3
CD	cluster of differentiation
CFR	Code of Federal Regulations
CHO	Chinese hamster ovary
CI	confidence interval
CNS	central nervous system
COVID-19	coronavirus disease 2019
CR	complete response
CRS	cytokine release syndrome
CV	coefficient of variation
CYP	cytochrome P450
DLT	dose-limiting toxicity
DNA	deoxyribonucleic acid
DOR	duration of response
DPd	daratumumab SC in combination with pomalidomide and dexamethasone
DR	daratumumab SC in combination with lenalidomide
DRd	daratumumab SC in combination with lenalidomide and dexamethasone
DVd	daratumumab SC in combination with bortezomib and dexamethasone
DVRd	daratumumab SC in combination with bortezomib, lenalidomide and dexamethasone
ECLIA	electrochemiluminescence immunoassay
eCRF	electronic Case Report Form
EDTA	ethylenediaminetetraacetic acid
EEA	European Economic Area
ELISA	enzyme-linked immunosorbent assay
EMA	European Medicines Agency
EMD	extramedullary disease
EPd	elotuzumab, pomalidomide and dexamethasone
E-R	exposure-response
EU	European Union
FACS	fluorescence-activated cell sorting
FDA	Food and Drug Administration
GLP	Good Laboratory Practice
GPRC5D	G protein-coupled receptor family C group 5 member D
hBCMA	human B cell maturation antigen
HBV	Hepatitis B virus
HDT	high-dose chemotherapy
HEK	human embryonic kidney
HLA-DR	human leukocyte antigen DR subtype
IB	Investigator's Brochure
ICANS	immune effector cell-associated neurotoxicity syndrome
ICE	Immune Effector Cell-associated Encephalopathy

ICH	International Council for Harmonisation
IFN- γ	interferon-gamma
IgG	immunoglobulin G
IgG4	immunoglobulin G4
IgG-4 PAA	immunoglobulin G4-proline, alanine, alanine
IHC	immunohistochemistry
IL	interleukin
IMiD	immunomodulatory drug
IMWG	International Myeloma Working Group
IP	intraperitoneal(ly)
IPPI	Investigational Product Preparation Instructions
IRC	Independent Review Committee
ISH	in situ hybridization
ISS	International Staging System
IV	intravenous
JNJ-79635322-D	JNJ-79635322 in combination with daratumumab
JNJ-79635322-DR	JNJ-79635322 in combination with daratumumab and lenalidomide
JRD	Janssen Research & Development, LLC
Kd	carfilzomib and dexamethasone
LAG-3	lymphocyte activation gene 3
MAD	Mutual Acceptance of Data
MD	Maryland
MedDRA	Medical Dictionary for Regulatory Activities
MGUS	monoclonal gammopathy of undetermined significance
MHC	major histocompatibility complex
MI	Michigan
M-proteins	monoclonal proteins
MRD	minimal residual disease
MS	mass spectrometry
MSD	MesoScale Discovery
NA	not applicable
NC	North Carolina
NCI-CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NE	not estimable
NF- κ B	nuclear factor kappa-light-chain-enhancer of activated B cells
NK	natural killer
NM	New Mexico
NOEL	no observed effect level
NSG	NOD/scid γ c-/-
NV	Nevada
OECD	Organisation for Economic Co-operation and Development
ORR	overall response rate
OS	overall survival
PA	Pennsylvania
PBMC	peripheral blood mononuclear cell
PBS	phosphate-buffered saline
PD-1	programmed cell death protein-1
PFS	progression-free survival
PI	proteasome inhibitor
PK	pharmacokinetic(s)
PML	progressive multifocal leukoencephalopathy
PR	partial response
PT	preferred term
PVd	pomalidomide, bortezomib, and dexamethasone
QW	weekly
QXW	every X weeks
qPCR	quantitative polymerase chain reaction
RP2D	recommended Phase 2 dose

RP2R	recommended Phase 2 regimen
RNA	ribonucleic acid
RSI	Reference Safety Information
SAR	serious adverse reaction
sBCMA	soluble B cell maturation antigen
SC	subcutaneous(ly)
sCR	stringent complete response
SD	standard deviation
SOC	system organ class
SUSAR	Suspected Unexpected Serious Adverse Reaction
Tal-DR	talquetamab in combination with daratumumab SC and lenalidomide
Tal-P	talquetamab in combination with pomalidomide
Tal-Tec	teclistamab in combination with talquetamab
T cell(s)	T lymphocyte(s)
TEAE	treatment-emergent adverse event
Tec-D	teclistamab in combination with daratumumab
Tec-DR	teclistamab with daratumumab SC and lenalidomide
Tec-DVRd	teclistamab with daratumumab SC, bortezomib, lenalidomide, and dexamethasone
Tec-Len	teclistamab in combination with lenalidomide
TIM-3	T cell immunoglobulin and mucin domain 3
TK	toxicokinetic
TNF	tumor necrosis factor
Treg	regulatory T cell
UK	United Kingdom
US(A)	United States (of America)
VGPR	very good partial response
w/v	weight per volume

Definitions of Terms

AUC	area under the serum concentration versus time curve
AUC _{Day22-29}	area under the serum concentration versus time curve from Day 22 to Day 29
AUC _{last}	area under the serum concentration versus time curve from time 0 to the time corresponding to the last quantifiable concentration
AUC _{tau}	area under the serum concentration versus time curve during the dosing interval
C _{ave,1stdose}	predicted average concentration of the first treatment dose
C _{max}	maximum observed serum concentration
C _{trough}	trough concentration
C _{trough,ss}	predicted steady-state trough concentration
EC ₅₀	concentration at 50% of maximal effect
EC ₉₀	concentration at 90% of maximal effect
IC ₅₀	half-maximal inhibitory concentration
T _{max}	individual time to reach the maximum concentration

SUMMARY

This summary provides only the key findings for each section and does not include all the information for JNJ-64007957 (hereafter referred to as teclistamab). Full information is available in the IB using the hyperlinked headings provided below.

INTRODUCTION

Teclistamab is a full-size, IgG-4 PAA lambda light chain bispecific antibody that targets the CD3 receptor expressed on the surface of T cells and BCMA, which is expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B cells and plasma cells. With its dual binding sites, teclistamab is able to draw CD3+ T cells in close proximity to BCMA+ cells, resulting in T cell activation and subsequent lysis of BCMA+ cells.

Teclistamab is being developed for the treatment of patients with multiple myeloma. Teclistamab monotherapy has been approved by the EMA, FDA, and other health authorities for the treatment of patients with relapsed/refractory multiple myeloma.

PHYSICAL, CHEMICAL, AND PHARMACEUTICAL PROPERTIES AND FORMULATIONS

Teclistamab has a molecular weight of 146.261 kDa for the predominant G0F/G0F glycoform and isoelectric points ranging from pI 8.00 to 8.65. Teclistamab is formulated as a solution for SC injection.

NONCLINICAL STUDIES

Nonclinical Pharmacology

- Nonclinical in vitro and in vivo data support teclistamab as a bispecific antibody that selectively promotes the T cell-dependent elimination of human cells expressing BCMA.
- Teclistamab binds specifically to BCMA-expressing multiple myeloma cells and was shown to mediate in vitro T cell-dependent cytotoxicity in multiple myeloma cell lines, primary myeloma patient bone marrow mononuclear cells and to completely inhibit the growth of a BCMA⁺ cell line in a murine model of multiple myeloma.

Pharmacokinetics and Metabolism in Animals

Exposure ($C_{\max}$ and AUC) increased in a dose-proportional manner in cynomolgus monkeys following 5 weekly IV doses of 0.1 to 30 mg/kg.

Toxicology

- In the pivotal GLP toxicity study in cynomolgus monkeys, the NOEL for 5 weekly IV doses of teclistamab was 30 mg/kg, the highest tested dose and an expected pharmacologically active dose. This NOEL corresponded to a $C_{\max}$ (on Day 22) of 1084.01 $\mu\text{g/mL}$ and $\text{AUC}_{\text{Day22-29}}$ of 3549.19 $\mu\text{g}\cdot\text{day/mL}$. ADAs were detected in 21 of 30 teclistamab-treated animals. Fourteen of these animals had exposure comparable to that of ADA-negative animals in the same dose groups.
- In a GLP SC local tolerance study of teclistamab (10 mg/mL) in New Zealand White rabbits (not a pharmacologically relevant species) to support transition from IV to SC administration in humans, no adverse injection site observations or effects at the injection site indicated local tolerance of the formulation.
- Teclistamab is not expected to be teratogenic based on a weight-of-evidence risk assessment.

EFFECTS IN HUMANS

- The recommended treatment dose is 1.5 mg/kg weekly teclistamab SC, preceded by step-up doses of 0.06 and 0.3 mg/kg. This dose was approved for monotherapy based on results from the ongoing MajesTEC-1 study, which is a first-in-human study of teclistamab in adult participants with relapsed or refractory multiple myeloma. In patients who have a response for a minimum of 6 months, a reduced dosing frequency of 1.5 mg/kg SC Q2W until disease progression or unacceptable toxicity may be considered.
- Additional studies are ongoing in participants with newly diagnosed or relapsed/refractory multiple myeloma to evaluate teclistamab as monotherapy (MMY1002 Japan, MajesTEC-4,

MajesTEC-9, and MajesTEC-10) or in combination regimens (TriMM-2, TriMM-3, RedirecTT-1, MajesTEC-2, MajesTEC-5, MajesTEC-3, MajesTEC-4, MajesTEC-7, TAURUS, and MonumenTAL-6).

Pharmacokinetics and Product Metabolism

MajesTEC-1 Study (Monotherapy)

Teclistamab exhibited approximately dose-proportional PK following SC administration across the dose range of 0.08 to 3 mg/kg. Mean accumulation ratio between the first and 13th weekly treatment dose was 4.2- and 5.3-fold for C_{max} and AUC_{tau}, respectively. Mean bioavailability following SC weekly administration for the treatment dose was 72%.

Population PK analysis showed that teclistamab clearance changes over time, with a mean (CV%) maximal reduction from baseline to the 13th treatment dose of 40.8% (56%). The geometric mean (CV%) clearance is 0.472 L/day (64%) at the 13th treatment dose. Patients who discontinue teclistamab after the 13th treatment dose are expected to have a 50% reduction from C_{max} in teclistamab concentration at a median (5th to 95th percentile) time of 15 (7 to 33) days after T_{max} and a 97% reduction from C_{max} in teclistamab concentration at a median time of 69 (32 to 163) days after T_{max}. Results of population PK analysis indicate that mild or moderate renal impairment and mild hepatic impairment did not significantly influence the PK of teclistamab. Limited data were available from patients with severe renal impairment, and no data were available from patients with moderate or severe hepatic impairment. Additionally, results of population PK indicated that soluble BCMA did not impact the PK of teclistamab.

TriMM-2, TriMM-3, RedirecTT-1, and MajesTEC-2 Studies (Combination Therapy)

Teclistamab serum concentrations in TriMM-2, TriMM-3, RedirecTT-1, and MajesTEC-2 were generally within the range of the values observed in participants treated with teclistamab monotherapy in MajesTEC-1.

Immunogenicity

In the MajesTEC-1 study, 1 of 239 participants (0.4%) receiving teclistamab SC developed ADAs of low titer. These ADAs were

neutralizing antibodies to teclistamab and seemed to have no impact on safety in this participant. None (0%) of the 186 participants who were ADA evaluable for the recommended dose were identified as positive for antibodies to teclistamab. In the combination studies, of the 124 participants (TriMM-2), 22 participants (TriMM-3), 188 participants (RedirecTT-1), and 137 participants (MajesTEC-2) who were ADA evaluable, none (0%) were identified as positive for antibodies to teclistamab.

Pharmacodynamics

MajesTEC-1 Study (Monotherapy SC Administration)

Participants treated with teclistamab SC doses ranging from 0.08 to 6 mg/kg weekly show that administration of teclistamab leads to pharmacodynamic changes following step-up dose(s) and within the first cycle that were characteristic of the mechanism of action for teclistamab (eg, T cell redistribution, activation, and cytokine production).

Within 1 month, the majority of responders had reduction in soluble BCMA, and a greater reduction in soluble BCMA was observed in patients with deeper responses to teclistamab.

TriMM-2, RedirecTT-1, and MajesTEC-2 Studies (Combination Therapy)

Participants treated with teclistamab in combination regimens exhibited pharmacodynamic changes consistent with the mechanism of action of teclistamab monotherapy and/or the combination treatment partner.

Efficacy

MajesTEC-1 Study (Monotherapy)

Efficacy was evaluated in 150 participants treated with 1.5 mg/kg teclistamab SC monotherapy weekly (clinical cutoff: 09 November 2021). The ORR (PR or better) was 62.7% (95% CI: 54.4%, 70.4%), with 88 participants (58.7%) having a VGPR or better and 48 participants (32%) having a CR or better.

TriMM-2 and RedirecTT-1 Studies (Combination Therapy)

The ORR (PR or better) was 68.9% for TriMM-2 RP2D (clinical cutoff: 31 January 2024; n=61) and 78.9% for RedirecTT-1 RP2R (clinical

cutoff: 18 March 2025; n=90). VGPR or better was achieved by 63.9% and 70.0% of participants, respectively, and CR or better was achieved by 44.3% and 54.4% of participants, respectively.

Safety and Tolerability

- The primary safety analysis for MajesTEC-1 (clinical cutoff: 07 September 2021) includes 165 participants treated with 1.5 mg/kg teclistamab SC weekly. The most frequently reported TEAEs ($\geq 20\%$) were CRS (71.5%), neutropenia (65.5%), anemia (49.7%), thrombocytopenia (38.2%), lymphopenia (33.9%), injection site erythema (25.5%), fatigue (24.8%), nausea (24.2%), headache (21.8%), and diarrhea (20.6%).
- Of the 20 deaths (12.1%) reported within 30 days of the last dose of teclistamab; 6 were due to TEAEs, none of which were related to study drug. Serious TEAEs were experienced by 88 participants (53.3%).
- Grade 3 or 4 TEAEs were experienced by 152 participants (92.1%), with the majority (73.9%) being considered related to study drug. CRS was experienced by 118 participants (71.5%); the majority were Grade 1 or 2. There were no CRS events leading to treatment discontinuation nor to death. ICANS was reported in 5 participants, all were Grade 1 or 2.
- Safety data from key teclistamab dosing cohorts in combination studies are generally comparable with the safety profile observed in the MajesTEC-1 monotherapy study.
- Important identified risks for teclistamab are CRS, neurologic toxicity (including ICANS), and serious infections.

Marketing Experience

Teclistamab first received marketing authorization in the European Union on 23 August 2022, was approved in the US on 25 October 2022, and has subsequently been approved in over 60 countries/territories. Based on the 56,351,480 mg distributed worldwide from launch to 31 August 2025, the estimated exposure to teclistamab is 9,884 person-years.

The surveillance of spontaneous and solicited cases of AEs reported with the use of teclistamab indicates that the safety profile of the drug in the post-marketing setting is consistent with the drug's known safety profile established from clinical studies.

SUMMARY OF DATA AND GUIDANCE FOR INVESTIGATORS

A table providing a complete list of ADRs is presented in [Table 1](#) in [Section 5](#).

REFERENCE SAFETY INFORMATION

The SARs identified for assessment of expectedness are listed in [Section 6](#).

1. INTRODUCTION

Teclistamab (also known as JNJ-64007957) is being developed for the treatment of multiple myeloma. Teclistamab monotherapy has been approved by the EMA, FDA, and other health authorities for the treatment of patients with relapsed/refractory multiple myeloma. The active ingredient teclistamab is a humanized antibody that specifically recognizes the BCMA receptor, which is expressed at a high level in multiple myeloma cells, and the CD3 receptor complex expressed on T cells.

1.1. Multiple Myeloma

Multiple myeloma is a malignant plasma cell disorder that accounts for approximately 10% of all hematologic cancers (Kyle 2008). It evolves from a disease of MGUS, an asymptomatic premalignant stage with clonal plasma cell proliferation present in more than 3% of the population above the age of 50 years. MGUS progresses directly to multiple myeloma at a rate of about 1% per year (Kyle 2002; Kyle 2008; Kyle 2009). Furthermore, MGUS has a risk to progress to smoldering multiple myeloma, originally identified as an intermediate stage evolving from MGUS, but subsequent studies define it as a separate and distinct clonal disorder with a higher risk (10%) to progress to multiple myeloma (Korde 2011; Kyle 2010; Patel 2004; Sundararajan 2016).

Mechanistically, multiple myeloma is characterized by production of M-proteins comprised of pathological immunoglobulins or fragments of such, which have lost their function (Kyle 2009; Palaologou 2014). The proliferation of multiple myeloma cells leads to subsequent displacement from the normal bone marrow niche, overproduction of M-proteins, characteristic osteolytic lesions, increased susceptibility to infections, hypercalcemia, renal insufficiency or failure, and neurological complications (Korde 2011; Palaologou 2014).

Treatment options for multiple myeloma have substantially improved over time and vary depending on the aggressiveness of the disease, underlying prognostic factors, physical condition of the patient, and existing comorbidities. Therapeutic options include PIs, IMiDs, alkylating agents, monoclonal antibodies, antibody drug conjugate, histone deacetylase inhibitor, nuclear protein export inhibitor, CAR-T cell therapy, bispecific antibodies, and stem cell transplantation.

Despite these therapeutic achievements, the disease recurs and is associated with additional risk factors (eg, comorbidities or increasing age), thus warranting the need for novel therapeutic approaches. Multiple myeloma remains an incurable malignancy for the vast majority of patients and represents an unmet medical need with significant morbidity and mortality. Functionally high-risk multiple myeloma populations with poor outcomes, such as patients with EMD for whom there are no approved standard of care treatment regimens, constitute a specific area of particularly significant unmet medical need. In addition to improved treatment of relapsed/refractory patients, improvement in upfront treatment options for multiple myeloma is critical prior to disease becoming refractory. The disease is most sensitive to therapy at the time of diagnosis, and initial treatment, therefore, provides the highest probability of achieving a long disease-free interval.

1.2. B cell Maturation Antigen

BCMA (also known as CD269 and TNF receptor superfamily member 17), a 20 kD receptor plays a critical role in B cell maturation and subsequent differentiation into plasma cells. BCMA binds 2 ligands: A proliferation-inducing ligand (APRIL; CD256) and B cell activating factor ([B cell activating factor receptor] BAFF; CD257) (Patel 2004). APRIL and BAFF are type II transmembrane proteins that are readily cleaved by Furin and secreted as soluble trimers by many cells (B cells [autocrine], monocytes, dendritic cells, T cells, osteoclasts, etc) and can bind to the BCMA receptor. Different from other surface markers, BCMA is exclusively expressed in B-lineage cells and is selectively induced during plasma cell differentiation (Darce 2007).

BCMA receptor is a 184 amino acid protein that neither has a secretory signal sequence nor any specific protease cleavage site in the N-terminal 54 amino acid extracellular domain. However, the N-terminal fragment is observed as a soluble protein in the serum as a result of gamma secretase activity that cleaves BCMA protein at the transmembrane domain (Laurent 2015). Inhibition of gamma secretase treatment results in significant increase of BCMA surface protein in human primary B cells (Laurent 2015). High levels of sBCMA were measured in multiple myeloma patient serum samples and correlated with the plasma cell counts (Sanchez 2012).

BCMA messenger ribonucleic acid and protein were universally detected in multiple myeloma cell lines and in all malignant plasma cells from multiple myeloma patients by us and others (Carpenter 2013; Novak 2004). Similarly, in multiple myeloma cell lines and patient samples, BCMA is more stably expressed compared with a key plasma cell marker (CD138) that is also expressed on normal fibroblasts and epithelial cells (Palaiologou 2014). BCMA expression is selective for B cell lineage and was not detected in any major tissues except for infiltrating plasma cells as determined by IHC methods (Carpenter 2013). Taken together, the selective expression of BCMA on the B cell lineage makes it an appealing target for T cell-mediated therapy to treat plasma cell disorders like multiple myeloma (Frerichs 2020; Frigyesi 2014; Tai 2015).

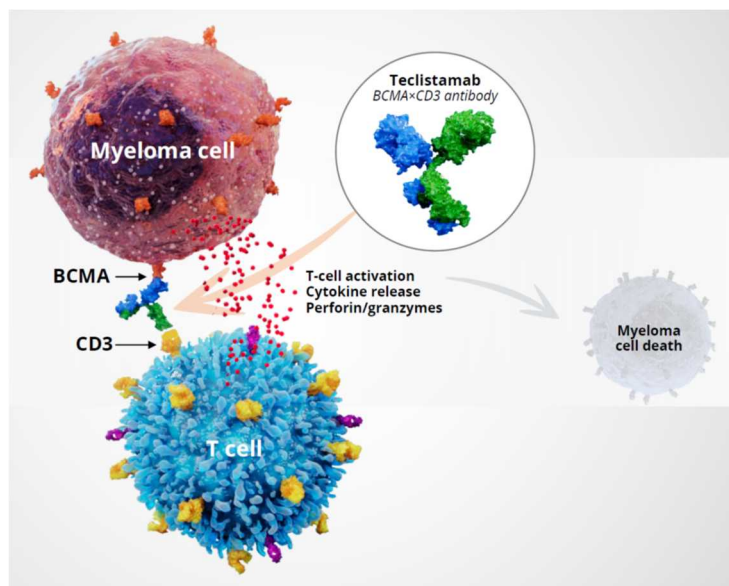
BCMA has been established as a validated target in multiple myeloma, with multiple therapeutic modalities demonstrating promising efficacy and an acceptable safety profile in pretreated patients (Huehls 2015; Strohl 2019; Shah 2020). Idecabtagene vicleucel and ciltacabtagene autoleucel, both CAR-T therapies targeting BCMA (Berdeja 2021; Munshi 2021), have been approved for the treatment of pretreated relapsed/refractory multiple myeloma.

1.3. Teclistamab

Teclistamab is a full-size, IgG-4 PAA lambda light chain bispecific antibody that targets the CD3 receptor expressed on the surface of T cells and BCMA, which is expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B cells and plasma cells. With its dual binding sites, teclistamab is able to draw CD3+ T cells in close proximity to BCMA+ cells, resulting in T cell activation and subsequent lysis of BCMA+ cells which is mediated by secreted perforin and various granzymes stored in the secretory vesicles of cytotoxic T cells. This effect occurs without regard to T cell receptor specificity or reliance on MHC Class 1 molecules on the surface of antigen presenting cells for activation, leading to cell death of the BCMA+ cells (Figure 1).

Teclistamab was developed by generating a controlled fragment antigen binding arm exchange from 2 parental antibodies (Labrijn 2013): (1) an anti-BCMA antibody that originated from Open Monoclonal Technology rat immunization using the human BCMA-fragment crystallizable recombinant protein and (2) an anti-CD3 ϵ antibody that originated from a public domain antibody known as SP34, which was further humanized and affinity matured. Teclistamab binds to human and cynomolgus CD3 and BCMA, but not to rodent CD3, and only weakly to rodent BCMA.

Figure 1: Schematic Overview of the Mode-of-Action of Teclistamab



2. PHYSICAL, CHEMICAL, AND PHARMACEUTICAL PROPERTIES AND FORMULATIONS

2.1. Product Identification

Teclistamab is a humanized IgG-4 PAA-based bispecific antibody directed against BCMA and the CD3 receptors, produced by cultivation of recombinant CHO cells, followed by isolation, chromatographic purification, and formulation.

2.2. Physical and Chemical Characteristics

Teclistamab has a molecular mass of 146.261 kD for the predominant G0F/G0F glycoform and isoelectric points ranging from pI 8.00 to 8.65. The absorptivity constant for teclistamab at 280 nm was theoretically determined to be 1.58 (mg/mL)⁻¹cm⁻¹.

2.3. Formulation Information

The formulation components of the 10 and 90 mg/mL drug products include teclistamab, Sodium acetate trihydrate, Glacial acetic acid, Sucrose, Polysorbate 20, EDTA, and water for injection.

The drug products are supplied as vials that must be stored at controlled refrigerated temperatures.

When used for SC administration, the drug product should be administered per instructions provided in the IPPI.

2.4. Other Pertinent Information

Detailed instructions on handling and storage conditions will accompany clinical drug supplies to the clinical study sites. The storage conditions and expiry dates will be indicated on the label. The IPPI should be referred to for selected formulations used for each clinical study.

3. NONCLINICAL STUDIES

All nonclinical studies listed in this IB for teclistamab were conducted in accordance with best scientific principles. Pivotal nonclinical safety studies were conducted in conformance with GLP, 21 CFR, Part 58 and/or the principles of OECD-GLP in a test facility that was part of the national GLP monitoring program of an EU Member State, an OECD Member Country, or fully adherent to the Mutual Acceptance of Data in the period that the study was conducted. An overview of the nonclinical studies is provided in [Appendix 1](#). A separate summary table listing the GLP safety studies with information on GLP compliance is provided in [Appendix 1.4](#).

3.1. Nonclinical Pharmacology

3.1.1. Identification of a Toxicology Species for Teclistamab

The cynomolgus monkey was the most pharmacologically relevant animal model to evaluate the potential toxicity of teclistamab, based on >90% sequence identity of cBCMA with hBCMA extracellular domain, teclistamab in vitro binding to cBCMA and cCD3, and teclistamab functional activity (measured by cytotoxicity and T cell activation assays) against cell lines overexpressing cBCMA. However, teclistamab had approximately 36-fold lower binding affinity and 2- to 20-fold lower functional activity (cytotoxicity and T cell activation) for cBCMA than for hBCMA. Therefore, nonclinical safety data from the in vivo cynomolgus monkey studies may have limited utility for human risk assessment.

Rodents were not a pharmacologically relevant species because teclistamab does not bind to rodent CD3 and binds only weakly to rodent BCMA. Further, CD3 bispecifics require the formation of a trimolecular complex by the binding of the CD3 bispecific to CD3 on T cells and to tumor associated antigen (BCMA) on target cells in order to elicit pharmacologic activity.

3.1.2. Primary Pharmacodynamics

3.1.2.1. Teclistamab In Vitro and In Vivo Pharmacology

Preclinical in vitro and in vivo experimental data support teclistamab as a bispecific antibody that selectively promotes the T cell-dependent elimination of human cells expressing BCMA.

3.1.2.2. BCMA Expression on Hematological Tissues

To evaluate the expression of BCMA and CD3 on leukocytes, ex vivo whole blood from normal human donors and frozen bone marrow from multiple myeloma patients were stained with teclistamab. No BCMA expression was observed on basophils, plasmacytoid dendritic cells, monocytes, neutrophils, and eosinophils using cell specific markers in whole blood from healthy human donors. However, BCMA was detected in frozen bone marrow mononuclear cell samples ([Figure 4](#)). As expected, teclistamab stained T cells in whole blood.

3.1.2.3. BCMA Expression on Normal Tissues

BCMA is a well-characterized, highly restricted target with expression limited to B cell lineage cells including, particularly in the interfollicular region of germinal centers, lymphocytes and plasma cells present in hematolymphoid organs (bone marrow, spleen, tonsil, lymph node, and thymus) as well as interstitial/resident lymphocytes and plasma cells present in various tissues (skin, testis, salivary glands, stomach, duodenum, colon, rectum, and lung) (Bu 2018; Carpenter 2013; Chiu 2007; Marella 2022; Zhang 2023; Studies Histo-06092020 and PATHLJ23-007).

Previously reported normal tissue BCMA expression (Bu 2018; Carpenter 2013; Van Oekelen 2021; Zhang 2023) included a limited number of anatomical locations within the brain; therefore, expression of BCMA in human normal (non-diseased) brain was investigated. This study employed 2 independent IHC assays and in situ hybridization and included 107 formalin fixed, paraffin-embedded brain samples (cerebrum, basal ganglia, cerebellum, brainstem; 63 unique donors). BCMA protein was not detected in human normal (non-diseased) brain in this investigation (Marella 2022; Study Histo-06092020).

To assess potential for exaggerated pharmacology when teclistamab and talquetamab are utilized in combination, co-expression of BCMA and GPRC5D was evaluated in select human normal lymphoid tissues (bone marrow, lymph node, spleen, and tonsil) and the gastrointestinal tract (colon) by hybridization chain reaction RNA fluorescence ISH and IHC (PATHLJ23-007). BCMA⁺ cells were predominantly found in lymphoid tissues, particularly the tonsil (average of 11.30%), whereas a notably high average percentage of GPRC5D⁺ cells (3.99%) or CD138⁺ plasma cells (20.03%) were observed among nucleated cells in the lamina propria of the colon. Importantly, co-localization of BCMA and GPRC5D in CD138⁺ plasma cells was very limited, typically below 1% in all tissues assessed. The low percentage of BCMA and GPRC5D co-expressing plasma cells in normal tissues suggests that different subsets of plasma cells may be targeted by teclistamab and talquetamab, respectively.

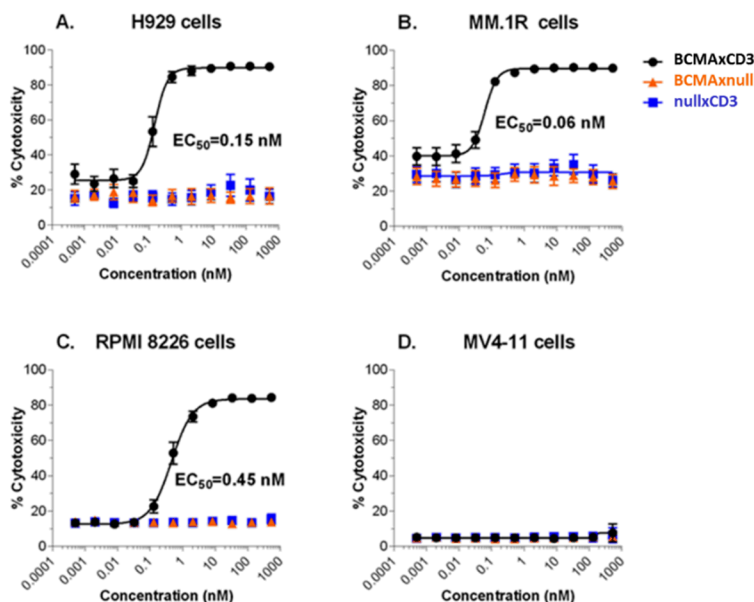
3.1.2.4. Effect of Teclistamab on BCMA Signaling and Ligand Binding

BCMA mediates downstream signaling such as NF-κB and p38 through its ligands APRIL and BAFF. Treatment with teclistamab led to no agonistic activation of BCMA-mediated signaling with no signs of increased phosphorylation on p38 (Pillariseti 2020).

3.1.2.5. Teclistamab-mediated T Cell-dependent Cytotoxicity of Multiple Myeloma Cell Lines

Treatment with teclistamab led to T cell-mediated cytotoxicity after 48 hours of incubation with BCMA⁺ multiple myeloma cell lines (H929, MM.1R, and RPMI 8226) and T cells from 6 different healthy donors resulted in significant cytotoxicity (Study DD16321). Importantly, there was no lysis of the BCMA-negative cell line MV4-11 or with control antibodies (unrelated arm × CD3 or BCMA × unrelated arm; see Figure 2). Concomitantly, teclistamab induced potent T cell activation when incubated with BCMA⁺ multiple myeloma cells and healthy donor pan T cells (Pillariseti 2020).

Figure 2: T Cell-mediated Teclistamab Antibody-dependent Cytotoxicity of Multiple Myeloma Cell Lines

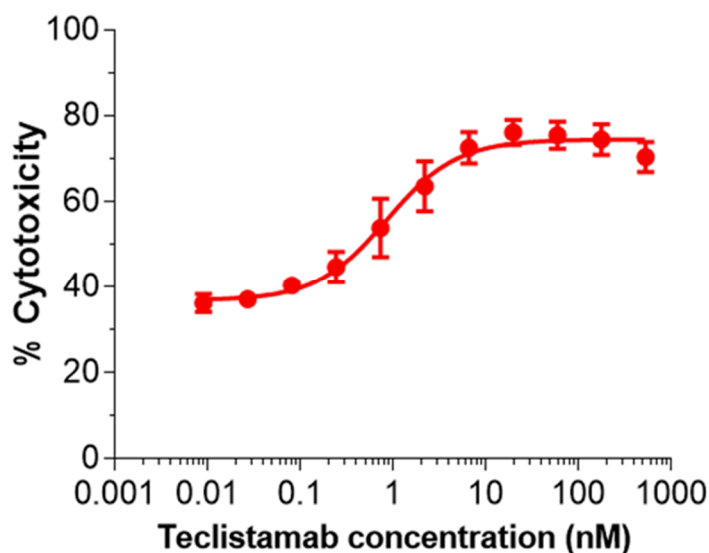


Note: Teclistamab and negative control molecules were incubated at increasing concentrations with multiple myeloma cell lines and healthy donor pan T cells at an effector:target ratio of 5:1 in the presence of fragment crystallizable blocker. After 48 hours of incubation the percentage cytotoxicity was then assessed by flow cytometry and EC_{50} s calculated using GraphPad Prism Software. The data above represents the average of 6 different T cell donors.
Source: Study DD16321.

3.1.2.6. Teclistamab-mediated T Cell-dependent Cytotoxicity of Multiple Myeloma Cell Line in Healthy Whole Blood Assay

For a more clinically relevant model, an in vitro whole blood model system was developed to evaluate the efficacy of teclistamab. BCMA positive multiple myeloma cells were spiked into the blood of 6 healthy donors, along with increasing concentrations of teclistamab for 48 hours to test target cell cytotoxicity, T cell activation, and cytokine release (Study TR2016T-005). Treatment with teclistamab resulted in dose-dependent cytotoxicity as shown in [Figure 3](#), with a concomitant dose-dependent T cell activation ([Pillarisetti 2020](#)).

Figure 3: Dose Response Curve of H929 Cell Cytotoxicity in Whole Blood After 48-hour Incubation with Teclistamab



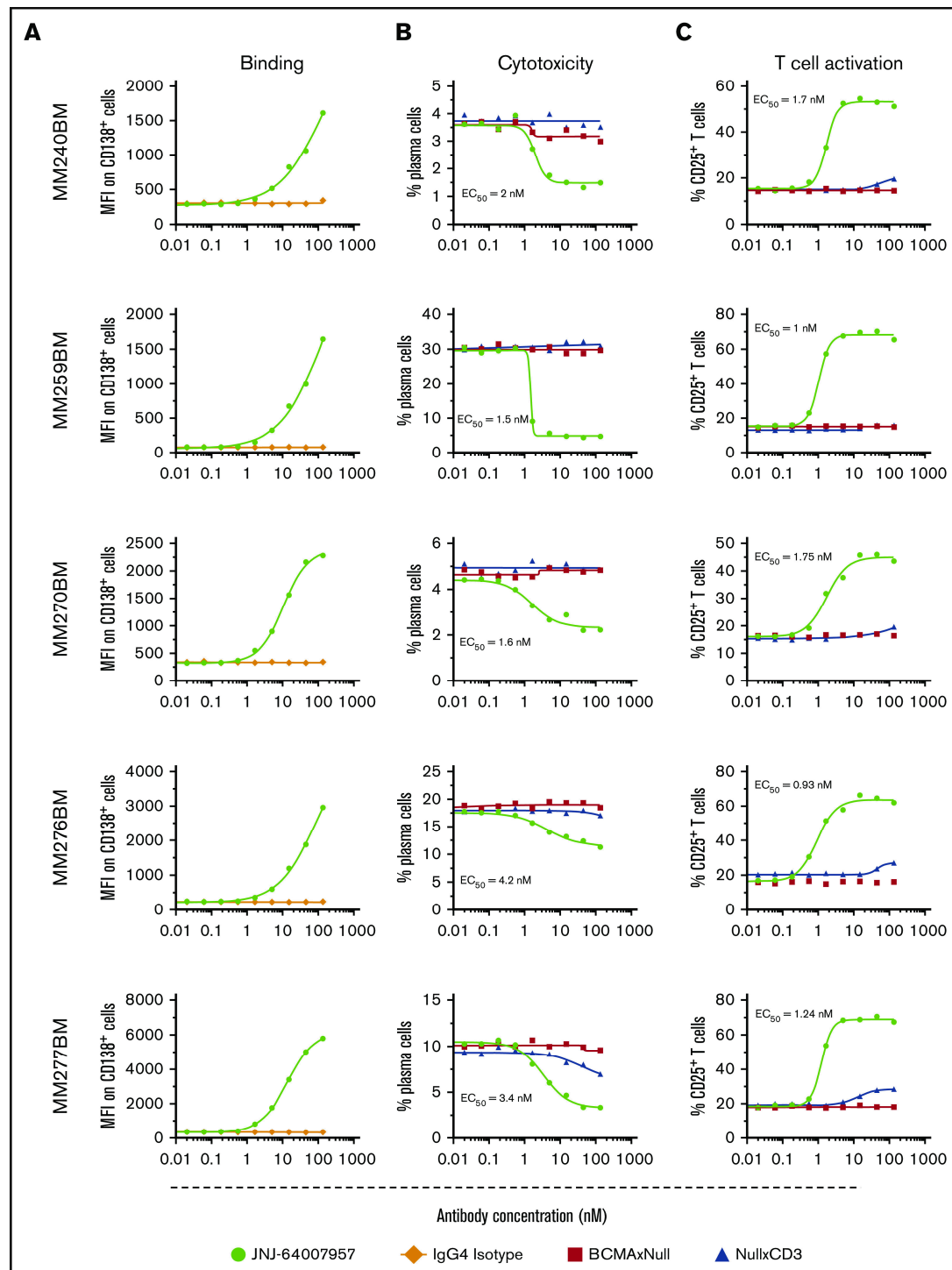
Note: Cytotoxicity was measured by flow cytometry. The graph above depicts the means of 6 individual donors $\pm$ standard error of the mean produced with GraphPad Prism Software.

Source: Study TR2016T-005.

3.1.2.7. Teclistamab Binding, Cytotoxicity and T Cell Activation Assays Using Patient-derived CD138⁺ Multiple Myeloma Bone Marrow Cells

The ability of teclistamab to induce killing using primary multiple myeloma samples (n=5) in co-culture with T cells from healthy donors was assessed (Study DD16321). Antibody binding and T cell activation potential were also measured. Teclistamab bound to and induced killing of all patient samples in a dose-dependent manner after 48 hours as measured by loss of CD138⁺ plasma cells (Figure 4). T cell activation data correlated with the results obtained from cell killing assays, as expected. Control null antibodies did not lead to significant killing or T cell activation.

Figure 4: Cytotoxic Potency of Teclistamab Antibody Against Human Primary Multiple Myeloma Plasma Cells



Frozen bone marrow-derived mononuclear cells from 5 different patients (multiple myeloma; patient numbers on the Y axes) were used to assess teclistamab (JNJ-64007957) binding, compared with IgG4 isotype control (left panel), plasma cell cytotoxicity (middle) and T cell activation (right). Teclistamab binds to plasma cells in a dose-dependent manner in all donor samples and the mean fluorescence intensities were recorded on the Y-axis. For the cytotoxicity assay, T cells from normal healthy donor (# M7077) were exogenously added to patient bone marrow aspirate mononuclear cell samples and incubated with teclistamab, BCMA × null or CD3 × null for 48 hours. A total of 100,000 T cells were added to each bone marrow sample. Note the loss of live plasma cells (CD138⁺) and the concomitant up-regulation of CD25 on T cells in response to teclistamab treatment. The donor-specific IC₅₀ values for cytotoxicity and EC₅₀ values for T cell activation are indicated on the graphs.

Source: Study DD16321; Pillarisetti 2020.

3.1.2.8. Teclistamab Cytotoxicity Assays Using Autologous CD138⁺ Multiple Myeloma Bone Marrow Cells

Lysis of multiple myeloma cells by teclistamab was assessed in samples from patients with newly diagnosed multiple myeloma (n=11), daratumumab-naïve relapsed/refractory multiple myeloma (n=21), and daratumumab-refractory multiple myeloma (n=17). Significantly higher lysis (p=0.031) was observed in daratumumab-refractory patients. Teclistamab-mediated multiple myeloma cell lysis was associated with activation (CD25) and degranulation (CD107a) of CD4⁺ and CD8⁺ T cells ([Frerichs 2020](#)).

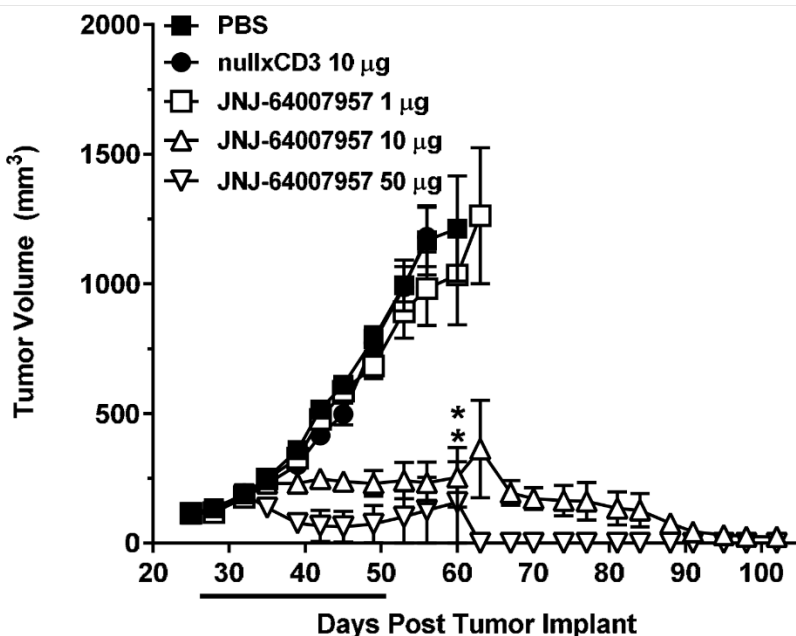
Improvement in tumor reduction may be aided by the immune-stimulatory effects of daratumumab; therefore, the study also analyzed sequential bone marrow aspirates from multiple myeloma patients before and after daratumumab treatment (n=8). Significantly improved (p=0.0004) multiple myeloma cell lysis by teclistamab was observed in samples obtained after disease progression during daratumumab treatment compared with samples collected before daratumumab initiation ([Frerichs 2020](#)).

3.1.2.9. Effect of Teclistamab in Murine T Cell Redirection Tumor Models

Efficacy of teclistamab was evaluated in 2 BCMA⁺ human multiple myeloma models in PBMC humanized NSG mice; either in a prophylactic model where treatment was initiated at the time of tumor cell implantation, or as an established model where treatment was initiated after palpable tumors were formed. In the prophylactic H929 model, teclistamab had antitumor efficacy with significant reduction of tumor formation and growth compared with PBS-treated control mice, at dose levels of either 0.5 or 1 µg/animal (0.025 or 0.05 mg/kg), whereas CD3×null or BCMA×null bispecific antibodies failed to suppress tumorigenesis in the model ([Pillarisetti 2020](#)).

In the repeat RPMI 8226 xenograft study, teclistamab showed a dose-dependent inhibition of tumor growth, 10 or 50 µg/animal dose completely regressed the tumor growth and a lower dose of 1 µg/animal failed to show reduction in the tumor volume ([Figure 5](#); Study DD20099).

Figure 5: Teclistamab-mediated Cytotoxicity of BCMA⁺ Multiple Myeloma Tumors in Murine Models



Note: Mice were treated with teclistamab (JNJ-64007957) at 1, 10, and 50 µg/animal (equivalent to 0.05, 0.5, and 2.5 mg/kg for a 20 g mouse, respectively) IP every 3-4 days (q3d or q4d) for 8 total treatments on Days 26, 29, 33, 36, 40, 43, 47, and 50 post tumor cell implantation. CD3xNull was dosed at 0.5 mg/kg with the same schedule and regimen.

Source: Study DD20099.

3.1.3. Secondary Pharmacodynamics

Binding in an in vitro tissue cross reactivity study (Study T-2016-013) is presented in Section 3.3.6.

3.1.4. Safety Pharmacology

Separate safety pharmacology studies were not conducted with teclistamab; however, cardiovascular, respiratory, and observational CNS safety pharmacology endpoints were incorporated into the design of the 5-week, repeat-dose toxicity GLP study with an 8-week recovery period in which cynomolgus monkeys were administered once weekly IV doses of 0, 1, 10, or 30 mg/kg teclistamab (Study T-2016-030; see Section 3.3.2). Electrocardiograms (leads I, II, III, aVR, aVL, and aVF) were recorded once pretreatment and during Week 5 and qualitatively evaluated for abnormalities. Electrocardiograms were not recorded at the end of the recovery period due to the absence of findings at the end of the dosing phase of the study. Blood pressure, heart rate, respiratory rate, and body temperature measurements were recorded once predose and 2 to 3 hours after each dose. CNS endpoints were evaluated via clinical observations conducted daily and twice after each dose (at 3 to 4 and 6 to 7 hours).

There were no teclistamab-related effects on examined cardiovascular, respiratory, or CNS parameters at doses of up to 30 mg/kg/week. Additionally, there is restricted expression of BCMA on B-lineage cells, no expression detected in normal (non-diseased) adult human brain (see Section 3.1.2) and in vitro tissue cross-reactivity studies with cynomolgus and human tissues demonstrated that teclistamab did not result in specific membranous staining of cardiac, lung,

brain, peripheral nerve, or spinal cord tissues. Hypotension and tachycardia were observed in cynomolgus monkeys following treatment with other CD3 redirectors, which are possibly related to cytokine release. However, there were no significant increases in circulating cytokines in cynomolgus monkeys dosed with teclistamab.

3.2. Pharmacokinetics and Metabolism in Animals

The PK/TK profile of teclistamab has been characterized in cynomolgus monkeys after a single IV dose and repeated weekly IV doses for 5 weeks, and in Gottingen minipigs after a single SC dose. Immunogenicity was also assessed in the repeat-dose GLP toxicology study in cynomolgus monkeys. ECLIA were used to quantify serum concentrations of teclistamab and to detect the presence of ADAs.

3.2.1. Methods of Analysis

Cynomolgus Monkey Serum

A qualified ECLIA method on the MSD platform (CP2015Q-060) was used during early development to determine concentrations of teclistamab in cynomolgus monkey serum samples obtained in the single-dose and 5-week repeat-dose arms of the non-GLP exploratory IV tolerability study. This method was subsequently validated (CP2016V-044) and used to determine concentrations of teclistamab in cynomolgus monkey serum samples obtained in the GLP 5-week repeat-dose toxicity IV study with an 8-week recovery period. For both the qualified and validated method, the lowest quantifiable concentration of teclistamab in a serum sample was 0.15630 µg/mL.

A validated bridging MSD ECLIA (CP2016V-069) was used to detect antibodies directed against teclistamab in cynomolgus monkey serum samples obtained in the pivotal GLP 5-week IV toxicity study with an 8-week recovery period. Study samples were evaluated in the screening method that distinguished potential ADA-positive samples from ADA-negative samples. Samples that screened potentially positive were then further evaluated in the specificity method. Samples that confirmed positive were subsequently evaluated in the titration assay.

Gottingen Minipig Serum

A fit-for-purpose ECLIA method on the MSD platform (CP2021RMQ-057) was used to quantify serum concentrations of teclistamab in the single-dose SC PK study in Gottingen minipigs. The lowest quantifiable concentration in a serum sample was 0.04 µg/mL.

3.2.2. Absorption and Pharmacokinetics

3.2.2.1. Pharmacokinetics, Toxicokinetics, and Immunogenicity in Monkeys

The PK/TK evaluations in cynomolgus monkeys supported selection of dose levels and dosing frequency, confirmed exposure to teclistamab in the toxicity studies, and indicated that the PK properties of teclistamab are predictable. Dose-proportional increases in exposure (C_{max} and AUC)

were observed in cynomolgus monkeys after a single dose (1 or 10 mg/kg) and after weekly dosing (0.1, 1, 10, or 30 mg/kg) for 5 weeks, with no apparent sex-related differences (Study T-2015-030).

Serum concentrations of teclistamab were adequately maintained throughout the dosing periods in the studies conducted in cynomolgus monkeys, except for approximately 10% of the treated animals, likely due to the presence of ADAs. In the pivotal GLP, 5-week, repeat-dose, toxicity study in cynomolgus monkeys, mean accumulation ratios of teclistamab ranged from 1.65 to 2.04 following up to 30 mg/kg/week repeated dosing, indicating moderate drug accumulation (Study T-2016-030).

Immune responses to teclistamab in cynomolgus monkeys were observed in the pivotal GLP 5-week repeat-dose toxicity study. While ADAs were detected in 21 of 30 monkeys, 14 of those monkeys had exposure comparable to that of ADA-negative monkeys in the same dose groups, and all, except for 2 treated monkeys, still had continuous exposure to teclistamab during the study. While most ADA-positive monkeys had teclistamab exposures comparable to the ADA-negative monkeys, there is potential that ADA will have an increasing impact on exposure over a longer dosing period therefore limiting the ability to sustain exposures for longer term monkey studies. Immunogenicity in monkeys toward human proteins is not expected to be predictive of human immunogenicity ([Bugelski 2004](#)).

3.2.2.2. Single-dose Subcutaneous Pharmacokinetics in Gottingen Minipigs

The PK profile of teclistamab in male Gottingen minipigs (4/group) following a single SC dose of 150 mg of teclistamab in 3 formulations at varying drug concentrations (90, 150, and 200 mg/mL) was similar in all the animals across all formulations tested with comparable exposures (Study CP2020PK-086). The mean C_{max} ranged from 58.22 to 67.26 $\mu\text{g/mL}$ and AUC_{last} ranged from 906.76 to 1104.94 $\mu\text{g}\cdot\text{day/mL}$. ADA testing was not conducted in the study.

3.2.3. Distribution

Traditional distribution studies (ie, tissue distribution studies with radiolabeled material; protein binding studies) typical for small molecules were not conducted for teclistamab as it is an antibody produced from 2 monoclonal antibodies with a molecular weight of approximately 146 kD. Due to its molecular size, teclistamab is expected to be primarily confined to the vascular space with only limited distribution to the extracellular space, which is typical of IgG-based monoclonal antibodies.

3.2.4. Metabolism and Excretion

Similar to other IgG4-based antibodies, teclistamab is presumably catabolized and eliminated via processes involved in the turnover and degradation of endogenous IgG. Thus, no specific studies to evaluate the metabolism and elimination of teclistamab have been conducted.

3.2.5. Pharmacokinetic Drug Interactions

No nonclinical PK drug interaction studies have been conducted. As an IgG4-based antibody with a large molecular weight (approximately 146 kD), teclistamab is not expected to undergo any direct metabolism-based small molecule drug interactions, to affect drug-metabolizing enzymes,

or to be a substrate for CYP enzymes or transporters. However, during CRS (if observed), cytokine release may transiently downregulate CYP enzymes.

3.3. Toxicology

The nonclinical toxicology program characterized the general toxicity of teclistamab in cynomolgus monkeys following weekly IV administration, the initial clinical administration route, in an exploratory 5-week tolerability study that included a single-dose phase and in a pivotal 5-week toxicity study with an 8-week recovery period (Studies T-2015-030 and T-2016-030). In addition to the standard toxicological evaluations, the pivotal GLP study included safety pharmacology (cardiovascular, respiratory, and observational CNS), ADA, and immunotoxicity assessments. A local tolerance GLP study of teclistamab SC was conducted in male New Zealand White rabbits, a generally accepted species for tolerability/irritancy testing, to support transition from IV to SC administration in humans. Because rabbits are not a pharmacologically relevant species due to poor sequence homology of rabbit CD3 with human CD3, the study tested the local tolerance of the formulation at a teclistamab concentration of 10 mg/mL.

Pregnancy risk was considered through a weight-of-evidence assessment. In vitro studies assessed tissue cross-reactivity in human tissues and select monkey tissues, cytokine release, serum compatibility and hemolytic potential of teclistamab.

Pivotal nonclinical safety studies were conducted in conformance with GLP, 21 CFR, Part 58 and/or the principles of OECD-GLP in a test facility that was part of the national GLP monitoring program of a European Union Member State, an OECD Member Country, or fully adherent to the Mutual Acceptance of Data in the period that the study was conducted.

A 3-month toxicity study was not conducted due to: 1) restricted expression of BCMA on the B cell lineage limiting the potential for toxicity on other normal cells and tissues, 2) the incidence of ADAs that, in some cases, impacted exposure to teclistamab, and 3) the absence of pharmacologic and toxicologic effects in the cynomolgus monkey studies. As teclistamab is a biologic compound that is not expected to interact with DNA, no genotoxicity testing was conducted or is planned. Carcinogenicity studies are not planned because teclistamab is in development for a systemic cancer that is generally regarded as incurable. Reproductive and developmental toxicology studies and specifically embryo-fetal development studies have not been performed for teclistamab and are not planned based on a weight-of-evidence assessment of reproductive risk.

3.3.1. Single-Dose Toxicity

A single IV dose of 1 or 10 mg/kg (highest tested dose) of teclistamab was well tolerated in cynomolgus monkeys and there were no test-article related changes that were considered adverse in the single-dose phase of a tolerability study (Study T-2015-030).

3.3.2. Repeat-Dose Toxicity

Weekly IV administration of teclistamab for 5 weeks was well tolerated in male cynomolgus monkeys at doses of 0.1, 1, or 10 mg/kg, with no adverse effects, in a tolerability study and in male and female cynomolgus monkeys at doses of 1, 10, or 30 mg/kg, with no treatment-related findings, in the pivotal toxicity GLP study (Study T-2016-030). The NOEL for 5 weekly IV doses of teclistamab was 30 mg/kg, which corresponded to a C_{max} on Day 22 of 1084.01 µg/mL and an area under the serum concentration versus time curve from Day 22 to Day 29 ($AUC_{Day22-29}$) of 3549.19 µg·day/mL.

All teclistamab doses were expected to be pharmacologically active, as mean serum concentrations of teclistamab throughout the treatment periods were higher than the EC_{50} (0.09 to 0.48 µg/mL) for cytotoxicity with cynomolgus monkey T cells against cBCMA expressing target cells. The lack of pharmacodynamic (eg, cytokine release or transient lymphocyte decreases) or toxicological response to teclistamab was attributed to a combination of a lower number of plasma cells (and consequently low expression of BCMA) in a healthy cynomolgus monkey and limited cross-reactivity of teclistamab to cynomolgus monkey relative to humans. The lack of pharmacology may be related to the fact that binding and cytotoxicity of teclistamab are lower in monkeys than in humans. Additionally, there are differences in BCMA expression in a normal cynomolgus monkey and a tumor-bearing patient.

3.3.3. Genotoxicity and Carcinogenicity

No genotoxicity or carcinogenicity studies have been performed for teclistamab.

3.3.4. Reproduction and Developmental Studies

No reproductive and developmental toxicity studies have been conducted for teclistamab. Pregnancy risk was considered through a weight-of-evidence assessment and teclistamab is not expected to be teratogenic based on the restricted expression of BCMA on plasma cell lineage compared with other normal cells and tissues and the on-target specificity of teclistamab.

3.3.5. Local Tolerance

Teclistamab was well tolerated at the SC injection site in male New Zealand White rabbits administered 20 mg (10 mg/mL), in a GLP local tolerance study (Study T-2018-019). There were no adverse dermal observations and no teclistamab-related gross or microscopic findings in the injection sites or draining lymph nodes. As rabbits are not a pharmacologically relevant species, this study tested the local tolerance of the formulation, which contains the same components as the clinical SC formulation.

In the repeat-dose IV toxicity studies in cynomolgus monkeys administered up to 30 mg/kg/week teclistamab for 5 weeks, there were no teclistamab-related effects at injections sites based on clinical observations and histopathology evaluation (Study T-2016-030).

3.3.6. Other Toxicity Studies

No unexpected binding was observed in an in vitro tissue cross-reactivity study with teclistamab in human and select cynomolgus monkey tissues (Study T-2016-031, including Study T-2015-051). Teclistamab formulations were not hemolytic and did not cause precipitation in human serum (Study T-2016-047 and Study T-2016-048). Cytokine release testing in diluted (1:10) healthy human donor whole blood (without addition of exogenous tumor cell lines) demonstrated that teclistamab induced statistically significant but low-level increases in IL-8, IFN- γ , and TNF- α versus a negative control at concentrations ≥ 82 ng/mL (Study T-2016-046).

3.4. Conclusions for Nonclinical Studies

The nonclinical in vitro and in vivo experimental data demonstrate that teclistamab selectively promotes the T cell-dependent elimination of human cells expressing BCMA on their surface. Teclistamab specifically binds to and induces potent T cell-dependent cytotoxicity of hBCMA-positive multiple myeloma cell lines and primary multiple myeloma bone marrow cells obtained from multiple myeloma patients and proved efficacious in the clinically relevant H929 whole blood in vitro model, as well as in prophylactic and established xenograft tumor models in NSG mice. The TK profile of teclistamab is well characterized in cynomolgus monkeys.

Teclistamab exhibited no effects in cynomolgus monkeys up to the highest tested dose and an expected pharmacologically active dose of 30 mg/kg/week IV, in a 5-week GLP toxicity study. Although cynomolgus monkey was considered the most pharmacologically relevant animal model for teclistamab, results from the monkey should be interpreted with caution as there was no evidence of pharmacology. Typical hallmarks of activity associated with CD3 bispecific antibodies such as transient decreases in lymphocytes, increases in circulating cytokines, and an acute phase response ([Saber 2017](#)) were not observed. Both binding affinity and in vitro bioactivity of teclistamab were lower in monkeys than in humans. Additionally, differences in BCMA and CD3 expression in a normal cynomolgus monkey and tumor-bearing patient further limit the translation of results.

In conclusion, teclistamab has exhibited efficacy in numerous multiple myeloma cell lines and in patient-derived primary myeloma cells. Teclistamab has also demonstrated significant reductions in xenograft/tumor growth in rodent models. There were no adverse findings identified in the pivotal toxicology program. These results support the IV and SC administration of teclistamab in patients with multiple myeloma and the results indicate teclistamab may have a significant therapeutic potential in treating multiple myeloma patients.

4. EFFECTS IN HUMANS

4.1. Overview

As of the data cutoff date of this IB (22 August 2025), approximately 2,814 participants were treated with teclistamab in the clinical development program, with approximately 1,134 participants exposed to teclistamab in monotherapy studies and approximately 1,680 participants exposed to teclistamab in combination therapy studies. Fourteen studies in

participants with multiple myeloma are ongoing as of 22 August 2025. Details of the design of each study are provided in [Appendix 2](#).

The primary analysis has been performed for the monotherapy dose-escalation study of teclistamab (Study 64007957MMY1001; [MajesTEC-1](#)) in participants with relapsed/refractory multiple myeloma. Based on these data, teclistamab monotherapy has been approved by the EMA, FDA, and other health authorities for the treatment of patients with relapsed/refractory multiple myeloma at a dose of 1.5 mg/kg teclistamab SC administered weekly, with the first treatment dose preceded by step-up doses of 0.06 and 0.3 mg/kg – the recommended dose established in MajesTEC-1. In patients who have a response for a minimum of 6 months, a reduced dosing frequency of 1.5 mg/kg Q2W until disease progression or unacceptable toxicity may be considered.

Safety information for teclistamab is summarized in Section [4.3.2](#). This includes monotherapy safety data in Section [4.3.2.1](#) from the primary analysis of MajesTEC-1 for participants treated with the recommended dose; data from other MajesTEC-1 cohorts, including those treated with monotherapy doses higher than the recommended dose; and safety data from the Japanese monotherapy Study 64007957MMY1002 ([MMY1002 Japan](#)). Safety data pertinent to planned and ongoing Phase 3 studies from Phase 1b/2 combination studies in participants with multiple myeloma are presented in Section [4.3.2.2](#), including data from Studies 64407564MMY1002 ([TriMM-2](#)), 64407564MMY1005 ([TriMM-3](#)), 64007957MMY1003 ([RedirecTT-1](#)), 64007957MMY1004 ([MajesTEC-2](#)), and GMMG-HD10/DSMM-XX/64007957MMY2003 ([MajesTEC-5](#)). Summaries of the safety data from the Safety Run-in phases of the ongoing Phase 3 combination Studies EMN30/64007957MMY3003 ([MajesTEC-4](#)) and 64007957MMY3005 ([MajesTEC-7](#)) are also provided in Section [4.3.2.2](#).

Data for Studies 64007957MMY3001 ([MajesTEC-3](#)), 64007957MMY3006 ([MajesTEC-9](#)), 64007957MMY1008 ([MajesTEC-10](#)), and 64407564MMY3009 ([MonumenTAL-6](#)), and for the randomized phases of Studies, EMN30/64007957MMY3003 ([MajesTEC-4](#)) and 64007957MMY3005 ([MajesTEC-7](#)) are blinded and therefore are not presented in this IB.

PK results from MajesTEC-1 are presented in Section [4.2](#), along with PK data from combination studies TriMM-2, TriMM-3, RedirecTT-1, and MajesTEC-2.

Pivotal efficacy data from MajesTEC-1 are presented in Section [4.3.1](#), along with efficacy data from combination studies TriMM-2, TriMM-3, and RedirecTT-1.

Of note, units for step-up doses and treatment doses of teclistamab in the text of this document reflect approved labeling (mg/kg). Tables and figures included in this IB may include the units used in the study protocol (µg/kg).

4.1.1. Ongoing and Completed Clinical Studies

A summary of teclistamab monotherapy and combination studies is provided in [Appendix 2](#). There are currently no completed studies with teclistamab.

4.2. Pharmacokinetics and Product Metabolism

4.2.1. Teclistamab Monotherapy Pharmacokinetics

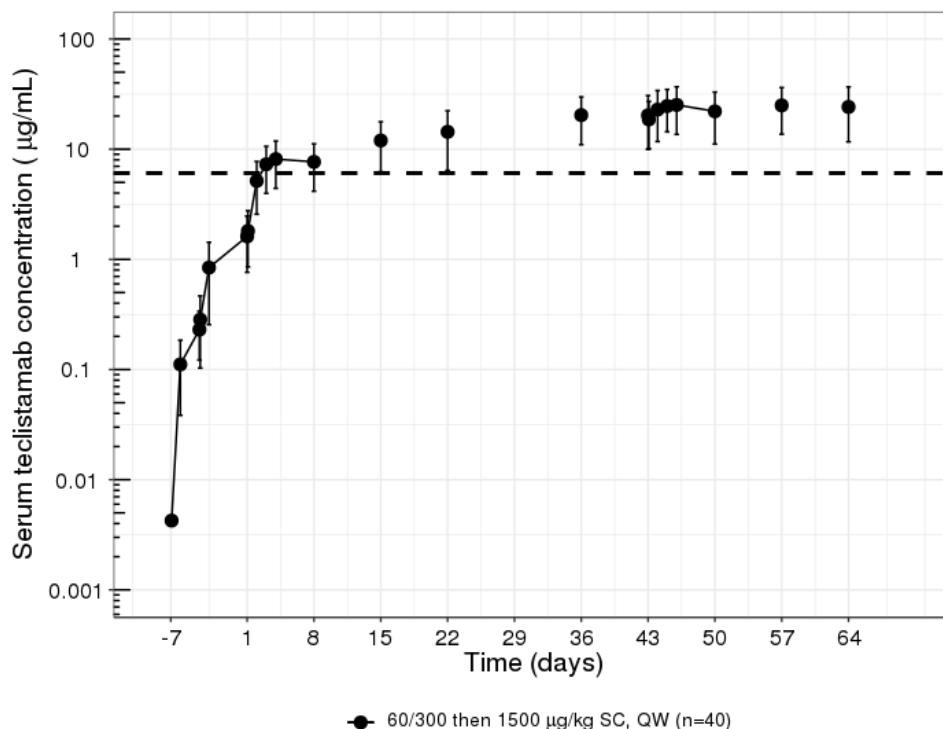
The data cutoff dates for monotherapy PK analyses in this IB were 01 December 2021 for population PK, 16 March 2022 for E-R analyses, and 09 August 2021 for noncompartmental PK analysis in MajesTEC-1.

SC Administration

In Phase 1 of MajesTEC-1, teclistamab serum exposure ($C_{\max}$ and AUC_{τ}) increased in an approximately dose-proportional manner following the first SC treatment dose in Cycle 1 across the range of 0.08 to 6 mg/kg. Based on the available data in Cycle 3, mean accumulation ratios following SC weekly dosing ranged from 1.80 to 3.18 for $C_{\max}$ and from 1.80 to 3.64 for AUC_{τ} (calculated based on the first treatment dose data in Cycle 3 and Cycle 1 for doses ranging from 0.08 to 3 mg/kg weekly). Exposure increased in an approximately dose-proportional manner following the multiple SC weekly dosing across the range of 0.08 to 3 mg/kg. A total of 40 participants treated with RP2D (1.5 mg/kg teclistamab SC weekly) had evaluable teclistamab PK data in Phase 1 and the mean PK profile is shown in [Figure 6](#).

From population PK analysis, 90% of steady-state exposure was achieved after 12 weekly treatment doses of teclistamab 1.5 mg/kg. The geometric mean (CV%) of $C_{\max}$, C_{trough} , and AUC_{τ} following the 13th treatment dose of teclistamab 1.5 mg/kg was 23.8 µg/mL (55%), 21.1 µg/mL (63%), and 3838 µg·h/mL (57%), respectively. The mean accumulation ratio between the first and 13th weekly treatment dose of teclistamab 1.5 mg/kg was 4.2-fold for $C_{\max}$, 4.1-fold for C_{trough} , and 5.3-fold for AUC_{τ} . The mean bioavailability of teclistamab was 72% when administered SC. The median (range) $T_{\max}$ of teclistamab after the first and 13th treatment doses was 139 (19-168) hours and 72 (24 to 168) hours, respectively. The mean (CV%) volume of distribution of teclistamab was 5.63 L (29%). Teclistamab clearance decreased over time, with a mean (CV%) maximal reduction from baseline to the 13th treatment dose of 40.8% (56%). The geometric mean (CV%) clearance is 0.472 L/day (64%) at the 13th treatment dose. Patients who discontinue teclistamab after the 13th weekly treatment dose are expected to have a 50% reduction from $C_{\max}$ in teclistamab concentration at a median (5th to 95th percentile) time of 15 (7 to 33) days after $T_{\max}$ and a 97% reduction from $C_{\max}$ in teclistamab concentration at a median time of 69 (32 to 163) days after $T_{\max}$.

Figure 6: Mean (SD) Serum Concentration-time Profiles of Teclistamab After SC Administration of Teclistamab at 0.06/0.3 then 1.5 mg/kg Weekly (RP2D) in Subjects with Multiple Myeloma (Phase 1); Pharmacokinetics Analysis Set (64007957MMY1001; Pivotal RP2D [Phase 1 only])



Step-up doses are shown using negative times (days).

Dash line represents the maximum EC_{90} value identified in an ex vivo cytotoxicity assay using bone marrow mononuclear cells from subjects with multiple myeloma (ie, 6.039 µg/mL, n=5).

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No clinically meaningful differences (ie, <20% to 25%) in the exposure to teclistamab were observed in participants with different body weight when teclistamab was administered on the weight proportional dosing regimen. Exposure of teclistamab largely overlapped across body weight subgroups. The disease status variables including multiple myeloma type (IgG vs non-IgG) and ISS staging (II vs I and III vs I) affected teclistamab exposure. The simulated $C_{ave,1stdose}$ and $C_{trough,ss}$ were approximately 32% and 34% lower in participants with IgG type of multiple myeloma, respectively, compared with those with non-IgG type of multiple myeloma. The simulated $C_{ave,1stdose}$ and $C_{trough,ss}$ were approximately 17% and 26% lower in participants with ISS Stage II, respectively, compared with those with ISS Stage I. The simulated $C_{ave,1stdose}$ and $C_{trough,ss}$ were approximately 29% and 42% lower in participants with ISS Stage III, respectively, compared with those with ISS Stage I. However, further clinical efficacy subgroup analyses and E-R analyses demonstrated that these covariates had no clinically relevant effect on efficacy at the recommended dose regimen.

Population PK analysis indicated that mild or moderate renal impairment and mild hepatic impairment did not influence teclistamab PK. Limited data were available from patients with severe renal impairment, and no data were available from patients with moderate or severe hepatic impairment. Results of population PK analysis also suggested soluble BCMA did not affect

teclistamab serum concentrations and was not a significant covariate of teclistamab PK.

An E-R trend was observed for ORR assessed by investigator based on IMWG 2011 criteria in SC participants in Phase 1 where ORR increased with teclistamab exposure across SC doses ranging from 0.08 to 3 mg/kg weekly, approaching plateau (ie, maximum response) at the recommended dose of 1.5 mg/kg weekly.

In participants who received 1.5 mg/kg teclistamab SC weekly, E-R analyses indicated a near flat E-R trend for ORR assessed by IRC based on IMWG 2016 criteria. Responders and non-responders had comparable and overlapping exposure range. The prognostic factors that were significantly associated with the ORR response in the multivariate analysis were baseline soluble BCMA and PD-1 expression. In addition, DOR, progression-free survival, and overall survival were not significantly correlated with teclistamab exposures at the recommended dose.

No apparent positive E-R trend was observed in the incidence of Grade ≥ 3 TEAEs of anemia, neutropenia, lymphopenia, thrombocytopenia, and infections across the predicted exposure quartiles in participants who received teclistamab SC.

Pharmacokinetics in Asian Population

No race difference has been observed in teclistamab PK from the MajesTEC-1 China cohort and the MMY1002 Japan study.

4.2.2. Teclistamab Pharmacokinetics in Combination Therapy Studies

Based on the data in TriMM-2, TriMM-3, RedirecTT-1, and MajesTEC-2, teclistamab serum concentrations in combination therapy were generally within the range of the values observed in participants treated with teclistamab monotherapy in MajesTEC-1. Preliminary analysis showed that popPK model developed for monotherapy characterized teclistamab PK in combination studies.

4.3. Safety and Efficacy

4.3.1. Efficacy

4.3.1.1. MajesTEC-1 Study (MMY1001)

Primary Analysis

As of the clinical cutoff of 09 November 2021 for the primary analysis of efficacy, 150 participants treated with the recommended dose of 1.5 mg/kg teclistamab SC weekly were evaluated for the efficacy analysis. Of these, 40 were treated in Phase 1 and 110 were treated in Cohort A of Phase 2 of the study. The ORR (PR or better), as assessed by the IRC based on IMWG 2016 criteria, was 62.7% (95% CI: 54.4%, 70.4%), with 58.7% of participants having a VGPR or better and 32.0% of participants having a CR or better. Median DOR (time from first response to disease progression or death due to any cause) was not reached. The percentage of participants estimated to be in response at 12 months was 67.2% (95% CI: 49.4%, 79.9%). Further details of the primary efficacy results are available in [Appendix 3](#) (Table: [MMY1001 Efficacy](#)).

Follow-up Analysis

As of the clinical cutoff of 22 August 2023, 38 of the total 165 participants treated with the recommended dose of teclistamab in MajesTEC-1 (40 in Phase 1 and 125 in Cohort A in Phase 2) remained on treatment and the majority of these had changed dosing schedule (n=37 [97.4%], including 12 participants on Q2W dosing, 22 participants on Q4W dosing, and 3 participants on Q8W dosing). Among the participants who switched to 1.5 mg/kg SC Q2W, median time to switch to Q2W dosing was 11.3 months (range: 3.2 to 29.5) and median follow-up after the schedule change was 18.7 months (range: 2.2 to 35.1). Among all responders (n=104 participants, including 65 participants who received Q2W dosing), the median DOR was 24.0 months (95% CI: 17.0, NE). The percentage of participants estimated to be in response at 30 months was 45.0% (95% CI: 34.8%, 54.7%).

4.3.1.2. TriMM-2 Study (MMY1002)

RP2D Population (Teclistamab 1.5 mg/kg Weekly or 3 mg/kg Q2W + Daratumumab SC)

Primary Analysis:

As of the clinical cutoff of 31 January 2024 for the primary analysis of efficacy, 61 participants treated with the RP2D of teclistamab 1.5 mg/kg weekly (21 participants) or 3 mg/kg Q2W (40 participants), preceded by step-up doses, in combination with daratumumab SC, were evaluated for the efficacy analysis. With a median follow-up of 11.96 months (range: 0.3 to 41.2), the ORR (PR or better), as assessed by the investigator, was 68.9%, with 68.9% of participants having clinical benefit (minimal response or better), 63.9% of participants having a VGPR or better, and 44.3% of participants having a CR or better.

The median time to first response by investigator assessment was 0.95 months (range: 0.8 to 14.5), 3.17 months (range: 0.8 to 25.6) to best response, 1.87 months (range: 0.9 to 14.5) to VGPR or better, and 4.96 months (range: 1.4 to 16.9) to CR or better.

The median DOR (time from first response to disease progression or death due to any cause) was not reached. The percentage of responders estimated to remain in response at 6, 12, and 24 months was 92.6% (95% CI: 78.8%, 97.6%), 73.8% (95% CI: 56.6%, 85.0%) and 66.9% (95% CI: 48.7%, 79.9%), respectively.

Final Analysis:

With a median follow-up of 11.83 months (range: 0.3 to 54.4) as of 30 April 2025 (final analysis), there was no change in ORR, clinical benefit rate, or VGPR or better rate among the 61 participants treated with the RP2D, compared with the primary analysis. A total of 45.9% of participants had a CR or better.

The median time to first response, best response, and VGPR or better were unchanged from the primary analysis. The median time to CR or better was 5.72 months (range: 1.4 to 30.1).

The median DOR was not reached; the percentage of responders estimated to remain in response at 6, 12 and 24 months was 92.6% (95% CI: 78.8%, 97.6%), 74.1% (95% CI: 57.1%, 85.2%) and 67.5% (95% CI: 49.6%, 80.2%), respectively.

Teclistamab 0.72 or 0.75 mg/kg Weekly + Daratumumab SC + Pomalidomide Cohort

As of 30 April 2025, 10 participants treated with teclistamab 0.72 or 0.75 mg/kg weekly, in combination with daratumumab SC and pomalidomide, were evaluated for the final efficacy analysis. With a median follow-up of 19.58 months (range: 1.2 to 51.1), the ORR (PR or better), as assessed by the investigator, was 70.0%, with 70.0% of participants having clinical benefit (minimal response or better), 70.0% of participants having a VGPR or better, and 50.0% of participants having a CR or better.

The median time to first response (PR or better) by investigator assessment was 0.95 months (range: 0.9 to 1.2), 3.22 months (range: 0.9 to 17.9) to best response, 0.95 months (range: 0.9 to 4.9) to VGPR or better, and 3.22 months (range: 1.9 to 11.1) to CR or better.

The estimated median DOR (time from first response to disease progression or death due to any cause) was 25.59 months (95% CI: 12.45, NE). The percentage of responders estimated to remain in response at 12 and 24 months was 100.0% (95% CI: 100.0%, 100.0%) and 66.7% (95% CI: 19.5%, 90.4%), respectively.

4.3.1.3. TriMM-3 Study (MMY1005)

Teclistamab (1.5 or 3 mg/kg) Q2W + Cetrelimab Q2W

As of 22 May 2025, 22 participants treated with teclistamab 1.5 or 3 mg/kg Q2W (preceded by step-up doses), in combination with cetrelimab Q2W, were evaluated for the efficacy analysis. With a median follow-up of 23.59 months (range: 1.3+ to 31.3), the ORR (PR or better), as assessed by the investigator, was 68.2%, with 54.5% of participants having VGPR or better, and 50.0% of participants having CR or better. A total of 31.8% of participants had sCR.

The median time to first response (PR or better) by investigator assessment was 1.41 months (range: 0.9 to 7.2), 6.83 (range: 1.0 to 20.8) to best response, 5.22 months (range: 1.0 to 9.0) to VGPR or better, and 6.83 (range: 1.9 to 20.8) to CR or better.

The median follow-up for responders was 25.49 months (range: 7.2 to 31.3) and the median DOR (time from initial response of PR or better to progressive disease or death) was not reached. The percentage of responders estimated to remain in response at 12 months was 86.7% (95% CI: 56.4%, 96.5%).

4.3.1.4. RedirecTT-1 Study (MMY1003)

Primary Efficacy Endpoint

As of 18 March 2025, 90 participants treated with the RP2R of teclistamab 3 mg/kg Q2W SC (preceded by step-up doses of 0.06, 0.3, and 1.5 mg/kg) in combination with talquetamab

0.8 mg/kg Q2W SC (preceded by step-up doses of 0.01, 0.06, and 0.3 mg/kg) in Phase 2 were evaluated for efficacy. With a median follow-up of 12.6 months (range: 0.5+ to 19.5), the ORR (PR or better) as assessed by the IRC was 78.9% (95% CI: 69.0%, 86.8%). Subgroup analyses showed that the ORR by IRC assessment was consistent across pre-specified, clinically relevant, subgroups.

Secondary Efficacy Endpoints

As of 18 March 2025, best response as assessed by the IRC was VGPR or better in 63 participants (70.0% [95% CI: 59.4%, 79.2%]), and CR or better in 49 participants (54.4% [95% CI: 43.6%, 65.0%]).

The median time to first response (PR or better) by IRC assessment was 2.6 months (range: 1.0 to 5.8), 4.7 months (range: 1.0 to 11.9) to best response, 3.1 months (range: 1.6 to 10.5) to VGPR or better, and 5.1 months (range: 1.6 to 11.9) to CR or better.

Results for DOR, PFS, and OS were not mature; with a median follow-up for responders of 13.4 months (range: 1.2+ to 19.5), the estimated median DOR (time from initial response of PR or better to progressive disease or death) was 13.8 months (95% CI: 11.50, NE) and the percentage of responders estimated to remain in response at 12 months was 64.1% (95% CI: 48.3%, 76.3%). Estimated median PFS was 15.4 months (95% CI: 10.8, NE), and the percentage of participants remaining event-free at 12 months was 61.0% (95% CI: 49.6%, 70.6%). The estimated OS rate at 12 months was 74.5% (95% CI: 63.4%, 82.7%).

4.3.2. Safety and Tolerability

Study protocols require reporting of any AE until 100 days (most Phase 1 studies) or 30 days (Phase 1 of MajesTEC-2, MMY1002 [Japan] and RedirecTT-1, Phase 2, and Phase 3) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier. AEs were coded using MedDRA Version 25.1, unless otherwise stated. All events discussed are treatment-emergent (ie, TEAEs). Incidences are reported as percentages for cohorts containing ≥ 20 participants and as numbers of participants for cohorts containing < 20 participants. Relatedness to study drug was assessed by the investigator. Severity is graded according to NCI-CTCAE Version 4.03 or 5.0 per protocol except for 2 AEs of clinical interest: CRS and ICANS. The grading system for CRS and ICANS is defined as follows:

- Events of CRS were graded according to the ASTCT grading system ([Lee 2019](#)), except for events of CRS reported in Phase 1 of MajesTEC-1 which were graded according to the CRS revised grading system ([Lee 2014](#)).
- Events of ICANS were graded according to ASTCT guidelines ([Lee 2019](#)). This consensus grading scale requires the ICE scores, and this tool was administered to any participant as indicated after the first symptoms of ICANS were suspected until resolution. Non-ICANS neurotoxicity as well as symptoms of ICANS are graded based on NCI-CTCAE in all teclistamab studies.

For the purposes of this IB, neurologic AEs are defined as a TEAE in the Nervous System Disorder or Psychiatric Disorders SOCs regardless of investigator judgement of relatedness to teclistamab. The subset of neurologic AEs that are judged by the investigator as teclistamab-related correspond to neurotoxicity events.

An analysis of immune-mediated AEs was performed by searching for events coded to the immune-mediated/autoimmune disorders (narrow) Standardized MedDRA Query reported in clinical studies as of a data cutoff of 22 February 2025. No safety signal was identified.

4.3.2.1. Teclistamab Safety in Monotherapy Studies

4.3.2.1.1. MajesTEC-1 Study (MMY1001)

4.3.2.1.1.1. Primary Analysis in Participants Treated at the Recommended Dose

Overview of Adverse Events

For this study, AEs were coded using MedDRA Version 24.0.

The clinical cutoff date for the primary safety analysis was 07 September 2021. The safety analysis presented below included 165 participants treated with 1.5 mg/kg teclistamab SC weekly, preceded by step-up doses of 0.06 and 0.3 mg/kg. Of these, 40 participants were treated in Phase 1 and 125 participants were treated in Cohort A of Phase 2 of the study.

All 165 participants experienced at least 1 TEAE. The most frequently reported TEAEs ($\geq 20\%$ of participants) were CRS (71.5%), neutropenia (65.5%), anemia (49.7%), thrombocytopenia (38.2%), lymphopenia (33.9%), injection site erythema (25.5%), fatigue (24.8%), nausea (24.2%), headache (21.8%), and diarrhea (20.6%). Two participants experienced immune-mediated TEAEs of immune-mediated lung disease; both events were Grade 2 in severity and both resolved (1 with sequelae). Refer to [Appendix 2](#) (Tables: [MMY1001 Safety Summary](#) and [MMY1001 TEAE](#)) for further details.

Deaths, Serious Adverse Events, and Other Significant Adverse Events

Deaths:

At primary analysis cutoff, 40 participants (24.2%) had died. The most frequently reported primary cause of death was progressive disease for 30 participants (18.2%).

Twenty participants (12.1%) died ≤ 30 days of the last dose of teclistamab; of these, 13 participants died due to progressive disease, 6 participants died due to AEs that were unrelated to study drug (4 deaths due to COVID-19, 1 due to pneumonia, and 1 due to hemoperitoneum), and 1 participant died due to “other” reason (respiratory failure due to pneumonia, which was not considered a TEAE because subsequent therapy had already been started. Three participants died due to an AE (COVID-19) > 30 days of the last dose of teclistamab that was considered treatment-emergent since the initial diagnosis of the preferred term occurred within 30 days of the last dose and no

subsequent therapy was administered. Refer to [Appendix 2 \(MMY1001 Deaths\)](#) for further details.

Serious Treatment-emergent Adverse Events:

Serious TEAEs were experienced by 88 participants (53.3%); these were considered related to study drug in 33 participants (20.0%). The most frequent serious TEAEs (>2% of participants) were CRS (7.9%), COVID-19 (7.3%), pneumonia (6.7%), general physical health deterioration (5.5%), acute kidney injury (4.8%), pyrexia (3.0%), and *Pneumocystis jirovecii* pneumonia (2.4%). Refer to [Appendix 2 \(MMY1001 Serious TEAEs\)](#) for further details.

Grade 3 or 4 Adverse Events:

Grade 3 or 4 TEAEs were experienced by 152 participants (92.1%); these were considered related to study drug in 122 participants (73.9%). The most frequent Grade 3 or 4 events (>5% of participants) were neutropenia (57.0%), anemia (34.5%), lymphopenia (32.1%), thrombocytopenia (21.2%), pneumonia (9.1%), leukopenia (7.3%), COVID-19 (6.7%), and hypophosphatemia (5.5%). Refer to [Appendix 2 \(MMY1001 Grade 3 or 4\)](#) for further details.

Treatment Discontinuation:

One participant (0.6%) experienced a TEAE that led to treatment discontinuation (serious, Grade 3 adenoviral pneumonia judged by the investigator as very likely related to teclistamab).

Cytokine Release Syndrome:

CRS was experienced by 118 participants (71.5%). Nearly all CRS events were Grade 1 or 2, with the exception of 1 participant who experienced a Grade 3 CRS with concurrent Grade 3 pneumonia, which resolved after 49.5 hours. The median onset time of CRS from the time of injection was 2.0 days (range of 1 to 6 days). All events resolved, with a median duration of 2.0 days (range of 1 to 9 days), and no participants discontinued treatment due to CRS.

Most events of CRS (any grade) occurred early in treatment. Seventy participants (42.4%) had CRS associated with Step-up Dose 1, 57 (34.5%) for Step-up Dose 2, and 40 (24.2%) for the first treatment dose. The incidence of any grade CRS associated with the second treatment dose was notably lower (4.8%), and this comparatively low incidence was maintained or decreased for subsequent doses. Only 4 participants experienced CRS for the first time after the first treatment dose, and all experienced their first occurrence of CRS during Cycle 1. Refer to [Appendix 2 \(Table: MMY1001 CRS Summary\)](#) for further details. Symptoms of treatment-emergent CRS by SOC and preferred term are presented in [Appendix 2 \(Table: MMY1001TE-CRS\)](#).

A total of 109 participants (66.1%) received supportive measures as treatment for CRS (36.4% received tocilizumab, 12.7% received supplemental low-flow oxygen, 7.9% received steroids, and 0.6% received a single vasopressor). Management of CRS using tocilizumab and steroids alone or in combination was per investigator decision. Treatment of CRS events with either agent alone was more frequent than with both agents in combination. Further details on CRS events treated with tocilizumab and/or steroids are in [Appendix 2 \(Table: MMY1001 CRS Treatment\)](#).

Neurotoxicity Events:

At least 1 any grade neurotoxicity event was reported for 21 participants (12.7%). The following events were reported in more than 1 participant: headache (8.5%), ICANS (see below), encephalopathy (1.2% in a grouped term in which only the preferred term of confusional state was reported), and tremor (1.2% in a grouped term in which only the preferred term of tremor was reported). Refer to [Appendix 2](#) (Tables: [MMY1001 Neurotoxicity](#) and [MMY1001 Grade 3 or 4 neurotoxicity](#)) for details on neurotoxicity events.

At least 1 event of ICANS was reported for 5 participants. All events of ICANS were Grade 1 (1.8%) or Grade 2 (1.2%), and all events resolved. No participants discontinued treatment due to ICANS. The median time to onset of symptoms of ICANS was 4 days (range of 2 to 5 days) and median duration of ICANS was 3 days (range of 1 to 20 days). Most events occurred relatively early in treatment (0.6% had ICANS associated with Step-up Dose 1 and 2.4% had ICANS during Cycle 1). ICANS occurring after Cycle 1 included one Grade 1 event that occurred on Cycle 3 Day 8, and 1 participant who experienced recurrent ICANS events (5), the last of which occurred at Cycle 2 Day 8.

Seven of the 9 ICANS events (77.8%) were concurrent with CRS (during or within 7 days of resolution of CRS). Of the 5 participants with ICANS, 4 experienced ICANS beginning on the same day or 1 day following an event of CRS; 1 of these participants also experienced subsequent events of ICANS, some of which were not associated with CRS. One participant did not experience CRS prior to ICANS. Refer to [Appendix 2](#) (Table: [MMY1001 ICANS](#)) for more details on ICANS.

Infection TEAEs:

Infection TEAEs were reported for 104 participants (63.0%) and were reported with a maximum severity of Grade 3 or 4 for 51 participants (30.9%). Eight participants (4.8%) experienced Grade 5 infections, including 7 (4.2%) with COVID-19 and 1 (0.6%) with pneumonia. Refer to [Appendix 2](#) (Table: [MMY1001 Infections](#)) for more details on infections.

4.3.2.1.1.2. Follow-up Analysis in Participants Treated at the Recommended Dose

With additional follow-up of the pivotal population of 165 participants who received teclistamab at the recommended dose in MajesTEC-1 (through the clinical cutoff of 22 August 2023), the safety profile remained consistent with what was described for the primary analysis, along with a notable decrease of new high-grade infections after 12 months on treatment (refer to figure in [Appendix 2](#) [[MMY1001 Infections by Event Onset Time](#)]). As of the clinical cutoff for the follow-up analysis, 35 participants (21.2%) died due to a TEAE, including 18 from COVID-19. Two events of CRS (Grade 1) were reported since the clinical cutoff for the primary analysis, both in the same participant with a prior event of CRS, and after a delay in treatment. No new events of ICANS were reported since the clinical cutoff for the primary analysis. One participant experienced a Grade 5 immune-mediated TEAE of Guillain-Barré syndrome.

Data are available as of 22 August 2023 regarding the incidence of CRS following prolonged dosing intervals among participants treated at pivotal RP2D in MajesTEC-1. Sixty-one participants in this population had a prolonged dosing interval of >28 days due to dose delay or other reasons. Fifty-nine of these 61 participants did not experience CRS upon restarting treatment with teclistamab, representing a total of 126 occurrences of prolonged dosing intervals without CRS. In the 100 occurrences of a dosing interval from >28 to 62 days, most participants (78.0%) did not receive repeat step-up doses prior to restarting treatment. For all but 1 of the remaining 26 occurrences of prolonged dosing intervals (all of which were ≥ 63 days in duration), the participants received at least 1 repeat step-up dose. Two participants who experienced a prolonged dosing interval experienced CRS (Grade 1 or 2) upon restarting treatment with teclistamab. Both participants experienced dosing interruptions lasting >28 to 62 days and had received repeat step-up doses prior to restarting treatment.

4.3.2.1.1.3. China Cohort Participants Treated at the Recommended Dose

As of the data cutoff (27 September 2023), 26 participants enrolled in MajesTEC-1 in China were treated with the recommended dose of 1.5 mg/kg teclistamab SC weekly (preceded by step-up doses of 0.06 and 0.3 mg/kg). All 26 participants have experienced at least 1 TEAE, with lymphopenia (100.0%) and leukopenia, CRS and neutropenia (96.2% each) being the most frequently reported. Serious TEAEs were reported for 76.9% of participants, most frequently COVID-19 (57.7%), and Grade 3 or 4 TEAEs were reported for all 26 participants, most frequently lymphopenia (88.5%). Four participants (15.4%) died due to a TEAE: due to cardiac failure, pneumonia, acute myocardial infarction and multiple organ dysfunction syndrome (1 participant each). No TEAEs led to discontinuation of teclistamab. The CRS events were Grade 1 or 2 and occurred primarily during step-up dosing or the first treatment dose. The median onset time of CRS from the time of injection was 2.0 days. Supportive measures to treat CRS included tocilizumab for 57.7% of participants, IV fluids for 23.1%, oxygen for 11.5%, and steroids for 7.7%. Neurologic TEAEs were reported for 57.7% of participants, and 34.6% experienced neurotoxicity (primarily headache [19.2%]); there were no events reported as ICANS. Infection TEAEs were reported for 96.2% of participants and were Grade ≥ 3 for 73.1%.

4.3.2.1.1.4. Safety Data for Other Notable MajesTEC-1 Treatment Regimens

Safety data as of the data cutoff (22 August 2024) are presented for treatment regimens at doses higher than the recommended dose for teclistamab SC monotherapy. The data from these cohorts are generally consistent with those from participants treated at the recommended dose of 1.5 mg/kg weekly. No DLTs were found with doses of up to 6 mg/kg or a fixed dose of 600 mg; safety data for these dosing regimens are not discussed here because the Sponsor does not intend to pursue these dosing regimens further.

Teclistamab 3 mg/kg Weekly

As of the data cutoff, 5 participants were treated with teclistamab 3 mg/kg weekly for all cycles, preceded by step-up doses of 0.06, 0.3, and 1.5 mg/kg.

All 5 participants have experienced at least 1 TEAE. The TEAEs reported for more than 1 participant were neutropenia (5 participants); anemia, cough, and headache (4 participants each); decreased appetite, fatigue, injection site rash, insomnia, leukopenia, and thrombocytopenia (3 participants each); and CRS, diarrhea, fall, hypogammaglobulinemia, lipase increased, nausea, edema peripheral, sepsis, upper respiratory tract infection, and weight decreased (2 participants each). Serious TEAEs were reported for all 5 participants, with CRS and sepsis being reported in more than 1 participant (2 participants each). Grade 3 or 4 TEAEs were reported for all 5 participants, most frequently neutropenia (in all 5 participants). One participant died due to a TEAE of sepsis. No TEAEs led to discontinuation of teclistamab. The CRS events in the 2 participants were Grade 1 and occurred during step-up dosing. Supportive measures to treat CRS included IV fluids for 1 participant. Neurologic TEAEs were reported for all 5 participants, and 1 participant experienced neurotoxicity (dysgeusia, headache, insomnia, and parosmia); there were no events reported as ICANS. Infection TEAEs were reported for 4 participants and were Grade ≥ 3 for 1 participant (sepsis).

Teclistamab 3 mg/kg Q4W

As of the data cutoff, 10 participants were treated with step-up doses of 0.06, 0.3, and 1.5 mg/kg followed by treatment doses of 3 mg/kg Q4W. Dexamethasone pretreatment was used through Cycle 1 Day 3.

All 10 participants experienced at least 1 TEAE. The most frequently reported TEAEs (≥ 3 participants) were neutropenia (7 participants); arthralgia, CRS, fatigue, and dyspnea (5 participants each); anemia, COVID-19, decreased appetite, diarrhea, hypogammaglobulinemia, and headache (4 participants each); and cough, fall, injection site erythema, nausea, pneumonia, and thrombocytopenia (3 participants each). Serious TEAEs were reported for 8 participants, most frequently COVID-19, CRS, and pneumonia (2 participants each). Grade 3 or 4 TEAEs were reported for all 10 participants, most frequently neutropenia (6 participants). A TEAE of pneumonia led to death in 1 participant. A TEAE of sepsis led to discontinuation of teclistamab in 1 participant. The CRS events were Grade 1 or 2 and occurred during step-up dosing or the first treatment dose. The median onset time of CRS from the time of injection was 2.0 days. Supportive measures to treat CRS included tocilizumab and IV fluids for 1 participant each. Neurologic TEAEs were reported for 8 participants, and 3 participants experienced neurotoxicity (headache in 2 participants; and somnolence and ageusia in 1 participant each). Infection TEAEs were reported for 9 participants and were Grade 3 or 4 for 5 participants.

4.3.2.1.2. Study MMY1002 (Japan)

As of the data cutoff (22 September 2023), 31 participants were treated with the recommended dose of teclistamab SC 1.5 mg/kg in Phase 1 and Phase 2 combined, 5 participants were treated with teclistamab SC 0.72 mg/kg weekly, and 4 participants were treated with teclistamab SC 3 mg/kg weekly. Of the total 40 participants treated in the study, 97.5% experienced at least 1 TEAE, most frequently ($\geq 20\%$ of participants) CRS (72.5%), neutropenia (72.5%), hypogammaglobulinemia (45.0%), pyrexia (42.5%), lymphopenia (32.5%), anemia (27.5%), and injection site erythema (25.0%). No DLTs were observed. At primary analysis cutoff,

5 participants (16.1%) treated with teclistamab SC 1.5 mg/kg in Phase 2 died; of these, 2 participants died due to TEAEs that were unrelated to study drug (large intestinal perforation and multiple organ dysfunction syndrome in 1 participant each), and 3 participants died due to progressive disease. Serious TEAEs were experienced by 18 participants (45.0%); these were considered related to study drug in 9 participants (22.5%). The most frequent Grade 3 or 4 event ($\geq 50\%$ of participants) was neutropenia (67.5%). At the recommended dose, CRS events were Grade 1 or 2 and occurred primarily during step-up dosing or the first treatment dose, the median onset time of CRS from the time of injection was 2.0 days, and supportive measures to treat CRS included tocilizumab for 64.5% of participants, steroids for 9.7%, and oxygen for 3.2%. At least 1 neurotoxicity event was reported for 5 participants (12.5%). The only event to be reported in >1 participant was headache, reported in 3 participants (7.5%). No participants reported ICANS events. Injection site reactions were reported for 17 participants (42.5%), most frequently injection site erythema (25.0%), injection site pruritus (7.5%), and erythema and skin reaction (5.0% each). Infection TEAEs were reported for 27 participants (67.5%) and were reported with a maximum severity of Grade 3 or 4 for 5 participants (12.5%).

4.3.2.2. Teclistamab Safety in Combination Therapy Studies

All data presented for the combination studies are for teclistamab administered by SC injection.

4.3.2.2.1. TriMM-2 Study (MMY1002)

Participants with multiple myeloma who have received at least 3 prior lines of therapy, including a PI and an IMiD, or have disease that is double refractory to a PI and an IMiD are included in this study. Safety data are presented for key cohorts treated with teclistamab and daratumumab SC combination therapy. The safety data for the combination of teclistamab and daratumumab do not indicate any different safety signals from the known safety profiles of the individual drugs. However, as detailed below, a higher rate of fatal infections was observed in cohorts that were administered fixed dose teclistamab combined with daratumumab SC compared with cohorts administered weight-based teclistamab combined with daratumumab SC, with all deaths on fixed dose teclistamab occurring in participants whose disease had previously been refractory to an anti-CD38 monoclonal antibody. No DLTs were found with teclistamab doses below 6 mg/kg in combination with daratumumab; safety data for the 6 mg/kg dosing regimen is not discussed here because the Sponsor does not intend to pursue this dosing regimen further.

RP2D Population (Teclistamab 1.5 mg/kg Weekly or 3 mg/kg Q2W + Daratumumab SC)

Primary Analysis:

As of the clinical cutoff of 31 January 2024 (primary analysis), 21 participants were treated with weekly teclistamab 1.5 mg/kg (preceded by step-up doses of 0.06 and 0.3 mg/kg) and 40 participants were treated with Q2W teclistamab 3 mg/kg (preceded by step-up doses of 0.06, 0.3, and 1.5 mg/kg) in combination with daratumumab SC, in Part 1 dose escalation and Part 2 dose expansion. These 61 participants are considered the RP2D population.

All 61 participants in the RP2D population experienced at least 1 TEAE. No DLTs were observed. The most frequently reported TEAEs ($\geq 20\%$ of participants) were CRS (73.8%); neutropenia (68.9%); anemia (60.7%); diarrhea (45.9%); thrombocytopenia (42.6%); COVID-19 (41.0%); fatigue (37.7%); cough (36.1%); arthralgia and pyrexia (31.1% each); nausea (29.5%); headache (27.9%); back pain (26.2%); asthenia (24.6%); upper respiratory tract infection (23.0%); and constipation and hypogammaglobulinemia (21.3% each).

Serious TEAEs were reported for 80.3% of participants, most frequently CRS (18.0%), COVID-19 (16.4%), and pneumonia (11.5%). Grade 3 or 4 TEAEs were reported for 93.4% of participants, most frequently neutropenia (62.3%), anemia (45.9%), and thrombocytopenia (32.8%). Seven participants (11.5%) died due to a TEAE: COVID-19 (2 participants) and 1 participant each due to enterococcal sepsis, septic shock, hepatic failure, pseudomonal sepsis, and adenocarcinoma gastric. Eight participants (13.1%) experienced TEAEs reported as leading to treatment discontinuation of both study drugs. Most frequently, these events were reported in the SOC of Infection and Infestations (4 participants). The CRS events were Grade 1 (49.2%) or 2 (24.6%) and occurred primarily during step-up dosing or the first treatment dose. The median onset time of CRS from the time of injection was 2.0 days. Supportive measures to treat CRS included tocilizumab for 22 participants (36.1%), steroids for 4 participants (6.6%), and oxygen for 3 participants (4.9%). Neurologic TEAEs were reported for 72.1% of participants, most frequently headache (27.9%) and insomnia (18.0%); 34.4% of participants experienced neurotoxicity (none were Grade ≥ 3), most frequently dysgeusia (11.5%) and headache (9.8%). ICANS (Grade 1 or 2) was reported for 2 participants (3.3%), both associated with concurrent CRS and both recovered. Infection TEAEs were reported for 82.0% of participants and were Grade 3 or 4 for 45.9%. Five participants (8.2%) experienced a fatal infection TEAE (see above).

Final Analysis:

With additional follow-up of the 61 participants treated at RP2D at the final analysis (through the clinical cutoff of 30 April 2025), the safety profile remained consistent with what was described for the primary analysis. There was 1 new event of CRS (in a participant who had experienced at least 1 prior TEAE of CRS), and no new events of ICANS, Grade 5 TEAEs, or DLTs.

Teclistamab 0.72 or 0.75 mg/kg Weekly + Daratumumab SC + Pomalidomide Cohort

As of 30 April 2025, 9 participants were treated with teclistamab 0.72 or 0.75 mg/kg weekly, preceded by step-up doses of 0.06 and 0.24 mg/kg, in combination with daratumumab SC and pomalidomide, and 1 participant received teclistamab and daratumumab but not pomalidomide.

All 10 participants experienced at least 1 TEAE, with the most frequently reported TEAEs (≥ 3 participants) being CRS (7 participants), arthralgia and neutropenia (6 participants each), cough and pyrexia (5 participants each), constipation, COVID-19, dizziness, fall, fatigue, headache, hypokalemia, hyponatremia, peripheral sensory neuropathy, sinusitis, and upper respiratory tract infection (4 participants each), and asthenia, diarrhea, hypermagnesemia, injection site erythema, lymphopenia, nasal congestion, nausea, oropharyngeal pain, pneumonia, pollakiuria, thrombocytopenia, urinary tract infection, and weight decreased (3 participants each).

Serious TEAEs were reported for 8 participants, with pneumonia (3 participants) and CRS (2 participants) being the only serious TEAEs reported for more than 1 participant. Grade 3 or 4 TEAEs were reported for 9 participants, most frequently neutropenia (6 participants). Three participants died during the study: 2 participants died due to an AE and 1 participant died due to disease progression. Grade 5 TEAEs were reported for 2 participants: COVID-19 pneumonia and pneumonia (1 participant each). One participant was reported with DLTs of thrombocytopenia and neutropenia (both Grade 4). Two participants experienced TEAEs leading to teclistamab discontinuation: pneumonia in 1 participant, who also discontinued pomalidomide, and bronchopulmonary aspergillosis and viral upper respiratory tract infection in the second participant, who discontinued all study drugs. The CRS events were Grade 1 or 2 and occurred primarily during step-up dosing or Cycle 1. The median onset time of CRS from the time of injection was 2.0 days. Supportive measures to treat CRS included tocilizumab for 6 participants, and steroids and oxygen for 1 participant each. Neurologic TEAEs were reported for 8 participants, and 4 participants experienced neurotoxicity (none were Grade 3 or 4); ICANS was reported for 1 participant. Infection TEAEs were reported for 9 participants and were Grade 3 or 4 for 5 participants. Two participants experienced a fatal infection TEAE (see above).

Fatal Infections in Participants Treated with Fixed Dose Teclistamab in Combination with Daratumumab SC

A total of 31 participants were enrolled into fixed dose teclistamab-daratumumab cohorts that evaluated a regimen in which teclistamab was administered at a treatment dose of 100 mg (for participants ≤ 60 kg), 150 mg (for participants >60 kg) weekly for Cycles 1 and 2, 200/300 mg Q2W for Cycles 3 to 6, and 200/300 mg Q4W for Cycles 7+. In each cohort, treatment doses were preceded by step-up doses.

As of 08 February 2023 and prompting an Urgent Safety Measure (see below), 8 cases (26%) of fatal infection were reported in the 31 participants who were treated with teclistamab fixed dose in combination with daratumumab. The median duration of follow-up for the fixed dose cohort was approximately 7 months. With a median follow-up of approximately 11 months, rates of fatal infections with weight-based dosing of teclistamab (1.5 mg/kg weekly or 3 mg/kg Q2W; $n=61$) in combination with daratumumab (5%) were comparable to that with weight-based dosing of teclistamab monotherapy with a similar duration of follow-up.

Participants in both the weight-based and fixed dose cohorts were pretreated with a median of 5 prior lines of therapy. The majority of participants were previously treated with at least an IMiD, a PI, and an anti-CD38 monoclonal antibody, and more than half of the participants had disease that was already refractory to an anti-CD38 therapy. All 8 fatal infections in the fixed dose regimen occurred in participants who were refractory to daratumumab and all occurred during the first 6 months of treatment, with 4 of these infections starting within the first 8 weeks of treatment. Three of the fatal infections occurred in participants with active COVID-19 infection, 3 were related to bacterial infections, 1 was due to adenovirus, and 1 event of sepsis did not reveal a pathogen. Notably, only 2 of these 8 participants had received intravenous immunoglobulin and only during hospitalization for the fatal infection.

These data led to the implementation of an Urgent Safety Measure by the Sponsor and subsequent amendment of all ongoing protocols to convert participants who were receiving fixed dose teclistamab to weight-based dosing. This included termination of fixed dosing in other teclistamab studies as a clinical development decision.

4.3.2.2.2. TriMM-3 Study (MMY1005)

Teclistamab (1.5 or 3 mg/kg) Q2W + Cetrelimab Q2W

As of 22 May 2025, 22 participants were treated with either teclistamab 1.5 mg/kg Q2W (preceded by step-up doses of 0.06, 0.24, and 0.75 mg/kg) or 3 mg/kg Q2W (preceded by step-up doses of 0.06, 0.3, and 1.5 mg/kg) in combination with cetrelimab Q2W. Three participants received teclistamab but not cetrelimab.

All 22 participants dosed with teclistamab and cetrelimab have experienced at least 1 TEAE. No DLTs were observed. The most frequently reported TEAEs ($\geq 20\%$ of participants) were CRS and thrombocytopenia (54.5% each), anemia (50.0%), neutropenia (45.5%), asthenia, back pain, cough, diarrhea, headache, injection site erythema, lymphopenia, and pneumonia (27.3% each), and COVID-19, hyperamylasemia, hyperglycemia, hypogammaglobulinemia, nausea, edema peripheral, and productive cough (22.7% each).

Serious TEAEs were reported for 54.5% of participants, most frequently pneumonia (13.6%) and hip fracture (9.1%). Grade 3 or 4 TEAEs were reported for 86.4% of participants, most frequently neutropenia (45.5%). Three participants died during the study: 1 participant died due to an AE (pseudomonas infection, reported as a Grade 5 TEAE), 1 participant died due to disease progression, and 1 participant died due to "Other: worsening of multiple myeloma disease". TEAEs leading to teclistamab interruption were reported for 2 participants (pseudomonas infection in 1 participant, and bicytopenia and acute myeloid leukemia in 1 participant). The CRS events were Grade 1 (50.0%) or 2 (4.5%) and most occurred primarily during step-up dosing. The median onset time of CRS from the time of injection was 2.5 days. Supportive measures to treat CRS included tocilizumab for 6 participants (27.3%), and oxygen for 1 participant (4.5%). Neurologic TEAEs were reported for 54.5% of participants, most frequently headache (27.3%) and insomnia and peripheral sensory neuropathy (13.6% each); 27.3% of participants experienced neurotoxicity related to at least 1 study drug (none were Grade ≥ 3). There were no reports of ICANS. Infection TEAEs were reported for 77.3% of participants and were Grade ≥ 3 for 31.8%. One participant experienced a fatal infection AE (see above).

4.3.2.2.3. RedirecTT-1 Study (MMY1003)

Safety data are presented for teclistamab and talquetamab combination therapy at the RP2R as of 18 March 2025 and at Dose Level 6 as of 22 August 2024. Overall, the safety profile observed with the teclistamab and talquetamab combination is generally consistent with teclistamab and talquetamab administered as monotherapy treatments.

Teclistamab 3 mg/kg Q2W + Talquetamab 0.8 mg/kg SC Q2W (RP2R)

As of 18 March 2025, 134 participants were treated with teclistamab 3 mg/kg Q2W (preceded by step-up doses of 0.06, 0.3, and 1.5 mg/kg) in combination with talquetamab 0.8 mg/kg SC Q2W (preceded by step-up doses of 0.01, 0.06, and 0.3 mg/kg), in Phase 1 and Phase 2 combined.

All 134 participants have experienced at least 1 TEAE. The most frequently reported TEAEs ($\geq 20\%$ of participants) were CRS (78.4%), neutropenia (71.6%), dysgeusia (58.2%), anemia and weight decreased (47.8% each), dry mouth (44.0%), diarrhea (41.8%), cough (38.8%), nail disorder and thrombocytopenia (36.6% each), dry skin (35.8%), pyrexia (34.3%), skin exfoliation (31.3%), COVID-19 (29.9%), hypogammaglobulinemia and nausea (29.1% each), fatigue and dysphagia (27.6%), upper respiratory tract infection (25.4%), hypokalemia (24.6%), decreased appetite (21.6%), and aspartate aminotransferase increased and pneumonia (20.1% each). Serious TEAEs were reported for 86 participants (64.2%), most frequently COVID-19 (8.2%), febrile neutropenia (6.7%) and CRS (5.2%). Grade 3 or 4 TEAEs were reported for 120 participants (89.6%), most frequently neutropenia (61.9%), anemia (29.1%), and thrombocytopenia (23.9%).

At least 1 TEAE of infection (any grade) was reported for 112 participants (83.6%), most frequently ($\geq 5\%$ of participants) COVID-19 (29.9%), upper respiratory tract infection (25.4%), pneumonia (20.1%), urinary tract infection (14.9%), oral candidiasis (8.2%), viral upper respiratory tract infection (7.5%), rhinovirus infection (6.7%), sinusitis (6.0%), and nasopharyngitis (5.2%). Grade 3 or 4 infection TEAEs were reported in 46 participants (34.3%).

A total of 33 participants (24.6%) died during the study, including 17 participants (12.7%) who died due to an AE. Grade 5 TEAEs were reported for 16 participants (11.9%): 10 participants (7.5%) had a fatal infection-related TEAE (COVID-19 pneumonia [4 participants] and Klebsiella sepsis, pneumonia, pneumonia fungal, pneumonia klebsiella, progressive multifocal leukoencephalopathy and pseudomonal sepsis [1 participant each]), and the remaining 6 died due to non-infectious TEAEs, of whom 3 died in the context of progression of disease, although the primary cause of death was reported as a TEAE (general physical health deterioration, euthanasia, and cerebral hemorrhage).

DLTs were evaluated during the dose escalation portion (Part 1) of Phase 1. One participant treated with RP2R reported 3 events of Grade 4 thrombocytopenia. The first event was reported after the 0.06 mg/kg step-up dose of teclistamab and 0.01 mg/kg step-up dose of talquetamab. Both study drugs were interrupted, then treatment with talquetamab and teclistamab resumed. The investigator reported the events as non-serious and related to study treatment. As of 18 March 2025, all events were resolving.

The CRS events were Grade 1 or 2 and occurred primarily during step-up dosing. The median onset time of CRS from the time of injection was 2.0 days. Tocilizumab was administered to 47.8% of participants for treatment of CRS, and other supportive measures included corticosteroids (13.4%) and oxygen (4.5%). Neurologic TEAEs were reported for 87.3% of participants, most frequently dysgeusia (58.2%) and headache (19.4%); 26.1% of participants experienced neurotoxicity (mostly Grade 1 or 2). Thirteen participants (9.7%) experienced events of ICANS

(mostly Grade 1 or 2). Infection TEAEs were reported for 83.6% of participants and were maximum toxicity Grade 3 or 4 for 34.3%. Ten participants experienced a fatal infection TEAE (see above).

Teclistamab 3 mg/kg Q4W + Talquetamab 0.8 mg/kg SC Q4W (Dose Level 6)

As of 22 August 2024, 20 participants were treated with teclistamab 3 mg/kg Q4W (preceded by step-up doses of 0.06, 0.3, and 1.5 mg/kg) in combination with talquetamab 0.8 mg/kg SC Q4W (preceded by step-up doses 0.01, 0.06, and 0.3 mg/kg), in the Part 1 dose escalation and Part 2 dose expansion combined (Phase 1).

All 20 participants have experienced at least 1 TEAE. The most frequently reported TEAEs ($\geq 20\%$ of participants) were CRS (80.0%); neutropenia (70.0%); anemia, dry mouth, headache, and thrombocytopenia (45.0% each); diarrhea, hypogammaglobulinemia, and weight decreased (40.0% each); dysgeusia and pruritus (35.0% each); cough, decreased appetite, dry skin, nail dystrophy, fatigue, nausea, and pyrexia (25.0% each); asthenia, COVID-19, dysphagia, dyspnea, nail disorder, pneumonia, skin exfoliation, and upper respiratory tract infection (20.0% each). Serious TEAEs were reported for 12 participants (60.0%), most frequently COVID-19 pneumonia, pneumonia, and pneumonia hemophilus (10.0% each). Grade 3 or 4 TEAEs were reported for 17 participants (85.0%), most frequently neutropenia (65.0%), anemia (30.0%), and thrombocytopenia (15.0%). One participant (5.0%) died due to a TEAE of COVID-19 pneumonia. No participants reported DLTs. The CRS events were Grade 1 or 2 and occurred primarily during step-up dosing or the first treatment dose. The median onset time of CRS from the time of injection was 2.0 days. Supportive measures to treat CRS included tocilizumab for 65.0% of participants and corticosteroids for 10.0% of participants. Neurologic TEAEs were reported for 75.0% of participants and neurotoxicity for 40.0% of participants. One participant experienced an event of ICANS. Infection TEAEs were reported for 80.0% of participants and were Grade 3 or 4 for 45.0%. One participant experienced a fatal infection TEAE (see above).

4.3.2.2.4. MajesTEC-2 Study (MMY1004)

Safety data are presented for relevant treatment regimens as of a data cutoff of 22 August 2024. The safety data for the combination of teclistamab and daratumumab do not indicate any different safety signals from the known safety profiles of the individual drugs.

Teclistamab 1.5 mg/kg Weekly + Lenalidomide

Participants with multiple myeloma who received at least 2 prior lines of therapy, including exposure to a PI, an IMiD, and an anti-CD38 monoclonal antibody are treated in this cohort. As of the data cutoff, 19 participants were treated, all of whom experienced at least 1 TEAE. The most frequently reported TEAEs (≥ 4 participants) were neutropenia (14 participants); CRS (13 participants); diarrhea (11 participants); cough and nausea (8 participants each); constipation and fatigue (7 participants each); back pain, headache, pneumonia, thrombocytopenia, and upper respiratory tract infection (6 participants each); anemia, bone pain, COVID-19, dyspnea, hypogammaglobulinemia, injection site erythema, and pruritus (5 participants each); and hypokalemia, hypomagnesemia, insomnia, oedema peripheral, pyrexia, rhinovirus infection,

vomiting, pain in extremity, procedural complications, productive cough, and weight decreased (4 participants each). Serious TEAEs were reported in 16 participants, most frequently pneumonia (6 participants). Grade 3 or 4 TEAEs were reported for 18 participants, most frequently neutropenia (13 participants). TEAEs led to discontinuation of teclistamab in 6 participants: 1 participant each due to acute kidney injury, COVID-19, lower respiratory tract infection, neuroendocrine carcinoma, sepsis, and weight decreased. Three participants (15.8%) died due to a TEAE: 1 participant each due to acute kidney injury, COVID-19, and sepsis. No participants reported DLTs. The CRS events were Grade 1 or 2 and occurred during step-up dosing or early treatment doses. The median onset time of CRS from the time of injection was 2.0 days. Supportive measures to treat CRS included tocilizumab for 8 participants, steroids for 2 participants, and oxygen for 1 participant. Neurologic TEAEs were reported for 13 participants. Neurotoxicity was reported for 7 participants (primarily headache [3 participants]), with 1 participant experiencing ICANS (Grade 1). Infection TEAEs were reported for 16 participants and were Grade ≥ 3 for 9 participants.

Teclistamab 1.5 mg/kg Weekly + Daratumumab SC + Lenalidomide

Participants with newly diagnosed multiple myeloma, or participants with multiple myeloma who have received 1 to 3 prior lines of therapy, including exposure to a PI and an IMiD, are treated in this cohort; safety data are presented separately for these groups below.

Participants with Newly Diagnosed Multiple Myeloma

As of the data cutoff, 11 participants were treated, all of whom experienced at least 1 TEAE. The most frequently reported TEAEs (≥ 3 participants) were upper respiratory tract infection (8 participants), CRS (6 participants); diarrhea, fatigue, insomnia, and nausea (5 participants each); gamma-glutamyltransferase increased, headache, hypogammaglobulinemia, hypophosphatemia, neutropenia, and rash maculopapular (4 participants each); and alanine aminotransferase increased, constipation, cough, and thrombocytopenia (3 participants each). Serious TEAEs were reported for 5 participants, with no preferred terms reported in more than 1 participant. Grade 3 or 4 TEAEs were reported for 9 participants, most frequently neutropenia (4 participants). No participants discontinued teclistamab due to a TEAE and no deaths have occurred. One participant was reported with a DLT of aspartate aminotransferase increased (Grade 4). The CRS events were Grade 1 or 2 and occurred primarily during step-up dosing or early treatment doses. The median onset time of CRS from the time of injection was 3.0 days. Supportive measures to treat CRS included tocilizumab for 6 participants and steroids for 1 participant. Neurologic TEAEs were reported for 9 participants, and 3 participants experienced neurotoxicity (headache [2 participants] and dysgeusia [1 participant]); there were no events of ICANS. Infection TEAEs were reported for 9 participants and were Grade ≥ 3 for 2 participants.

Participants with Relapsed or Refractory Multiple Myeloma

As of the data cutoff, 19 participants were treated, all of whom have experienced at least 1 TEAE. The most frequently reported TEAEs (≥ 4 participants) were CRS (17 participants); neutropenia (16 participants); fatigue and diarrhea (10 participants each); COVID-19 and nausea

(9 participants); cough, insomnia, and pneumonia (8 participants each); alanine aminotransferase increased, anemia, headache, hypophosphatemia, and thrombocytopenia (7 participants each); aspartate aminotransferase increased, blood alkaline phosphatase increased, decreased appetite, hypocalcemia, injection site erythema, and pyrexia (6 participants each); arthralgia, dyspnea, hyponatremia, lipase increased, muscle spasms, peripheral neuropathy, rash, and upper respiratory tract infection (5 participants each); and bone pain, constipation, gamma-glutamyltransferase increased, hyperbilirubinemia, hypoalbuminemia, hypokalemia, hypotension, pruritus, sinus tachycardia, weight decreased, and vomiting (4 participants each). Serious TEAEs were reported for 17 participants, most frequently pneumonia (6 participants). Grade 3 or 4 TEAEs were reported for all 19 participants, most frequently neutropenia (17 participants). TEAEs led to discontinuation of teclistamab for 4 participants: 1 participant due to COVID-19 pneumonia, 1 due to metapneumovirus pneumonia, 1 due to multiple organ dysfunction syndrome, and 1 due to inflammation and neuralgia. One participant died due to a TEAE of multiple organ dysfunction syndrome. The CRS events were Grade 1 or 2 and occurred during step-up dosing or early treatment doses. The median onset time of CRS from the time of injection was 2.0 days. Supportive measures for CRS included tocilizumab for 11 participants and steroids for 2 participants. Neurologic TEAEs were reported for 16 participants, and 7 participants experienced neurotoxicity (primarily headache [3 participants]); there were no events of ICANS. Infection TEAEs were reported for 18 participants and were Grade ≥ 3 for 14 participants.

Teclistamab Weekly (0.72 mg/kg or 1.5 mg/kg) + Daratumumab SC + Pomalidomide

As of the data cutoff, 17 participants were treated with teclistamab weekly (0.72 mg/kg or 1.5 mg/kg), in combination with daratumumab SC and pomalidomide. All 17 participants experienced at least 1 TEAE, with the most frequently reported TEAEs (≥ 5 participants) being neutropenia (15 participants); cough (11 participants); diarrhea and hypokalemia (9 participants each); CRS, pyrexia, and upper respiratory tract infection (8 participants each); anemia, dyspnea, fatigue, injection site erythema, and thrombocytopenia (7 participants each); blood lactate dehydrogenase increased and hypogammaglobulinemia (6 participants each); and blood alkaline phosphatase increased, COVID-19 pneumonia, lipase increased, and weight decreased (5 participants each). Serious TEAEs were reported for 13 participants, with COVID-19 pneumonia (5 participants) and anemia (2 participants) being the only serious TEAEs reported for more than 1 participant. Grade 3 or 4 TEAEs were reported for 16 participants, most frequently neutropenia (15 participants). Two participants died due to TEAEs of COVID-19 pneumonia. Five participants experienced TEAEs leading to teclistamab discontinuation: COVID-19 pneumonia (2 participants), colitis, diarrhea, weight decreased, diarrhea, and decreased appetite (1 participant each). The CRS events were all Grade 1 and occurred during step-up dosing. The median onset time of CRS from the time of injection was 2.0 days. Supportive measures to treat CRS included tocilizumab for 3 participants, and no participants received steroids or oxygen. Neurologic TEAEs were reported for 9 participants, and 3 participants experienced neurotoxicity (none were Grade ≥ 3); ICANS was not reported for any participants. Infection TEAEs were reported for 16 participants and were Grade ≥ 3 for 12 participants. Two participants experienced a fatal infection TEAE (see above).

4.3.2.2.5. MajesTEC-4 Study (EMN30/MMY3003)

4.3.2.2.5.1. Safety Run-in 1: Teclistamab 1.5 mg/kg SC + Lenalidomide

As of 03 March 2025, 32 participants with newly diagnosed multiple myeloma who have completed induction therapy followed by an ASCT, with or without consolidation, were treated with teclistamab in combination with lenalidomide in Safety Run-in 1 of MajesTEC-4. The safety data for the combination of teclistamab and lenalidomide do not indicate any different safety signals from the known safety profiles of the individual drugs.

Safety Run-in 1 was initiated with weight-based teclistamab dosing for all participants, per the original protocol. After approval of an amendment to the protocol, participants who were already enrolled were switched from weight-based to fixed dosing. Participants enrolled in Safety Run-in 1 after implementation of the amendment, started study treatment with fixed dose teclistamab. Following implementation of an Urgent Safety Measure (refer to Section 4.3.2.2.1), all participants receiving fixed dose teclistamab were transitioned to weight-based teclistamab.

Of the total 32 participants treated in Safety Run-in 1, 15 participants started treatment with weight-based teclistamab (of whom 12 switched to fixed dose teclistamab) and 17 participants started treatment with fixed dose teclistamab. Following the Urgent Safety Measure (refer to Section 4.3.2.2.1), no further participants received fixed dose teclistamab.

All 32 participants experienced at least 1 TEAE. The most frequently reported TEAEs ($\geq 20\%$ of participants) were neutropenia (93.8%), hypogammaglobulinemia (87.5%), upper respiratory tract infection (68.8%), CRS (50.0%), diarrhea and cough (46.9% each), COVID-19 (40.6%), fatigue (31.3%), leukopenia and pneumonia (25.0% each), and hypokalemia, injection site erythema, influenza like illness, and nasopharyngitis (21.9% each).

Serious TEAEs were reported for 17 participants (53.1%). Grade 3 and Grade 4 TEAEs were reported for 10 participants (31.3%) and 22 participants (68.8%), respectively, with neutropenia the most frequently reported for each grade. One participant died during the study, with cause of death reported as “severe immunosuppression after transplantation”. No participants died due to AEs. Six participants (18.8%) experienced TEAEs leading to teclistamab discontinuation. The CRS events reported were Grade 1 or 2 and most occurred during step-up dosing or early treatment doses. Ten participants (31.3%) experienced a neurologic TEAE, most commonly peripheral sensory neuropathy in 4 participants (12.5%), and dizziness, headache, and paresthesia in 2 participants (6.3%) each. No participants were reported with neurotoxicity. Infection TEAEs (TEAEs in the SOC of Infections and Infestations) were reported for 31 participants (96.9%) and were Grade 3 and Grade 4 for 11 participants (34.4%) and 1 participant (3.1%), respectively.

4.3.2.2.5.2. Safety Run-in 2

Tec-Len Cohort: Teclistamab 3 mg/kg SC + Lenalidomide

As of 03 March 2025, 32 participants with newly diagnosed multiple myeloma who have completed induction therapy followed by an ASCT, with or without consolidation, were treated with teclistamab in combination with lenalidomide in Safety Run-in 2 of MajesTEC-4. The safety

data for the combination of teclistamab and lenalidomide do not indicate any different safety signals from the known safety profiles of the individual drugs.

All 32 participants experienced at least 1 TEAE. The most frequently reported TEAEs ($\geq 20\%$ of participants) were neutropenia (75.0%), hypogammaglobulinemia (56.3%), CRS and upper respiratory tract infection (40.6% each), injection site erythema (37.5%), diarrhea (34.4%), cough and fatigue (25.0% each), and COVID-19 and peripheral sensory neuropathy (21.9% each).

Serious TEAEs were reported for 13 participants (40.6%). Grade 3 and Grade 4 TEAEs were reported for 14 participants (43.8%) and 16 participants (50.0%), respectively, with neutropenia the most frequently reported for each grade. Two participants (6.3%) died in the Tec-Len cohort, both due to AEs (COVID-19 pneumonia and radiculopathy in 1 participant each, both reported as TEAEs with an outcome of death). Two participants (6.3%) experienced TEAEs leading to teclistamab discontinuation. The CRS events reported were Grade 1 and most occurred during step-up dosing or early treatment doses. Fifteen participants (46.9%) experienced a neurologic TEAE, most commonly peripheral sensory neuropathy in 7 participants (21.9%) and headache in 4 participants (12.5%). No participants were reported with neurotoxicity. Infection TEAEs (TEAEs in the SOC of Infections and Infestations) were reported for 28 participants (87.5%) and were Grade 3 and Grade 4 for 8 participants (25.0%) and 2 participants (6.3%), respectively.

Tec Cohort: Teclistamab 3 mg/kg SC

As of 03 March 2025, 30 participants with newly diagnosed multiple myeloma who have completed induction therapy followed by an ASCT, with or without consolidation, were treated with teclistamab monotherapy in Safety Run-in 2 of MajesTEC-4. The safety data are consistent with the known safety profile of teclistamab monotherapy.

All 30 participants experienced at least 1 TEAE. The most frequently reported TEAEs ($\geq 20\%$ of participants) were hypogammaglobulinemia (83.3%), neutropenia (66.7%), CRS (43.3%), upper respiratory tract infection (40.0%), cough (33.3%), COVID-19 and injection site erythema (30.0% each), diarrhea (26.7%), and fatigue and lymphopenia (20.0%).

Serious TEAEs were reported for 8 participants (26.7%). Grade 3 and Grade 4 TEAEs were reported for 9 participants (30.0%) and 11 participants (36.7%), respectively, with neutropenia the most frequently reported for each grade. One participant died in the Tec cohort, due to progressive disease. One participant experienced a TEAE leading to teclistamab discontinuation. The CRS events reported were Grade 1 or 2 and most occurred during step-up dosing or early treatment doses. Thirteen participants (43.3%) experienced a neurologic TEAE; the PTs reported in more than 1 participant were peripheral sensory neuropathy, headache, paresthesia, dizziness, and dysgeusia (2 participants [6.7%] each). No participants were reported with neurotoxicity. Infection TEAEs (TEAEs in the SOC of Infections and Infestations) were reported for 25 participants (83.3%) and were Grade 3 and Grade 4 for 5 participants (16.7%) and 1 participant (3.3%), respectively.

4.3.2.2.6. MajesTEC-5 Study (GMMG-HD10/DSMM-XX/MMY2003)

As of 22 August 2025, 59 participants with newly diagnosed transplant-eligible multiple myeloma were treated in Arms A, A1, B, and C of the study, including 30 participants with teclistamab in combination with daratumumab SC, lenalidomide, and dexamethasone as induction therapy followed by ASCT and teclistamab with daratumumab SC with or without lenalidomide maintenance therapy; 19 participants with teclistamab in combination with daratumumab SC, bortezomib, lenalidomide, and dexamethasone as induction therapy followed by ASCT and teclistamab with daratumumab SC maintenance therapy; and 10 participants with teclistamab in combination with daratumumab SC and lenalidomide as maintenance therapy. As of 10 July 2025, 20 participants were treated in Arm D, with teclistamab in combination with daratumumab SC, lenalidomide, and dexamethasone as induction therapy followed by teclistamab in combination with talquetamab in lieu of ASCT. The safety data for these combination regimens to date do not indicate any new safety signals different from the known safety profiles of the individual drugs; additional details are provided below. Preliminary data indicate that stem cell mobilization and collection are not impaired by the addition of teclistamab to the induction regimen.

Arm A: Teclistamab 1.5 mg/kg weekly + Daratumumab SC + Lenalidomide + Dexamethasone Induction Therapy, Followed by ASCT and Teclistamab 3 mg/kg Q4W + Daratumumab SC ± Lenalidomide

As of 22 August 2025, 10 participants started induction treatment before transplant: teclistamab step-up doses of 0.06 and 0.3 mg/kg followed by 2 treatment doses of 1.5 mg/kg (Cycle 1) and 1.5 mg/kg weekly (Cycles 2-6), in combination with daratumumab SC, lenalidomide, and dexamethasone (Cycles 1-4). Nine participants received maintenance treatment: teclistamab step-up doses of 0.06 and 0.3 mg/kg followed by treatment doses of 1.5 mg/kg weekly (Cycle 1) and 3 mg/kg Q4W (Cycles 2-18) in combination with daratumumab SC and lenalidomide. All 10 participants experienced at least 1 TEAE. The most frequently reported TEAEs (≥ 3 participants) were hypogammaglobulinemia and lymphopenia (10 participants each), diarrhea and pyrexia (8 participants each), neutropenia (7 participants), CRS, leukopenia, nasopharyngitis, and upper respiratory tract infection (6 participants each), anemia and rash (5 participants each), blood alkaline phosphatase increased and thrombocytopenia (4 participants each), and alanine aminotransferase increased, gamma-glutamyltransferase increased, hyperglycemia, injection site erythema, muscle spasms, and urinary tract infection (3 participants each).

Serious TEAEs were reported for 7 participants, most frequently pyrexia (3 participants). Grade 3 or 4 TEAEs were reported for all 10 participants, most frequently lymphopenia (9 participants). No TEAEs led to discontinuation of teclistamab or death. The CRS events were Grade 1, and predominantly occurred during step-up dosing or early treatment doses. The median onset time of CRS from the time of injection was 38.2 hours. No participants received tocilizumab, corticosteroids, or oxygen as supportive measures for CRS; 1 participant received IV fluids. Neurologic TEAEs were reported for 8 participants; there were no events of ICANS. Infection TEAEs (TEAEs in the SOC of Infections and Infestations) were reported for all 10 participants and were Grade ≥ 3 for 4 participants.

All 10 participants underwent stem cell mobilization; median stem cell yield was $8.6 \times 10^6/\text{kg}$. Of these 10 participants, 2 participants (20.0%) received plerixafor.

Arm A1: Teclistamab 3 mg/kg Q4W + Daratumumab SC + Lenalidomide + Dexamethasone Induction Therapy, Followed by ASCT and Teclistamab 3 mg/kg Q4W + Daratumumab SC

As of 22 August 2025, 20 participants started induction treatment before transplant: teclistamab step-up doses of 0.06 and 0.3 mg/kg followed by 2 treatment doses of 1.5 mg/kg weekly (Cycle 1) and 3 mg/kg Q4W (Cycles 2-6), in combination with daratumumab SC, lenalidomide, and dexamethasone. Eighteen participants started maintenance treatment: teclistamab step-up doses of 0.06 and 0.3 mg/kg followed by 2 treatment doses of 1.5 mg/kg weekly (Cycle 1) and 3 mg/kg Q4W (Cycles 2-18) in combination with daratumumab SC.

All 20 participants experienced at least 1 TEAE. The most frequently reported TEAEs ($\geq 20\%$ of participants) were CRS (70.0%), neutropenia (65.0%), upper respiratory tract infection (55.0%), hypogammaglobulinemia and pyrexia (50.0% each), hypokalemia and lymphopenia (45.0% each), anemia (40.0%), thrombocytopenia (35.0%), gamma-glutamyltransferase increased (30.0%), diarrhea, lipase increased, peripheral sensory neuropathy, and rash (25.0% each), and COVID-19, hyperkalemia, leukopenia, nasopharyngitis, and nausea (20.0% each).

Serious TEAEs were reported for 10 participants (50.0%), most frequently CRS and pyrexia (2 participants [10.0%] each). Grade 3 or 4 TEAEs were reported for 19 participants (95.0%), most frequently neutropenia (13 participants [65.0%]). No TEAEs led to death; 1 participant experienced a TEAE leading to teclistamab discontinuation. The CRS events were Grade 1 and 2, and predominantly occurred during step-up dosing or early treatment doses. The median onset time of CRS from the time of injection was 48.0 hours. Supportive measures for CRS included tocilizumab (2 participants) and IV fluids (2 participants); no participants received corticosteroids or oxygen. Neurologic TEAEs were reported for 9 participants (45.0%); there were no events of ICANS. Infection TEAEs (TEAEs in the SOC of Infections and Infestations) were reported for 19 participants (95.0%) and were Grade ≥ 3 for 10 participants (50.0%).

All 20 participants underwent stem cell mobilization; median stem cell yield was $7.7 \times 10^6/\text{kg}$. Of these 20 participants, 11 participants (55.0%) received plerixafor.

Arm B: Teclistamab 3 mg/kg Q4W + Daratumumab SC + Bortezomib + Lenalidomide + Dexamethasone Induction Therapy, Followed by ASCT and Teclistamab 3 mg/kg Q4W + Daratumumab SC

As of 22 August 2025, 19 participants started induction treatment before transplant: teclistamab step-up doses of 0.06 and 0.3 mg/kg followed by 2 treatment doses of 1.5 mg/kg (Cycle 1) and 3 mg/kg Q4W (Cycles 2-6), in combination with daratumumab SC, bortezomib, lenalidomide, and dexamethasone (Cycles 1-2). Eighteen participants started maintenance treatment: teclistamab step-up doses of 0.06 and 0.3 mg/kg followed by 2 treatment doses of 1.5 mg/kg weekly (Cycle 1) and 3 mg/kg Q4W (Cycles 2-18) in combination with daratumumab SC.

All 19 participants experienced at least 1 TEAE. The most frequently reported TEAEs ($\geq 20\%$ of participants) were neutropenia (78.9%), CRS (68.4%), lymphopenia (63.2%), leukopenia and rash (47.4%), nausea, and thrombocytopenia (42.1% each), anemia, hypogammaglobulinemia, and pyrexia (36.8% each), upper respiratory tract infection (31.6%), constipation, diarrhea, edema peripheral, and gamma-glutamyltransferase increased (26.3% each), and blood alkaline phosphatase increased, COVID-19, C-reactive protein increased, hypokalemia, and peripheral sensory neuropathy (21.1% each).

Serious TEAEs were reported for 10 participants (52.6%), no PTs were reported in more than 1 participant. Grade 3 or 4 TEAEs were reported for 16 participants (84.2%), most frequently neutropenia (13 participants [68.4%]) and lymphopenia (12 participants [63.2%]). No TEAEs led to death; 2 participants experienced TEAEs leading to teclistamab discontinuation. The CRS events were Grade 1 or 2, and occurred during step-up dosing or early treatment doses. The median onset time of CRS from the time of injection was 48.0 hours. Supportive measures for CRS included tocilizumab (4 participants), and corticosteroids and oxygen (1 participant each). Neurologic TEAEs were reported for 14 participants (73.7%); there were no events of ICANS. Infection TEAEs (TEAEs in the SOC of Infections and Infestations) were reported for 12 participants (63.2%) and were Grade ≥ 3 for 5 participants (26.3%).

Seventeen participants (89.5%) underwent stem cell mobilization; median stem cell yield was $7.5 \times 10^6/\text{kg}$. Of these 17 participants, 7 participants (41.2%) received plerixafor.

Arm C: Teclistamab + Daratumumab SC $\pm$ Lenalidomide (Maintenance)

As of 22 August 2025, 10 participants were enrolled in Arm C, and 9 participants received post-transplant maintenance treatment with teclistamab step-up doses of 0.06 and 0.3 mg/kg, followed by 2 treatment doses of 1.5 mg/kg (Cycle 1) and 3 mg/kg Q4W (Cycles 2-18), in combination with daratumumab SC and lenalidomide. One participant discontinued after the first dose of daratumumab SC on Study Day 1, before receiving any dose of teclistamab and lenalidomide. Of note, participants in Arm C were initially treated with teclistamab biweekly dosing schedule (1.5 mg/kg weekly [Cycles 1-2] followed by 3 mg/kg [Cycles 3-18] Q2W) and transitioned to Q4W dosing of teclistamab (per protocol amendment).

All 10 participants experienced at least 1 TEAE. The most frequently reported TEAEs (≥ 3 participants) were lymphopenia and neutropenia (9 participants each), diarrhea, hypogammaglobulinemia, leukopenia, and upper respiratory tract infection (5 participants each), rash (4 participants), and constipation, COVID-19, febrile neutropenia, thrombocytopenia, and urinary tract infection (3 participants each).

Serious TEAEs were reported for 6 participants, most frequently febrile neutropenia (2 participants). Grade 3 or 4 TEAEs were reported for all 10 participants, most frequently neutropenia (9 participants). No TEAEs led to death; 1 participant experienced a TEAE leading to teclistamab discontinuation (viral infection). No participant experienced CRS events during maintenance therapy. Neurologic TEAEs were reported for 3 participants; there were no events of

ICANS. Infection TEAEs (TEAEs in the SOC of Infections and Infestations) were reported for 9 participants and were Grade ≥ 3 for 3 participants.

Arm D: Teclistamab 3 mg/kg Q4W + Daratumumab SC + Lenalidomide + Dexamethasone Induction Therapy, Followed by Teclistamab 3 mg/kg Q4W + Talquetamab 0.8 mg/kg Q4W in lieu of ASCT

As of 10 July 2025, 20 participants completed induction treatment with teclistamab step-up doses of 0.06 and 0.3 mg/kg followed by 2 treatment doses of 1.5 mg/kg (Cycle 1) and 3 mg/kg Q4W (Cycles 2-6), in combination with daratumumab SC, lenalidomide, and dexamethasone (Cycles 1-2). Nineteen participants continued treatment with teclistamab 3 mg/kg Q4W (Cycles 1-18) in combination with talquetamab step-up doses of 0.01, 0.06, and 0.4 mg/kg followed by 1 treatment dose of 0.8 mg/kg (Cycle 1) and 0.8 mg/kg Q4W (Cycles 2-18).

Nineteen participants (95.0%) experienced at least 1 TEAE. The most frequently reported TEAEs ($\geq 20\%$ of participants) were cough and CRS (45.0% each), diarrhea, hypogammaglobulinemia, neutropenia, and rash (40.0% each), pyrexia (35.0%), upper respiratory tract infection (30.0%), ageusia, dysgeusia, hypokalemia, nausea, and palmar-plantar erythrodysesthesia syndrome (25.0% each), and dry mouth, hypokalemia, lymphopenia, and respiratory tract infection (20.0% each).

Serious TEAEs were reported for 9 participants (45.0%), most frequently respiratory tract infection (2 participants [10.0%]). Grade 3 or 4 TEAEs were reported for 17 participants (85.0%), most frequently neutropenia (8 participants [40.0%]). No TEAEs led to teclistamab discontinuation or death. The CRS events were Grade 1 or 2, and mostly occurred during step-up dosing or early treatment doses. The median onset time of CRS from the time of injection was 48.0 hours. Supportive measures for CRS included tocilizumab (2 participants) and corticosteroids (1 participant). Neurologic TEAEs were reported for 12 participants (60.0%); there were no events of ICANS. Infection TEAEs were reported for 15 participants (75.0%) and were Grade ≥ 3 for 5 participants (25.0%).

Fifteen participants (75.0%) underwent stem cell mobilization, and median stem cell yield was $4.9 \times 10^6/\text{kg}$. Of these 15 participants, 7 participants (46.7%) received plerixafor.

4.3.2.2.7. MajesTEC-7 Study (MMY3005)

4.3.2.2.7.1. Safety Run-in 1 (Tec-DR)

As of 10 July 2024, 26 participants with newly diagnosed multiple myeloma were treated with teclistamab starting with 2 step-up doses followed by a treatment dose of 1.5 mg/kg weekly at Cycle 1-2; 3 mg/kg Q2W at Cycle 3-6; and 3 mg/kg Q4W at Cycle 7+, in combination with daratumumab SC and lenalidomide (Tec-DR).

All 26 participants experienced at least 1 TEAE. Serious TEAEs were reported for 18 participants (69.2%); the most frequently reported ($\geq 10\%$ of participants) were CRS and COVID-19 (11.5% each). Grade 3 or 4 TEAEs were reported in 25 participants (96.2%). Infection TEAEs were reported for all participants and were Grade 3 or 4 for 34.6%. One participant experienced a fatal

infection of pneumonia influenza that was considered related to teclistamab. One participant discontinued teclistamab due to a serious TEAE of transitional cell carcinoma. The CRS events were all Grade 1 or 2 and occurred primarily during step-up dosing or the first treatment dose. Neurotoxicity TEAEs were reported in 7.7% of participants; ICANS was reported in 1 participant.

4.3.2.2.7.2. Safety Run-in 2 (Tec-DR)

In Safety Run-in 2, participants started treatment with a lead-in cycle of DRd at Cycle 1 with administration of teclistamab starting in Cycle 2 (2 step-up doses followed by 1.5 mg/kg treatment doses) and 3 mg/kg Q4W dosing as of Cycle 3. Emerging data revealed a potentially increased risk of higher-grade CRS events (total of 2 events of Grade 3 CRS) associated with the DRd lead-in dosing strategy, which led to the implementation of an Urgent Safety Measure on 24 January 2024. The strategy of a lead-in cycle is not being further pursued in the Randomized Part of MajesTEC-7 nor will it be implemented in any other study across the teclistamab development program.

As of 10 July 2024, 29 participants with newly diagnosed multiple myeloma were enrolled in Safety Run-in 2. Following the Urgent Safety Measure, only 20 participants who received the first full treatment dose of teclistamab (ie, 1.5 mg/kg teclistamab planned for Cycle 2 Day 8) continued treatment with Tec-DR; 3 participants who received at least 1 dose of teclistamab switched to treatment with DRd and 6 participants who did not initiate dosing with teclistamab continued treatment with DRd. The safety population described below is comprised of 23 participants (20 who continued treatment with Tec-DR and 3 who received at least 1 dose of teclistamab).

All 23 participants experienced at least 1 TEAE and at least 1 Grade 3 or 4 TEAE. Serious TEAEs were reported for 17 (73.9%) participants. Study treatment was discontinued by 6 (26.1%) participants, including 5 (21.7%) participants due to a TEAE. Infections were reported in 22 (95.7%) participants, with Grade 3 or 4 infections reported for 12 (52.2%) participants. Four (17.4%) participants experienced treatment-emergent Grade 5 infections, one each due to COVID-19, COVID-19 pneumonia, septic shock, and pneumonia. CRS events occurred in 13 (56.5%) participants, mostly Grade 1 or 2, occurring primarily during step-up dosing. Two participants experienced Grade 3 CRS and no participants experienced a Grade 4 or 5 CRS event. No participants reported neurotoxicity TEAEs, including ICANS.

4.4. Biomarker Evaluations

4.4.1. Pharmacodynamics

MajesTEC-1 Study (MMY1001)

Within the first month of treatment with teclistamab, activation and redistribution of T cells, reduction of B cells and induction of serum cytokines were observed.

Following administration of teclistamab SC weekly at 1.5 mg/kg, a rapid decrease in sBCMA was observed in a majority of the responders (PR or better) within the first month of treatment, and greater reduction in sBCMA was observed in participants with deeper responses to teclistamab. Responders to teclistamab also showed a trend of sBCMA reduction over time. On Cycle 4 Day 1,

a majority of responders had a decrease in sBCMA (63 of 72 participants [87.5%]), and all non-responders had an increase in sBCMA (9 of 9 participants [100%]).

TriMM-2 Study (MMY1002)

Pharmacodynamic analyses for patients treated with teclistamab plus daratumumab in the RP2D cohorts were available as of 31 January 2024. Following treatment, participants exhibited pharmacodynamic changes consistent with the mechanism of action of teclistamab and daratumumab. Treatment with teclistamab plus daratumumab resulted in changes including T cell margination, as indicated by reductions in absolute counts of CD4⁺ and CD8⁺ T cells in peripheral blood immediately after administration, followed by recovery. Treatment also led to induction of T cell activation, as indicated by max fold change increases in expression of markers such as PD-1, LAG-3, TIM-3, HLA-DR, and CD25 on CD4⁺ or CD8⁺ T cells. Notably, teclistamab administration led to induction of CD38⁺ CD8⁺ T cells after the first step-up dose, despite concurrent daratumumab dosing. A reduction in the frequency of CD38⁺ Tregs and absolute counts of NK cells was observed, as well as maximum fold change inductions in the serum levels of cytokines such as IL-10, IL-6, TNF- α , IFN- γ , and IL-2R α in Cycle 1. Reductions of CD19⁺ B cells were observed beginning in Cycle 1 and persistent decreases were observed at Cycle 3.

Following teclistamab plus daratumumab dosing, the majority of responders in the RP2D cohorts had a decrease in sBCMA on Cycle 3 Day 1 (32 of 38 participants [84.2%]), and all non-responders had an increase in sBCMA on Cycle 3 Day 1 (all 3 participants [100.0%]) when compared with baseline values. Additionally, a greater reduction in sBCMA was observed in participants with deeper responses to teclistamab.

RedirecTT-1 Study (MMY1003)

As of 18 March 2025, pharmacodynamic results indicate that following treatment, participants exhibited pharmacodynamic changes consistent with the mechanisms of action of teclistamab and talquetamab. Treatment with the combination of teclistamab with talquetamab resulted in T cell margination, followed by a T cell recovery observed in all dose levels tested. T cell activation was also evidenced by the upregulation of phenotypic markers in CD8⁺ T cells, including CD38, CD25, HLA-DR, and PD-1. The magnitude of T cell activation was variable across dose levels. Cytokine induction was also observed in all dose levels tested, as indicated by increases in serum (IL-6, IFN- γ , TNF- α , IL-2R α). Median inductions were variable but comparable in talquetamab 0.4 mg/kg + teclistamab 1.5 mg/kg QW, talquetamab 0.8 mg/kg + teclistamab 1.5 mg/kg Q2W, talquetamab 0.8 mg/kg + teclistamab 3 mg/kg Q2W (RP2R) and talquetamab 0.8 mg/kg + teclistamab 3 mg/kg Q4W dose levels. A reduction in absolute counts of CD19⁺ B cells was observed across all dose levels tested.

MajesTEC-2 Study (MMY1004)

Pharmacodynamic analyses for patients treated with teclistamab plus daratumumab and pomalidomide, teclistamab plus lenalidomide, or teclistamab plus daratumumab and lenalidomide were available as of 22 August 2024. Following treatment, subjects exhibited T cell margination,

indicated by the reduction in the total numbers of peripheral CD4⁺ and CD8⁺ T cells, followed by subsequent T cell recovery. This is consistent with the mechanisms of action of teclistamab, daratumumab, lenalidomide, and pomalidomide. Treatment also led to induction of T cell activation, indicated by the max fold change in expression of markers such as PD-1, LAG-3, HLA-DR, TIM-3 and CD25 on peripheral CD4⁺ or CD8⁺ T cells.

Addition of pomalidomide or lenalidomide led to re-stimulation in expression of markers such as HLA-DR and LAG-3 on peripheral CD4⁺ or CD8⁺ T cells, consistent with lenalidomide and pomalidomide mechanisms of action. In participants treated with teclistamab plus daratumumab and pomalidomide, or teclistamab plus daratumumab and lenalidomide decreased proportions of CD38⁺/CD4⁺ or CD38⁺/CD8⁺ T cells, CD38⁺ Tregs and total number of NK cells were observed through Cycle 3, consistent with daratumumab mechanism of action. Combination treatment led to early increases in the levels of serum cytokines such as IL-10, IL-6, TNF- α , IFN- γ , and soluble IL-2R α . Reductions in the total number of CD19⁺ B cells were observed in Cycle 1, with persistent decreases through Cycle 3.

4.5. Immunogenicity (Anti-drug Antibodies)

As of 07 June 2023 (data cutoff for immunogenicity data in MajesTEC-1), 1 of 239 participants (0.4%) receiving teclistamab SC as monotherapy developed ADAs with a low titer of 20 (equal to the minimum required dilution of the assay). These ADAs were neutralizing antibodies to teclistamab and seemed to have no impact on safety in this participant. Of the 186 participants who were ADA evaluable for the recommended dose, none were identified as positive for antibodies to teclistamab.

Based on preliminary data from the combination studies, of the 124 participants (TriMM-2), 22 participants (TriMM-3), 188 participants (RedirecTT-1), and 137 participants (MajesTEC-2) who were ADA evaluable, none (0%) were identified as positive for antibodies to teclistamab.

4.6. Marketing Experience

Teclistamab first received marketing authorization in the European Union on 23 August 2022, was approved in the US on 25 October 2022, and has subsequently been approved in over 60 countries/territories.

Based on the 56,351,480 mg distributed worldwide from launch to 31 August 2025, the estimated exposure to teclistamab is 9,884 person-years.

The surveillance of spontaneous and solicited cases of AEs reported with the use of teclistamab indicates that the safety profile of the drug in the post-marketing setting is consistent with the drug's known safety profile established from clinical studies.

5. SUMMARY OF DATA AND GUIDANCE FOR INVESTIGATORS

5.1. Description of Teclistamab

Teclistamab is a humanized IgG-4 PAA bispecific antibody targeting the CD3 receptor complex expressed on the surface of T cells and BCMA on B cells.

5.2. Clinical Pharmacokinetics

Teclistamab exhibited approximately dose-proportional PK following SC administration across a dose range of 0.08 mg/kg to 3 mg/kg in monotherapy. From population PK analysis, 90% of steady-state exposure was achieved after 12 weekly treatment doses of teclistamab 1.5 mg/kg. The mean bioavailability of teclistamab was 72% when administered SC. The mean accumulation ratio between the first and 13th weekly treatment dose of teclistamab 1.5 mg/kg was 4.2-fold for $C_{\max}$, 4.1-fold for C_{trough} , and 5.3-fold for AUC_{tau} .

The PK of teclistamab were consistent whether used as monotherapy or in combination.

Distribution

Based on the population PK model, the mean (CV%) volume of distribution was 5.63 L (29%).

Excretion

Population PK analysis showed that teclistamab clearance decreases over time, with a mean (CV%) maximal reduction from baseline to the 13th weekly treatment dose of 40.8% (56%). The geometric mean (CV%) clearance is 0.472 L/day (64%) at the 13th weekly treatment dose. Patients who discontinue teclistamab after the 13th weekly treatment dose are expected to have a 50% reduction from $C_{\max}$ in teclistamab concentration at a median (5th to 95th percentile) time of 15 (7 to 33) days after $T_{\max}$ and a 97% reduction from $C_{\max}$ in teclistamab concentration at a median time of 69 (32 to 163) days after $T_{\max}$.

Population PK analysis (based on MajesTEC-1) showed that soluble BCMA did not impact teclistamab serum concentrations.

Specific Populations

Age and Sex

The PK of teclistamab in pediatric patients have not been investigated. Results of population PK analyses indicate that age (24 to 84 years) and sex did not influence the PK of teclistamab.

Renal Impairment

No formal studies of teclistamab in patients with renal impairment have been conducted. Results of population PK analyses indicate that mild or moderate renal impairment did not significantly influence the PK of teclistamab. Limited data are available from patients with severe renal impairment.

Hepatic Impairment

No formal studies of teclistamab in patients with hepatic impairment have been conducted. Results of population PK analyses indicate that mild hepatic impairment did not significantly influence the PK of teclistamab. No data are available in patients with moderate and severe hepatic impairment.

5.3. Pharmacodynamics

Within the first month of treatment with teclistamab, activation and redistribution of T cells, reduction of B cells and induction of serum cytokines were observed.

Within one month, the majority of responders had reduction in soluble BCMA, and a greater reduction in soluble BCMA was observed in patients with deeper responses to teclistamab.

Participants treated with teclistamab in combination regimens exhibited pharmacodynamic changes consistent with the mechanism of action of teclistamab monotherapy and/or the combination treatment partner.

5.4. Indications and Use

Teclistamab is approved and indicated as monotherapy for the treatment of adult patients with relapsed or refractory multiple myeloma. Teclistamab is also being evaluated as monotherapy and in combination regimens in ongoing studies in participants with newly diagnosed or relapsed/refractory multiple myeloma, including earlier lines of therapy.

5.5. Contraindications

None.

5.6. Precautions and Warnings

The data below describe the safety profile of 165 participants with relapsed or refractory multiple myeloma who received the recommended dose regimen of SC teclistamab monotherapy in MajesTEC-1, unless otherwise noted.

Cytokine Release Syndrome

CRS, including life-threatening or fatal reactions, may occur in patients receiving teclistamab. The majority of CRS events observed following teclistamab administration were Grade 1 and Grade 2. The median time to onset of CRS was 2 (range: 1 to 6) days after the most recent dose with a median duration of 2 (range: 1 to 9) days.

Clinical signs and symptoms of CRS may include, but are not limited to, fever, chills, hypotension, tachycardia, hypoxia, headache, and elevated liver enzymes. Potentially life-threatening complications of CRS may include cardiac dysfunction, adult respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation.

Initiate therapy according to teclistamab step-up dosing schedule to reduce risk of CRS. Failure to follow the recommended doses or dosing schedule for initiation of therapy or re-initiation of therapy after dose delays may result in increased frequency and severity of AEs related to mechanism of action. Administer pretreatment medications (corticosteroids, antihistamine, and antipyretics) prior to each dose of the teclistamab step-up dosing schedule to reduce risk of CRS and monitor patients following administration accordingly. In patients who experienced CRS following their previous dose, administer pretreatment medications prior to the next dose of teclistamab.

Counsel patients to seek medical attention should signs or symptoms of CRS occur. At the first sign of CRS, immediately evaluate patient for hospitalization and institute treatment with supportive care, tocilizumab and/or corticosteroids, based on severity. In MajesTEC-1, tocilizumab, corticosteroids, and tocilizumab in combination with corticosteroids were used to treat 32%, 11% and 3% of CRS events, respectively. The use of myeloid growth factors, particularly granulocyte macrophage-colony stimulating factor, should be avoided during CRS. Withhold treatment with teclistamab until CRS resolves.

Neurologic Toxicities

Serious, life-threatening, or fatal neurologic toxicities, including ICANS, have occurred following treatment with teclistamab. The majority of neurologic toxicity events were Grade 1 or 2. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS.

Monitor patients for signs or symptoms of neurologic toxicities during treatment and treat promptly.

Counsel patients to seek medical attention should signs or symptoms of neurologic toxicity occur. At the first sign of neurologic toxicity, including ICANS, immediately evaluate patient and institute treatment based on severity.

For ICANS or other neurologic toxicities, withhold treatment with teclistamab and manage adverse reactions per guidelines described in the individual study protocol.

Infections

Severe, life-threatening, or fatal infections have been reported in patients receiving teclistamab. New or reactivated viral infections occurred during therapy with teclistamab.

Monitor patients for signs and symptoms of infection prior to and during treatment with teclistamab and treat appropriately. Prophylactic antimicrobials should be administered according to local institutional guidelines. For all grades of infection, do not administer teclistamab step-up dosing schedule in participants with active infection. For a Grade 3 or 4 infection, withhold subsequent treatment doses of teclistamab until infection improves to Grade 2 or better. If absolute neutrophil count less than $0.5 \times 10^9/L$, withhold teclistamab until absolute neutrophil count is $0.5 \times 10^9/L$ or higher.

PML, which can be fatal, has also been reported in subjects receiving teclistamab. Monitor any new onset of or changes in pre-existing neurological signs or symptoms. If PML is suspected, withhold treatment with teclistamab and initiate appropriate diagnostic testing. Discontinue teclistamab if PML is confirmed.

Hepatitis B Virus Reactivation

HBV reactivation can occur in patients treated with drugs directed against B cells, and in some cases, may result in fulminant hepatitis, hepatic failure, and death.

Patients with evidence of positive HBV serology should be monitored for clinical and laboratory signs of HBV reactivation while receiving teclistamab, and for at least 6 months following the end of treatment.

In patients who develop reactivation of HBV while on teclistamab, withhold treatment with teclistamab and manage per local institutional guidelines.

Hypogammaglobulinemia

Hypogammaglobulinemia has been reported in patients receiving teclistamab. Monitor immunoglobulin levels during treatment with teclistamab and treat according to local institutional guidelines, including infection precautions, antibiotic or antiviral prophylaxis, and administration of immunoglobulin replacement therapy. Further guidance is provided in the individual clinical study protocols.

Vaccines

Immune response to vaccines may be reduced when taking teclistamab. The safety of immunization with live viral vaccines during or following teclistamab treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 4 weeks prior to the start of treatment, during treatment, and at least 4 weeks after treatment.

Neutropenia

Neutropenia and febrile neutropenia have been reported in patients who received teclistamab. Monitor complete blood cell counts at baseline and periodically during treatment and provide supportive care per local institutional guidelines. Patients with neutropenia should be monitored for signs of infection. Withhold treatment with teclistamab based on severity.

5.7. Drug Interactions

No drug interaction studies have been performed with teclistamab.

The initial release of cytokines associated with the start of teclistamab treatment could suppress CYP enzymes. Based on physiologically based PK modeling, the highest risk of drug-drug interaction is predicted to be from initiation of teclistamab step-up dosing schedule up to 7 days after the first treatment dose or during a CRS event. During this time period, monitor for toxicity or drug concentrations (eg, cyclosporine) in patients who are receiving concomitant CYP substrates with a narrow therapeutic index. The dose of the concomitant drug should be adjusted as needed.

5.8. Carcinogenicity, Mutagenicity, and Impairment of Fertility

No genotoxicity or carcinogenicity studies have been performed to assess the carcinogenic or genotoxic potential of teclistamab. No studies have been conducted to evaluate the effects of teclistamab on fertility in males or females. In the 5-week repeat-dose IV toxicity study in cynomolgus monkeys, there were no notable effects in the male and female reproductive organs at doses up to 30 mg/kg/week (approximately 22 times the maximum recommended human dose based on AUC exposure).

5.9. Pregnancy and Breastfeeding

Pregnancy

There are no available data on the use of teclistamab in pregnant women or animal data to assess the risk of teclistamab in pregnancy. Human IgG is known to cross the placenta after the first trimester of pregnancy. Therefore, teclistamab has the potential to be transmitted from the mother to the developing fetus. Teclistamab is not recommended for women who are pregnant. Teclistamab is associated with hypogammaglobulinemia, therefore, assessment of immunoglobulin levels in newborns of mothers treated with teclistamab should be considered.

Breastfeeding

It is not known whether teclistamab is excreted in human or animal milk, affects breastfed infants, or affects milk production. Because of the potential for SARs in breastfed infants from teclistamab, advise patients not to breastfeed during treatment with teclistamab and for at least 5 months after the last dose.

Females and Males of Reproductive Potential

Pregnancy Testing

Pregnancy status for females of child-bearing potential should be verified prior to starting treatment with teclistamab.

Contraception

Advise females of reproductive potential to use effective contraception during treatment and for 5 months after the final dose of teclistamab.

Advise male patients with a female partner of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of teclistamab.

5.10. Immunogenicity (Anti-drug Antibodies)

As of 07 June 2023 (data cutoff for immunogenicity data in MajesTEC-1), 1 of 239 participants (0.4%) receiving teclistamab SC as monotherapy developed ADAs with a low titer of 20 (equal to the minimum required dilution of the assay). These ADAs were neutralizing antibodies to teclistamab and seemed to have no impact on safety in this participant. Of the 186 participants who were ADA evaluable for the recommended dose, none were identified as positive for antibodies to teclistamab.

Based on preliminary data from the combination studies, of the 124 participants (TriMM-2), 22 participants (TriMM-3), 188 participants (RedirecTT-1), and 137 participants (MajesTEC-2) who were ADA evaluable, none (0%) were identified as positive for antibodies to teclistamab.

5.11. Use in Specific Populations (Geriatric and Pediatric)

The safety and efficacy of teclistamab have not been established in pediatric patients aged 17 years and younger.

Of the 165 patients treated with teclistamab in MajesTEC-1 at the recommended dose, 48% were 65 years of age or older, and 15% were 75 years of age or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

5.12. Use in Renal/Hepatic Dysfunction/Failure

No formal studies have been conducted in patients with renal or hepatic impairment.

5.13. Effects on Ability to Drive and Use Machines

Due to the potential for ICANS, patients receiving teclistamab are at risk of depressed level of consciousness. Patients should avoid driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of teclistamab step-up dosing schedule and in the event of new onset of any neurological symptoms.

5.14. Overdosage and Abuse Potential

The maximum tolerated dose of teclistamab has not been determined. In clinical studies, doses of up to 6 mg/kg have been administered. In the event of an overdose, the patient should be monitored for any signs or symptoms of adverse effects and appropriate symptomatic treatment should be instituted immediately.

5.15. How Supplied

Detailed information on dose preparation, handling, and storage conditions will accompany the clinical drug supplies to the clinical study site(s). The storage conditions and expiry will be indicated on the label of the drug product.

5.16. Adverse Drug Reactions

SARs in the ADR table below may be used for expectedness determination for the purposes of expedited reporting for non-UK/EU/EEA regions, in accordance with applicable local regulations.

The Sponsor's medical experts evaluated safety data from MajesTEC-1 (registrational study) up to 22 August 2025, according to the definition of ADRs from the ICH E6(R2): Good Clinical Practice, Consolidated Guideline (ICH, 2016). ADRs identified are presented in [Table 1](#). There are no new ADRs added with this Edition of the IB.

Table 1: Adverse Drug Reactions Associated with Teclistamab; All Treated Analysis Set (Study 64007957MMY1001)

System Organ Class	Preferred Term	Frequency Category	Number of participants exposed to teclistamab RP2D (N=165)	
			Frequency n (%)	
			Any Grade	Grade 3 or 4
Infections and infestations	Upper respiratory tract infection ^{*a}	Very common	61 (37.0%)	4 (2.4%)
	<i>Bronchitis</i>	Very common	22 (13.3%)	0
	<i>Upper respiratory tract infection^d</i>	Very common	18 (10.9%)	0
	<i>Nasopharyngitis</i>	Common	16 (9.7%)	0
	<i>Sinusitis^a</i>	Common	14 (8.5%)	2 (1.2%)
	<i>Rhinitis</i>	Common	6 (3.6%)	0
	<i>Respiratory tract infection^d</i>	Common	4 (2.4%)	0
	<i>Viral upper respiratory tract infection^d</i>	Common	4 (2.4%)	1 (0.6%)
	<i>Pharyngitis</i>	Uncommon	1 (0.6%)	0
	<i>Respiratory tract infection bacterial^a</i>	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Rhinovirus infection^d</i>	Uncommon	1 (0.6%)	0
	<i>Tracheitis</i>	Uncommon	1 (0.6%)	0
	<i>Pneumonia^{*a}</i>	Very common	46 (27.9%)	32 (19.4%)
	<i>Pneumonia^{ab}</i>	Very common	30 (18.2%)	21 (12.7%)
	<i>Pneumocystis jirovecii pneumonia^{ab}</i>	Common	7 (4.2%)	7 (4.2%)
	<i>Lower respiratory tract infection^d</i>	Common	4 (2.4%)	1 (0.6%)
	<i>Pneumonia pseudomonal^{ab}</i>	Common	3 (1.8%)	2 (1.2%)
	<i>Enterobacter pneumonia</i>	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Lower respiratory tract infection viral</i>	Uncommon	1 (0.6%)	0
	<i>Metapneumovirus pneumonia^a</i>	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Pneumonia adenoviral^a</i>	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Pneumonia bacterial^d</i>	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Pneumonia klebsiella</i>	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Pneumonia moraxella^a</i>	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Pneumonia pneumococcal</i>	Uncommon	1 (0.6%)	0
	<i>Pneumonia respiratory syncytial viral^a</i>	Uncommon	1 (0.6%)	0
	<i>Pneumonia staphylococcal^d</i>	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Pneumonia viral^a</i>	Uncommon	1 (0.6%)	0
	<i>COVID-19^{*a}</i>	Very common	30 (18.2%)	20 (12.1%)
	<i>COVID-19^{ab}</i>	Very common	29 (17.6%)	20 (12.1%)
	<i>Asymptomatic COVID-19</i>	Common	2 (1.2%)	0
	<i>Urinary tract infection^{*a}</i>	Very common	23 (13.9%)	10 (6.1%)
	<i>Urinary tract infection^a</i>	Common	11 (6.7%)	3 (1.8%)
	<i>Cystitis</i>	Common	5 (3.0%)	1 (0.6%)
	<i>Escherichia urinary tract infection^a</i>	Common	5 (3.0%)	2 (1.2%)
	<i>Cystitis escherichia^a</i>	Common	3 (1.8%)	3 (1.8%)
	<i>Urinary tract infection bacterial</i>	Common	3 (1.8%)	2 (1.2%)
	<i>Cystitis klebsiella</i>	Uncommon	1 (0.6%)	0
	<i>Sepsis^{*a}</i>	Common	13 (7.9%)	11 (6.7%)
	<i>Bacteraemia^a</i>	Common	3 (1.8%)	2 (1.2%)
	<i>Pseudomonal sepsis^{ab}</i>	Common	3 (1.8%)	3 (1.8%)
	<i>Sepsis^{ab}</i>	Common	3 (1.8%)	3 (1.8%)

Table 1: Adverse Drug Reactions Associated with Teclistamab; All Treated Analysis Set (Study 64007957MMY1001)

System Organ Class	Preferred Term	Frequency Category	Number of participants exposed to teclistamab RP2D (N=165)	
			Frequency n (%)	
			Any Grade	Grade 3 or 4
Blood and lymphatic system disorders	<i>Pseudomonas</i> bacteraemia ^a	Common	2 (1.2%)	1 (0.6%)
	<i>Meningococcal</i> sepsis ^a	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Neutropenic</i> sepsis ^a	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Staphylococcal</i> bacteraemia	Uncommon	1 (0.6%)	1 (0.6%)
	Cellulitis ^a	Common	7 (4.2%)	5 (3.0%)
	Progressive Multifocal Leukoencephalopathy ^a	Uncommon	1 (0.6%)	1 (0.6%)
	Neutropenia ^a	Very common	117 (70.9%)	106 (64.2%)
	Anemia ^{a,a}	Very common	90 (54.5%)	61 (37.0%)
	Anaemia ^a	Very common	86 (52.1%)	61 (37.0%)
	Iron deficiency	Common	5 (3.0%)	0
	Iron deficiency anaemia	Common	4 (2.4%)	0
	Thrombocytopenia ^d	Very common	66 (40.0%)	35 (21.2%)
	Lymphopenia	Very common	57 (34.5%)	54 (32.7%)
	Leukopenia ^d	Very common	29 (17.6%)	12 (7.3%)
Immune system disorders	Febrile neutropenia ^a	Common	6 (3.6%)	5 (3.0%)
	Hypogammaglobulinaemia ^{a,c}	Very common	123 (74.5%)	3 (1.8%)
	<i>Hypogammaglobulinaemia</i>	Very common	123 (74.5%)	3 (1.8%)
	<i>Immunoglobulins decreased</i>	Uncommon	1 (0.6%)	0
	Cytokine release syndrome ^a	Very common	119 (72.1%)	1 (0.6%)
Metabolism and nutrition disorders	Hypokalaemia ^d	Very common	23 (13.9%)	8 (4.8%)
	Hypomagnesaemia	Very common	22 (13.3%)	0
	Decreased appetite	Very common	20 (12.1%)	1 (0.6%)
	Hypophosphataemia	Very common	20 (12.1%)	10 (6.1%)
	Hypercalcaemia ^a	Very common	19 (11.5%)	5 (3.0%)
	Hyponatraemia ^a	Common	13 (7.9%)	8 (4.8%)
	Hypocalcaemia	Common	12 (7.3%)	0
	Hyperkalaemia	Common	8 (4.8%)	2 (1.2%)
	Hyperamylasaemia	Common	6 (3.6%)	4 (2.4%)
	Hypoalbuminaemia	Common	4 (2.4%)	1 (0.6%)
	Hypoglycaemia	Common	4 (2.4%)	0
	Headache ^d	Very common	39 (23.6%)	1 (0.6%)
	Neuropathy peripheral ^{a,a}	Very common	26 (15.8%)	1 (0.6%)
	<i>Hypoaesthesia</i>	Common	9 (5.5%)	0
Nervous system disorders	<i>Peripheral sensory neuropathy</i>	Common	8 (4.8%)	0
	<i>Paraesthesia</i>	Common	6 (3.6%)	0
	<i>Sciatica</i> ^a	Common	3 (1.8%)	1 (0.6%)
	<i>Dysaesthesia</i>	Uncommon	1 (0.6%)	0
	<i>Hypoaesthesia oral</i>	Uncommon	1 (0.6%)	0
	<i>Neuralgia</i>	Uncommon	1 (0.6%)	0
	<i>Paraesthesia oral</i>	Uncommon	1 (0.6%)	0
	Encephalopathy ^{a,a}	Common	16 (9.7%)	0
	<i>Confusional state</i> ^a	Common	10 (6.1%)	0

Table 1: Adverse Drug Reactions Associated with Teclistamab; All Treated Analysis Set (Study 64007957MMY1001)

System Organ Class	Preferred Term	Frequency Category	Number of participants exposed to teclistamab RP2D (N=165)	
			Frequency n (%)	
			Any Grade	Grade 3 or 4
Vascular disorders	<i>Lethargy^a</i>	Common	4 (2.4%)	0
	<i>Somnolence</i>	Common	3 (1.8%)	0
	<i>Depressed level of consciousness</i>	Uncommon	1 (0.6%)	0
	<i>Memory impairment</i>	Uncommon	1 (0.6%)	0
	<i>Immune effector cell-associated neurotoxicity syndrome^d</i>	Common	5 (3.0%)	0
	<i>Hypertension*</i>	Very common	21 (12.7%)	9 (5.5%)
	<i>Hypertension</i>	Very common	20 (12.1%)	9 (5.5%)
	<i>Essential hypertension</i>	Uncommon	1 (0.6%)	0
	<i>Hemorrhage^{*a}</i>	Very common	20 (12.1%)	5 (3.0%)
	<i>Epistaxis</i>	Common	8 (4.8%)	2 (1.2%)
	<i>Haematuria</i>	Common	6 (3.6%)	0
	<i>Haematoma</i>	Common	3 (1.8%)	0
	<i>Lower gastrointestinal haemorrhage^a</i>	Common	2 (1.2%)	2 (1.2%)
	<i>Melaena</i>	Common	2 (1.2%)	1 (0.6%)
	<i>Conjunctival haemorrhage</i>	Uncommon	1 (0.6%)	0
	<i>Haemoperitoneum^a</i>	Uncommon	1 (0.6%)	1 (0.6%)
	<i>Haemorrhoidal haemorrhage</i>	Uncommon	1 (0.6%)	0
	<i>Mouth haemorrhage</i>	Uncommon	1 (0.6%)	0
Respiratory, thoracic and mediastinal disorders	<i>Subdural haematoma^a</i>	Uncommon	1 (0.6%)	0
	<i>Hypotension^a</i>	Very common	18 (10.9%)	4 (2.4%)
	<i>Cough^{*a}</i>	Very common	39 (23.6%)	0
	<i>Cough^a</i>	Very common	33 (20.0%)	0
	<i>Productive cough</i>	Common	8 (4.8%)	0
	<i>Allergic cough</i>	Uncommon	1 (0.6%)	0
	<i>Upper-airway cough syndrome</i>	Uncommon	1 (0.6%)	0
	<i>Dyspnea^{*a}</i>	Very common	22 (13.3%)	3 (1.8%)
	<i>Dyspnoea^d</i>	Very common	17 (10.3%)	1 (0.6%)
	<i>Dyspnoea exertional</i>	Common	3 (1.8%)	0
	<i>Acute respiratory failure^a</i>	Common	2 (1.2%)	2 (1.2%)
	<i>Hypoxia^a</i>	Common	16 (9.7%)	6 (3.6%)
Gastrointestinal disorders	<i>Diarrhoea^a</i>	Very common	47 (28.5%)	6 (3.6%)
	<i>Nausea^a</i>	Very common	45 (27.3%)	1 (0.6%)
	<i>Constipation</i>	Very common	34 (20.6%)	0
	<i>Vomiting</i>	Very common	21 (12.7%)	1 (0.6%)
	<i>Abdominal pain^{*a}</i>	Very common	20 (12.1%)	2 (1.2%)
	<i>Abdominal pain^a</i>	Common	11 (6.7%)	1 (0.6%)
	<i>Abdominal pain upper</i>	Common	7 (4.2%)	1 (0.6%)
	<i>Abdominal discomfort</i>	Common	3 (1.8%)	0
Musculoskeletal and connective tissue disorders	<i>Musculoskeletal pain^{*a}</i>	Very common	85 (51.5%)	14 (8.5%)
	<i>Arthralgia</i>	Very common	36 (21.8%)	1 (0.6%)
	<i>Bone pain^a</i>	Very common	29 (17.6%)	6 (3.6%)
	<i>Back pain^a</i>	Very common	27 (16.4%)	4 (2.4%)

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			Frequency n (%)	
			Any Grade	Grade 3 or 4
General disorders and administration site conditions	<i>Pain in extremity^a</i>	Very common	21 (12.7%)	1 (0.6%)
	<i>Musculoskeletal chest pain^a</i>	Very common	17 (10.3%)	3 (1.8%)
	<i>Myalgia</i>	Common	13 (7.9%)	0
	<i>Neck pain</i>	Common	5 (3.0%)	0
	<i>Musculoskeletal pain</i>	Common	2 (1.2%)	0
	Muscle spasms	Very common	17 (10.3%)	0
	Fatigue ^{*a}	Very common	67 (40.6%)	5 (3.0%)
	<i>Fatigue^a</i>	Very common	46 (27.9%)	4 (2.4%)
	<i>Asthenia</i>	Very common	18 (10.9%)	1 (0.6%)
	<i>Malaise</i>	Common	6 (3.6%)	0
	Injection site reaction ^{*a}	Very common	62 (37.6%)	1 (0.6%)
	<i>Injection site erythema</i>	Very common	43 (26.1%)	0
	<i>Injection site pruritus</i>	Common	13 (7.9%)	0
	<i>Injection site rash</i>	Common	10 (6.1%)	0
	<i>Injection site bruising</i>	Common	3 (1.8%)	0
	<i>Injection site inflammation</i>	Common	3 (1.8%)	0
	<i>Injection site swelling</i>	Common	3 (1.8%)	0
	<i>Injection site cellulitis^a</i>	Common	2 (1.2%)	1 (0.6%)
	<i>Injection site oedema</i>	Common	2 (1.2%)	0
	<i>Injection site reaction</i>	Common	2 (1.2%)	0
	<i>Injection site discomfort</i>	Uncommon	1 (0.6%)	0
	<i>Injection site haematoma</i>	Uncommon	1 (0.6%)	0
	<i>Injection site induration</i>	Uncommon	1 (0.6%)	0
	Pyrexia ^a	Very common	45 (27.3%)	1 (0.6%)
	Pain ^{*a}	Very common	34 (20.6%)	3 (1.8%)
	<i>Oropharyngeal pain</i>	Common	9 (5.5%)	0
	<i>Non-cardiac chest pain</i>	Common	7 (4.2%)	0
	<i>Pain</i>	Common	7 (4.2%)	1 (0.6%)
	<i>Pain in jaw</i>	Common	6 (3.6%)	0
	<i>Toothache</i>	Common	5 (3.0%)	1 (0.6%)
	<i>Ear pain</i>	Common	2 (1.2%)	0
	<i>Groin pain</i>	Common	2 (1.2%)	0
	<i>Flank pain</i>	Uncommon	1 (0.6%)	0
	<i>Tumour pain^a</i>	Uncommon	1 (0.6%)	1 (0.6%)
Investigations	Edema [*]	Very common	23 (13.9%)	0
	<i>Oedema peripheral</i>	Very common	18 (10.9%)	0
	<i>Fluid overload</i>	Common	4 (2.4%)	0
	<i>Face oedema</i>	Uncommon	1 (0.6%)	0
	<i>Peripheral swelling</i>	Uncommon	1 (0.6%)	0
	Blood alkaline phosphatase increased	Very common	18 (10.9%)	3 (1.8%)
	Gamma-glutamyltransferase increased	Common	16 (9.7%)	5 (3.0%)
	Transaminase elevation [*]	Common	16 (9.7%)	4 (2.4%)

Table 1: Adverse Drug Reactions Associated with Teclistamab; All Treated Analysis Set (Study 64007957MMY1001)

System Organ Class	Preferred Term	Frequency Category	Number of participants exposed to teclistamab RP2D (N=165)	
			Frequency n (%)	
			Any Grade	Grade 3 or 4
	<i>Alanine aminotransferase increased</i>	Common	14 (8.5%)	3 (1.8%)
	<i>Aspartate aminotransferase increased</i>	Common	9 (5.5%)	2 (1.2%)
	Lipase increased	Common	10 (6.1%)	2 (1.2%)
	Blood creatinine increased ^a	Common	9 (5.5%)	0

Key: RP2D = recommended phase 2 dose, CRS = cytokine release syndrome, ICANS = immune effector cell-associated neurotoxicity.

Note: RP2D includes Phase 1 RP2D treatment group and Phase 2 Cohort A.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

Note: Adverse events are graded according to the NCI-CTCAE Version 4.03, with the exception of ICANS and CRS. CRS was originally graded by Lee criteria (Lee et al 2014) in Phase 1 and by ASTCT consensus grading system (Lee et al 2019) in Phase 2, with conversion of grade in Phase 1 to ASTCT based on data in eCRF. Toxicity grade for CRS by ASTCT is presented in this table, for both Phase 1 and Phase 2. Toxicity grade for ICANS by ASTCT is also presented in this table.

Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 24.0

Note: The output includes the diagnosis of CRS and ICANS; the symptoms of CRS or ICANS are excluded.

* Group term that includes multiple Preferred Terms (PTs) which are indented and italicized.

^a Serious ADR

^b Life threatening events are considered expected for reporting purposes.

^c Hypogammaglobulinaemia includes patients with adverse events of hypogammaglobulinaemia, hypoglobulinaemia, blood immunoglobulin G decreased; and/or patients with laboratory IgG levels below 500 mg/dL following treatment with Teclistamab.

^d Identified as a serious ADR using data from other clinical trials where this term was reported as serious with ≥ 2 events in the Global Safety Database.

Note: Frequency Grouping: Frequencies are defined as Very common ($\geq 1/10$), Common ($\geq 1/100$ to $< 1/10$), Uncommon ($\geq 1/1,000$ to $< 1/100$). Within each frequency grouping, where relevant, adverse reactions are presented in order of decreasing frequency.

Modified from: [tsfadr01.rtf] [xcp_oncology/z_64007957_dsur/dbr_dsur_2025_08/re_ib_2025_08/tsfadr01.sas] 23SEP2025, 19:35

6. REFERENCE SAFETY INFORMATION

The information within this section outlines expected SARs for regulatory reporting purposes, in compliance with UK/EU/EEA-specific regulatory requirements and does not present a comprehensive overview of the safety profile of teclistamab.

[Table 2](#) provides a cumulative list of SARs that have occurred more than once as of the DSUR data lock point of 22 August 2025 from 10 ongoing teclistamab clinical studies (MajesTEC-1, MMY1002 Japan, TriMM-2, TriMM-3, RedirecTT-1, MajesTEC-2, MajesTEC-5, MajesTEC-4 [Safety Run-in only], MajesTEC-7 [Safety Run-in only], and TAURUS) and are considered expected in accordance with applicable local regulations. Data from MajesTEC-3, MajesTEC-4 (randomized phase), MajesTEC-7 (randomized phase), MajesTEC-10, MonumenTAL-6, and MajesTEC-9 are blinded and therefore are not included in the analysis of SARs. Some SARs in [Table 2](#) were not reported as serious for the RP2D in MajesTEC-1 but were reported as serious at least twice in other clinical trials and as such are reported in [Table 2](#).

Reports of suspected SARs that are not listed in [Table 2](#) are subject to expedited reporting, in accordance with applicable local regulations.

No fatal SARs are considered expected by the Sponsor for the purposes of expedited reporting of SUSARs.

The sponsor has identified 6 PTs under the SOC of Infections and Infestations considered as expected when life-threatening: pneumonia, COVID-19, sepsis, pneumonia pseudomonal, pneumocystis jirovecii pneumonia, and pseudomonal sepsis (6, 7, 6, 3, 3, and 2 cases, respectively). The severity and nature of these events are fully characterized in Section 4.8 of the Summary of Product Characteristics of teclistamab and therefore can be considered as expected. The risk of life-threatening SARs is mitigated through the safety measures presented in Section 5.6. These measures are described in the protocol and informed consent forms for all ongoing studies and are included in all relevant risk communications to investigators and treating physicians, thus maintaining teclistamab's favorable benefit-risk profile. The sponsor therefore considers that there is a robust justification for the life-threatening events currently included in the reference safety information.

The Reference Safety Information table below uses the latest available MedDRA version. There was no impact to the list of preferred terms according to the latest updated MedDRA version.

Table 2: Serious Adverse Reactions for Teclistamab Considered Expected for Safety Reporting Purposes; All Treated Analysis Set (Study 54767414MMY2089, 64007957MMY1001, 64007957MMY1002, 64007957MMY1003, 64007957MMY1004, 64007957MMY2003, 64007957MMY3003, 64007957MMY3005, 64407564MMY1002, & 64407564MMY1005)

System Organ Class (SOC)	Serious Adverse Reaction (SAR) by Preferred Term	All SARs Frequency n(%) (N=1363)	Life Threatening SARs n(%)	Frequency Category	Synonymous Medical Terms by Preferred Term ^a
Immune system disorders Infections and infestations	Cytokine release syndrome	123 (9.0%)	Not applicable	Common	COVID-19 pneumonia, SARS-CoV-2 viraemia, SARS-CoV-2 test positive
	Pneumonia	94 (6.9%)	6 (0.4%)	Common	
	COVID-19	56 (4.1%)	7 (0.5%)	Common	
	Sepsis	15 (1.1%)	6 (0.4%)	Common	
	Pneumonia bacterial	12 (0.9%)	Not applicable	Uncommon	
	Pneumonia pseudomonal	12 (0.9%)	3 (0.2%)	Uncommon	
	Pneumonia viral	12 (0.9%)	Not applicable	Uncommon	
	Respiratory tract infection	12 (0.9%)	Not applicable	Uncommon	
	Upper respiratory tract infection	12 (0.9%)	Not applicable	Uncommon	
	Pneumocystis jirovecii pneumonia	10 (0.7%)	3 (0.2%)	Uncommon	
	Urinary tract infection	8 (0.6%)	Not applicable	Uncommon	
	Lower respiratory tract infection	6 (0.4%)	Not applicable	Uncommon	
	Pseudomonal sepsis	6 (0.4%)	2 (0.1%)	Uncommon	
	Sinusitis	4 (0.3%)	Not applicable	Uncommon	
	Metapneumovirus pneumonia	3 (0.2%)	Not applicable	Uncommon	
	Bacteraemia	2 (0.1%)	Not applicable	Uncommon	
	Cellulitis	2 (0.1%)	Not applicable	Uncommon	
	Escherichia urinary tract infection	2 (0.1%)	Not applicable	Uncommon	
	Neutropenic sepsis	2 (0.1%)	Not applicable	Uncommon	
	Pneumonia klebsiella	2 (0.1%)	Not applicable	Uncommon	
	Pneumonia pneumococcal	2 (0.1%)	Not applicable	Uncommon	
	Pneumonia respiratory syncytial viral	2 (0.1%)	Not applicable	Uncommon	
	Pneumonia staphylococcal	2 (0.1%)	Not applicable	Uncommon	
	Rhinovirus infection	2 (0.1%)	Not applicable	Uncommon	
	Viral upper respiratory tract infection	2 (0.1%)	Not applicable	Uncommon	
Blood and lymphatic system disorders	Febrile neutropenia	48 (3.5%)	Not applicable	Common	neutrophil count decreased haemoglobin decreased, haematocrit decreased
	Neutropenia	17 (1.2%)	Not applicable	Common	
	Anaemia	6 (0.4%)	Not applicable	Uncommon	
	Thrombocytopenia	4 (0.3%)	Not applicable	Uncommon	
	Leukopenia	2 (0.1%)	Not applicable	Uncommon	white blood cell count decreased
General disorders and administration site conditions	Pyrexia	31 (2.3%)	Not applicable	Common	body temperature increased
Nervous system disorders	Immune effector cell-associated neurotoxicity syndrome	14 (1.0%)	Not applicable	Common	
	Headache	4 (0.3%)	Not applicable	Uncommon	
Gastrointestinal disorders	Diarrhoea	9 (0.7%)	Not applicable	Uncommon	
Metabolism and nutrition disorders	Hypokalaemia	2 (0.1%)	Not applicable	Uncommon	
Psychiatric disorders	Confusional state	2 (0.1%)	Not applicable	Uncommon	
Respiratory, thoracic and mediastinal disorders	Dyspnoea	2 (0.1%)	Not applicable	Uncommon	

Table 2: Serious Adverse Reactions for Teclistamab Considered Expected for Safety Reporting Purposes; All Treated Analysis Set (Study 54767414MMY2089, 64007957MMY1001, 64007957MMY1002, 64007957MMY1003, 64007957MMY1004, 64007957MMY2003, 64007957MMY3003, 64007957MMY3005, 64407564MMY1002, & 64407564MMY1005)

System Organ Class (SOC)	Serious Adverse Reaction (SAR) by Preferred Term	All SARs Frequency n(%) (N=1363)	Life Threatening SARs n(%)	Frequency Category	Synonymous Medical Terms by Preferred Term ^a
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n = Number of participants who experienced SAR assessed as related.
N = Number of participants exposed to Teclistamab.
^a These events would not be subject to expedited reporting.
Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1,000$ to $< 1/100$); rare ($\geq 1/10,000$ to $< 1/1,000$); very rare ($< 1/10,000$).
Note: Events occurring in more than one participant are included in this table.
Adverse events are coded using MedDRA Version 28.0.

Modified from [tsfadr02.rtf] [xcp_oncology/z_64007957_dsur/dbr_dsur_2025_08/re_ib_2025_08/tsfadr02.sas] 23SEP2025, 19:36

7. REFERENCES

- Berdeja JG, Madduri D, Usmani SZ, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): a phase 1b/2 open-label study [published correction appears in Lancet. 2021 Oct 2;398(10307):1216]. Lancet. 2021;398(10297):314-324.
- Bu DX, Singh R, Choi EE, et al. Pre-clinical validation of B cell maturation antigen (BCMA) as a target for T cell immunotherapy of multiple myeloma. *Oncotarget*. 2018;9(40):25764-25780.
- Bugelski PJ, Treacy G. Predictive power of preclinical studies in animals for the immunogenicity of recombinant therapeutic proteins in humans. *Curr Opin Mol Ther*. 2004;6(1):10-16.
- Carpenter RO, Evbuomwan MO, Pittaluga S, et al. B-cell maturation antigen is a promising target for adoptive T-cell therapy of multiple myeloma. *Clin Cancer Res*. 2013;19(8):2048-2060.
- Chiu A, Xu W, He B, et al. Hodgkin lymphoma cells express TACI and BCMA receptors and generate survival and proliferation signals in response to BAFF and APRIL. *Blood*. 2007;109(2):729-739.
- Darce JR, Arendt BK, Chang SK, Jelinek DF. Divergent effects of BAFF on human memory B cell differentiation into Ig-secreting cells. *J Immunol*. 2007 May 1;178(9):5612-5622.
- Frerichs KA, Broekmans MEC, Marin Soto JA, et al. Preclinical activity of JNJ-7957, a novel BCMA×CD3 bispecific antibody for the treatment of multiple myeloma, is potentiated by daratumumab. *Clin Cancer Res*. 2020;26(9):2203-2215.
- Frigyesi I, Adolffson J, Ali M et al. Robust isolation of malignant plasma cells in multiple myeloma. *Blood*. 2014;123(9):1336-1340.
- Huehls AM, Coupet TA, Sentman CL. Bispecific T-cell engagers for cancer immunotherapy. *Immunology and cell biology*. 2015;93(3):290-6.
- Korde N, Kristinsson SY, Landgren O. Monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM): novel biological insights and development of early treatment strategies. *Blood*. 2011;117(21):5573-5581.
- Kyle RA, Therneau TM, Rajkumar SV, et al. A long-term study of prognosis in monoclonal gammopathy of undetermined significance. *N Engl J Med*. 2002;346(8):564-569.
- Kyle RA, Rajkumar SV. Multiple myeloma. *Blood*. 2008;111(6):2962-2972.
- Kyle RA, Rajkumar SV. Criteria for diagnosis, staging, risk stratification and response assessment of multiple myeloma. *Leukemia*. 2009;23(1):3-9.
- Kyle RA, Durie BG, Rajkumar SV, et al. Monoclonal gammopathy of undetermined significance (MGUS) and smoldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management. *Leukemia*. 2010;24(6):1121-1127.
- Labrijn AF, Meesters JI, de Goeij BE, et al. Efficient generation of stable bispecific IgG1 by controlled Fab-arm exchange. *Proc Natl Acad Sci U S A*. 2013;110(13):5145-5150.
- Laurent SA, Hoffman FS, Kuhn PH, et al. γ -Secretase directly sheds the survival receptor BCMA from plasma cells. *Nat Commun*. 2015;6:7333.
- Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. *Blood*. 2014;124(2):188-195.
- Lee DW, Santomasso BD, Locke FL, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biol Blood Marrow Transplant*. 2019;25(4):625-638.
- Marella M, Yao X, Carreira V, et al. Comprehensive BCMA Expression Profiling in Adult Normal Human Brain Suggests a Low Risk of On-target Neurotoxicity in BCMA-targeting Multiple Myeloma Therapy. *J Histochem Cytochem*. 2022;70(4):273-287.
- Munshi NC, Anderson LD Jr, Shah N, et al. Idecabtagene Vicleucel in Relapsed and Refractory Multiple Myeloma. *N Engl J Med*. 2021;384(8):705-716.

- Novak AJ, Darce JR, Arendt BK, et al. Expression of BCMA, TACI, and BAFF-R in multiple myeloma: a mechanism for growth and survival. *Blood*. 2004;103(2):689-694.
- Palaiologou M, Delladetsima I, Tiniakos D. CD138 (syndecan-1) expression in health and disease. *Histol Histopathol*. 2014;29(2):177-189.
- Patel DR, Wallweber HJ, Yin J, et al. Engineering an APRIL-specific B cell maturation antigen. *J Biol Chem*. 2004;279(16):16727-16735.
- Pillarisetti K, Powers G, Luistro L, et al. Teclistamab is an active T cell-redirecting bispecific antibody against B-cell maturation antigen for multiple myeloma. *Blood Adv*. 2020;4(18):4538-4549.
- Saber H, Del valle P, Ricks TK, Leighton JK. An FDA oncology analysis of CD3 bispecific constructs and first-in-human dose selection. *Regul Toxicol Pharmacol*. 2017;90:144-152.
- Sanchez E, Li M, Kitto A, et al. Serum B-cell maturation antigen is elevated in multiple myeloma and correlates with disease status and survival. *Br J Haematol*. 2012;158(6):727-738.
- Shah N, Chari A, Scott E, Mezzi K, Usmani SZ. B-cell maturation antigen (BCMA) in multiple myeloma: rationale for targeting and current therapeutic approaches. *Leukemia*. 2020;34(4):985-1005.
- Strohl WR, Naso M. Bispecific T-cell redirection versus chimeric antigen receptor (CAR)-T cells as approaches to kill cancer cells. *Antibodies*. 2019;8(3):41.
- Sundararajan S, Kumar A, Korde N, Agarwal A. Smoldering multiple myeloma: emerging concepts and therapeutics. *Curr Hematol Malig Rep*. 2016;11(2):102-110.
- Tai YT, Anderson KC. Targeting B cell maturation antigen in multiple myeloma. *Immunotherapy*. 2015;7(11):1187-1199.
- Van Oekelen O, Aleman A, Upadhyaya B, et al. Neurocognitive and hypokinetic movement disorder with features of parkinsonism after BCMA-targeting CAR-T cell therapy. *Nat Med*. 2021;27(12):2099-2103.
- Zhang M, Gray F, Cushman I, et al. A novel BCMA immunohistochemistry assay reveals a heterogenous and dynamic BCMA expression profile in multiple myeloma. *Mod Pathol*. 2023;36(4):100050.

APPENDIX 1: OVERVIEW OF NONCLINICAL STUDIES OF TECLISTAMAB

Appendix 1.1: Pharmacology Overview

Type of Study	Test System	Route (Vehicle/Formulation)	Dose Batch Number	GLP	Test Facility	Study Number
Primary Pharmacodynamics						
Binding affinity and functional activity	Recombinant expression system, PBMCs from multiple species, FACS, ELISA	In vitro		No	JRD Spring House, PA, USA	DD16323
Cross-reactivity to human and cynomolgus monkey BCMA protein	Recombinant protein, surface plasmon resonance binding	In vitro		No	JRD Spring House, PA, USA	DS-TEC-72238
Cross-reactivity to human and cynomolgus monkey CD3 protein	Human and cynomolgus monkey primary T cells, FACS	In vitro		No	JRD Spring House, PA, USA	DS-TEC-93455
Binding profile in whole blood	FACS	In vitro		No	JRD Spring House, PA, USA	DD16322
BCMA IHC antibody validation and expression on normal non-hematological tissues	IHC	In vitro		No	Asterand Biosciences Detroit, MI, USA & JRD Spring House, PA, USA	DD16320
BCMA protein expression in multiple myeloma cell lines	FACS	In vitro		No	JRD Spring House, PA, USA	DD16320
BCMA mRNA expression in cell lines	Microarray data set	Computational		No	JRD Spring House, PA, USA	DD16320
BCMA endogenous expression in human brain	Human brain tissues, IHC	In vitro		No	JRD San Diego, CA, USA	Histo-06092020
BCMA and GPRC5D normal tissue co-expression	Human normal lymphoid and gastrointestinal tract tissues, IHC and ISH	In vitro		No	JRD San Diego, CA, USA	PATHLJ23-007
Binding profile on multiple myeloma cell lines	Human endogenous BCMA-expressing cell lines, FACS	In vitro		No	JRD Spring House, PA, USA	DD16321
BCMA receptor density on multiple myeloma plasma cells	FACS	In vitro		No	JRD Spring House, PA, USA	DD16320
Antagonistic effect on ligand mediated signaling	P38 phosphorylation assay	In vitro		No	JRD Spring House, PA, USA	DD16322
Soluble BCMA levels in multiple myeloma patient plasma samples	Mass Spectrometry	In vitro		No	Caprion Biosciences Montreal, Quebec, Canada & JRD Spring House, PA, USA	DD16322
Soluble factors (sBCMA, APRIL, BAFF) effect on binding to BCMA ⁺ cells	FACS	In vitro		No	JRD Spring House, PA, USA	DD16322
Soluble factors (soluble BCMA, APRIL, BAFF) effect on functional activity	FACS	In vitro		No	JRD Spring House, PA, USA	DD16322

Type of Study	Test System	Route (Vehicle/Formulation)	Dose Batch Number	GLP	Test Facility	Study Number
T cell-dependent cytotoxicity in BCMA-expressing cell lines	Human endogenous BCMA-expressing cell lines, human pan T cells, FACS	In vitro		No	JRD Spring House, PA, USA	DD16321
Teclistamab-mediated T cell activation	Human endogenous BCMA-expressing cell lines, human pan T cells, FACS	In vitro		No	JRD Spring House, PA, USA	DD16321
Effect on T cell activation in absence of target cells	FACS	In vitro		No	JRD Spring House, PA, USA	DD16322
Teclistamab-mediated cytokine release	Human endogenous BCMA-expressing cell lines (RPMI-8226), human pan T cells, MSD	In vitro		No	JRD Spring House, PA, USA	DD16321
Teclistamab-mediated T cell-dependent cytotoxicity of frozen primary multiple myeloma bone marrow samples	Human multiple myeloma patient bone marrow samples, FACS	In vitro		No	JRD Spring House, PA, USA	DD16321
Comparison of HEK vs CHO produced teclistamab	FACS	In vitro		No	JRD Spring House, PA, USA	DD16322
Comparison of different batches	FACS	In vitro		No	JRD Spring House, PA, USA	DD16322
Effect of parental antibody concentrations on teclistamab efficacy	FACS	In vitro		No	JRD Spring House, PA, USA	DD16322
Efficacy of teclistamab in H929 or RPMI 8226 model of human multiple myeloma in PBMC humanized NSG mice	Prophylactic H929 or SC RPMI 8226 (BCMA ⁺) inoculation, engrafted human healthy PBMCs	IV (PBS)	H929 model: 0.5, 1 µg/mouse (0.025, 0.05 mg/kg) RPMI 8226 model: 0.1, 1 µg/mouse (0.005, 0.05 mg/kg)	No	JRD Spring House, PA, USA	DD16334
Efficacy of teclistamab in RPMI-8226 established T cell model	SC RPMI-8226 (BCMA ⁺) inoculation, engrafted human healthy PBMCs	IP (PBS)	1, 10, 50 µg/mouse (0.05, 0.5, 2.5 mg/kg)	No	Charles River Discovery Services Morrisville, NC, USA	DD20099
Efficacy of teclistamab in a H929 whole blood model of human multiple myeloma	Healthy human whole blood spiked with H929 cells	In vitro		No	JRD Spring House, PA, USA	TR2016T-005
Secondary Pharmacology	No studies conducted					
Safety Pharmacology						
Cardiovascular, central nervous, and respiratory system, assessments conducted as part of the pivotal repeat-dose toxicity study	Cynomolgus monkey (5-week toxicity study with 8-week recovery period) (5/sex/group dosing phase, 2/sex/recovery phase)	IV (formulation buffer ^a ; diluent: sterile saline)	0 ^a , 1, 10, 30 mg/kg/week Batch number: GBS5I	Yes	Charles River Laboratories Reno, NV, USA	T-2016-030

a. Formulation buffer: An aqueous solution of 10 mM sodium acetate, 8% (w/v) sucrose, 0.04% (w/v) polysorbate 20, 20 µg/mL EDTA, at pH 5.2. Control animals were administered sterile saline.

Abbreviations: See [List of Abbreviations and Definitions of Terms](#).

Appendix 1.2: Pharmacokinetics Overview

Type of Study	Test System	Route (Vehicle/Formation)	Batch Number	GLP	Test Facility	Study Number
Absorption						
Single-dose PK and repeat-dose TK in exploratory single- and 5-week repeat-dose tolerability study	Cynomolgus monkey (3 males/group)	IV (PBS; diluent: sterile saline)	8617	No	Charles River Laboratories Reno, NV, USA	T-2015-030
Repeat-dose TK and ADA in pivotal 5-week toxicity GLP study with an 8-week recovery period	Cynomolgus monkey (5/sex/group dosing phase, 2/sex/recovery phase)	IV (formulation buffer ^a ; diluent: sterile saline)	GBS5I	Yes	Charles River Laboratories Reno, NV, USA	T-2016-030
Single-dose PK of 3 formulations	Gottingen minipig (4 males/group)	SC (formulations 1, 2, 3)	AN7475, API-150, API-200	No	JRD Spring House, PA, USA	CP2020PK-086
Distribution	No studies conducted					
Metabolism	No studies conducted					
Excretion	No studies conducted					
Pharmacokinetic Drug Interactions	No studies conducted					
Other	No studies conducted					

a. Formulation buffer: An aqueous solution of 10 mM sodium acetate, 8% (w/v) sucrose, 0.04% (w/v) polysorbate 20, 20 µg/mL EDTA, at pH 5.2. Control animals were administered sterile saline.

Abbreviations: See [List of Abbreviations and Definitions of Terms](#).

Appendix 1.3: Toxicology Overview

Type of Study	Species and Strain	Route (Vehicle/Formulation)	Duration of Dosing	Doses ^a	Batch Number	TK	GLP	Test Facility	Study Number
Single-dose Toxicity	No studies conducted								
Repeat-dose Toxicity									
Exploratory single and 5-week repeat-dose tolerability study	Cynomolgus monkey (3 males/group)	IV (PBS; diluent: sterile saline)	once	1, 10 mg/kg	8617	Yes	No	Charles River Laboratories Reno, NV, USA	T-2015-030
			5 weeks	0 ^c , 0.1, 1, 10 mg/kg/week					
				(0, 0.05, 0.5, 5 mg/mL; 2 mL/kg dose volume) (Days 1, 8, 15, 22, 29)					
Pivotal 5-week repeat-dose toxicity study with an 8-week recovery period	Cynomolgus monkey (5/sex/group dosing phase, 2/sex/recovery phase)	IV (formulation buffer ^b ; diluent: sterile saline)	5 weeks	0, 1, 10, 30 mg/kg/week	GBS5I	Yes	Yes	Charles River Laboratories Reno, NV, USA	T-2016-030
				(0 ^c , 0.33, 3.33, 10 mg/mL; 3 mL/kg dose volume)					
				(Days 1, 8, 15, 22, 29)					
Genotoxicity	No studies conducted								
Carcinogenicity	No studies conducted								
Reproduction Toxicity	No studies conducted								
Local Tolerance	New Zealand White rabbit (6 males/group)	SC (formulation buffer ^b)	once	0 ^d , 20 mg (10 mg/mL; 2 mL volume)	P73101A	No	Yes	Charles River Laboratories Saint Constant, Canada	T-2018-019
Other Toxicity Studies									
Tissue cross-reactivity	Normal human tissues (cryosections)	In vitro (formulation buffer ^b ; diluent: PBS + 1% BSA)	NA	4, 20 µg/mL biotinylated teclistamab	MOS00123254 (GBS5I for unlabeled protein)	No	Yes	Charles River Laboratories Frederick, MD, USA	T-2016-031
Tissue cross-reactivity	Human and cynomolgus monkey normal tissues (cryosections)	In vitro (diluent: PBS + 1% BSA)	NA	1, 5 µg/mL biotinylated teclistamab	MOS00089892	No	No	Charles River Laboratories Frederick, MD, USA	T-2015-051 (included in T-2016-031)
Hemolytic potential	Human whole blood	In vitro (formulation buffer ^b)	NA	0.010 to 10 mg/mL	GBS5I	No	No	JRD Spring House, PA, USA	T-2016-048
Serum compatibility	Human serum	In vitro (formulation buffer ^b)	NA	0.010 to 10 mg/mL	GBS5I	No	No	JRD Spring House, PA, USA	T-2016-047

Type of Study	Species and Strain	Route (Vehicle/Formulation)	Duration of Dosing	Doses ^a	Batch Number	TK	GLP	Test Facility	Study Number
Cytokine release	Human whole blood	In vitro (diluent: PBS)	NA	1.016 to 20,000 ng/mL	GBS5I	No	No	JRD Spring House, PA, USA	T-2016-046

- a. The highest NOEL is underlined.
b. Formulation buffer: An aqueous solution of 10 mM sodium acetate, 8% (w/v) sucrose, 0.04% (w/v) polysorbate 20, 20 µg/mL EDTA, at pH 5.2.
c. Control animals were administered sterile saline.
d. The SC local tolerance rabbit study control group received sterile saline on the right side and formulation buffer on the left side of the scapular region.

Abbreviations: See [List of Abbreviations and Definitions of Terms](#).

Appendix 1.4: GLP Compliance of GLP Nonclinical Studies

Study Title	Study Code	Date of Study Start ^a	Date of Completion of the Final Report ^b	Test Facility(es)/Test Site(s) in Which the Study was Conducted (Name and Complete Address)	For Studies Conducted in European Union, OECD or Fully MAD-adherent Countries: Indicate (Y/N/NA) Whether a Successful Inspection by its National GLP Compliance Monitoring Authority Took Place Within 3 Years Before or After Final Study Report Date
JNJ-64007957 (BCMAxCD3): A 5-week, Intravenous Repeat-dose Toxicity Study in Cynomolgus Monkeys with an 8-week Recovery Period	T-2016-030	22 Apr 2016	18 May 2017 (Amendment 1 12 Jun 2017)	Test facility Charles River Laboratories, Inc. 6995 Longley Lane, Reno, NV, 89511, USA Test site - Ophthalmology interpretation Eye Care for Animals 9720 S. Virginia Street, Suite D, Reno, NV 89511, USA Test site - Cardiology evaluation VetMed Consultants, Inc. Physical address: 3600 Cerrillos Road, Suite 714A, Santa Fe, NM 87507, USA Mailing address: 1704-B Llano Street, Suite 279, Santa Fe, NM 87505, USA Test site - Toxicokinetic and ADA bioanalysis and interpretation Janssen Research & Development, LLC 1400 McKean Road, Spring House, PA 19477, USA	Yes
JNJ-64007957 (BCMAxCD3) and JNJ-64407564 (GPRC5DxCD3): A Single Dose SC Local Tolerance Study in New Zealand White Rabbits	T-2018-019	27 Aug 2018	12 Nov 2018	Test facility Charles River Laboratories, Inc. 905 Sheehy Drive, Horsham, PA, 19044, USA Test site – Pathology peer review Janssen Research & Development, LLC 1400 McKean Road, Spring House, PA 19477, USA	Yes
A Tissue Cross-reactivity Study of Biotinylated JNJ-64007657 in Normal Tissues	T-2016-031	23 Jun 2016	17 Aug 2016	Test facility Charles River Laboratories, Inc. 15 Worman's Mill Court, Suite I, Frederick, MD, 21701, USA	Yes

a. Original protocol sign-off date

b. Final report sign-off date (and amendment issue date(s), if applicable)

Abbreviations: See [List of Abbreviations and Definitions of Terms](#).

APPENDIX 2: SUMMARY OF TECLISTAMAB MONOTHERAPY AND COMBINATION STUDIES

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
Teclistamab Monotherapy Studies in Multiple Myeloma				
64007957MMY1001 (MajesTEC-1) Ongoing/ Primary analysis completed	Phase: 1/2 First-in-human, open-label, dose escalation/dose expansion, multicenter study Adults ≥18 years of age, with relapsed or refractory multiple myeloma Part 1 (Phase 1 dose escalation): To identify the proposed RP2D(s) and schedule assessed to be safe for teclistamab Part 2 (Phase 1 dose expansion): To characterize the safety and tolerability of teclistamab at the proposed RP2D(s) Part 3 (Phase 2): To evaluate the efficacy of teclistamab at the RP2D	Part 1: <u>IV administration:</u> approximately 100 participants <u>SC administration:</u> approximately 150 participants Part 2: a maximum of 40 participants were to be treated at each of the proposed RP2D(s). Part 3: <u>Cohort A</u> (participants without prior anti-BCMA therapy): approximately 100 participants <u>China cohort</u> (participants without prior anti-BCMA therapy): approximately 25 participants. <u>Cohort C</u> (participants with prior anti-BCMA therapy): approximately 38 participants	teclistamab (IV and SC) Until disease progression or unacceptable toxicity	Teclistamab IV n=84 Teclistamab SC non-RP2D n=177 Teclistamab SC RP2D (1.5 mg/kg weekly) Phase 1: n=40 Phase 2 Cohort A: n=128 ^a Phase 2 China cohort RP2D: n=26 Phase 2 Cohort C RP2D: n=40 Total: n=495 ^a

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
64007957MMY1002 (MMY1002 Japan) Ongoing	Phase: 1/2 Open-label, single-arm, multicenter study Japanese participants ≥ 20 years of age, with relapsed or refractory multiple myeloma Phase 1: To evaluate the safety and tolerability in Japanese participants with relapsed/refractory multiple myeloma at RP2D identified in Study 64007957MMY1001 Phase 2: To evaluate the efficacy of teclistamab at RP2D for Japanese participants	Phase 1: At least 3 participants to be enrolled in each cohort (0.72, 1.5, 3.0 mg/kg, and 6.0 mg/kg) with a maximum of 18 participants enrolled in this study. Phase 2: Approximately 24 participants to be enrolled.	teclistamab SC Until disease progression or unacceptable toxicity	Teclistamab SC non-RP2D: n=9 Teclistamab SC RP2D (1.5 mg/kg weekly) Phase 1: n=5 Phase 2: n=26 Total: n=40
64007957MMY3006 (MajesTEC-9) Ongoing	Phase: 3 Part 1: Randomized, open-label, multicenter study comparing teclistamab monotherapy (Arm A) versus investigator's choice of PVd or Kd (PVd/Kd; Arm B) Part 2: Single-arm, non-randomized, multicenter study to evaluate an alternative teclistamab step-up dose regimen Adults ≥ 18 years of age with multiple myeloma who have previously received 1 to 3 prior line(s) of therapy, including an anti-CD38 monoclonal antibody and lenalidomide	Part 1: Approximately 590 participants will be randomized 1:1 Part 2: Approximately 60 additional participants will be enrolled	Part 1 Arm A and Part 2: teclistamab SC Part 1 Arm B: pomalidomide oral + bortezomib SC + dexamethasone oral <i>or</i> carfilzomib IV + dexamethasone oral/IV Until disease progression or intolerable toxicity	Part 1: n=574 Part 2: n=19 Total: n=593

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
	Part 1: To compare the efficacy of teclistamab with PVd/Kd Part 2: To evaluate the safety profile of alternative step-up dose of teclistamab			
64007957MMY1008 (MajesTEC-10) Ongoing	Phase 1 Randomized, open-label, multicenter study to compare the PK of pre-change and post-change teclistamab (Part 1) and an additional statistical analysis to assess aggregate results of the efficacy and safety of teclistamab (Part 2) Adults with relapsed/refractory multiple myeloma who have received 1 to 3 prior lines of therapy, including an anti-CD38 monoclonal antibody, lenalidomide, and a PI Part 1: To assess PK comparability between pre-change teclistamab and post-change teclistamab Part 2: To evaluate the efficacy of teclistamab in the aggregate population	A minimum of approximately 100 participants randomized in a 1:1 ratio to Arm A (pre-change teclistamab) or Arm B (post-change teclistamab). Enrollment may be continued to ensure inclusion of at least 40 PK-evaluable participants in each arm	teclistamab SC Until disease progression or intolerable toxicity	n=105

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
Teclistamab Combination Therapy Studies in Multiple Myeloma				
64407564MMY1002 (TriMM-2) Ongoing	Phase: 1b Open-label, multicenter, multi-cohort study of daratumumab in combination with bispecific antibodies (teclistamab or talquetamab [a T cell redirecting antibody targeting GPRC5D]) with or without pomalidomide Adults with multiple myeloma who have received ≥ 3 prior lines of therapy including a PI and an IMiD or who have disease that is double refractory to a PI and an IMiD Part 1 (dose escalation): To identify RP2Ds for each treatment combination Part 2 (dose expansion): To characterize the safety of each RP2D for selected treatment combination(s)	Part 1: At least 30 participants Part 2: Up to approximately 40 participants evaluated at each of the RP2Ds for each treatment combination	daratumumab SC teclistamab (IV or SC) talquetamab (IV or SC) pomalidomide (oral) Until disease progression or unacceptable toxicity	Part 1: daratumumab + teclistamab IV n=6 daratumumab + teclistamab SC n=40 daratumumab + fixed dose ^b teclistamab SC n=33 daratumumab + teclistamab SC + pomalidomide n=10 ^c Part 2: daratumumab + teclistamab SC n=38 Total: n=127

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
64407564MMY1005 (TriMM-3) Ongoing	Phase: 1b Open-label, nonrandomized, multicenter, dose-escalation study with dose expansion of talquetamab in combination with cetrelimab or teclistamab in combination with cetrelimab Adults ≥ 18 years of age with relapsed or refractory multiple myeloma who are not a candidate for available therapy with established clinical benefit. To identify the safe dose(s) of cetrelimab in combination with talquetamab or teclistamab. To characterize the safety and tolerability of talquetamab or teclistamab when administered in combination with cetrelimab.	Dose escalation: At least 16 participants (at least 4 per dose level) Dose expansion: Up to approximately 40 participants per treatment regimen	teclistamab SC talquetamab SC cetrelimab IV Until disease progression or unacceptable toxicity	Teclistamab SC + cetrelimab IV: n=25 ^d
64007957MMY1003 (RedirecTT-1) Ongoing	Phase: 1b/2 Open-label, multicenter study of the combination of teclistamab and talquetamab with or without daratumumab SC Part 1 and Part 2 (Phase 1b): Adults ≥ 18 years of age with measurable multiple myeloma that is relapsed or refractory to established therapies or who are intolerant of established therapies	Part 1: Up to approximately 75 participants will be enrolled Part 2: Up to approximately 20 participants will be enrolled per RP2R	teclistamab SC talquetamab SC daratumumab SC Until disease progression unless judged to be in the best interest of participant to continue after discussion with sponsor, or unacceptable toxicity	Part 1: n=87 Part 2: n=51 Part 3: n=90 Total: n=228

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
	- <u>Cohorts without daratumumab:</u> Prior lines of therapy must include a PI, an IMiD, and an anti-CD38 therapy, in any order. - <u>Cohorts with daratumumab:</u> Prior lines of therapy must include a PI and an IMiD. Has disease that is considered refractory to an anti-CD38 monoclonal antibody per IMWG (best response of stable disease or progression during treatment or within 60 days of completing therapy with an anti-CD38 monoclonal antibody). Treatment with an anti-CD38 therapy is allowed ≥ 90 days prior to study treatment if the participant did not discontinue prior treatment due to AEs related to anti-CD38 therapy. Part 3 (Phase 2): Adults ≥ 18 years of age with relapsed or refractory multiple myeloma and EMD exposed to a PI, IMiD, and an anti-CD38 monoclonal antibody with evidence of progressive disease on or after their last regimen. Part 1: To identify the RP2R(s) and schedule for the study treatment. Part 2: To characterize the safety of the RP2R(s) for the study treatment. Part 3: To evaluate the anticancer activity of talquetamab and teclistamab combination therapy in participants with relapsed or	Part 3: Approximately 90 participants will be enrolled		

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
	refractory multiple myeloma and EMD.			
64007957MMY1004 (MajesTEC-2)	Phase: 1b	At least 20 participants will be enrolled for each treatment regimen	Regimen A: teclistamab SC + daratumumab SC + pomalidomide oral	Regimen A: n=17
Ongoing	Open-label, nonrandomized, multicenter, dose-escalation study of teclistamab combination regimens		Regimen B: teclistamab SC + daratumumab SC + lenalidomide oral + bortezomib SC or IV (21-day cycles)	Regimen B: n=22
	Adults ≥18 years with newly diagnosed or relapsed/refractory multiple myeloma who meet treatment-specific requirements		Regimen C: teclistamab SC + nirogacestat oral	Regimen C: n=28
	To characterize the safety and tolerability of teclistamab when administered in different combination regimens		Regimen D: teclistamab SC + lenalidomide oral	Regimen D: n=31
	To identify the optimal dose(s) of teclistamab combination regimens		Regimen E: teclistamab SC + daratumumab SC + lenalidomide oral	Regimen E: n=42
			Regimen F: teclistamab SC + daratumumab SC + lenalidomide oral + bortezomib SC (28-day cycles)	Total: n=140
			Until disease progression or unacceptable toxicity	
GMMG-HD10/DSMM-XX 64007957MMY2003 (MajesTEC-5)	Phase: 2	A maximum of approximately 320 participants. Arm A will enroll approximately 10 participants. Arm A1 and Arm B will initially enroll	Arm A and Arm A1: teclistamab SC + daratumumab SC + lenalidomide oral + dexamethasone oral or IV (induction) and teclistamab	Arm A: n=10 (induction phase, of whom 9 also started maintenance treatment)
Ongoing	Open-label, multicenter study of combination regimens including Tec-DRd and Tec-DVRd as induction therapy with Tec-DR and Tec-D as			Arm A1: n=20 (induction phase, of whom 18 also

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
	post-transplant maintenance therapy, and Tec-DRd as induction therapy followed by Tal-Tec in lieu of ASCT.	approximately 20 participants each and may be expanded up to a total of 80 participants (Arms A1 and B combined). Arm C will enroll approximately 10 participants and based on evolving data, Arm C1 may be opened to enroll approximately 10 participants. Arm D will initially enroll approximately 20 participants and may enroll up to 60 participants. Arm E will initially enroll approximately 10 participants and may enroll up to 30 participants.	SC + daratumumab SC ± lenalidomide oral (maintenance) Arm B: teclistamab SC + daratumumab SC + bortezomib SC + lenalidomide oral + dexamethasone oral or IV (induction) and teclistamab SC + daratumumab SC (maintenance) Arm C and Arm C1: teclistamab SC + daratumumab SC ± lenalidomide oral (maintenance) Arm D: teclistamab SC + daratumumab SC + lenalidomide oral + dexamethasone oral or IV (induction) and teclistamab SC + talquetamab SC (replacement for HDT+ASCT) Arm E: talquetamab SC + daratumumab SC + lenalidomide oral + dexamethasone oral or IV (induction) and teclistamab SC + daratumumab SC (maintenance)	started maintenance treatment) Arm B: n=19 (induction phase, of whom 18 also started maintenance treatment) Arm C: n=10 (maintenance phase) Arm D: n=20 (induction phase, of whom 19 also started Tal-Tec) Total: n=79

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
64007957MMY3001 (MajesTEC-3) Ongoing	Phase: 3	Approximately 560 participants will be randomized in a 1:1 ratio to Arm A or Arm B	All Arms: 6 cycles for induction therapy and 18 cycles for maintenance therapy	Total: n=573
	Open-label, randomized, multicenter study Adults ≥18 years of age with multiple myeloma who have previously received 1 to 3 prior line(s) of therapy, including a PI and lenalidomide. If a participant has received only 1 prior line of therapy, the participant's disease must be lenalidomide refractory. To compare the efficacy of teclistamab in combination with daratumumab with DPd/DVd		Arm A: teclistamab SC + daratumumab SC Arm B: Investigator's choice of daratumumab SC + pomalidomide oral + dexamethasone oral or IV <i>or</i> daratumumab SC + bortezomib SC + dexamethasone oral or IV Until progressive disease or intolerable toxicity	

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
EMN30/64007957MMY3003 (MajesTEC-4) Ongoing	Phase: 3 Open-label, randomized, multicenter study of teclistamab in combination with lenalidomide and teclistamab alone versus lenalidomide alone as maintenance therapy following ASCT Adults ≥ 18 years of age with newly diagnosed multiple myeloma who have completed induction therapy followed by ASCT, with or without consolidation To compare the efficacy of teclistamab in combination with lenalidomide to lenalidomide, and the efficacy of teclistamab to lenalidomide in the maintenance setting	Approximately 1500 participants will be randomized 1:1:1, following 3 Safety Run-in cohorts, each enrolling approximately 20 participants	Safety Run-in 1: teclistamab SC + lenalidomide oral Safety Run-in 2: teclistamab SC + lenalidomide oral or teclistamab SC Arm A: teclistamab SC + lenalidomide oral Arm B: lenalidomide oral Arm C: teclistamab SC For 2 years, or until disease progression or intolerable toxicity	Safety Run-in 1: n=32 Safety Run-in 2: n=62 Randomized part: n=491 Total: n=585
64007957MMY3005 (MajesTEC-7) Ongoing	Phase: 3 Randomized, open-label, multicenter study comparing Tec-DR versus DRd and Tal-DR vs DRd Adults ≥ 18 years of age with newly diagnosed multiple myeloma who are ineligible or not intended for ASCT as initial therapy To compare the efficacy of Tec-DR vs DRd and Tal-DR vs DRd	Approximately 1500 participants will be randomized 1:1:1, following 3 Safety Run-in cohorts, each enrolling approximately 30 participants	teclistamab SC + daratumumab SC + lenalidomide oral <i>or</i> talquetamab SC + daratumumab SC + lenalidomide oral <i>or</i> daratumumab SC + lenalidomide oral + dexamethasone oral or IV Until progressive disease or intolerable toxicity	Safety Run-in 1 (Tec-DR): n=26 Safety Run-in 2 (Tec-DR): n=23 Safety Run-in 3 (Tal-DR): n=22 Randomized Part: n=802

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
EMN33/54767414MMY2089 (TAURUS) Ongoing	Phase 2 Open-label, multicenter study to compare bone marrow-based MRD techniques (by next-generation sequencing, next-generation flow cytometry) and blood-based M-protein MS-MRD technique Adults (18 to 70 years of age, inclusive) with newly diagnosed multiple myeloma for whom high-dose therapy and ASCT is part of the intended treatment plan To compare MRD measurements by next-generation sequencing (bone marrow) and MS (M-protein measurement in peripheral blood) at key timepoints in transplant-eligible participants with newly diagnosed multiple myeloma combined across cohorts: • Cohort 1: post-consolidation • Cohort 2: 3 cycles of Tal-Tec • Cohort 3: 3 cycles of JNJ-79635322-D • Cohort 4: 3 cycles of JNJ-79635322-DR	Approximately 200 participants in Part 1 of the study. In Part 2 of the study, participants will proceed to Cohort 1 or, up to 25 of the 200 participants, will have the option to participate in Cohort 2. An additional 40 participants will have the option to participate in Cohort 3 or Cohort 4, 20 participants each.	Cohort 1: daratumumab SC + bortezomib SC + lenalidomide oral + dexamethasone oral or IV (induction and consolidation) Cohort 2: daratumumab SC + bortezomib SC + lenalidomide oral + dexamethasone oral or IV (induction) + teclistamab SC + talquetamab SC Cohort 3: daratumumab SC + bortezomib SC + lenalidomide oral + dexamethasone oral or IV then JNJ-79635322 SC + daratumumab SC Cohort 4: JNJ-79635322 SC + daratumumab SC + lenalidomide oral Cohort 1: Up to 6 cycles of DVRd Cohort 2: 6 cycles of DVRd and up to 12 cycles of teclistamab + talquetamab Cohort 3: 6 cycles of DVRd and up to 12 cycles of JNJ-79635322-D	Cohort 1: n=200 Cohort 2: n=25

Study Identifier Study Status	Phase Study Design Study Population Primary Objective(s)	Total Planned Number of Participants	Study Drug(s): Route of Administration Duration of Treatment	Total Treated
64407564MMY3009 (MonumenTAL-6)	Phase 3	Approximately 795 participants randomized in a 1:1:1 ratio to receive Tal-P (Arm A), Tal-Tec (Arm B), or EPd or PVd (Arm C)	Cohort 4: 18 cycles of JNJ-79635322-DR Arm A: talquetamab SC + pomalidomide oral Arm B: teclistamab SC + talquetamab SC Arm C: elotuzumab IV + pomalidomide oral + dexamethasone oral <i>or</i> pomalidomide oral + bortezomib SC + dexamethasone oral For 26 cycles (talquetamab/teclistamab) or until progressive disease or toxicity. Pomalidomide may be continued in Arm A after Cycle 26 if no discontinuation criteria are met.	Total: n=226

- Three participants were planned to receive fixed dose teclistamab in Cohort D but switched to weight-based teclistamab following an Urgent Safety Measure (see Section 4.3.2.2.1). These participants are in Cohort A but are not included in the “pivotal RP2D” data above and in Appendix 3.
- All participants transitioned to weight-based dosing after an Urgent Safety Measure (see Section 4.3.2.2.1). Safety data that led to the Urgent Safety Measure were from 31 participants treated with a 2-tiered teclistamab fixed-dose regimen in TriMM-2, as described in Section 4.3.2.2.1.
- As of the 22 August 2025 clinical cutoff date for this IB, n=9 participants were assigned to Tec-D with pomalidomide 4 mg and n=1 to Tec-D with pomalidomide 2 mg.
- Three participants received teclistamab but did not receive cetrelimab.

APPENDIX 3: CLINICAL TABLES AND FIGURES FOR STUDY MAJESTEC-1 (64007957MMY1001)

Appendix 3.1: Primary Safety Analysis

Study 64007957MMY1001 (Pivotal RP2D): Summary of Overall Best Confirmed Response based on Independent Review Committee (IRC) Assessment; Efficacy Analysis Set

	RP2D					
	Phase 1		Phase 2 Cohort A		Total	
	n (%)	95% CI for %	n (%)	95% CI for %	n (%)	95% CI for %
Analysis set: Efficacy	40		110		150	
Response category						
Stringent complete response (sCR)	13 (32.5%)	(18.6%, 49.1%)	25 (22.7%)	(15.3%, 31.7%)	38 (25.3%)	(18.6%, 33.1%)
Complete response (CR)	4 (10.0%)	(2.8%, 23.7%)	6 (5.5%)	(2.0%, 11.5%)	10 (6.7%)	(3.2%, 11.9%)
Very good partial response (VGPR)	8 (20.0%)	(9.1%, 35.6%)	32 (29.1%)	(20.8%, 38.5%)	40 (26.7%)	(19.8%, 34.5%)
Partial response (PR)	1 (2.5%)	(0.1%, 13.2%)	5 (4.5%)	(1.5%, 10.3%)	6 (4.0%)	(1.5%, 8.5%)
Minimal response (MR)	0	(NE, NE)	1 (0.9%)	(0.0%, 5.0%)	1 (0.7%)	(0.0%, 3.7%)
Stable disease (SD)	7 (17.5%)	(7.3%, 32.8%)	19 (17.3%)	(10.7%, 25.7%)	26 (17.3%)	(11.6%, 24.4%)
Progressive disease (PD)	7 (17.5%)	(7.3%, 32.8%)	17 (15.5%)	(9.3%, 23.6%)	24 (16.0%)	(10.5%, 22.9%)
Not evaluable	0	(NE, NE)	5 (4.5%)	(1.5%, 10.3%)	5 (3.3%)	(1.1%, 7.6%)
Overall response (sCR + CR + VGPR + PR)	26 (65.0%)	(48.3%, 79.4%)	68 (61.8%)	(52.1%, 70.9%)	94 (62.7%)	(54.4%, 70.4%)
VGPR or better (sCR + CR + VGPR)	25 (62.5%)	(45.8%, 77.3%)	63 (57.3%)	(47.5%, 66.7%)	88 (58.7%)	(50.3%, 66.6%)
CR or better (sCR + CR)	17 (42.5%)	(27.0%, 59.1%)	31 (28.2%)	(20.0%, 37.6%)	48 (32.0%)	(24.6%, 40.1%)

Key: CI = confidence interval; NE = not estimable; RP2D = recommended Phase 2 dose; IRC = independent review committee; IMWG = international myeloma working group

Note: Response was assessed by IRC, based on IMWG consensus criteria (2016).

Note: Percentages calculated with the number of subjects in the efficacy analysis set as denominator.

Note: Exact 95% confidence intervals are provided.

[TEFRESP01RP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_EFFICACY_ADDENDUM\RE_EFFICACY_ADDENDUM\PROD\TEFRESP01RP2D.SAS] 13DEC2021, 23:14

**Study 64007957MMY1001 (Pivotal RP2D): Overall Summary of Treatment-emergent Adverse Events;
All Treated Analysis Set**

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Any TEAE	40 (100.0%)	125 (100.0%)	165 (100.0%)
Study drug-related ^a	37 (92.5%)	115 (92.0%)	152 (92.1%)
Maximum toxicity grade			
Grade 1	0	1 (0.8%)	1 (0.6%)
Grade 2	4 (10.0%)	8 (6.4%)	12 (7.3%)
Grade 3	16 (40.0%)	32 (25.6%)	48 (29.1%)
Grade 4	19 (47.5%)	67 (53.6%)	86 (52.1%)
Grade 5	1 (2.5%)	17 (13.6%)	18 (10.9%)
Any serious TEAE	19 (47.5%)	69 (55.2%)	88 (53.3%)
Study drug-related ^a	6 (15.0%)	27 (21.6%)	33 (20.0%)
TEAE leading to discontinuation of study drug ^b	0	1 (0.8%)	1 (0.6%)
TEAE with outcome death ^c	1 (2.5%)	17 (13.6%)	18 (10.9%)
Death due to COVID-19	0	7 (5.6%)	7 (4.2%)
COVID-19 TEAEs	5 (12.5%)	10 (8.0%)	15 (9.1%)
COVID-19 serious TEAEs	3 (7.5%)	9 (7.2%)	12 (7.3%)

Key: TEAE = treatment-emergent adverse event; RP2D = recommended Phase 2 dose; CRS = cytokine release syndrome;
ICANS = immune effector cell-associated neurotoxicity syndrome

^a TEAEs related to study drug

^b Includes those subjects indicated as having discontinued treatment due to an adverse event on the end of treatment CRF page.

^c TEAE with outcome death on the AE eCRF page.

Note: Adverse events are graded according to the NCI-CTCAE Version 4.03, with the exception of ICANS and CRS. CRS was originally graded by Lee criteria (Lee et al 2014) in Phase 1 and by ASTCT consensus grading system (Lee et al 2019) in Phase 2, with conversion of grade in Phase 1 to ASTCT based on data in eCRF. Toxicity grade for CRS by ASTCT is presented in this table, for both Phase 1 and Phase 2. Toxicity grade for ICANS by ASTCT is also presented in this table.

Note: The output includes the diagnosis of CRS and ICANS; the symptoms of CRS or ICANS are excluded.

Note: Percentages calculated with the number of subjects in the all treated analysis set as denominator.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

[TSFAE01RP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFAE01RP2D.SAS] 07OCT2021, 21:23

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set			
	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Subjects with 1 or more TEAEs	40 (100.0%)	125 (100.0%)	165 (100.0%)
MedDRA system organ class / preferred term			
Blood and lymphatic system disorders	37 (92.5%)	110 (88.0%)	147 (89.1%)
Neutropenia	29 (72.5%)	79 (63.2%)	108 (65.5%)
Anaemia	23 (57.5%)	59 (47.2%)	82 (49.7%)
Thrombocytopenia	17 (42.5%)	46 (36.8%)	63 (38.2%)
Lymphopenia	5 (12.5%)	51 (40.8%)	56 (33.9%)
Leukopenia	14 (35.0%)	15 (12.0%)	29 (17.6%)
Febrile neutropenia	0	5 (4.0%)	5 (3.0%)
Iron deficiency anaemia	1 (2.5%)	2 (1.6%)	3 (1.8%)
Leukocytosis	0	3 (2.4%)	3 (1.8%)
Hyperviscosity syndrome	1 (2.5%)	1 (0.8%)	2 (1.2%)
Lymphocytosis	0	2 (1.6%)	2 (1.2%)
Eosinophilia	0	1 (0.8%)	1 (0.6%)
Hypoglobulinaemia	0	1 (0.8%)	1 (0.6%)
Lymphatic obstruction	0	1 (0.8%)	1 (0.6%)
Microcytic anaemia	0	1 (0.8%)	1 (0.6%)
Neutrophilia	0	1 (0.8%)	1 (0.6%)
Thrombocytosis	1 (2.5%)	0	1 (0.6%)
General disorders and administration site conditions	33 (82.5%)	91 (72.8%)	124 (75.2%)
Injection site erythema	15 (37.5%)	27 (21.6%)	42 (25.5%)
Fatigue	16 (40.0%)	25 (20.0%)	41 (24.8%)
Pyrexia	5 (12.5%)	24 (19.2%)	29 (17.6%)
Oedema peripheral	5 (12.5%)	10 (8.0%)	15 (9.1%)
Asthenia	1 (2.5%)	13 (10.4%)	14 (8.5%)
Injection site pruritus	4 (10.0%)	8 (6.4%)	12 (7.3%)
Injection site rash	3 (7.5%)	7 (5.6%)	10 (6.1%)
Chills	1 (2.5%)	8 (6.4%)	9 (5.5%)
General physical health deterioration	2 (5.0%)	7 (5.6%)	9 (5.5%)
Pain	2 (5.0%)	5 (4.0%)	7 (4.2%)
Non-cardiac chest pain	0	6 (4.8%)	6 (3.6%)
Gait disturbance	0	5 (4.0%)	5 (3.0%)
Malaise	2 (5.0%)	3 (2.4%)	5 (3.0%)
Influenza like illness	0	4 (3.2%)	4 (2.4%)
Chest pain	1 (2.5%)	2 (1.6%)	3 (1.8%)
Injection site bruising	0	3 (2.4%)	3 (1.8%)
Injection site swelling	0	3 (2.4%)	3 (1.8%)
Injection site inflammation	2 (5.0%)	0	2 (1.2%)
Injection site oedema	1 (2.5%)	1 (0.8%)	2 (1.2%)
Application site erythema	0	1 (0.8%)	1 (0.6%)
Catheter site erythema	1 (2.5%)	0	1 (0.6%)
Catheter site haematoma	1 (2.5%)	0	1 (0.6%)
Catheter site pain	0	1 (0.8%)	1 (0.6%)
Early satiety	1 (2.5%)	0	1 (0.6%)
Face oedema	0	1 (0.8%)	1 (0.6%)
Hernia	1 (2.5%)	0	1 (0.6%)
Inflammation	0	1 (0.8%)	1 (0.6%)
Injection site discomfort	0	1 (0.8%)	1 (0.6%)
Injection site haematoma	0	1 (0.8%)	1 (0.6%)
Injection site induration	0	1 (0.8%)	1 (0.6%)
Injection site reaction	0	1 (0.8%)	1 (0.6%)
Mucosal inflammation	1 (2.5%)	0	1 (0.6%)

Study 64007957MMY1001 (Pivotal RP2D):	Number of Subjects With Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set		
	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Multiple organ dysfunction syndrome	0	1 (0.8%)	1 (0.6%)
Organ failure	0	1 (0.8%)	1 (0.6%)
Peripheral swelling	0	1 (0.8%)	1 (0.6%)
Vaccination site discomfort	0	1 (0.8%)	1 (0.6%)
Vaccination site swelling	0	1 (0.8%)	1 (0.6%)
Immune system disorders	29 (72.5%)	92 (73.6%)	121 (73.3%)
Cytokine release syndrome	28 (70.0%)	90 (72.0%)	118 (71.5%)
Hypogammaglobulinaemia	6 (15.0%)	11 (8.8%)	17 (10.3%)
Drug hypersensitivity	0	1 (0.8%)	1 (0.6%)
Infections and infestations	25 (62.5%)	79 (63.2%)	104 (63.0%)
Pneumonia	7 (17.5%)	15 (12.0%)	22 (13.3%)
COVID-19	4 (10.0%)	10 (8.0%)	14 (8.5%)
Upper respiratory tract infection	4 (10.0%)	10 (8.0%)	14 (8.5%)
Bronchitis	3 (7.5%)	7 (5.6%)	10 (6.1%)
Urinary tract infection	3 (7.5%)	6 (4.8%)	9 (5.5%)
Nasopharyngitis	4 (10.0%)	4 (3.2%)	8 (4.8%)
Sinusitis	4 (10.0%)	4 (3.2%)	8 (4.8%)
Infection	1 (2.5%)	5 (4.0%)	6 (3.6%)
Rhinitis	2 (5.0%)	4 (3.2%)	6 (3.6%)
Cellulitis	1 (2.5%)	4 (3.2%)	5 (3.0%)
Pneumocystis jirovecii pneumonia	1 (2.5%)	4 (3.2%)	5 (3.0%)
Oral herpes	0	4 (3.2%)	4 (2.4%)
Conjunctivitis	0	3 (2.4%)	3 (1.8%)
Cystitis	0	3 (2.4%)	3 (1.8%)
Escherichia urinary tract infection	0	3 (2.4%)	3 (1.8%)
Lower respiratory tract infection	0	3 (2.4%)	3 (1.8%)
Oral fungal infection	0	3 (2.4%)	3 (1.8%)
Otitis media	1 (2.5%)	2 (1.6%)	3 (1.8%)
Pseudomonal sepsis	0	3 (2.4%)	3 (1.8%)
Respiratory tract infection	2 (5.0%)	1 (0.8%)	3 (1.8%)
Sepsis	2 (5.0%)	1 (0.8%)	3 (1.8%)
Urinary tract infection bacterial	0	3 (2.4%)	3 (1.8%)
Viral upper respiratory tract infection	2 (5.0%)	1 (0.8%)	3 (1.8%)
Clostridium difficile colitis	0	2 (1.6%)	2 (1.2%)
Cystitis escherichia	0	2 (1.6%)	2 (1.2%)
Enterocolitis infectious	1 (2.5%)	1 (0.8%)	2 (1.2%)
Gastroenteritis	0	2 (1.6%)	2 (1.2%)
Injection site cellulitis	0	2 (1.6%)	2 (1.2%)
Oral candidiasis	0	2 (1.6%)	2 (1.2%)
Pneumonia pseudomonal	0	2 (1.6%)	2 (1.2%)
Pseudomonal bacteraemia	0	2 (1.6%)	2 (1.2%)
Adenovirus infection	0	1 (0.8%)	1 (0.6%)
Adenovirus reactivation	0	1 (0.8%)	1 (0.6%)
Aspergillus infection	0	1 (0.8%)	1 (0.6%)
Asymptomatic COVID-19	1 (2.5%)	0	1 (0.6%)
BK virus infection	0	1 (0.8%)	1 (0.6%)
Bacteraemia	0	1 (0.8%)	1 (0.6%)
Cystitis klebsiella	0	1 (0.8%)	1 (0.6%)
Cytomegalovirus infection reactivation	0	1 (0.8%)	1 (0.6%)
Cytomegalovirus viraemia	0	1 (0.8%)	1 (0.6%)
Diverticulitis	0	1 (0.8%)	1 (0.6%)
Empyema	1 (2.5%)	0	1 (0.6%)
Enterobacter pneumonia	0	1 (0.8%)	1 (0.6%)
Erysipelas	0	1 (0.8%)	1 (0.6%)

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set			
	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Escherichia infection	0	1 (0.8%)	1 (0.6%)
Fungal skin infection	0	1 (0.8%)	1 (0.6%)
Furuncle	1 (2.5%)	0	1 (0.6%)
Hepatitis B reactivation	0	1 (0.8%)	1 (0.6%)
Herpes zoster	1 (2.5%)	0	1 (0.6%)
Impetigo	1 (2.5%)	0	1 (0.6%)
Meningococcal sepsis	0	1 (0.8%)	1 (0.6%)
Metapneumovirus pneumonia	0	1 (0.8%)	1 (0.6%)
Moraxella infection	0	1 (0.8%)	1 (0.6%)
Orchitis	1 (2.5%)	0	1 (0.6%)
Pharyngitis	0	1 (0.8%)	1 (0.6%)
Pneumonia adenoviral	0	1 (0.8%)	1 (0.6%)
Pneumonia klebsiella	0	1 (0.8%)	1 (0.6%)
Pneumonia moraxella	1 (2.5%)	0	1 (0.6%)
Pneumonia pneumococcal	0	1 (0.8%)	1 (0.6%)
Pneumonia respiratory syncytial viral	0	1 (0.8%)	1 (0.6%)
Pneumonia staphylococcal	0	1 (0.8%)	1 (0.6%)
Pneumonia viral	0	1 (0.8%)	1 (0.6%)
Pseudomonas infection	0	1 (0.8%)	1 (0.6%)
Respiratory tract infection bacterial	0	1 (0.8%)	1 (0.6%)
Rhinovirus infection	1 (2.5%)	0	1 (0.6%)
Skin candida	0	1 (0.8%)	1 (0.6%)
Skin infection	0	1 (0.8%)	1 (0.6%)
Staphylococcal bacteraemia	0	1 (0.8%)	1 (0.6%)
Stomatococcal infection	0	1 (0.8%)	1 (0.6%)
Tracheitis	0	1 (0.8%)	1 (0.6%)
Vestibular neuronitis	0	1 (0.8%)	1 (0.6%)
Gastrointestinal disorders	26 (65.0%)	70 (56.0%)	96 (58.2%)
Nausea	15 (37.5%)	25 (20.0%)	40 (24.2%)
Diarrhoea	13 (32.5%)	21 (16.8%)	34 (20.6%)
Constipation	5 (12.5%)	24 (19.2%)	29 (17.6%)
Vomiting	11 (27.5%)	7 (5.6%)	18 (10.9%)
Abdominal pain	1 (2.5%)	4 (3.2%)	5 (3.0%)
Dyspepsia	2 (5.0%)	3 (2.4%)	5 (3.0%)
Stomatitis	3 (7.5%)	2 (1.6%)	5 (3.0%)
Toothache	0	5 (4.0%)	5 (3.0%)
Abdominal pain upper	1 (2.5%)	3 (2.4%)	4 (2.4%)
Abdominal discomfort	1 (2.5%)	2 (1.6%)	3 (1.8%)
Flatulence	2 (5.0%)	1 (0.8%)	3 (1.8%)
Gastroesophageal reflux disease	1 (2.5%)	2 (1.6%)	3 (1.8%)
Odynophagia	0	3 (2.4%)	3 (1.8%)
Abdominal distension	1 (2.5%)	1 (0.8%)	2 (1.2%)
Dry mouth	0	2 (1.6%)	2 (1.2%)
Mouth ulceration	0	2 (1.6%)	2 (1.2%)
Dental caries	0	1 (0.8%)	1 (0.6%)
Food poisoning	1 (2.5%)	0	1 (0.6%)
Gastric ulcer	0	1 (0.8%)	1 (0.6%)
Gastritis	0	1 (0.8%)	1 (0.6%)
Gastrointestinal wall thickening	0	1 (0.8%)	1 (0.6%)
Haemoperitoneum	0	1 (0.8%)	1 (0.6%)
Haemorrhoidal haemorrhage	0	1 (0.8%)	1 (0.6%)
Haemorrhoids	0	1 (0.8%)	1 (0.6%)
Hypoaesthesia oral	0	1 (0.8%)	1 (0.6%)
Impaired gastric emptying	0	1 (0.8%)	1 (0.6%)
Irritable bowel syndrome	1 (2.5%)	0	1 (0.6%)
Lip blister	0	1 (0.8%)	1 (0.6%)
Lip swelling	0	1 (0.8%)	1 (0.6%)

Study 64007957MMY1001 (Pivotal RP2D):		Number of Subjects With Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set		
	RP2D			
	Phase 1	Phase 2 Cohort A	Total	
Lip ulceration	0	1 (0.8%)	1 (0.6%)	
Lower gastrointestinal				
haemorrhage	1 (2.5%)	0	1 (0.6%)	
Melaena	1 (2.5%)	0	1 (0.6%)	
Mouth haemorrhage	1 (2.5%)	0	1 (0.6%)	
Obstructive pancreatitis	1 (2.5%)	0	1 (0.6%)	
Paraesthesia oral	0	1 (0.8%)	1 (0.6%)	
Swollen tongue	0	1 (0.8%)	1 (0.6%)	
Tongue dry	1 (2.5%)	0	1 (0.6%)	
Musculoskeletal and connective				
tissue disorders	20 (50.0%)	70 (56.0%)	90 (54.5%)	
Bone pain	7 (17.5%)	19 (15.2%)	26 (15.8%)	
Arthralgia	7 (17.5%)	18 (14.4%)	25 (15.2%)	
Back pain	4 (10.0%)	21 (16.8%)	25 (15.2%)	
Pain in extremity	5 (12.5%)	13 (10.4%)	18 (10.9%)	
Musculoskeletal chest pain	7 (17.5%)	9 (7.2%)	16 (9.7%)	
Myalgia	3 (7.5%)	9 (7.2%)	12 (7.3%)	
Muscle spasms	3 (7.5%)	6 (4.8%)	9 (5.5%)	
Pain in jaw	2 (5.0%)	4 (3.2%)	6 (3.6%)	
Muscular weakness	0	5 (4.0%)	5 (3.0%)	
Neck pain	1 (2.5%)	4 (3.2%)	5 (3.0%)	
Fracture pain	0	2 (1.6%)	2 (1.2%)	
Joint range of motion decreased	2 (5.0%)	0	2 (1.2%)	
Musculoskeletal pain	0	2 (1.6%)	2 (1.2%)	
Arthritis	0	1 (0.8%)	1 (0.6%)	
Flank pain	1 (2.5%)	0	1 (0.6%)	
Foot deformity	1 (2.5%)	0	1 (0.6%)	
Gouty arthritis	0	1 (0.8%)	1 (0.6%)	
Groin pain	0	1 (0.8%)	1 (0.6%)	
Joint stiffness	0	1 (0.8%)	1 (0.6%)	
Muscle discomfort	1 (2.5%)	0	1 (0.6%)	
Muscle rigidity	0	1 (0.8%)	1 (0.6%)	
Osteoarthritis	1 (2.5%)	0	1 (0.6%)	
Osteolysis	0	1 (0.8%)	1 (0.6%)	
Osteoporosis	0	1 (0.8%)	1 (0.6%)	
Pathological fracture	0	1 (0.8%)	1 (0.6%)	
Rotator cuff syndrome	1 (2.5%)	0	1 (0.6%)	
Metabolism and nutrition disorders	18 (45.0%)	70 (56.0%)	88 (53.3%)	
Hypophosphataemia	4 (10.0%)	17 (13.6%)	21 (12.7%)	
Hypomagnesaemia	4 (10.0%)	16 (12.8%)	20 (12.1%)	
Hypokalaemia	5 (12.5%)	14 (11.2%)	19 (11.5%)	
Decreased appetite	4 (10.0%)	14 (11.2%)	18 (10.9%)	
Hypercalcaemia	4 (10.0%)	14 (11.2%)	18 (10.9%)	
Hypocalcaemia	2 (5.0%)	10 (8.0%)	12 (7.3%)	
Hyponatraemia	1 (2.5%)	11 (8.8%)	12 (7.3%)	
Hyperglycaemia	2 (5.0%)	9 (7.2%)	11 (6.7%)	
Hyperkalaemia	1 (2.5%)	6 (4.8%)	7 (4.2%)	
Hyperuricaemia	1 (2.5%)	6 (4.8%)	7 (4.2%)	
Hyperamylasaemia	1 (2.5%)	5 (4.0%)	6 (3.6%)	
Dehydration	1 (2.5%)	3 (2.4%)	4 (2.4%)	
Fluid overload	0	4 (3.2%)	4 (2.4%)	
Hypoalbuminaemia	0	4 (3.2%)	4 (2.4%)	
Iron deficiency	1 (2.5%)	2 (1.6%)	3 (1.8%)	
Folate deficiency	1 (2.5%)	1 (0.8%)	2 (1.2%)	
Hyperphosphataemia	1 (2.5%)	1 (0.8%)	2 (1.2%)	
Fluid retention	0	1 (0.8%)	1 (0.6%)	
Hypercholesterolaemia	1 (2.5%)	0	1 (0.6%)	
Hyperlactacidaemia	0	1 (0.8%)	1 (0.6%)	
Hyperlipidaemia	0	1 (0.8%)	1 (0.6%)	

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set			
	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Hyperproteinaemia	0	1 (0.8%)	1 (0.6%)
Hypertriglyceridaemia	0	1 (0.8%)	1 (0.6%)
Hypoglycaemia	1 (2.5%)	0	1 (0.6%)
Malnutrition	0	1 (0.8%)	1 (0.6%)
Tumour lysis syndrome	0	1 (0.8%)	1 (0.6%)
Vitamin B12 deficiency	1 (2.5%)	0	1 (0.6%)
Nervous system disorders	21 (52.5%)	48 (38.4%)	69 (41.8%)
Headache	10 (25.0%)	26 (20.8%)	36 (21.8%)
Hypoesthesia	3 (7.5%)	5 (4.0%)	8 (4.8%)
Dizziness	3 (7.5%)	4 (3.2%)	7 (4.2%)
Peripheral sensory neuropathy	1 (2.5%)	4 (3.2%)	5 (3.0%)
Tremor	2 (5.0%)	3 (2.4%)	5 (3.0%)
Immune effector cell-associated neurotoxicity syndrome	0	4 (3.2%)	4 (2.4%)
Paraesthesia	4 (10.0%)	0	4 (2.4%)
Presyncope	3 (7.5%)	1 (0.8%)	4 (2.4%)
Dysgeusia	2 (5.0%)	1 (0.8%)	3 (1.8%)
Sciatica	1 (2.5%)	2 (1.6%)	3 (1.8%)
Somnolence	1 (2.5%)	2 (1.6%)	3 (1.8%)
Lethargy	1 (2.5%)	1 (0.8%)	2 (1.2%)
Anosmia	0	1 (0.8%)	1 (0.6%)
Carpal tunnel syndrome	0	1 (0.8%)	1 (0.6%)
Cogwheel rigidity	0	1 (0.8%)	1 (0.6%)
Depressed level of consciousness	0	1 (0.8%)	1 (0.6%)
Dysaesthesia	0	1 (0.8%)	1 (0.6%)
Hypokinesia	0	1 (0.8%)	1 (0.6%)
Memory impairment	0	1 (0.8%)	1 (0.6%)
Neuralgia	0	1 (0.8%)	1 (0.6%)
Peroneal nerve palsy	0	1 (0.8%)	1 (0.6%)
Psychomotor hyperactivity	0	1 (0.8%)	1 (0.6%)
Restless legs syndrome	1 (2.5%)	0	1 (0.6%)
Sedation	0	1 (0.8%)	1 (0.6%)
Spinal cord compression	0	1 (0.8%)	1 (0.6%)
Vlth nerve paralysis	0	1 (0.8%)	1 (0.6%)
Respiratory, thoracic and mediastinal disorders	17 (42.5%)	45 (36.0%)	62 (37.6%)
Cough	6 (15.0%)	15 (12.0%)	21 (12.7%)
Dyspnoea	5 (12.5%)	7 (5.6%)	12 (7.3%)
Hypoxia	1 (2.5%)	10 (8.0%)	11 (6.7%)
Epistaxis	4 (10.0%)	4 (3.2%)	8 (4.8%)
Oropharyngeal pain	2 (5.0%)	4 (3.2%)	6 (3.6%)
Dysphonia	1 (2.5%)	4 (3.2%)	5 (3.0%)
Productive cough	2 (5.0%)	2 (1.6%)	4 (2.4%)
Hiccups	0	3 (2.4%)	3 (1.8%)
Nasal congestion	2 (5.0%)	1 (0.8%)	3 (1.8%)
Pleural effusion	1 (2.5%)	2 (1.6%)	3 (1.8%)
Pulmonary embolism	1 (2.5%)	2 (1.6%)	3 (1.8%)
Acute respiratory failure	0	2 (1.6%)	2 (1.2%)
Immune-mediated lung disease	1 (2.5%)	1 (0.8%)	2 (1.2%)
Respiratory distress	0	2 (1.6%)	2 (1.2%)
Rhinorrhoea	1 (2.5%)	1 (0.8%)	2 (1.2%)
Sneezing	1 (2.5%)	1 (0.8%)	2 (1.2%)
Acute respiratory distress syndrome	0	1 (0.8%)	1 (0.6%)
Allergic cough	0	1 (0.8%)	1 (0.6%)
Asthmatic crisis	0	1 (0.8%)	1 (0.6%)
Atelectasis	1 (2.5%)	0	1 (0.6%)
Dyspnoea exertional	1 (2.5%)	0	1 (0.6%)
Increased bronchial secretion	0	1 (0.8%)	1 (0.6%)

Study 64007957MMY1001 (Pivotal RP2D):		Number of Subjects With Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set		
		RP2D		
		Phase 1	Phase 2 Cohort A	Total
Lung opacity		0	1 (0.8%)	1 (0.6%)
Nasal dryness		0	1 (0.8%)	1 (0.6%)
Pneumothorax		0	1 (0.8%)	1 (0.6%)
Rhinitis allergic		1 (2.5%)	0	1 (0.6%)
Rhonchi		0	1 (0.8%)	1 (0.6%)
Sinus congestion		0	1 (0.8%)	1 (0.6%)
Sleep apnoea syndrome		0	1 (0.8%)	1 (0.6%)
Upper-airway cough syndrome		1 (2.5%)	0	1 (0.6%)
Investigations		17 (42.5%)	41 (32.8%)	58 (35.2%)
Blood alkaline phosphatase increased		3 (7.5%)	15 (12.0%)	18 (10.9%)
Gamma-glutamyltransferase increased		3 (7.5%)	11 (8.8%)	14 (8.5%)
Alanine aminotransferase increased		3 (7.5%)	7 (5.6%)	10 (6.1%)
Weight decreased		4 (10.0%)	4 (3.2%)	8 (4.8%)
Blood creatinine increased		2 (5.0%)	5 (4.0%)	7 (4.2%)
Lipase increased		2 (5.0%)	5 (4.0%)	7 (4.2%)
Weight increased		2 (5.0%)	5 (4.0%)	7 (4.2%)
Aspartate aminotransferase increased		2 (5.0%)	3 (2.4%)	5 (3.0%)
C-reactive protein increased		0	4 (3.2%)	4 (2.4%)
Blood lactate dehydrogenase increased		1 (2.5%)	2 (1.6%)	3 (1.8%)
Plasma cells increased		0	2 (1.6%)	2 (1.2%)
Troponin increased		0	2 (1.6%)	2 (1.2%)
Blood creatine phosphokinase increased		0	1 (0.8%)	1 (0.6%)
Blood phosphorus increased		1 (2.5%)	0	1 (0.6%)
Blood thyroid stimulating hormone increased		0	1 (0.8%)	1 (0.6%)
Body temperature increased		1 (2.5%)	0	1 (0.6%)
International normalised ratio increased		1 (2.5%)	0	1 (0.6%)
Monocyte count increased		0	1 (0.8%)	1 (0.6%)
Vascular disorders		9 (22.5%)	33 (26.4%)	42 (25.5%)
Hypertension		1 (2.5%)	17 (13.6%)	18 (10.9%)
Hypotension		4 (10.0%)	6 (4.8%)	10 (6.1%)
Hot flush		2 (5.0%)	2 (1.6%)	4 (2.4%)
Haematoma		1 (2.5%)	2 (1.6%)	3 (1.8%)
Flushing		1 (2.5%)	1 (0.8%)	2 (1.2%)
Venous thrombosis limb		0	2 (1.6%)	2 (1.2%)
Deep vein thrombosis		0	1 (0.8%)	1 (0.6%)
Essential hypertension		0	1 (0.8%)	1 (0.6%)
Peripheral embolism		0	1 (0.8%)	1 (0.6%)
Phlebitis		0	1 (0.8%)	1 (0.6%)
Superior vena cava occlusion		0	1 (0.8%)	1 (0.6%)
Thrombophlebitis		0	1 (0.8%)	1 (0.6%)
Thrombophlebitis superficial		1 (2.5%)	0	1 (0.6%)
Renal and urinary disorders		6 (15.0%)	30 (24.0%)	36 (21.8%)
Acute kidney injury		3 (7.5%)	10 (8.0%)	13 (7.9%)
Dysuria		2 (5.0%)	5 (4.0%)	7 (4.2%)
Haematuria		0	6 (4.8%)	6 (3.6%)
Renal impairment		0	6 (4.8%)	6 (3.6%)
Hydronephrosis		0	2 (1.6%)	2 (1.2%)
Nephrolithiasis		0	2 (1.6%)	2 (1.2%)
Pollakiuria		1 (2.5%)	1 (0.8%)	2 (1.2%)
Urinary retention		0	2 (1.6%)	2 (1.2%)
Chronic kidney disease		0	1 (0.8%)	1 (0.6%)

Study 64007957MMY1001 (Pivotal RP2D):		Number of Subjects With Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set		
	RP2D			
	Phase 1	Phase 2 Cohort A	Total	
Micturition urgency	1 (2.5%)	0	1 (0.6%)	
Myeloma cast nephropathy	0	1 (0.8%)	1 (0.6%)	
Renal cyst	0	1 (0.8%)	1 (0.6%)	
Urinary hesitation	0	1 (0.8%)	1 (0.6%)	
Psychiatric disorders	13 (32.5%)	20 (16.0%)	33 (20.0%)	
Confusional state	5 (12.5%)	6 (4.8%)	11 (6.7%)	
Insomnia	4 (10.0%)	6 (4.8%)	10 (6.1%)	
Anxiety	1 (2.5%)	5 (4.0%)	6 (3.6%)	
Agitation	0	2 (1.6%)	2 (1.2%)	
Delirium	0	2 (1.6%)	2 (1.2%)	
Depression	2 (5.0%)	0	2 (1.2%)	
Apathy	0	1 (0.8%)	1 (0.6%)	
Hallucination	1 (2.5%)	0	1 (0.6%)	
Libido disorder	0	1 (0.8%)	1 (0.6%)	
Skin and subcutaneous tissue disorders	10 (25.0%)	17 (13.6%)	27 (16.4%)	
Night sweats	2 (5.0%)	4 (3.2%)	6 (3.6%)	
Pruritus	1 (2.5%)	4 (3.2%)	5 (3.0%)	
Hyperhidrosis	2 (5.0%)	2 (1.6%)	4 (2.4%)	
Rash	2 (5.0%)	2 (1.6%)	4 (2.4%)	
Actinic keratosis	0	2 (1.6%)	2 (1.2%)	
Alopecia	2 (5.0%)	0	2 (1.2%)	
Dry skin	0	2 (1.6%)	2 (1.2%)	
Rash pruritic	1 (2.5%)	1 (0.8%)	2 (1.2%)	
Blister	0	1 (0.8%)	1 (0.6%)	
Decubitus ulcer	0	1 (0.8%)	1 (0.6%)	
Drug eruption	1 (2.5%)	0	1 (0.6%)	
Eczema	1 (2.5%)	0	1 (0.6%)	
Erythema	1 (2.5%)	0	1 (0.6%)	
Ingrowing nail	0	1 (0.8%)	1 (0.6%)	
Onychomadesis	1 (2.5%)	0	1 (0.6%)	
Petechiae	0	1 (0.8%)	1 (0.6%)	
Rash maculo-papular	0	1 (0.8%)	1 (0.6%)	
Injury, poisoning and procedural complications	7 (17.5%)	15 (12.0%)	22 (13.3%)	
Fall	2 (5.0%)	4 (3.2%)	6 (3.6%)	
Contusion	1 (2.5%)	4 (3.2%)	5 (3.0%)	
Clavicle fracture	0	2 (1.6%)	2 (1.2%)	
Femur fracture	0	2 (1.6%)	2 (1.2%)	
Rib fracture	1 (2.5%)	1 (0.8%)	2 (1.2%)	
Drain site complication	1 (2.5%)	0	1 (0.6%)	
Gastrostomy failure	0	1 (0.8%)	1 (0.6%)	
Humerus fracture	0	1 (0.8%)	1 (0.6%)	
Infusion related reaction	1 (2.5%)	0	1 (0.6%)	
Ligament sprain	0	1 (0.8%)	1 (0.6%)	
Limb injury	1 (2.5%)	0	1 (0.6%)	
Muscle contusion	0	1 (0.8%)	1 (0.6%)	
Procedural pain	0	1 (0.8%)	1 (0.6%)	
Scapula fracture	0	1 (0.8%)	1 (0.6%)	
Subdural haematoma	0	1 (0.8%)	1 (0.6%)	
Tooth fracture	0	1 (0.8%)	1 (0.6%)	
Vaccination complication	0	1 (0.8%)	1 (0.6%)	
Cardiac disorders	7 (17.5%)	10 (8.0%)	17 (10.3%)	
Sinus tachycardia	3 (7.5%)	6 (4.8%)	9 (5.5%)	
Cardiac arrest	0	2 (1.6%)	2 (1.2%)	
Sinus bradycardia	2 (5.0%)	0	2 (1.2%)	
Angina pectoris	0	1 (0.8%)	1 (0.6%)	
Atrial flutter	0	1 (0.8%)	1 (0.6%)	
Cardiac failure	1 (2.5%)	0	1 (0.6%)	

Study 64007957MMY1001 (Pivotal RP2D):		Number of Subjects With Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set		
	RP2D			
	Phase 1	Phase 2 Cohort A	Total	
Left ventricular failure	0	1 (0.8%)	1 (0.6%)	
Supraventricular tachycardia	1 (2.5%)	0	1 (0.6%)	
Tachycardia	1 (2.5%)	0	1 (0.6%)	
Ventricular tachycardia	0	1 (0.8%)	1 (0.6%)	
Eye disorders	5 (12.5%)	6 (4.8%)	11 (6.7%)	
Vision blurred	2 (5.0%)	2 (1.6%)	4 (2.4%)	
Amaurosis fugax	0	1 (0.8%)	1 (0.6%)	
Blepharitis	1 (2.5%)	0	1 (0.6%)	
Cataract	1 (2.5%)	0	1 (0.6%)	
Conjunctival haemorrhage	0	1 (0.8%)	1 (0.6%)	
Diplopia	1 (2.5%)	0	1 (0.6%)	
Dry eye	0	1 (0.8%)	1 (0.6%)	
Exophthalmos	1 (2.5%)	0	1 (0.6%)	
Eyelid ptosis	1 (2.5%)	0	1 (0.6%)	
Photopsia	1 (2.5%)	0	1 (0.6%)	
Retinal detachment	0	1 (0.8%)	1 (0.6%)	
Retinal tear	0	1 (0.8%)	1 (0.6%)	
Vitreous floaters	0	1 (0.8%)	1 (0.6%)	
Hepatobiliary disorders	4 (10.0%)	7 (5.6%)	11 (6.7%)	
Hyperbilirubinaemia	3 (7.5%)	2 (1.6%)	5 (3.0%)	
Hepatic cytolysis	0	4 (3.2%)	4 (2.4%)	
Cholestasis	0	2 (1.6%)	2 (1.2%)	
Cholecystitis acute	0	1 (0.8%)	1 (0.6%)	
Cholelithiasis	1 (2.5%)	0	1 (0.6%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (2.5%)	9 (7.2%)	10 (6.1%)	
Seborrhoeic keratosis	0	2 (1.6%)	2 (1.2%)	
Basal cell carcinoma	0	1 (0.8%)	1 (0.6%)	
Leptomeningeal myelomatosis	0	1 (0.8%)	1 (0.6%)	
Malignant pleural effusion	0	1 (0.8%)	1 (0.6%)	
Plasma cell leukaemia	0	1 (0.8%)	1 (0.6%)	
Skin papilloma	1 (2.5%)	0	1 (0.6%)	
Transitional cell carcinoma	0	1 (0.8%)	1 (0.6%)	
Tumour obstruction	0	1 (0.8%)	1 (0.6%)	
Tumour pain	0	1 (0.8%)	1 (0.6%)	
Ear and labyrinth disorders	1 (2.5%)	4 (3.2%)	5 (3.0%)	
Vertigo	0	2 (1.6%)	2 (1.2%)	
Deafness unilateral	1 (2.5%)	0	1 (0.6%)	
Ear pain	0	1 (0.8%)	1 (0.6%)	
Hypoacusis	0	1 (0.8%)	1 (0.6%)	
Endocrine disorders	0	3 (2.4%)	3 (1.8%)	
Adrenal insufficiency	0	1 (0.8%)	1 (0.6%)	
Hypothyroidism	0	1 (0.8%)	1 (0.6%)	
Inappropriate antidiuretic hormone secretion	0	1 (0.8%)	1 (0.6%)	
Reproductive system and breast disorders	1 (2.5%)	2 (1.6%)	3 (1.8%)	
Balanoposthitis	0	1 (0.8%)	1 (0.6%)	
Benign prostatic hyperplasia	0	1 (0.8%)	1 (0.6%)	
Erectile dysfunction	1 (2.5%)	0	1 (0.6%)	
Prostatitis	0	1 (0.8%)	1 (0.6%)	
Product issues	1 (2.5%)	0	1 (0.6%)	
Thrombosis in device	1 (2.5%)	0	1 (0.6%)	

Study 64007957MMY1001 (Pivotal RP2D):	Number of Subjects With Treatment-emergent Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set		
	RP2D		
	Phase 1	Phase 2 Cohort A	Total

Key: TEAE = treatment-emergent adverse event; RP2D = recommended Phase 2 dose; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome

Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 24.0.

Note: The output includes the diagnosis of CRS and ICANS; the symptoms of CRS or ICANS are excluded

Note: Percentages calculated with the number of subjects in the all treated analysis set as denominator.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

[TSFAE02RP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFAE02RP2D.SAS] 04NOV2021, 11:57

Study 64007957MMY1001 (Pivotal RP2D): Summary of Deaths and Cause of Death; All Treated Analysis Set

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Total number of subjects who died during study	10 (25.0%)	30 (24.0%)	40 (24.2%)
Primary cause of death			
Adverse event	0	9 (7.2%)	9 (5.5%)
Study drug related ^a	0	0	0
AE(s) unrelated	0	9 (7.2%)	9 (5.5%)
Adverse event - COVID-19	0	7 (5.6%)	7 (4.2%)
Disease progression	9 (22.5%)	21 (16.8%)	30 (18.2%)
Other	1 (2.5%)	0	1 (0.6%)
Other - COVID-19 related	0	0	0
Total number of subjects who died within 30 days of last study treatment dose	2 (5.0%)	18 (14.4%)	20 (12.1%)
Primary cause of death			
Adverse event	0	6 (4.8%)	6 (3.6%)
Study drug related ^a	0	0	0
AE(s) unrelated	0	6 (4.8%)	6 (3.6%)
Adverse event - COVID-19	0	4 (3.2%)	4 (2.4%)
Disease progression	1 (2.5%)	12 (9.6%)	13 (7.9%)
Other	1 (2.5%)	0	1 (0.6%)
Other - COVID-19 related	0	0	0
Total number of subjects who died within 60 days of first study treatment dose	2 (5.0%)	16 (12.8%)	18 (10.9%)
Primary cause of death			
Adverse event	0	6 (4.8%)	6 (3.6%)
Study drug related ^a	0	0	0
AE(s) unrelated	0	6 (4.8%)	6 (3.6%)
Adverse event - COVID-19	0	4 (3.2%)	4 (2.4%)
Disease progression	1 (2.5%)	10 (8.0%)	11 (6.7%)
Other	1 (2.5%)	0	1 (0.6%)
Other - COVID-19 related	0	0	0

Key: AE = adverse event; RP2D = recommended Phase 2 dose

^a Related if assessed by the investigator as possibly, probably, or very likely related to study agent.

Note: Percentages calculated with the number of subjects in the all treated analysis set as denominator.

[TSFDTH01RP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFDTH01RP2D.SAS] 07OCT2021, 21:36

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Serious Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Subjects with 1 or more serious TEAE	19 (47.5%)	69 (55.2%)	88 (53.3%)
MedDRA system organ class / preferred term			
Infections and infestations	12 (30.0%)	37 (29.6%)	49 (29.7%)
COVID-19	3 (7.5%)	9 (7.2%)	12 (7.3%)
Pneumonia	4 (10.0%)	7 (5.6%)	11 (6.7%)
Pneumocystis jirovecii pneumonia	1 (2.5%)	3 (2.4%)	4 (2.4%)
Cellulitis	1 (2.5%)	2 (1.6%)	3 (1.8%)
Pseudomonal sepsis	0	3 (2.4%)	3 (1.8%)
Sepsis	2 (5.0%)	1 (0.8%)	3 (1.8%)
Enterocolitis infectious	1 (2.5%)	1 (0.8%)	2 (1.2%)
Infection	1 (2.5%)	1 (0.8%)	2 (1.2%)
Pseudomonal bacteraemia	0	2 (1.6%)	2 (1.2%)
Sinusitis	1 (2.5%)	1 (0.8%)	2 (1.2%)
Adenovirus infection	0	1 (0.8%)	1 (0.6%)
Bacteraemia	0	1 (0.8%)	1 (0.6%)
Clostridium difficile colitis	0	1 (0.8%)	1 (0.6%)
Cystitis escherichia	0	1 (0.8%)	1 (0.6%)
Empyema	1 (2.5%)	0	1 (0.6%)
Erysipelas	0	1 (0.8%)	1 (0.6%)
Escherichia urinary tract infection	0	1 (0.8%)	1 (0.6%)
Hepatitis B reactivation	0	1 (0.8%)	1 (0.6%)
Injection site cellulitis	0	1 (0.8%)	1 (0.6%)
Meningococcal sepsis	0	1 (0.8%)	1 (0.6%)
Metapneumovirus pneumonia	0	1 (0.8%)	1 (0.6%)
Pneumonia adenoviral	0	1 (0.8%)	1 (0.6%)
Pneumonia moraxella	1 (2.5%)	0	1 (0.6%)
Pneumonia respiratory syncytial viral	0	1 (0.8%)	1 (0.6%)
Pneumonia viral	0	1 (0.8%)	1 (0.6%)
Pseudomonas infection	0	1 (0.8%)	1 (0.6%)
Respiratory tract infection bacterial	0	1 (0.8%)	1 (0.6%)
Urinary tract infection	1 (2.5%)	0	1 (0.6%)
Vestibular neuronitis	0	1 (0.8%)	1 (0.6%)
General disorders and administration site conditions	3 (7.5%)	14 (11.2%)	17 (10.3%)
General physical health deterioration	2 (5.0%)	7 (5.6%)	9 (5.5%)
Pyrexia	1 (2.5%)	4 (3.2%)	5 (3.0%)
Chills	0	1 (0.8%)	1 (0.6%)
Fatigue	0	1 (0.8%)	1 (0.6%)
Multiple organ dysfunction syndrome	0	1 (0.8%)	1 (0.6%)
Organ failure	0	1 (0.8%)	1 (0.6%)
Immune system disorders	2 (5.0%)	11 (8.8%)	13 (7.9%)
Cytokine release syndrome	2 (5.0%)	11 (8.8%)	13 (7.9%)
Musculoskeletal and connective tissue disorders	1 (2.5%)	10 (8.0%)	11 (6.7%)
Bone pain	0	3 (2.4%)	3 (1.8%)
Musculoskeletal chest pain	0	2 (1.6%)	2 (1.2%)
Back pain	1 (2.5%)	0	1 (0.6%)
Fracture pain	0	1 (0.8%)	1 (0.6%)
Muscle rigidity	0	1 (0.8%)	1 (0.6%)
Osteolysis	0	1 (0.8%)	1 (0.6%)
Pain in extremity	0	1 (0.8%)	1 (0.6%)
Pathological fracture	0	1 (0.8%)	1 (0.6%)
Renal and urinary disorders	1 (2.5%)	8 (6.4%)	9 (5.5%)
Acute kidney injury	1 (2.5%)	7 (5.6%)	8 (4.8%)
Myeloma cast nephropathy	0	1 (0.8%)	1 (0.6%)

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Serious Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Respiratory, thoracic and mediastinal disorders	1 (2.5%)	8 (6.4%)	9 (5.5%)
Hypoxia	0	3 (2.4%)	3 (1.8%)
Immune-mediated lung disease	1 (2.5%)	1 (0.8%)	2 (1.2%)
Respiratory distress	0	2 (1.6%)	2 (1.2%)
Acute respiratory failure	0	1 (0.8%)	1 (0.6%)
Cough	0	1 (0.8%)	1 (0.6%)
Pleural effusion	0	1 (0.8%)	1 (0.6%)
Blood and lymphatic system disorders	1 (2.5%)	5 (4.0%)	6 (3.6%)
Febrile neutropenia	0	3 (2.4%)	3 (1.8%)
Hyperviscosity syndrome	1 (2.5%)	1 (0.8%)	2 (1.2%)
Anaemia	0	1 (0.8%)	1 (0.6%)
Neutropenia	0	1 (0.8%)	1 (0.6%)
Gastrointestinal disorders	2 (5.0%)	4 (3.2%)	6 (3.6%)
Diarrhoea	1 (2.5%)	2 (1.6%)	3 (1.8%)
Abdominal pain	0	1 (0.8%)	1 (0.6%)
Haemoperitoneum	0	1 (0.8%)	1 (0.6%)
Impaired gastric emptying	0	1 (0.8%)	1 (0.6%)
Nausea	0	1 (0.8%)	1 (0.6%)
Obstructive pancreatitis	1 (2.5%)	0	1 (0.6%)
Nervous system disorders	2 (5.0%)	4 (3.2%)	6 (3.6%)
Presyncope	1 (2.5%)	1 (0.8%)	2 (1.2%)
Cogwheel rigidity	0	1 (0.8%)	1 (0.6%)
Dizziness	1 (2.5%)	0	1 (0.6%)
Hypokinesia	0	1 (0.8%)	1 (0.6%)
Lethargy	0	1 (0.8%)	1 (0.6%)
Sciatica	0	1 (0.8%)	1 (0.6%)
Spinal cord compression	0	1 (0.8%)	1 (0.6%)
Tremor	0	1 (0.8%)	1 (0.6%)
Metabolism and nutrition disorders	0	5 (4.0%)	5 (3.0%)
Hypercalcaemia	0	3 (2.4%)	3 (1.8%)
Hyponatraemia	0	1 (0.8%)	1 (0.6%)
Tumour lysis syndrome	0	1 (0.8%)	1 (0.6%)
Injury, poisoning and procedural complications	0	4 (3.2%)	4 (2.4%)
Clavicle fracture	0	1 (0.8%)	1 (0.6%)
Fall	0	1 (0.8%)	1 (0.6%)
Gastrostomy failure	0	1 (0.8%)	1 (0.6%)
Humerus fracture	0	1 (0.8%)	1 (0.6%)
Subdural haematoma	0	1 (0.8%)	1 (0.6%)
Psychiatric disorders	1 (2.5%)	3 (2.4%)	4 (2.4%)
Confusional state	1 (2.5%)	2 (1.6%)	3 (1.8%)
Apathy	0	1 (0.8%)	1 (0.6%)
Cardiac disorders	1 (2.5%)	2 (1.6%)	3 (1.8%)
Cardiac arrest	0	2 (1.6%)	2 (1.2%)
Cardiac failure	1 (2.5%)	0	1 (0.6%)
Eye disorders	2 (5.0%)	0	2 (1.2%)
Diplopia	1 (2.5%)	0	1 (0.6%)
Exophthalmos	1 (2.5%)	0	1 (0.6%)
Eyelid ptosis	1 (2.5%)	0	1 (0.6%)
Vision blurred	1 (2.5%)	0	1 (0.6%)
Hepatobiliary disorders	0	2 (1.6%)	2 (1.2%)
Cholecystitis acute	0	1 (0.8%)	1 (0.6%)
Hepatic cytolysis	0	1 (0.8%)	1 (0.6%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	2 (1.6%)	2 (1.2%)
Transitional cell carcinoma	0	1 (0.8%)	1 (0.6%)
Tumour pain	0	1 (0.8%)	1 (0.6%)
Vascular disorders	0	2 (1.6%)	2 (1.2%)

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Serious Adverse Events by System Organ Class and Preferred Term; All Treated Analysis Set

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Hypotension	0	1 (0.8%)	1 (0.6%)
Superior vena cava occlusion	0	1 (0.8%)	1 (0.6%)
Ear and labyrinth disorders	1 (2.5%)	0	1 (0.6%)
Deafness unilateral	1 (2.5%)	0	1 (0.6%)
Investigations	1 (2.5%)	0	1 (0.6%)
Blood creatinine increased	1 (2.5%)	0	1 (0.6%)

Key: TEAE = treatment-emergent adverse event; RP2D = recommended Phase 2 dose; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome

Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 24.0.

The output includes the diagnosis of CRS and ICANS; the symptoms of CRS or ICANS are excluded.

Note: Percentages calculated with the number of subjects in the all treated analysis set with available data as denominator.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

[TSFAE05RP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFAE05RP2D.SAS] 16OCT2021, 14:10

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Grade 3 or 4 Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug; All Treated Analysis Set

	RP2D					
	Phase 1		Phase 2 Cohort A		Total	
	Total	Related	Total	Related	Total	Related
Analysis set: All Treated	40		125		165	
Subjects with 1 or more grade 3 or 4 TEAEs	36 (90.0%)	30 (75.0%)	116 (92.8%)	92 (73.6%)	152 (92.1%)	122 (73.9%)
MedDRA system organ class / preferred term						
Blood and lymphatic system disorders			104 (83.2%)	89 (71.2%)	137 (83.0%)	117 (70.9%)
Neutropenia	24 (60.0%)	24 (60.0%)	70 (56.0%)	65 (52.0%)	94 (57.0%)	89 (53.9%)
Anaemia	13 (32.5%)	5 (12.5%)	44 (35.2%)	20 (16.0%)	57 (34.5%)	25 (15.2%)
Lymphopenia	5 (12.5%)	5 (12.5%)	48 (38.4%)	36 (28.8%)	53 (32.1%)	41 (24.8%)
Thrombocytopenia	7 (17.5%)	3 (7.5%)	28 (22.4%)	19 (15.2%)	35 (21.2%)	22 (13.3%)
Leukopenia	7 (17.5%)	7 (17.5%)	5 (4.0%)	4 (3.2%)	12 (7.3%)	11 (6.7%)
Febrile neutropenia	0	0	4 (3.2%)	3 (2.4%)	4 (2.4%)	3 (1.8%)
Hyperviscosity syndrome	1 (2.5%)	0	1 (0.8%)	0	2 (1.2%)	0
Leukocytosis	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Infections and infestations	12 (30.0%)	4 (10.0%)	46 (36.8%)	14 (11.2%)	58 (35.2%)	18 (10.9%)
Pneumonia	5 (12.5%)	0	10 (8.0%)	5 (4.0%)	15 (9.1%)	5 (3.0%)
COVID-19	3 (7.5%)	1 (2.5%)	8 (6.4%)	0	11 (6.7%)	1 (0.6%)
Pneumocystis jirovecii pneumonia	1 (2.5%)	1 (2.5%)	4 (3.2%)	3 (2.4%)	5 (3.0%)	4 (2.4%)
Cellulitis	1 (2.5%)	1 (2.5%)	3 (2.4%)	0	4 (2.4%)	1 (0.6%)
Infection	1 (2.5%)	0	2 (1.6%)	0	3 (1.8%)	0
Pseudomonal sepsis	0	0	3 (2.4%)	1 (0.8%)	3 (1.8%)	1 (0.6%)
Sepsis	2 (5.0%)	0	1 (0.8%)	0	3 (1.8%)	0
Urinary tract infection	1 (2.5%)	0	2 (1.6%)	1 (0.8%)	3 (1.8%)	1 (0.6%)
Cystitis	0	0	2 (1.6%)	0	2 (1.2%)	0
Cystitis escherichia	0	0	2 (1.6%)	0	2 (1.2%)	0
Sinusitis	1 (2.5%)	0	1 (0.8%)	0	2 (1.2%)	0
Urinary tract infection bacterial	0	0	2 (1.6%)	1 (0.8%)	2 (1.2%)	1 (0.6%)
Adenovirus infection	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Bacteraemia	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Cytomegalovirus infection reactivation	0	0	1 (0.8%)	0	1 (0.6%)	0
Cytomegalovirus viraemia	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Diverticulitis	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Empyema	1 (2.5%)	1 (2.5%)	0	0	1 (0.6%)	1 (0.6%)
Enterobacter pneumonia	0	0	1 (0.8%)	0	1 (0.6%)	0
Enterocolitis infectious	1 (2.5%)	0	0	0	1 (0.6%)	0
Erysipelas	0	0	1 (0.8%)	0	1 (0.6%)	0
Escherichia infection	0	0	1 (0.8%)	0	1 (0.6%)	0
Escherichia urinary tract infection	0	0	1 (0.8%)	0	1 (0.6%)	0
Hepatitis B reactivation	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Injection site cellulitis	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Lower respiratory tract infection	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Meningococcal sepsis	0	0	1 (0.8%)	0	1 (0.6%)	0

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Grade 3 or 4 Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug; All Treated Analysis Set

	RP2D					
	Phase 1		Phase 2 Cohort A		Total	
	Total	Related	Total	Related	Total	Related
Metapneumovirus pneumonia	0	0	1 (0.8%)	0	1 (0.6%)	0
Moraxella infection	0	0	1 (0.8%)	0	1 (0.6%)	0
Pneumonia adenoviral	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Pneumonia klebsiella	0	0	1 (0.8%)	0	1 (0.6%)	0
Pneumonia moraxella	1 (2.5%)	1 (2.5%)	0	0	1 (0.6%)	1 (0.6%)
Pneumonia pseudomonal	0	0	1 (0.8%)	0	1 (0.6%)	0
Pneumonia staphylococcal	0	0	1 (0.8%)	0	1 (0.6%)	0
Pseudomonal bacteraemia	0	0	1 (0.8%)	0	1 (0.6%)	0
Pseudomonas infection	0	0	1 (0.8%)	0	1 (0.6%)	0
Respiratory tract infection bacterial	0	0	1 (0.8%)	0	1 (0.6%)	0
Staphylococcal bacteraemia	0	0	1 (0.8%)	0	1 (0.6%)	0
Stomatococcal infection	0	0	1 (0.8%)	0	1 (0.6%)	0
Vestibular neuritis	0	0	1 (0.8%)	0	1 (0.6%)	0
Viral upper respiratory tract infection	1 (2.5%)	0	0	0	1 (0.6%)	0
Metabolism and nutrition disorders	8 (20.0%)	1 (2.5%)	31 (24.8%)	8 (6.4%)	39 (23.6%)	9 (5.5%)
Hypophosphataemia	3 (7.5%)	1 (2.5%)	6 (4.8%)	3 (2.4%)	9 (5.5%)	4 (2.4%)
Hyponatraemia	1 (2.5%)	0	7 (5.6%)	1 (0.8%)	8 (4.8%)	1 (0.6%)
Hyperglycaemia	1 (2.5%)	0	5 (4.0%)	1 (0.8%)	6 (3.6%)	1 (0.6%)
Hypokalaemia	1 (2.5%)	1 (2.5%)	5 (4.0%)	2 (1.6%)	6 (3.6%)	3 (1.8%)
Hypercalcaemia	2 (5.0%)	0	3 (2.4%)	0	5 (3.0%)	0
Hyperamylasaemia	1 (2.5%)	0	3 (2.4%)	0	4 (2.4%)	0
Hyperkalaemia	0	0	2 (1.6%)	0	2 (1.2%)	0
Decreased appetite	0	0	1 (0.8%)	0	1 (0.6%)	0
Hyperlactacidaemia	0	0	1 (0.8%)	0	1 (0.6%)	0
Hyperuricaemia	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Hypoalbuminaemia	0	0	1 (0.8%)	0	1 (0.6%)	0
Tumour lysis syndrome	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Musculoskeletal and connective tissue disorders	4 (10.0%)	2 (5.0%)	12 (9.6%)	2 (1.6%)	16 (9.7%)	4 (2.4%)
Bone pain	3 (7.5%)	2 (5.0%)	2 (1.6%)	0	5 (3.0%)	2 (1.2%)
Back pain	0	0	4 (3.2%)	2 (1.6%)	4 (2.4%)	2 (1.2%)
Musculoskeletal chest pain	1 (2.5%)	0	1 (0.8%)	0	2 (1.2%)	0
Arthralgia	1 (2.5%)	0	0	0	1 (0.6%)	0
Fracture pain	0	0	1 (0.8%)	0	1 (0.6%)	0
Gouty arthritis	0	0	1 (0.8%)	0	1 (0.6%)	0
Joint range of motion decreased	1 (2.5%)	0	0	0	1 (0.6%)	0
Osteolysis	0	0	1 (0.8%)	0	1 (0.6%)	0
Pain in extremity	0	0	1 (0.8%)	0	1 (0.6%)	0
Pathological fracture	0	0	1 (0.8%)	0	1 (0.6%)	0
General disorders and administration site conditions	3 (7.5%)	0	8 (6.4%)	1 (0.8%)	11 (6.7%)	1 (0.6%)
General physical health deterioration	2 (5.0%)	0	4 (3.2%)	0	6 (3.6%)	0
Fatigue	1 (2.5%)	0	2 (1.6%)	0	3 (1.8%)	0

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Grade 3 or 4 Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug; All Treated Analysis Set

	RP2D					
	Phase 1		Phase 2 Cohort A		Total	
	Total	Related	Total	Related	Total	Related
Asthenia	0	0	1 (0.8%)	0	1 (0.6%)	0
Multiple organ dysfunction syndrome	0	0	1 (0.8%)	0	1 (0.6%)	0
Pain	0	0	1 (0.8%)	0	1 (0.6%)	0
Pyrexia	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Investigations	3 (7.5%)	0	8 (6.4%)	3 (2.4%)	11 (6.7%)	3 (1.8%)
Gamma-glutamyltransferase increased	2 (5.0%)	0	2 (1.6%)	1 (0.8%)	4 (2.4%)	1 (0.6%)
Blood alkaline phosphatase increased	0	0	3 (2.4%)	2 (1.6%)	3 (1.8%)	2 (1.2%)
Lipase increased	1 (2.5%)	0	1 (0.8%)	0	2 (1.2%)	0
Plasma cells increased	0	0	2 (1.6%)	0	2 (1.2%)	0
Alanine aminotransferase increased	1 (2.5%)	0	0	0	1 (0.6%)	0
Respiratory, thoracic and mediastinal disorders	1 (2.5%)	0	10 (8.0%)	3 (2.4%)	11 (6.7%)	3 (1.8%)
Hypoxia	0	0	3 (2.4%)	0	3 (1.8%)	0
Acute respiratory failure	0	0	2 (1.6%)	1 (0.8%)	2 (1.2%)	1 (0.6%)
Epistaxis	1 (2.5%)	0	1 (0.8%)	1 (0.8%)	2 (1.2%)	1 (0.6%)
Pulmonary embolism	0	0	2 (1.6%)	0	2 (1.2%)	0
Dyspnoea	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Pleural effusion	0	0	1 (0.8%)	0	1 (0.6%)	0
Respiratory distress	0	0	1 (0.8%)	0	1 (0.6%)	0
Gastrointestinal disorders	3 (7.5%)	0	7 (5.6%)	2 (1.6%)	10 (6.1%)	2 (1.2%)
Diarrhoea	2 (5.0%)	0	2 (1.6%)	2 (1.6%)	4 (2.4%)	2 (1.2%)
Abdominal pain	0	0	1 (0.8%)	0	1 (0.6%)	0
Abdominal pain upper	0	0	1 (0.8%)	0	1 (0.6%)	0
Haemoperitoneum	0	0	1 (0.8%)	0	1 (0.6%)	0
Impaired gastric emptying	0	0	1 (0.8%)	0	1 (0.6%)	0
Lower gastrointestinal haemorrhage	1 (2.5%)	0	0	0	1 (0.6%)	0
Nausea	0	0	1 (0.8%)	0	1 (0.6%)	0
Toothache	0	0	1 (0.8%)	0	1 (0.6%)	0
Vomiting	0	0	1 (0.8%)	0	1 (0.6%)	0
Vascular disorders	0	0	9 (7.2%)	3 (2.4%)	9 (5.5%)	3 (1.8%)
Hypertension	0	0	8 (6.4%)	3 (2.4%)	8 (4.8%)	3 (1.8%)
Hypotension	0	0	1 (0.8%)	0	1 (0.6%)	0
Renal and urinary disorders	1 (2.5%)	0	6 (4.8%)	0	7 (4.2%)	0
Acute kidney injury	1 (2.5%)	0	5 (4.0%)	0	6 (3.6%)	0
Myeloma cast nephropathy	0	0	1 (0.8%)	0	1 (0.6%)	0
Injury, poisoning and procedural complications	0	0	4 (3.2%)	0	4 (2.4%)	0
Fall	0	0	2 (1.6%)	0	2 (1.2%)	0
Clavicle fracture	0	0	1 (0.8%)	0	1 (0.6%)	0
Femur fracture	0	0	1 (0.8%)	0	1 (0.6%)	0
Humerus fracture	0	0	1 (0.8%)	0	1 (0.6%)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	0	4 (3.2%)	0	4 (2.4%)	0
Malignant pleural effusion	0	0	1 (0.8%)	0	1 (0.6%)	0

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Grade 3 or 4 Treatment-emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug; All Treated Analysis Set

	RP2D					
	Phase 1		Phase 2 Cohort A		Total	
	Total	Related	Total	Related	Total	Related
Plasma cell leukaemia	0	0	1 (0.8%)	0	1 (0.6%)	0
Transitional cell carcinoma	0	0	1 (0.8%)	0	1 (0.6%)	0
Tumour pain	0	0	1 (0.8%)	0	1 (0.6%)	0
Cardiac disorders	1 (2.5%)	0	2 (1.6%)	0	3 (1.8%)	0
Cardiac arrest	0	0	2 (1.6%)	0	2 (1.2%)	0
Cardiac failure	1 (2.5%)	0	0	0	1 (0.6%)	0
Supraventricular tachycardia	1 (2.5%)	0	0	0	1 (0.6%)	0
Hepatobiliary disorders	0	0	3 (2.4%)	1 (0.8%)	3 (1.8%)	1 (0.6%)
Cholestasis	0	0	2 (1.6%)	1 (0.8%)	2 (1.2%)	1 (0.6%)
Hepatic cytolysis	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Hyperbilirubinaemia	0	0	1 (0.8%)	0	1 (0.6%)	0
Immune system disorders	0	0	3 (2.4%)	2 (1.6%)	3 (1.8%)	2 (1.2%)
Hypogammaglobulinaemia	0	0	2 (1.6%)	1 (0.8%)	2 (1.2%)	1 (0.6%)
Cytokine release syndrome	0	0	1 (0.8%)	1 (0.8%)	1 (0.6%)	1 (0.6%)
Nervous system disorders	0	0	3 (2.4%)	0	3 (1.8%)	0
Headache	0	0	1 (0.8%)	0	1 (0.6%)	0
Sciatica	0	0	1 (0.8%)	0	1 (0.6%)	0
Spinal cord compression	0	0	1 (0.8%)	0	1 (0.6%)	0
Eye disorders	0	0	1 (0.8%)	0	1 (0.6%)	0
Retinal tear	0	0	1 (0.8%)	0	1 (0.6%)	0

Key: TEAE = treatment-emergent adverse event; RP2D = recommended Phase 2 dose; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome

Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 24.0.

Note: The output includes the diagnosis of CRS and ICANS; the symptoms of CRS or ICANS are excluded.

Note: Percentages calculated with the number of subjects in the all treated analysis set as denominator.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

Note: CRS was originally graded by Lee criteria (Lee et al 2014) in Phase 1 and by ASTCT consensus grading system (Lee et al 2019) in Phase 2, with conversion of grade in Phase 1 to ASTCT based on data in eCRF.

Toxicity grade by ASTCT is presented in this table, for both Phase 1 and Phase 2.

[TSFAE13ARP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFAE13ARP2D.SAS] 16OCT2021, 15:27

Study 64007957MMY1001 (Pivotal RP2D): Summary of Treatment-emergent Cytokine Release Syndrome (CRS) Events; All Treated Analysis Set

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Number of subjects with CRS	28 (70.0%)	90 (72.0%)	118 (71.5%)
Maximum toxicity grade			
Grade 1	19 (47.5%)	63 (50.4%)	82 (49.7%)
Grade 2	9 (22.5%)	26 (20.8%)	35 (21.2%)
Grade 3	0	1 (0.8%)	1 (0.6%)
Grade 4	0	0	0
Grade 5	0	0	0
Number of subjects with CRS leading to discontinuation of study drug	0	0	0
Number of subjects with multiple CRS events	12 (30.0%)	42 (33.6%)	54 (32.7%)
Grade of CRS worsened at any subsequent event	0	4 (3.2%)	4 (2.4%)
Number of subjects with supportive measures to treat CRS ^a	28 (70.0%)	81 (64.8%)	109 (66.1%)
Anti-IL6 receptor tocilizumab	16 (40.0%)	44 (35.2%)	60 (36.4%)
Multiple doses at any time during study	1 (2.5%)	4 (3.2%)	5 (3.0%)
>1 dose for a single CRS event	1 (2.5%)	3 (2.4%)	4 (2.4%)
Corticosteroids	5 (12.5%)	8 (6.4%)	13 (7.9%)
IV Fluids	9 (22.5%)	12 (9.6%)	21 (12.7%)
Vasopressor used	0	1 (0.8%)	1 (0.6%)
Single	0	1 (0.8%)	1 (0.6%)
Multiple	0	0	0
Oxygen used	5 (12.5%)	16 (12.8%)	21 (12.7%)
Blow-by	0	0	0
Nasal cannula low flow ($\leq 6\text{L/min}$)	5 (12.5%)	16 (12.8%)	21 (12.7%)
Nasal cannula high flow ($>6\text{L/min}$)	0	0	0
Face mask	0	0	0
Non-Rebreather mask	0	0	0
Venturi mask	0	0	0
Other	0	0	0
Positive pressure	0	0	0
Continuous Positive Airway Pressure	0	0	0
Bilevel Positive Airway Pressure	0	0	0
Intubation/ Mechanical Ventilation	0	0	0
Other	26 (65.0%)	73 (58.4%)	99 (60.0%)
Occurrence of CRS ^b			
Step-up Dose 1	18 (45.0%)	52 (41.6%)	70 (42.4%)
Step-up Dose 2	13 (32.5%)	44 (35.2%)	57 (34.5%)
Repeat Step-up ^c	0	1 (0.8%)	1 (0.6%)
Cycle 1 Day 1	7 (17.5%)	33 (26.4%)	40 (24.2%)
Cycle 1 Day 8	2 (5.0%)	6 (4.8%)	8 (4.8%)
Cycle 1 Day 15	2 (5.0%)	2 (1.6%)	4 (2.4%)
Cycle 1 Day 22	-	2 (1.6%)	2 (1.2%)
Cycle 2+	2 (5.0%)	3 (2.4%)	5 (3.0%)
Time from last injection of Teclistamab to new onset of CRS, hours ^d			
Number of CRS events		133	
Mean (SD)		34.874 (16.6779)	
Median		31.150	
Range		(3.83; 120.50)	

Time from last injection of Teclistamab to new onset of CRS, days			
Number of CRS events	45	145	190
Mean (SD)	2.2 (0.93)	2.5 (0.78)	2.4 (0.82)
Median	2.0	2.0	2.0
Range	(1; 6)	(1; 6)	(1; 6)
Duration of CRS, hours ^d			
Number of CRS events		127	
Mean (SD)		19.941 (22.3309)	
Median		12.000	
Range		(0.33; 151.05)	
Duration of CRS, days			
Number of CRS events	45	147	192
Mean (SD)	2.4 (1.60)	2.0 (1.22)	2.1 (1.32)
Median	2.0	2.0	2.0
Range	(1; 8)	(1; 9)	(1; 9)
Outcome of CRS			
N	45	147	192
Recovered or resolved	45 (100.0%)	147 (100.0%)	192 (100.0%)
Not recovered or not resolved	0	0	0
Recovered or resolved with sequelae	0	0	0
Recovering or resolving	0	0	0
Fatal	0	0	0
Unknown	0	0	0
Missing	0	0	0

Key: CRS = cytokine release syndrome; RP2D = recommended Phase 2 dose

^a Supportive measures to treat CRS and CRS symptoms are included.

^b Subjects may appear in more than one category. Occurrence is based on the last treatment visit on or prior to the day in which the TEAE occurred.

^c Prior to Cycle 1.

^d Hours only displayed for Phase 2, start and end times of CRS events were not collected uniformly in Phase 1.

Note: Percentages calculated with the number of subjects in the all treated analysis set as denominator, except for the outcome of CRS for which percentages are calculated with the number of CRS events in the all-treated analysis set as denominator.

Note: CRS was originally graded by Lee criteria (Lee et al 2014) in Phase 1 and by ASTCT consensus grading system (Lee et al 2019) in Phase 2, with conversion of grade in Phase 1 to ASTCT based on data in eCRF. Toxicity grade by ASTCT is presented in this table, for both Phase 1 and Phase 2.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

Note: Day 8 is not applicable for subjects on a biweekly or monthly dosing schedule, Day 15 is not applicable for subjects on a monthly dosing schedule, and Day 22 is not applicable for subjects on a monthly dosing schedule or Phase 1 subjects on a weekly dosing schedule (21-day cycle).

Note: Time from last injection to new onset is defined as date of last dose – start date of CRS +1. Duration is defined as end date of CRS – start date of CRS +1. For calculating in days, the date is used without time. For hours the date and time is used and those with time portion missing will be excluded.

[TSFAE18RP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFAE18RP2D.SAS] 26OCT2021, 11:46

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Symptoms of Cytokine Release Syndrome (CRS) by System Organ Class and Preferred Term; All Treated Analysis Set

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Subjects with 1 or more TE symptoms of CRS	28 (70.0%)	90 (72.0%)	118 (71.5%)
MedDRA system organ class / preferred term			
General disorders and administration site conditions	28 (70.0%)	90 (72.0%)	118 (71.5%)
Pyrexia	28 (70.0%)	89 (71.2%)	117 (70.9%)
Chills	6 (15.0%)	14 (11.2%)	20 (12.1%)
Fatigue	1 (2.5%)	1 (0.8%)	2 (1.2%)
Respiratory, thoracic and mediastinal disorders	5 (12.5%)	17 (13.6%)	22 (13.3%)
Hypoxia	5 (12.5%)	17 (13.6%)	22 (13.3%)
Tachypnoea	0	1 (0.8%)	1 (0.6%)
Vascular disorders	6 (15.0%)	16 (12.8%)	22 (13.3%)
Hypotension	5 (12.5%)	15 (12.0%)	20 (12.1%)
Capillary leak syndrome	0	1 (0.8%)	1 (0.6%)
Hypertension	1 (2.5%)	0	1 (0.6%)
Cardiac disorders	3 (7.5%)	9 (7.2%)	12 (7.3%)
Sinus tachycardia	3 (7.5%)	9 (7.2%)	12 (7.3%)
Nervous system disorders	7 (17.5%)	4 (3.2%)	11 (6.7%)
Headache	7 (17.5%)	4 (3.2%)	11 (6.7%)
Investigations	4 (10.0%)	4 (3.2%)	8 (4.8%)
Alanine aminotransferase increased	3 (7.5%)	3 (2.4%)	6 (3.6%)
Aspartate aminotransferase increased	4 (10.0%)	2 (1.6%)	6 (3.6%)
C-reactive protein increased	0	1 (0.8%)	1 (0.6%)
Gamma-glutamyltransferase increased	1 (2.5%)	0	1 (0.6%)
Gastrointestinal disorders	2 (5.0%)	2 (1.6%)	4 (2.4%)
Nausea	2 (5.0%)	2 (1.6%)	4 (2.4%)
Vomiting	0	1 (0.8%)	1 (0.6%)
Musculoskeletal and connective tissue disorders	1 (2.5%)	2 (1.6%)	3 (1.8%)
Myalgia	1 (2.5%)	1 (0.8%)	2 (1.2%)
Back pain	0	1 (0.8%)	1 (0.6%)
Hepatobiliary disorders	2 (5.0%)	0	2 (1.2%)
Hyperbilirubinaemia	2 (5.0%)	0	2 (1.2%)

Key: CRS = Cytokine Release Syndrome, TE = treatment-emergent; RP2D = recommended Phase 2 dose

Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 24.0.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

[TSFAE02ARP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFAE02ARP2D.SAS] 16OCT2021, 10:58

Study 64007957MMY1001 (Pivotal RP2D): Summary of Treatment-emergent Cytokine Release Syndrome (CRS) Events Treated with Tocilizumab and/or Steroids; All Treated Analysis Set

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Number of CRS events	45	147	192
Number of CRS events treated with tocilizumab but no steroids ^a	16 (35.6%)	47 (32.0%)	63 (32.8%)
Grade 1	8 (17.8%)	22 (15.0%)	30 (15.6%)
Grade 2	8 (17.8%)	24 (16.3%)	32 (16.7%)
Grade 3	0	1 (0.7%)	1 (0.5%)
Number of CRS events treated with steroids but no tocilizumab ^a	10 (22.2%)	11 (7.5%)	21 (10.9%)
Grade 1	10 (22.2%)	11 (7.5%)	21 (10.9%)
Number of CRS events treated with both tocilizumab and steroids ^a	1 (2.2%)	4 (2.7%)	5 (2.6%)
Grade 1	0	1 (0.7%)	1 (0.5%)
Grade 2	1 (2.2%)	3 (2.0%)	4 (2.1%)

Key: CRS=cytokine release syndrome; RP2D=recommended Phase 2 dose; ASTCT=American society for transplantation and cellular therapy

^a Tocilizumab and steroids to treat CRS and CRS symptoms are considered

Note: Percentages calculated with the number of CRS events in the all treated analysis set as denominator.

Note: CRS was originally graded by Lee criteria (Lee et al 2014) in Phase 1 and by ASTCT consensus grading system (Lee et al 2019) in Phase 2, with conversion of grade in Phase 1 to ASTCT based on data in eCRF. Toxicity grade by ASTCT is presented in this table, for both Phase 1 and Phase 2.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

[TSFAE24F2RP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFAE24F2RP2D.SAS] 05NOV2021, 10:04

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Neurotoxicity Events by System Organ Class and Preferred Term; All Treated Analysis Set			
	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Subjects with 1 or more TE neurotoxicity	5 (12.5%)	16 (12.8%)	21 (12.7%)
Terms with grouping			
System organ class			
Grouped term(s)			
Preferred term			
Nervous System Disorders	1 (2.5%)	2 (1.6%)	3 (1.8%)
Encephalopathy^{ab}	1 (2.5%)	1 (0.8%)	2 (1.2%)
Confusional state	1 (2.5%)	1 (0.8%)	2 (1.2%)
Tremor^a	1 (2.5%)	1 (0.8%)	2 (1.2%)
Tremor	1 (2.5%)	1 (0.8%)	2 (1.2%)
Terms without grouping (MedDRA SOC/PT)			
Nervous system disorders	5 (12.5%)	15 (12.0%)	20 (12.1%)
Headache	4 (10.0%)	10 (8.0%)	14 (8.5%)
Immune effector cell-associated neurotoxicity syndrome	0	4 (3.2%)	4 (2.4%)
Cogwheel rigidity	0	1 (0.8%)	1 (0.6%)
Dizziness	0	1 (0.8%)	1 (0.6%)
Dysgeusia	1 (2.5%)	0	1 (0.6%)
Hypoaesthesia	1 (2.5%)	0	1 (0.6%)
Hypokinesia	0	1 (0.8%)	1 (0.6%)
Lethargy	0	1 (0.8%)	1 (0.6%)
Psychiatric disorders	0	1 (0.8%)	1 (0.6%)
Apathy	0	1 (0.8%)	1 (0.6%)

Key: TE = treatment-emergent; RP2D = recommended Phase 2 dose; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome

^a Preferred term grouping.

^b All terms under encephalopathy are presented in this table under Nervous system disorders SOC.

Note: Neurotoxicity includes adverse events in the Nervous System Disorders SOC or Psychiatric Disorders SOC that are considered related by investigator. Symptoms of CRS and ICANS are excluded.

Note: Terms without grouping are the MedDRA Preferred terms representing unique adverse events not characterized in other grouped terms.

Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 24.0.

Note: Percentages calculated with the number of subjects in the all treated analysis set as denominator.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

Note: 1 of the events of confusional state reported in a subject treated at RP2D in Phase 1 is considered by the sponsor to be consistent with ICANS and presented as such in summaries of ICANS events.

Note: Grouped terms consider the following: Aphasia (aphasia, dysphasia), Delirium (agitation, delirium, delusion, disorientation, hallucination, restlessness), Encephalopathy (cognitive disorder, confusional state, depressed level of consciousness, disturbances in attention, encephalopathy, hypersomnia, leukoencephalopathy, memory impairment, mental status changes, paranoia, somnolence, stupor), Tremor (head titubation, tremor).

[TSFAE23RP2D.RTF] [JNJ-64007957/MMY1001_P3/DBR_CSR/RE_CSR/PROD/TSFAE23RP2D.SAS] 21OCT2021, 20:03

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Neurotoxicity Events by System Organ Class, Preferred Term and Grade 3 or 4; All Treated Analysis Set

	RP2D					
	Phase 1		Phase 2 Cohort A		Total	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Analysis set: All Treated	40		125		165	
Subjects with 1 or more TE neurotoxicity	5 (12.5%)	0	16 (12.8%)	0	21 (12.7%)	0
Terms with grouping						
System organ class						
Grouped term(s)						
Preferred term						
Nervous System						
Disorders	1 (2.5%)	0	2 (1.6%)	0	3 (1.8%)	0
Encephalopathy^{ab}	1 (2.5%)	0	1 (0.8%)	0	2 (1.2%)	0
Confusional state	1 (2.5%)	0	1 (0.8%)	0	2 (1.2%)	0
Tremor^a	1 (2.5%)	0	1 (0.8%)	0	2 (1.2%)	0
Tremor	1 (2.5%)	0	1 (0.8%)	0	2 (1.2%)	0
Terms without grouping (MedDRA SOC / PT)						
Nervous system disorders	5 (12.5%)	0	15 (12.0%)	0	20 (12.1%)	0
Headache	4 (10.0%)	0	10 (8.0%)	0	14 (8.5%)	0
Immune effector cell-associated neurotoxicity syndrome	0	0	4 (3.2%)	0	4 (2.4%)	0
Cogwheel rigidity	0	0	1 (0.8%)	0	1 (0.6%)	0
Dizziness	0	0	1 (0.8%)	0	1 (0.6%)	0
Dysgeusia	1 (2.5%)	0	0	0	1 (0.6%)	0
Hypoaesthesia	1 (2.5%)	0	0	0	1 (0.6%)	0
Hypokinesia	0	0	1 (0.8%)	0	1 (0.6%)	0
Lethargy	0	0	1 (0.8%)	0	1 (0.6%)	0
Psychiatric disorders	0	0	1 (0.8%)	0	1 (0.6%)	0
Apathy	0	0	1 (0.8%)	0	1 (0.6%)	0

Key: TE = treatment-emergent; RP2D = recommended Phase 2 dose; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome

^a Preferred term grouping.

^b All terms under encephalopathy are presented in this table under Nervous system disorders SOC.

Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 24.0.

Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

Note: Neurotoxicity includes adverse events in the Nervous System Disorders SOC or Psychiatric Disorders SOC that are considered related by investigator. Symptoms of CRS and ICANS are excluded.

Note: Neurotoxicity events are graded according to the NCI-CTCAE Version 4.03, with the exception of ICANS, which were evaluated according to the ASTCT consensus grading system.

Note: Terms without grouping are the MedDRA Preferred terms representing unique adverse events not characterized in other grouped terms.

Note: 1 of the events of confusional state reported in a subject treated at RP2D in Phase 1 is considered by the sponsor to be consistent with ICANS and presented as such in summaries of ICANS events.

Note: Grouped terms consider the following: Aphasia (aphasia, dysphasia), Delirium (agitation, delirium, delusion, disorientation, hallucination, restlessness), Encephalopathy (cognitive disorder, confusional state, depressed level of consciousness, disturbances in attention, encephalopathy, hypersomnia, leukoencephalopathy, memory impairment, mental status changes, paranoia, somnolence, stupor), Tremor (head titubation, tremor).

[TSFAE23ARP2D.RTF] [JNJ-64007957\MMY1001_P3\DR_CSR\RE_CSR\PROD\TSFAE23ARP2D.SAS] 21OCT2021, 19:57

Study 64007957MMY1001 (Pivotal RP2D): Summary of Treatment-emergent Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS); All Treated Analysis Set

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Analysis set: All Treated	40	125	165
Number of subjects with ICANS	1 (2.5%)	4 (3.2%)	5 (3.0%)
Maximum toxicity grade			
Grade 1	1 (2.5%)	2 (1.6%)	3 (1.8%)
Grade 2	0	2 (1.6%)	2 (1.2%)
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Number of subjects with ICANS leading to discontinuation of study drug	0	0	0
Number of subjects with multiple ICANS events	0	2 (1.6%)	2 (1.2%)
Number of subjects with supportive measures to treat ICANS ^a	0	4 (3.2%)	4 (2.4%)
IL-1 receptor antagonist anakinra	0	0	0
Anti-IL6 receptor tocilizumab	0	3 (2.4%)	3 (1.8%)
Corticosteroids	0	3 (2.4%)	3 (1.8%)
Dexamethasone	0	3 (2.4%)	3 (1.8%)
Methylprednisolone sodium succinate	0	0	0
Levetiracetam	0	1 (0.8%)	1 (0.6%)
Pethidine	0	0	0
Other	0	2 (1.6%)	2 (1.2%)
Occurrence of ICANS ^b			
Step-up Dose 1	0	1 (0.8%)	1 (0.6%)
Step-up Dose 2	0	0	0
Repeat Step-up ^c	0	0	0
Cycle 1 Day 1	1 (2.5%)	1 (0.8%)	2 (1.2%)
Cycle 1 Day 8	0	1 (0.8%)	1 (0.6%)
Cycle 1 Day 15	0	0	0
Cycle 1 Day 22	-	1 (0.8%)	1 (0.6%)
Cycle 2+	0	2 (1.6%)	2 (1.2%)
Time from last injection of Teclistamab to new onset of ICANS, hours ^d			
Number of ICANS events		8	
Mean (SD)		61.729 (21.4934)	
Median		60.775	
Range		(28.15; 95.23)	
Time from last injection of Teclistamab to new onset of ICANS, days			
Number of ICANS events	1	8	9
Mean (SD)	3.0 (-)	3.8 (1.04)	3.7 (1.00)
Median	3.0	4.0	4.0
Range	(3; 3)	(2; 5)	(2; 5)
Duration of ICANS, hours ^d			
Number of ICANS events		8	
Mean (SD)		128.552 (147.3058)	
Median		91.292	
Range		(7.85; 454.50)	
Duration of ICANS, days			
Number of ICANS events	1	8	9
Mean (SD)	1.0 (-)	6.4 (6.25)	5.8 (6.12)

Study 64007957MMY1001 (Pivotal RP2D): Summary of Treatment-emergent Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS); All Treated Analysis Set

	RP2D		
	Phase 1	Phase 2 Cohort A	Total
Median	1.0	5.0	3.0
Range	(1; 1)	(1; 20)	(1; 20)
Outcome of ICANS			
Number of ICANS events	1	8	9
Recovered or resolved	1 (100.0%)	8 (100.0%)	9 (100.0%)
Not recovered or not resolved	0	0	0
Recovered or resolved with sequelae	0	0	0
Recovering or resolving	0	0	0
Fatal	0	0	0
Unknown	0	0	0
Missing	0	0	0
Concurrent CRS ^e			
Yes	1 (100.0%)	6 (75.0%)	7 (77.8%)
No	0	2 (25.0%)	2 (22.2%)

Key: RP2D=recommended Phase 2 dose; TEAE = treatment-emergent adverse event; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome

^a Supportive measures to treat ICANS and ICANS symptoms are included.

^b Subjects may appear in more than one category. Occurrence is based on the last treatment visit on or prior to the day in which the TEAE occurred.

^c Prior to Cycle 1.

^d Hours only displayed for Phase 2, start and end times of Phase 1 ICANS event were not collected

^e Concurrent CRS considers ICANS events that occur during or within 7 days of the end date of CRS.

Note: Percentages calculated with the number of subjects in the all treated analysis set as denominator, except for the onset and outcome of ICANS and concurrent CRS for which percentages are calculated with the number of ICANS events in the all treated analysis set as denominator.

Note: Time from last injection to new onset is defined as date of last dose – start date of ICANS +1. Duration is defined as end date of ICANS – start date of ICANS +1. For calculating in days, the date is used without time. For hours the date and time is used and those with time portion missing will be excluded.

Note: The subject treated at RP2D in Phase 1 is reported in the database as experiencing a TEAE of confusional state. This event is considered by the sponsor to be consistent with ICANS and presented as such in this summary. The Ph1 TEAE considered as ICANS was originally graded by NCI-CTCAE version 4.03. and by ASTCT consensus grading system (Lee et al 2019) in Phase 2, with conversion of grade in Phase 1 to ASTCT based on data in eCRF. Toxicity grade by ASTCT is presented in this table, for both Phase 1 and Phase 2.

Note: Day 8 is not applicable for subjects on a biweekly or monthly dosing schedule, Day 15 is not applicable for subjects on a monthly dosing schedule, and Day 22 is not applicable for subjects on a monthly dosing schedule or Phase 1 subjects on a weekly dosing schedule (21-day cycle).

[TSFAE22RP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFAE22RP2D.SAS] 07OCT2021, 21:30

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Infections and Infestations by System Organ Class, Preferred Term, and Worst Toxicity Grade of 3 or Higher; All Treated Analysis Set

	RP2D								
	Phase 1			Phase 2 Cohort A			Total		
	Total	Grade 3 or 4	Grade 5	Total	Grade 3 or 4	Grade 5	Total	Grade 3 or 4	Grade 5
Analysis set: All Treated	40			125			165		
Subjects with 1 or more TE infections	25 (62.5%)	12 (30.0%)	0	79 (63.2%)	39 (31.2%)	8 (6.4%)	104 (63.0%)	51 (30.9%)	8 (4.8%)
MedDRA system organ class/preferred term									
Infections and infestations	25 (62.5%)	12 (30.0%)	0	79 (63.2%)	39 (31.2%)	8 (6.4%)	104 (63.0%)	51 (30.9%)	8 (4.8%)
Pneumonia	7 (17.5%)	5 (12.5%)	0	15 (12.0%)	9 (7.2%)	1 (0.8%)	22 (13.3%)	14 (8.5%)	1 (0.6%)
COVID-19	4 (10.0%)	3 (7.5%)	0	10 (8.0%)	2 (1.6%)	7 (5.6%)	14 (8.5%)	5 (3.0%)	7 (4.2%)
Upper respiratory tract infection	4 (10.0%)	0	0	10 (8.0%)	0	0	14 (8.5%)	0	0
Bronchitis	3 (7.5%)	0	0	7 (5.6%)	0	0	10 (6.1%)	0	0
Urinary tract infection	3 (7.5%)	1 (2.5%)	0	6 (4.8%)	2 (1.6%)	0	9 (5.5%)	3 (1.8%)	0
Nasopharyngitis	4 (10.0%)	0	0	4 (3.2%)	0	0	8 (4.8%)	0	0
Sinusitis	4 (10.0%)	1 (2.5%)	0	4 (3.2%)	1 (0.8%)	0	8 (4.8%)	2 (1.2%)	0
Infection	1 (2.5%)	1 (2.5%)	0	5 (4.0%)	2 (1.6%)	0	6 (3.6%)	3 (1.8%)	0
Rhinitis	2 (5.0%)	0	0	4 (3.2%)	0	0	6 (3.6%)	0	0
Cellulitis	1 (2.5%)	1 (2.5%)	0	4 (3.2%)	3 (2.4%)	0	5 (3.0%)	4 (2.4%)	0
Pneumocystis jirovecii pneumonia	1 (2.5%)	1 (2.5%)	0	4 (3.2%)	4 (3.2%)	0	5 (3.0%)	5 (3.0%)	0
Oral herpes	0	0	0	4 (3.2%)	0	0	4 (2.4%)	0	0
Conjunctivitis	0	0	0	3 (2.4%)	0	0	3 (1.8%)	0	0
Cystitis	0	0	0	3 (2.4%)	2 (1.6%)	0	3 (1.8%)	2 (1.2%)	0
Escherichia urinary tract infection	0	0	0	3 (2.4%)	1 (0.8%)	0	3 (1.8%)	1 (0.6%)	0
Lower respiratory tract infection	0	0	0	3 (2.4%)	1 (0.8%)	0	3 (1.8%)	1 (0.6%)	0
Oral fungal infection	0	0	0	3 (2.4%)	0	0	3 (1.8%)	0	0
Otitis media	1 (2.5%)	0	0	2 (1.6%)	0	0	3 (1.8%)	0	0
Pseudomonal sepsis	0	0	0	3 (2.4%)	3 (2.4%)	0	3 (1.8%)	3 (1.8%)	0
Respiratory tract infection	2 (5.0%)	0	0	1 (0.8%)	0	0	3 (1.8%)	0	0
Sepsis	2 (5.0%)	2 (5.0%)	0	1 (0.8%)	1 (0.8%)	0	3 (1.8%)	3 (1.8%)	0
Urinary tract infection bacterial	0	0	0	3 (2.4%)	2 (1.6%)	0	3 (1.8%)	2 (1.2%)	0
Viral upper respiratory tract infection	2 (5.0%)	1 (2.5%)	0	1 (0.8%)	0	0	3 (1.8%)	1 (0.6%)	0
Clostridium difficile colitis	0	0	0	2 (1.6%)	0	0	2 (1.2%)	0	0
Cystitis escherichia	0	0	0	2 (1.6%)	2 (1.6%)	0	2 (1.2%)	2 (1.2%)	0
Enterocolitis infectious	1 (2.5%)	1 (2.5%)	0	1 (0.8%)	0	0	2 (1.2%)	1 (0.6%)	0
Gastroenteritis	0	0	0	2 (1.6%)	0	0	2 (1.2%)	0	0
Injection site cellulitis	0	0	0	2 (1.6%)	1 (0.8%)	0	2 (1.2%)	1 (0.6%)	0
Oral candidiasis	0	0	0	2 (1.6%)	0	0	2 (1.2%)	0	0
Pneumonia pseudomonal	0	0	0	2 (1.6%)	1 (0.8%)	0	2 (1.2%)	1 (0.6%)	0
Pseudomonal bacteraemia	0	0	0	2 (1.6%)	1 (0.8%)	0	2 (1.2%)	1 (0.6%)	0
Adenovirus infection	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Adenovirus reactivation	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Aspergillus infection	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Asymptomatic COVID-19	1 (2.5%)	0	0	0	0	0	1 (0.6%)	0	0
BK virus infection	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Infections and Infestations by System Organ Class, Preferred Term, and Worst Toxicity Grade of 3 or Higher; All Treated Analysis Set

	RP2D								
	Phase 1			Phase 2 Cohort A			Total		
	Total	Grade 3 or 4	Grade 5	Total	Grade 3 or 4	Grade 5	Total	Grade 3 or 4	Grade 5
Bacteraemia	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Cystitis klebsiella	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Cytomegalovirus infection reactivation	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Cytomegalovirus viraemia	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Diverticulitis	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Empyema	1 (2.5%)	1 (2.5%)	0	0	0	0	1 (0.6%)	1 (0.6%)	0
Enterobacter pneumonia	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Erysipelas	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Escherichia infection	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Fungal skin infection	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Furuncle	1 (2.5%)	0	0	0	0	0	1 (0.6%)	0	0
Hepatitis B reactivation	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Herpes zoster	1 (2.5%)	0	0	0	0	0	1 (0.6%)	0	0
Impetigo	1 (2.5%)	0	0	0	0	0	1 (0.6%)	0	0
Meningococcal sepsis	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Metapneumovirus pneumonia	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Moraxella infection	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Orchitis	1 (2.5%)	0	0	0	0	0	1 (0.6%)	0	0
Pharyngitis	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Pneumonia adenoviral	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Pneumonia klebsiella	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Pneumonia moraxella	1 (2.5%)	1 (2.5%)	0	0	0	0	1 (0.6%)	1 (0.6%)	0
Pneumonia pneumococcal	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Pneumonia respiratory syncytial viral	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Pneumonia staphylococcal	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Pneumonia viral	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Pseudomonas infection	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Respiratory tract infection bacterial	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Rhinovirus infection	1 (2.5%)	0	0	0	0	0	1 (0.6%)	0	0
Skin candida	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Skin infection	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Staphylococcal bacteraemia	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Stomatococcal infection	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0
Tracheitis	0	0	0	1 (0.8%)	0	0	1 (0.6%)	0	0
Vestibular neuronitis	0	0	0	1 (0.8%)	1 (0.8%)	0	1 (0.6%)	1 (0.6%)	0

Study 64007957MMY1001 (Pivotal RP2D): Number of Subjects With Treatment-emergent Infections and Infestations by System Organ Class, Preferred Term, and Worst Toxicity Grade of 3 or Higher; All Treated Analysis Set

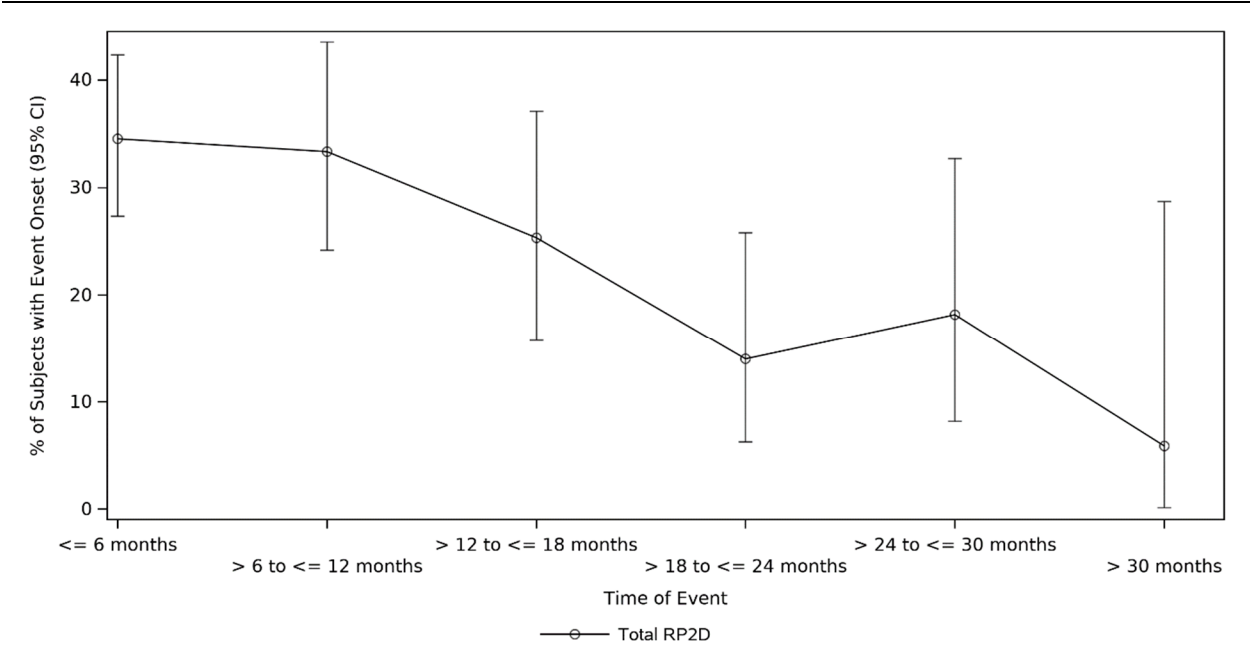
RP2D								
Phase 1			Phase 2 Cohort A			Total		
Total	Grade 3 or 4	Grade 5	Total	Grade 3 or 4	Grade 5	Total	Grade 3 or 4	Grade 5

Key: TE = treatment-emergent; RP2D = recommended Phase 2 dose
Note: Subjects are counted only once for any given event, regardless of the number of times they actually experienced the event. The event experienced by the subject with the maximum toxicity is used. If a subject has missing toxicity for a specific adverse event, the subject is only counted in the total column for that adverse event. Adverse events are coded using MedDRA Version 24.0.
Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.
Note: Percentages calculated with the number of subjects in the all treated analysis set as denominator.

[TSFAE31RP2D.RTF] [JNJ-64007957\MMY1001_P3\DBR_CSR\RE_CSR\PROD\TSFAE31RP2D.SAS] 07OCT2021, 21:35

Appendix 3.2: Follow-up Safety Analysis

Study 64007957MMY1001 (Pivotal RP2D): Percentage of Subjects with 1 or More Grade 3 or Higher Treatment-emergent Infections and Infestations (New Onsets) by Event Onset Time; All Treated Analysis Set



Keys: RP2D=recommended Phase 2 dose
Note: Includes subjects either treated or initiated any grade 3 or higher TEAE of infections/infestations within the specific window.
Note: For TEAE event with multiple grades, only the first record of grade 3 or higher sorted by event onset date is summarized in this table.
Note: Percentages are calculated with the number of subjects treated within each window as denominator. 95% exact confidence interval is displayed.
Note: Adverse events are reported until 100 days (Phase 1) or 30 days (Phase 2) after the last dose of teclistamab or until the start of subsequent anticancer therapy, if earlier.

[gsfae17brp2d.rtf] [jnj-64007957/mmy1001_p3/dbr_csr_aug_2023/re_csr_aug_2023/gsfac17brp2d.sas] 15OCT2023, 18:14