
Clinical Study Protocol - Addendum 1.0 India

Study Intervention	Rilvegostomig (AZD2936)
Study Code	D702NC00001
Addendum Version	1.0
Date	07 Oct 2025

India Addendum

**Phase III, Randomized, Open-label, Global, Multicenter Study of
Rilvegostomig or Durvalumab in Combination With Chemotherapy
as a First-line Treatment for Patients With Advanced Biliary Tract
Cancer (ARTEMIDE-Biliary02)**

Sponsor Name: AstraZeneca AB

1. DOCUMENT HISTORY

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Document	Date
Clinical Study Protocol – Addendum 1.0 India	07 Oct 2025
Original Protocol	08 Aug 2025

Overall Rationale for the Addendum:

To comply with the Indian regulatory authority requirement regarding reporting of Serious Adverse Events. The text derived from the original protocol included in the table together with the requirements mentioned in **bold** should be considered applicable for all the sites in India per regulatory requirements.

Section # and Name	Description of Change with Reason
8.4.1 Time Period and Frequency for Collecting AE and SAE Information	<u>Previous Text:</u> AEs and SAEs will be collected from the time of signature of the ICF and throughout the treatment period until the safety follow-up period is completed (90 [$\pm$ 7 days] days post last dose of study treatment). Collection and reporting of AEs and SAEs after the final DCO is described in Section 8.4.12. If the Investigator becomes aware of an SAE with a suspected causal relationship to the IMP/study intervention(s) that occurs after the end of the clinical study in a treated participant, the Investigator shall, without undue delay, report the SAE to AstraZeneca, as described in Section 8.4.13. <u>Revised Text:</u> AEs and SAEs will be collected from the time of signature of the ICF and throughout the treatment period until the safety follow-up period is completed (90 [$\pm$ 7 days] days post last dose of study treatment). Collection and reporting of AEs and SAEs after the final DCO is described in Section 8.4.12. If the Investigator becomes aware of an SAE with a suspected causal relationship to the IMP/study intervention(s) that occurs after the end of the clinical study in a treated participant, the Investigator shall, without undue delay, report the SAE to AstraZeneca, as described in Section 8.4.13. However, all the events occurring at the Indian sites (the reason whatsoever) that meet the criteria for seriousness from the time of signing the ICF for study procedures, throughout the treatment period, and until the follow-up period is completed (90 [+7] days after the discontinuation of all study interventions) and all SAEs with a suspected causal relationship to the study intervention that occurs after the end of follow up period, will be reported expeditiously as SAEs per local regulatory requirements to the Sponsor (appropriate AstraZeneca representatives), Indian regulatory authority and the concerned Ethics Committees in Table 5 format of New Drugs and Clinical Trials Rules, 2019. Reason for change: Per Indian regulatory requirements, all the events that meet criteria for seriousness have to be reported expeditiously to the Sponsor, Indian regulatory authority and the concerned Ethics Committees.
8.4.4 AEs Based on Examinations and Tests	<u>Previous Text:</u> Deterioration as compared to baseline in protocol-mandated laboratory values, vital signs (temperature, blood pressure, pulse rate, respiratory rate, and pulse oximetry), physical examination, ECGs, ECHO/MUGA scans, ECOG performance status should only be reported as AEs if they meet any of the following:

Section # and Name	Description of Change with Reason
	• Fulfils any of the SAE criteria • Are the reason for discontinuation of the IMP/study intervention(s) • Are clinically relevant as judged by the Investigator (which may include but is not limited to consideration as to whether intervention or non-planned visits were required or other action was taken with the IMP/study intervention(s), eg, dose adjustment or drug interruption). If deterioration in a laboratory value/vital sign is associated with clinical signs and symptoms, the sign or symptom will be reported as an AE and the associated laboratory result/vital sign will be considered as additional information. Wherever possible the reporting Investigator uses the clinical, rather than the laboratory term (eg, anemia vs low hemoglobin value). In the absence of clinical signs or symptoms, clinically relevant deteriorations in non-mandated parameters should be reported as AE(s). Deterioration of a laboratory value, which is unequivocally due to disease progression, should not be reported as an AE/SAE. Any new or aggravated clinically relevant abnormal medical finding at a physical examination as compared with the baseline assessment will be reported as an AE unless unequivocally related to the DUS. Please refer to Section 8.4.8. The results from the protocol-mandated laboratory tests and vital signs will be summarized in the CSR <u>Revised Text:</u> Deterioration as compared to baseline in protocol-mandated laboratory values, vital signs (temperature, blood pressure, pulse rate, respiratory rate, and pulse oximetry), physical examination, ECGs, ECHO/MUGA scans, ECOG performance status should only be reported as AEs if they meet any of the following: • Fulfils any of the SAE criteria • Are the reason for discontinuation of the IMP/study intervention(s) • Are clinically relevant as judged by the Investigator (which may include but is not limited to consideration as to whether intervention or non-planned visits were required or other action was taken with the IMP/study intervention(s), eg, dose adjustment or drug interruption). If deterioration in a laboratory value/vital sign is associated with clinical signs and symptoms, the sign or symptom will be reported as an AE and the associated laboratory result/vital sign will be considered as additional information. Wherever possible the reporting Investigator uses the clinical, rather than the laboratory term (eg, anemia vs low hemoglobin value). In the absence of clinical signs or symptoms, clinically relevant deteriorations in non-mandated parameters should be reported as AE(s). Deterioration of a laboratory value, which is unequivocally due to disease progression, should not be reported as an AE/SAE.

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	Any new or aggravated clinically relevant abnormal medical finding at a physical examination as compared with the baseline assessment will be reported as an AE unless unequivocally related to the DUS. Please refer to Section 8.4.8. The results from the protocol-mandated laboratory tests and vital signs will be summarized in the CSR However, all the events occurring at the Indian sites (the reason whatsoever) that meet the criteria for seriousness from the time of signing the ICF for study procedures, throughout the treatment period, and until the follow-up period is completed (90 [+7] days after the discontinuation of all study interventions) and all SAEs with a suspected causal relationship to the study intervention that occurs after the end of follow up period, will be reported expeditiously as SAEs per local regulatory requirements to the Sponsor (appropriate AstraZeneca representatives), Indian regulatory authority and the concerned Ethics Committees in Table 5 format of New Drugs and Clinical Trials Rules, 2019. Reason for change: Per Indian regulatory requirements, all the events that meet criteria for seriousness have to be reported expeditiously to the Sponsor, Indian regulatory authority and the concerned Ethics Committees.
8.4.7 Disease Progression	<u>Previous Text:</u> Disease progression can be considered as a worsening of a participant's condition attributable to the disease for which the IMP is being studied. It may be an increase in the severity of the DUS and/or increases in the symptoms of the disease. The development of new or progression of existing metastasis to the primary cancer under study should be considered as disease progression and not an AE. Events, which are unequivocally due to disease progression, should not be reported as AEs during the study. <u>Revised Text:</u> Disease progression can be considered as a worsening of a participant's condition attributable to the disease for which the IMP is being studied. It may be an increase in the severity of the DUS and/or increases in the symptoms of the disease. The development of new or progression of existing metastasis to the primary cancer under study should be considered as disease progression and not an AE. Events, which are unequivocally due to disease progression, should not be reported as AEs during the study. However, all the events occurring at the Indian sites (the reason whatsoever) that meet the criteria for seriousness from the time of signing the ICF for study procedures, throughout the treatment period, and until the follow-up period is completed (90 [+7] days after the discontinuation of all study interventions) and all SAEs with a suspected causal relationship to the study intervention that occurs after the end of follow up period, will be reported expeditiously as SAEs per local regulatory requirements to the Sponsor

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	(appropriate AstraZeneca representatives), Indian regulatory authority and the concerned Ethics Committees in Table 5 format of New Drugs and Clinical Trials Rules, 2019. Reason for change: Per Indian regulatory requirements, all the events that meet criteria for seriousness have to be reported expeditiously to the Sponsor, Indian regulatory authority and the concerned Ethics Committees.
8.4.10 Deaths	<u>Previous Text:</u> All deaths that occur during the study intervention period, or within the protocol-defined follow-up period after the administration of the last dose of study intervention, must be reported as follows: • Death clearly resulting from PD should be documented in the eCRF in the Statement of Death page. It should not be reported as an SAE. • Where death is not due (or not clearly due) to PD under study, the AE causing the death must be reported as an SAE within 24 hours. It should also be documented in the Statement of Death page in the eCRF. The report should contain a comment regarding the co-involvement of PD, if appropriate, and should assign the main and contributory causes of death. • Deaths with an unknown cause should always be reported as an SAE and documented in the Statement of Death page in the eCRF, but every effort should be made to determine a cause of death. A post-mortem may be helpful in the assessment of the cause of death, and if performed, a copy of the post-mortem results should be forwarded to AstraZeneca Patient Safety or its representative within the usual time frames. Deaths occurring after the protocol-defined follow-up period after the administration of the last dose of study intervention should be documented in the Statement of Death page. If the death occurred as a result of an event that started after the defined follow-up period and the event is considered to be due to a late-onset toxicity to study intervention, then it should also be reported as an SAE. <u>Revised Text:</u> All deaths that occur during the study intervention period, or within the protocol-defined follow-up period after the administration of the last dose of study intervention, must be reported as follows: • Death clearly resulting from PD should be documented in the eCRF in the Statement of Death page. It should not be reported as an SAE. • Where death is not due (or not clearly due) to PD under study, the AE causing the death must be reported as an SAE within 24 hours. It should also be documented in the Statement of Death page in the eCRF. The report should contain a comment regarding the co-involvement of PD, if appropriate, and should assign the main and contributory causes of death.

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	Deaths with an unknown cause should always be reported as an SAE and documented in the Statement of Death page in the eCRF, but every effort should be made to determine a cause of death. A post-mortem may be helpful in the assessment of the cause of death, and if performed, a copy of the post-mortem results should be forwarded to AstraZeneca Patient Safety or its representative within the usual time frames. Deaths occurring after the protocol-defined follow-up period after the administration of the last dose of study intervention should be documented in the Statement of Death page. If the death occurred as a result of an event that started after the defined follow-up period and the event is considered to be due to a late-onset toxicity to study intervention, then it should also be reported as an SAE. However, all the events occurring at the Indian sites (the reason whatsoever) that meet the criteria for seriousness from the time of signing the ICF for study procedures, throughout the treatment period, and until the follow-up period is completed (90 [+7] days after the discontinuation of all study interventions) and all SAEs with a suspected causal relationship to the study intervention that occurs after the end of follow up period, will be reported expeditiously as SAEs per local regulatory requirements to the Sponsor (appropriate AstraZeneca representatives), Indian regulatory authority and the concerned Ethics Committees in Table 5 format of New Drugs and Clinical Trials Rules, 2019. Reason for change: Per Indian regulatory requirements, all the events that meet criteria for seriousness have to be reported expeditiously to the Sponsor, Indian regulatory authority and the concerned Ethics Committees.

Study sites affected by this addendum:

This Clinical Study Protocol - Addendum affects all the study sites in India and will prevail if in conflict with any other section in the Clinical Study Protocol (CSP) (including its appendices).

Persons who initiated the Addendum

Ashish S. Rasam, Study Start-Up Associate Director (SSUAD)