

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Study Protocol:	TAK-226-3001
Study Title:	A Phase 3, Multicenter, Open Label, Randomized Trial to Compare the Efficacy and Safety of Elriterccept versus Epoetin Alfa for the Treatment of Anemia Due to IPSS-R Very Low, Low, or Intermediate Risk Myelodysplastic Syndromes in ESA-naïve Adult Participants Who Require Red Blood Cell Transfusions
Study Medication:	Elriterccept (TAK-226), referred to throughout the document as the “study drug”
Sponsor of the study:	Takeda Development Center Americas, Inc. 500 Kendall Street Cambridge, MA 02142 USA
Phase of the study:	III

Investigator:	Dr. Arijit Nag
Site Number (if applicable):	24003
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Country:	India

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Introduction

We are inviting you to participate in a clinical research study for Study drug (the “Takeda Study Drug(s)”) as you have anemia due to diagnosis of lower-risk myelodysplastic syndrome (MDS) needing blood transfusions. The company that is making payment for the study is Takeda (“Sponsor”).

Participating in the study is totally voluntary. You may refuse to take part or leave the study, at any time, without being penalized or loss of benefits to which you are otherwise entitled. It is up to you if you do or do not wish to participate.

Kindly take time to read this form cautiously.

This form tells you important information regarding the research study. It is important for you to know why the research is being conducted, the possible risks and benefits involved, and what you need to do before you decide whether you would like to participate in this research study. Kindly take time to read and discuss the information on given on this form cautiously.

You are encouraged to discuss the information with friends, family, and your doctors if you like.

The study will be explained to you by your study doctor or a member of the study team. Kindly ask your study doctor or a study team member if there is anything that is unclear. Additional information may also be given by them if you need it.

Your decision will not change the medical care you receive from your doctors now or in the future.

If you decide to participate, you should put a signature and date the consent at the end of this form. Even after putting a signature on the consent, you have the liberty to withdraw from the study at any time without providing any reason. You will be explained in this form how to leave and what that means to you.

If anything changes regarding the research study, you will be notified and asked to put a signature again if you agree to the changes.

Why is this study being conducted?

We are asking you to participate in a research study for an investigational treatment of anemia because of lower-risk myelodysplastic syndrome (LR-MDS). Your bone marrow are affected by LR-MDS causing it not to produce adequate mature red blood cells that result in low hemoglobin levels and symptoms of anemia. This research study are being offered to you because you need red-blood cell (RBC) transfusions for treating your symptoms of anemia and you have not obtained other therapies (with some exceptions that your study physician will review) for treating your symptoms of anemia or LR-MDS. ‘Investigational’ in this study means that the medication has not been approved as yet by regulatory authorities for treating anemia due to LR-MDS. Previous studies in patients with LR-MDS indicated the study drug may be given at a safe dose with manageable side effects. The previous studies in LR-MDS patients also showed some improvements in hemoglobin and reduced need for blood transfusions. The use of study treatment in comparison to a commonly used treatment will be evaluated in this study.

This study is being conducted to help respond to the following queries(s):

- How safe is study drug and what are the side effects that may be associated with it in comparison to epoetin alfa?
- How much does study drug improve anemia symptoms in comparison to epoetin alfa that is a commonly used therapy?

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- How much does study drug improve requirement for RBC transfusions in comparison to epoetin alfa?
- How much does study drug improve quality of life in comparison to epoetin alfa?

This research may permit study doctors to better know about the study drug effects on the body and to recognize future patients who can benefit.

What is the Takeda study drug?

Elritercept (TAK-226) is the Takeda study drug used in this study.

Elritercept (TAK-226) is a manufactured protein (called a recombinant fusion protein) designed to block other proteins in your body that interfere with blood cell production in the bone marrow. This permits the bone marrow to produce more cells that become mature red blood cells that might improve hemoglobin levels.

This study medication is administered by injection into the fat under the skin known as a subcutaneous injection. It is administered once every 28 days (once per month). The dose of study drug will not be administered if your hemoglobin level is increasing rapidly or is at a high level, or if the study medication is causing significant side effects.

What is the other study medication(s)?

The other drug used in this study is epoetin alfa to compare to the Takeda study drug.

Epoetin alfa is a manufactured protein called an erythropoiesis-stimulating agent (ESA) designed to act like a hormone (specialized protein known as erythropoietin) which stimulates the bone marrow to produce more red blood cells. Epoetin alfa was selected as the comparator drug as it is commonly used for initial treatment of anemia caused by LR-MDS. Epoetin alfa is recommended by international clinical practice guidelines.

Epoetin alfa is given by injection into the fat under the skin known as a subcutaneous injection. It is administered once every 7 days (once a week). The dose of study drug will not be administered if your hemoglobin level is increasing rapidly or is at a high level, or if the study medication is causing significant side effects.

If you are allotted to epoetin alfa treatment, your study physician may permit you to get some of the weekly injections at home or at another approved location. If permitted, a home healthcare provider may administer these injections or, if you have been appropriately given training, by yourself. If you are permitted to administer the epoetin alfa by yourself, then you will be asked to fill out a medication diary card and give it back to the site at your next study visit.

How is the study set up?

Patients suitable for the study are randomized into one of two treatment groups for the study.

You will be selected at random to receive one of the following two study treatments:

- Study medication: You have a 1 in 2 (50%) chance of receiving this treatment. This study medication will be administered as a subcutaneous injection once every 28 days (once a month).
- Epoetin alfa: You have a 1 in 2 (50%) chance of receiving this treatment. This study medication will be administered as a subcutaneous injection once every 7 days (once a week).

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When you are randomly assigned a treatment, this means you are put into a treatment group by chance (like tossing a coin).

How many people are in the study and how long will you participate in the study?

There will be 210 to 300 patients who will be taking part in this study. Patients must be adults aged 18 years or older with anemia needing blood transfusions due to LR-MDS who have not obtained other treatment. The study will occur at approximately 150 clinical sites in 28 countries worldwide. You will be in the study approximately 5-8 years based on how many patients enrolled before you.

What will occur during the study visits and what do you need to do?

If you decide to take part in this study, certain personal information will be collected by the study doctor and study staff. What procedures will be conducted to collect this information are explained in this section.

To take part in the study, you may also be asked to stop certain drugs you are presently consuming. The drugs you take now will be discussed by the study doctor before you begin the study and you will be informed whether you require to stop consuming any of them before you consume the study medication.

Blood, urine and bone marrow samples will be collected from you by this study as part of this study. The samples will be used to monitor your health condition during the study.

Also, some of these samples might be used for additional research on MDS looking at “markers” of the disease that may be found in the blood and bone marrow. The sponsor, its agents and its affiliated companies may use these sample(s) and test data:

- To help develop new methods to monitor and treat anemia due to diagnosis of LR-MDS.
- To create information required for additional research and diagnostic tests associated with diseases or conditions that study drug may treat.
- To help get country health authority approvals for study drug.
- To develop a better understanding of how disease-associated gene mutations (from your diseased tissue samples) correlate with safety and efficacy of study drug and MDS disease states.

4 time periods are included in this study:

1. **Screening Period:** This period begins at the time you give consent to take part in the study and ends when your study doctor has confirmed whether you are eligible for the study or not and may be randomized to the study treatment. During this period, several evaluations and tests will be conducted and the study doctor will review your medical history information. This period can take up to 6 weeks and may be increased by an additional 6 weeks (for a total of 12 weeks) if required for your doctor to confirm whether you are suitable for the study treatment.
 - **Rescreening:** If during the screening period your study doctor determines you have the applicable diagnosis of LR-MDS but you are not suitable for the study for other reasons you will not be permitted to begin the study. But if these reasons are conditions that can change or improve over time, your study doctor might offer to you to repeat the screening for the study. You would need to begin from the beginning with providing your consent and repeat the evaluations and tests, but you might not have to repeat the bone marrow test.

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- Randomization: If you are suitable for the study, then your information will be entered by your study doctor into an electronic system which is programmed to automatically assign you to either study drug or epoetin alfa treatment. Your study treatment will begin within 3 days of randomization.
2. **Treatment Period:** This is the time period from beginning of study treatment until your study doctor and you decide to stop the study treatment permanently. During this period you will be observed at the site or, if permitted, by a home healthcare provider every other week and at times weekly. During these visits there will be regularly repeated evaluations and tests done, any side effects or blood transfusions you have will be recorded by the study staff and you will fill out questionnaires about how you feel. You will be given the study drug during this period on a monthly basis if you are allotted to study drug treatment or on a weekly basis if you are allotted to epoetin alfa treatment.
 - If your study treatment stops prior to 6 months: You will be asked to still complete the questionnaires and information regarding blood transfusions up to 6 months.
 - End of Treatment Visit: When your study doctor and you decide to stop the study treatment you will be asked to come back for a study visit to complete some evaluations and tests to evaluate any effects from the treatment.
 3. **Safety Follow-Up Period:** This time period will take about 60 days beginning from the day after your End of Treatment Visit. You will be asked to come to the site at 1 month and 2 months after you complete the End of Treatment Visit for some evaluations and tests to evaluate any continuing effects from the treatment.
 4. **Survival Follow-Up Period:** This time period will begin on the day after your last safety follow-up visit and will continue until you have been on the study approximately 5-8 years or the study is discontinued. During this time you will be contacted every 3 months to check on your disease condition, to report any other treatment you are getting and to respond to some queries about your health condition.

Kindly see **Table 1** on the next page for the schedule of all tests and evaluations to be done at the time of the study. An explanation for each test and evaluation is given in **Table 2**.

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Table 1: Schedule of Activities

	Screening Period Up to 6 Weeks before Randomization	Treatment Period Day 1 to End of Treatment Visit	Safety Period Up to 60 Days following Last Dose	Follow-Up ~5 to 8 Years following Randomization
Informed Consent	X			
Medical History	X			
MDS Disease and Transfusion History	X			
Physical Exam	X	X	X	
Vital Signs	X	X	X	
Height	X			
Weight		X		
Electrocardiogram	X	X		
Echocardiogram	X	X		
Coagulation	X			
Hematology	X	X	X	
Chemistry	X	X	X	
Urinalysis	X	X	X	
Pregnancy Testing	X	X	X	
HBV, HCV and HIV Status Check	X			
Serum Erythropoietin (EPO)	X	X		
Peripheral Blood and Bone Marrow Sample Collection	X	X		
MDS Disease Evaluation	X	X		
Randomization		X		
Study medication vs. Epoetin Alfa Dosing		X		
Transfusion Verification		X		
Pharmacokinetic (PK) Evaluation		X		
Anti-Drug Antibody (ADA) Evaluation		X	X	

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Biomarker Evaluations	X	X	X	
Patient Reported Outcome Evaluations	X	X	X	X
Healthcare Resource Utilization Evaluation		X		
Adverse Event and Concomitant Treatment Evaluations	X	X	X	
Survival and Disease Condition				X
Subsequent Treatment				X

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Details of the tests and evaluations are given in Table 2.

Table 2: Activity Details

Informed Consent	Before you can begin the study, the study staff will speak with you about the study and you will need to put a signature on a consent form if you wish to take part.
Medical History	You will be asked how you are feeling, about your medical history, demographics (like year of birth, age, sex, race, and ethnicity), and about any drugs you are consuming. This will involve any prescription or non-prescription drugs. This helps us understand your overall health and if this study is appropriate for you.
MDS Disease and Transfusion History	Information about your diagnosis of MDS will be collected by your study doctor, including when you were diagnosed, the type of MDS you have, and how it has been treated. Tests to confirm the condition of your MDS disease will be done during the screening period including bone marrow and blood tests. Information about your earlier treatments with red blood cell or platelet transfusions, including the results of any blood work obtained beforehand will also be collected by your study doctor to see how much hemoglobin was in your blood before every transfusion. The number of transfusions administered to you in the previous 2 months when your hemoglobin was reduced will be counted. All of this information helps your study doctor to understand the status of your disease and if this study might be an option for treatment.
Physical Exam	A physical examination is a routine evaluation by your study doctor to check your overall physical health. It normally involves: looking at the body, feeling and tapping areas of the body, like your belly, and listening to sounds, like your lungs. After the first complete physical examination later repeat evaluations may be limited to a few areas of your body depending on your symptoms or physical complaints.
Vital Signs	Vital signs are your blood pressure, heart rate, respiratory rate (number of breaths per minute), and temperature measurements.
Height and Weight	Your height will be measured once at the start of the study. Your weight will be checked every month to ensure the appropriate dose of study medication is administered. To measure your weight, you will be asked to take out your shoes and any heavy clothing as well as empty your pockets.
Electrocardiogram (ECG)	An electrocardiogram (ECG) is a test that tells how the heart is functioning. You will have small, soft pads put temporarily on the chest, wrists and ankles and attached to a monitor that will indicate the electrical activity of your heart.
Echocardiogram (ECHO)	An echocardiogram (ECHO) is a test that uses sound waves (ultrasound) to make images of your heart to indicate how well the heart muscle and the structure of the heart is functioning. A probe known as a transducer is passed over your chest (transthoracic) or in your throat (transesophageal) to take images of your heart indicated on a video monitor. It may take up to 30 minutes to 1 hour to complete this exam.

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	If a transesophageal ECHO (TEE) is done, a thin, flexible tube with a small probe will be gently put down your throat into your food pipe (esophagus), which sits behind your heart, to take clear images using sound waves. You will get drugs to relax and numb your throat in advance.
Coagulation	A blood sample will be collected by needle stick (or an intravenous (IV) line if you have one) to check how well your blood clots.
Hematology	A blood sample will be collected by needle stick (or an intravenous (IV) line if you have one) for measuring the number and types of cells in your blood, like red blood cells, white blood cells, and platelets. The total amount of blood needed each time this test is done is approximately 4 mL or approximately 1 teaspoon. This test will be done again at least every 2 weeks or more often if required. The hemoglobin results from this test will be used to monitor your response to the study medication and to evaluate whether you might require blood transfusions.
Chemistry	A blood sample will be collected by needle stick (or an intravenous (IV) line if you have one) to check your general health and to measure components of your blood to find out how well your liver and kidneys are functioning. The total blood volume needed each time this test is done is approximately 6 mL or approximately 1½ teaspoons.
Urinalysis	A cup will be given to you to take to bathroom. You will be asked to pass urine into this cup. The urine collected will be used to conduct some tests. Some of the urine will also be sent to a clinical laboratory for testing.
Pregnancy Testing	If you are a female of childbearing potential, a urine sample is needed to test if you are pregnant. If the test is positive, then a blood test (approximately 5 mL or 1 teaspoon) will be needed to confirm. If you are pregnant, you will be unable to begin the study or will have to stop the study treatment if you have previously begun.
Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and Human Immunodeficiency Virus (HIV) Status Check	You will be asked regarding your history of HBV, HCV and HIV infection. If you have any of these viruses you cannot take part in the study. If you have never been tested or are not sure of your condition, then your study doctor may require a blood sample collected by needle stick (or an intravenous (IV) line if you have one) to test your blood for HBV, HCV and/or HIV. If the results indicate that you have hepatitis B, hepatitis C, and human immunodeficiency virus, you will be informed about this in confidence and be provided information regarding medical follow-up. Positive results for certain viruses that cause these infectious diseases may require to be reported to the local health authorities in your country, if needed by law.
Serum Erythropoietin (EPO)	A blood sample will be collected by needle stick (or an intravenous (IV) line if you have one) to evaluate how much of the hormone erythropoietin (serum EPO) is there in your blood. This hormone helps to balance the red blood cells amount produced in the bone marrow. If the level is very high this study treatment might not be a good option and you would not be suitable.
Peripheral Blood (for Blood Smear) and Bone Marrow Sample Collection	Bone marrow aspirate and bone marrow biopsy are included in bone marrow sample collection. These procedures are conducted to gather and check bone marrow, a spongy tissue inside some of your larger bones.

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	For the bone marrow aspirate, a special thin needle is placed into the hip bone to withdraw approximately 5 mL (1 teaspoon) of bone marrow fluid. For the bone marrow biopsy, a special hollow needle is placed into the hip bone to remove a small piece (approximately 1.5 cm or 0.5 inches long) of the solid part of the bone and bone marrow. This is approximately the thickness of a lead pencil. Some sedation or local anesthesia may be given to you to numb your skin to reduce any pain related to these procedures, but there can still be discomfort and bone pain for some time following these procedures. You may be given with medication by your study doctor if required for the discomfort. In addition to the bone marrow evaluation, a few drops of blood will be collected by needle stick (or an intravenous (IV) line if you are having one) and put on a slide. This blood smear will be sent, together with the bone marrow samples, to the study specific pathology laboratory to evaluate your MDS.
MDS Disease Evaluation	The peripheral blood sample (for blood smear) and bone marrow samples mentioned above will be sent to the study specific pathology laboratory during screening, after you complete 24 weeks and 48 weeks of treatment, and then as deemed needed by your study doctor until the end of study treatment visit (EOTx). A peripheral blood sample (for blood smear), bone marrow aspirate and bone marrow biopsy are needed at screening and after you finish 24 weeks of treatment. The bone marrow biopsy is optional after that. The MDS disease evaluation is conducted during screening, to confirm your diagnosis of LR-MDS and to determine whether you are suitable for the study. The MDS disease evaluation is conducted during study treatment, to know about the condition of your LR-MDS and to evaluate how much your disease reacts to the study treatment.
Randomization	You will be allotted at random to one of two treatment options by a computer program based on your disease stage and risk factors. When you are randomly assigned a treatment, this means you are put into a treatment group by chance (like tossing a coin).
Study drug Dosing	This is the investigational medication being tested in this study. It is administered under the skin by injection (subcutaneous injection) every 28 days (once per month).
Epoetin Alfa Dosing	This is the standard of care drug being in comparison to the investigational medication in this study. It is administered under the skin by injection (subcutaneous injection) every 7 days (once per week).
Transfusion Verification	You will be asked regarding any blood transfusions you have obtained since your last visit to the site. This involves any transfusions that may have been administered at a different clinic or hospital. If a transfusion does happen at a different clinic or hospital, then your study doctor will require to get copies of a report that documents the transfusion procedure, also the results from any blood tests (which include hemoglobin, platelets and iron related tests) conducted before the transfusion.
Pharmacokinetic (PK) Evaluation	If you are allotted to Study drug treatment, then blood samples collected by needle stick (or an intravenous (IV) line if you have one) will be taken for measuring how much study drug is in your blood and evaluate how

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	well the study drug is absorbed and broken down by your body. A part of this sample might be used for biomarker research purposes. The total amount of blood needed each time this test is done is approximately 16 mL or approximately 3 teaspoons per sample.
Anti-Drug Antibody (ADA) Evaluation	If you are allotted to Study drug treatment, then blood samples collected by needle stick (or an intravenous (IV) line if you have one) will be taken to check whether your immune system is making antibodies (proteins) to the study medication. This would happen if your body perceives the study medication as a foreign substance in your blood. The total amount of blood needed each time this test is done is approximately 8 mL or 1½ teaspoons.
Biomarker Evaluations	Some blood samples will be collected by needle stick (or an intravenous (IV) line if you have one) strictly for research objectives. Biomarkers are biological or chemical “markers” that can be found in blood and tissue samples of patients with MDS. Biomarker research may help us learn which patients are more likely to react to the study drug or more likely to develop side effects to the study drug. It also helps us determine what other effects the study medication is having on the body. You will not benefit from this research, but it might help people in the future. The biomarker evaluations in this study involve the following: ▪ A blood sample (approximately 8 mL or approximately 1½ teaspoons) will be taken once per month while you are taking study drug to test for known clinical biomarkers. ▪ Another blood sample (approximately 11 mL or approximately 2 teaspoons) will be taken at 7 timepoints within the first 12 weeks of study treatment and then quarterly after that to test for exploratory biomarkers. This blood sample will be used also for disease-associated genetic tests of your ribonucleic acid (RNA). ▪ An additional blood sample (approximately 3 mL or approximately ½ teaspoon) will be taken on your first day of treatment to test for disease specific genetic mutations.
Healthcare Resource Utilization Evaluation	Information will be taken during routine study visits, about the number, period, and reasons for any admittance in the hospital that have happened since your last visit to the site. Also, data will be collected on the number of unplanned site visits, diagnostic procedures, and treatment interventions that did not need admittance in the hospital.
Adverse Events	You will be asked whether you have observed any negative signs and symptoms or any alterations in your health. These changes are known as adverse events.
Concomitant Drugs/Procedures	You will be asked regarding any drugs you continue to consume or any new drugs you have began consuming. It is essential that you inform the study doctor regarding all the drugs you are consuming which includes: prescription medications, over-the-counter drugs, vitamins, herbal supplements, vaccines and anything else you may take. You may not consume any other drugs for treating your LR-MDS or participate in

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	another research study that involves consuming drugs while you are on this study treatment. You will also be asked regarding any blood transfusions or any other medical procedures or surgeries that you have undergone or are expected to have.
Survival Follow-up and Disease Condition	After the end of the safety follow-up period, you will join the survival follow-up period where you will be contacted, typically by telephone, every 3 months to find out how you are feeling and to give updates on your MDS disease condition. You will also be asked to complete the EQ-5D-5L questionnaire by phone.
Subsequent Treatment	During the survival follow-up period, you will be asked to report any treatments for MDS disease that you have begun since discontinuing the study treatment.

Patient Reported Outcomes (PROs) Evaluations Needed During the Study

EORTC QLQ-C30 (Questionnaire 1)	This questionnaire measures physical function, breathlessness, and tiredness. It is a 30-item, patient-reported multi-domain questionnaire designed to evaluate the functioning, well-being, and symptom experience of patients with cancer. [European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30]
FACT-An Anemia scale (Questionnaire 2)	This questionnaire is used to evaluate the effects of disease symptoms on functioning and health in patients with anemia. [Functional Evaluation of Cancer Therapy-Anemia]
EQ-5D-5L (Questionnaire 3)	This questionnaire contains 2 components: a descriptive system and a VAS (visual analogue scale). The instrument's descriptive system contains 5 items measuring problems with mobility, self-care, normal activities, pain/discomfort, and anxiety/depression. The instrument's VAS permits you to rate your own health on a 100-point scale.
Transfusion Burden Evaluation (Questionnaire 4)	This questionnaire contains a single item measuring the participant-perceived burden of any red blood cell transfusions (which include time commitment as well as physical and emotional burden) that have been done in the previous 4 weeks.
PGI-S items (Questionnaire 5)	With this questionnaire, you are asked to rate the severity of symptoms or functional limitations over the preceding week. [Patient Global Impression of Severity]

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PGI-C items (Questionnaire 6)	With this questionnaire, you are asked to assess changes in results since the beginning of trial intervention. [Patient Global Impression of Change]
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Minimum Blood Volumes

The total quantity of blood collected from you in the study will be based on how many cycles of treatment you get on the study. The minimum approximate blood volume to be taken at every visit is below:

Time Period	Blood Volume (tablespoons)
Screening Period	About 35 mL or approximately 2½ tablespoons
Study Treatment Period (through End of Treatment (EOTx) visit)	About 50-125 mL or approximately 3½-8½ tablespoons per month
Safety Follow-Up Period	About 18 mL or approximately 1 tablespoon per month
Survival Follow-Up Period	None
Additional monthly testing up to 1 year if you have antibodies to elritcept at end of the safety evaluation	About 8 mL or approximately ½ tablespoon each month
If you have a transfusion, sample for hemoglobin and chemistry	About 10 mL or approximately 1 tablespoon before every transfusion

Will there be devices and any type of technology used in the study?

Type of Electronic device and related technology	What company is giving you with this electronic device [and/or] related technology?	How is the electronic device [and/or] related technology being used?	When is this electronic device [and/or] related technology going to be used?
Tablets for Questionnaires (PROs – Patient reported outcomes)	Signant Health	To record answers to questionnaires	During the screening, treatment, safety follow-up and survival follow-up periods

All patient reported outcomes (PROs) evaluations should be completed using the electronic devices identified above and associated technology. You cannot take part in this study if you decide not to use the electronic devices and associated technology.

By giving your consent, you consent to use the electronic devices and associated technology as requested. Kindly note that:

- Takeda will have access to information that indirectly identifies you such as your study ID number.

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- Your personal information will be used to register you as a user of the electronic device and related technology.

Additional information about the electronic devices and associated technology will be given to you if you decide to enroll in the study. If you have queries about the use of the electronic devices and related technology, kindly ask your study doctor.

What will occur to your study samples and biomarker images?

All blood, urine, and bone marrow sample(s) collected from you during the study will be sent to the Sponsor's designated laboratory. The laboratory will temporarily store the sample(s) and arrange for tests that are associated with this study. The sample(s) will be labeled with a code and not your name.

The sponsor, its agents and affiliated companies will have access to the sample(s) taken. During the study, all sample(s) taken will be stored securely with limited access and the sponsor will require anybody who works with the sample(s) to agree to hold the research information and any individual results in confidence. The testing/storage facility might change, you may always request to know the location of your samples.

How will your samples be stored?

All blood and urine samples taken for standard clinical tests will be destroyed at or before the end of the study when all the test data has been analyzed.

All bone marrow aspirate, bone marrow biopsy and peripheral blood samples taken for the biomarker research will be kept by the Sponsor with its long-term storage partners. This involves the bone marrow aspirate, bone marrow biopsy and peripheral blood samples taken for MDS disease evaluation and biomarker/PK/ADA evaluations. After the completion of the study, these samples will be stored for up to 15 years unless there are local laws which need a shorter storage period, or you withdraw consent for sample storage and use. After that time, the samples will be destroyed. Records linking your identity will be kept by the study doctor with your samples as needed by applicable law.

Can I withdraw my consent for using my samples?

If you leave the study, you can also request that your sample(s), and material obtained from your sample(s), be destroyed at any time by getting in touch with your study doctor. As long as the records connecting your identity to your sample(s) prevail, your sample(s) may still be destroyed. However, the sponsor will be entitled to maintain and use any study results or information which was received from your sample(s) before your request to stop.

Will I receive my test results?

The samples taken from you for biomarker research, and the information and results from tests done with these samples, can be used individually or in combination with other data. The tests done with these samples are not intended to make determinations regarding your health or the possibility you will develop any illness, so no test results will be given to your doctor or placed into your medical record. By putting a signature on this consent form, you consent that we may store your samples and can use them for the research explained in this informed consent form.

Who is the owner of my samples and how will they be used?

The information collected from the sample(s) taken from you in this study will be analyzed and assessed by the sponsor, and may result in new discoveries, patents or products. You have no rights to and will not get

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payments of any kind for such discoveries, patents or products. By agreeing to take part in this clinical study, you are waiving any ownership rights that you may have in sample(s) taken from you during this study to the study sponsor.

In case the sponsor sells study drug to another company performing clinical research, your samples taken as part of this study can be shared with that company as part of that transaction.

How will your personal information be safeguarded for samples?

The confidentiality of your information to the fullest extent possible will be protected by us. Your samples and related data will be coded to safeguard your identity. Only the study doctor will have the key to the code key that may link your samples to your identifying information. The key will be stored securely and safeguarded. For additional information about how we safeguard your privacy, kindly see the section entitled <“How will your privacy be respected, and the confidentiality of your personal information be maintained?”>.

Biomarker Image Analysis

Biomarker testing may involve image analysis that is performed on your tissue biopsy after it is sectioned and put on a glass slide. This testing uses specialized image analysis computer software to count or measure various cell types in the tissue. This testing may help researchers learn how changes in cell populations may affect a disease or response to treatment. Analyses of samples from a large number of people can also help researchers learn more about other illnesses, possible links among illnesses, and new avenues for drug development.

Kindly understand that the biomarker images of bone marrow will be recorded and saved to a computer program and sent in a secure way to the sponsor and/or their commercial partners for central reading and analysis objectives. A unique code that is allotted to you will identify the recorded materials. Your name or other identifying information will not be used. These recordings may be viewed by personnel from the sponsor and the sponsor's partners for this study. The biomarker images will be kept private, and other person will not have access to these images in so far as allowed by law. Within the limits imposed by technology and the law, every effort will be made to keep the privacy of your information. Biomarker images will be kept in a secure location with limited access. The biomarker images will be stored for at least 25 years from the completion of the study, or if less, the maximum period allowed under applicable law or until withdrawal of consent. After that period, the biomarker images will be discarded.

Genetic Testing

Genetic testing will be done on your diseased bone marrow tissue and/or blood samples to identify mutations in key genes found in MDS and acute myeloid leukemia (AML). Genes are made of a type of molecule known as deoxyribonucleic acid, or DNA, and DNA varies widely from one individual to another. DNA is the genetic material that carries the instructions for your body's development and function. Each person's body have tens of thousands of genes (“genome”). Your genome or all of your genetic material will not be tested. Only a limited set of selected genes in your diseased bone marrow tissue and/or blood sample(s) will be tested.

Biomarker testing will include the analysis of all ribonucleic acid (RNA) from the cells in your blood. This will permit us to learn how genes are expressed in those cells during collection. This testing may help researchers learn how changes in the expression of genes are associated with disease or study drug treatment response. The RNA analysis is only for research purposes and is not a medical test. This means that the medical importance of the results might not be known, or that they may not be associated with any

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Sponsor Name: Takeda Development Center (TDC) Americas, Inc.

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medical condition. You, the study doctor, any insurance company, your employer, your family, or any physician who treats you will not be given the results of tests on your sample. These are research tests and not applicable to your medical care. Measures will be put in place by the sponsor and researchers to reduce the possibility for the results from this research being linked to you, but there is always the remote possibility that information obtained from your participation in the research may be revealed.

What are the side effects of the study medications and the risks of participating in the study?

You may have discomforts and risks during the study, from study drug and the study procedures. These may differ from individual to individual. Everybody participating in the study will be carefully monitored for side effects; however, doctors are not aware all the discomforts and risks that may occur. There is always the possibility that unknown risks may happen and some of which may be serious, fatal, or even lifethreatening. It is significant that you report all symptoms/health problems to the study doctor/staff, whether you consider these problems are because of the study medication or not. In case it is an emergency and you are not able to get in touch with the study team or doctor, you must contact local emergency services right away. If you have a severe reaction to the study medication, the study doctor may decide that you should be removed from the study for your safety.

The more commonly occurring discomforts and risks are mentioned below, as are the rare but serious discomforts and risks.

Furthermore, It is possible that there could be a failure of investigational product to give intended therapeutic effect. As the objective of this study is to evaluate the safety and effectiveness of an unapproved investigational product (study medication), it is possible that the study drug may not have the intended therapeutic effect.

What are the possible risks for consuming the Takeda medication?

As of 03 April 2025, about 109 participants with MDS have obtained at least 1 elritercept dose in clinical trials with most participants getting elritercept for 12 months.

Elritercept (TAK-226, the study drug) is an experimental drug and the risks to human subjects have not been completely assessed. With all drugs, there is the possibility of complications and side effects that are not known at this time. Other risks may occur that are unknown which might be serious. You will be monitored closely at the time of the study.

You may experience none, some or all of the side effects mentioned below, and they can be mild, moderate or severe. If you experience any of these side effects, or are concerned about them, speak with the study doctor.

Many side effects disappear shortly after treatment ends. However, sometimes side effects may be serious, long lasting, or permanent. If a severe side effect or reaction happens, your study doctor may require to stop your study drug treatment. Inform your study doctor right away about any new or abnormal symptoms or changes in your health that you become aware of or have concerns. Your study doctor will speak with you how to manage symptoms or side effects. The treatment of the side effects will be based on the type and severity of the symptom(s).

During screening before study treatment or during participation with study drug treatment if an earlier unknown medical condition is discovered, the study doctor will discuss:

- whether you are suitable to start or continue study treatment participation

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- whether you need a referral to your usual physician or to a specialist

The study drug may be a risk to an unborn child or nursing baby, so it is important to read the section on “Pregnancy, contraception and nursing” carefully, whether you are a male or female.

The following side effects were reported very commonly (observed in over 1 in 10 people) by the participants with myelodysplastic syndromes/neoplasms that obtained the study drug in another research study so far.

- Loose, watery stools
- Fatigue/weakness
- COVID-19
- Low red blood cells: can cause breathlessness/ breathing difficulty; feeling weak; lightheadedness; loss of appetite; numbness and tingling of hands and feet
- Giddiness (lightheadedness)
- Nosebleed
- Nausea (feeling ill to the stomach)
- Breathlessness
- Constipation (trouble passing stools)
- Fall
- Swelling in hands, feet, or ankles
- Cough
- Increase in blood pressure
- Urinary tract infection (symptoms of infection might involve fever, pain, redness, burning when peeing, difficulty peeing or blood in urine)
- Joint pain
- Headache
- Back pain
- Vomiting

It is possible for developing antibodies to the study drug, showing an immune reaction. At times, this can cause the drug to not work effectively or can cause allergic reactions (see below for more information). It can also cause a skin reaction where an injection (shot) was administered known as an injection site reaction, that can cause some redness and swelling.

Also, low platelets (can cause bruising or bleeding), fever, neutropenia (a condition in which the number of white bloods cells known as neutrophils is abnormally low that can increase the risk of infection), and lung infection (symptoms of infection might involve fever, chest pain, cough, and/or breathing difficulty) have been reported very commonly in another research study by the subjects with a blood condition known as myelofibrosis given treatment with study drug alone.

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What are the risks of epoetin alfa?

If you are allotted to get the comparator study drug epoetin alfa and not study drug, you may experience none, some or all of the side effects mentioned below that have been reported with epoetin alfa. The side effects to epoetin alfa study medication might be mild, moderate or severe. Other risks may occur that are unknown which might be serious. Inform your study doctor right away about any new or abnormal symptoms or changes in your health that you become aware of or if you have concerns. Your study doctor will speak with you how to manage symptoms or side effects. The treatment of the side effects will be based on the type and severity of the symptom(s).

- Loose, watery stools
- Nausea
- Vomiting
- Fever
- Headache
- High blood pressure and severe increase in blood pressure (called hypertensive crisis) may result in brain disorder, seizures, stabbing migraine-like headaches and possible stroke
- Increase in risk of blood clots in a vein (possible symptoms involve pain, swelling, and/or redness), or in an artery (may result in organ damage like stroke, failure to breathe, possible blindness, bleeding in brain, and/or heart attack) that may be fatal particularly in patients with pre-existing risk factors such as obesity and prior history of these events
- Chills, flu-like symptoms
- An allergic reaction of the skin at the site where an injection (shot) was administered, that can cause some redness and swelling
- Swelling in arms and/or legs
- Cough
- Seizure (particularly in patients with history of epilepsy and conditions such as brain and spinal cord infection or brain cancer)
- Joint pain, bone pain, muscle pain and/or body aches, arm and/or leg pain
- High blood platelet count (might lead to increased clotting)
- High blood levels of potassium (might lead to kidney failure or heart effects)
- Respiratory tract congestion (blockage or stuffiness in the airways, often because of excess mucus or inflammation)
- Decrease in bone marrow function and inability to make red blood cells causing a low red blood cell count called anemia, which include symptoms of tiredness, weakness, and pale skin
- Hypersensitivity and Anaphylactic reaction: Allergic reaction that may involve a rash, hives, fever, breathing difficulty, swelling beneath the skin, often around the eyes, lips, tongue, and throat (angioneurotic oedema), and low blood pressure. However, usually reversible with treatment, it may be severe or fatal

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- Worsening of genetic disorder known as porphyria that may involve symptoms like pain in the abdomen, confusion, anxiety, seizures, muscle pain, increase in sensitivity to sunlight leading to skin reactions like blisters and itching on sun-exposed areas

Other adverse reactions reported with epoetin alfa involves severe skin reactions such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) that can show up as various blisters, hives, and other lesions in various locations on the body which includes palms and soles, face and other extremities. This is serious and can be fatal. If you experience any of these side effects, inform your study doctor right away.

Allergic reaction risks: Any drug has a possible risk of an allergic reaction, that if not given treatment immediately, may become fatal. They are mild to moderate in severity. However, fatal reactions may happen at any drug dose. If you believe you are having a serious allergic reaction after taking study drug or epoetin alfa, you must look after emergency medical assistance right away. Kindly inform the study doctor right away if you experience any of these symptoms. Some symptoms of allergic reactions are as follows:

- Rash or itching
- Coughing, wheezing and breathing difficulty
- Giddiness (lightheadedness) and fainting
- Swelling surrounding the mouth, lips, tongue, throat and/or eyes
- Fast pulse rate
- Sweating

You will be monitored carefully by your study doctor for any signs or symptoms that you might be experiencing an allergic reaction, and appropriate care will be taken by the study doctor. If you do not understand what some of these side effects or risks mean, ask the study doctor to describe them to you.

Are there any other possible risks for participating in this study?

While clinical studies are designed to make sure of the safety and health of participants, there are still some risks and discomforts related to the study procedures that you must be aware of:

Collection of Blood Samples: During blood sample collection, you may experience slight pain and/or experience bruising where the needle was placed into the skin. You may also experience excess (too much) bleeding, blood clots, and infections where the needle was placed into the skin, but this is extremely rare. Fainting occasionally occurs During, or shortly after, withdrawal of blood. This event most frequently happens if you get up rapidly from a sitting or lying down position. If you feel faint, you must let study site staff know and lie down right away to avoid possible injury due to falling. Very rarely, some people experience short and long-term damage of vessels and nerves, that may be irreversible and may lead to long term pain and impairments.

Bone Marrow Aspirate and Biopsy: Potential side effects involve bleeding, infection, bruising, pain, or discomfort at the needle stick site. Based on the procedures at your trial center you may get a numbing drug which will be injected into the skin above the area of the bone to lessen the pain. In rare cases, there may be nerve damage. In very rare cases, people may experience an allergic reaction to the local anesthetic (numbing drug). The allergic reaction may involve rash/hives, flushing of the face, itching, wheezing, and tightness in the throat. A scar can also form at the aspiration/biopsy site. You may need to put a signature and date a separate consent form for the bone marrow biopsy and aspiration.

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Echocardiogram (ECHO): Some people might feel uncomfortable having to lie in one position and you might develop mild rash or skin irritation where the electrodes (sticky patches) were put. [If Transesophageal Echo \(TEE\) is done](#), possible side effects involve sore throat, infection, or aspiration in addition to possible esophageal injury, which include bleeding or perforation (very rare).

Electrocardiogram (ECG): You may experience mild irritation, redness, or itching where the recording patches are put.

Subcutaneous Injection: In a subcutaneous injection, a short needle is used to inject a treatment into the tissue layer between the skin and muscle. If you experience any of these reactions, your doctor must be contacted immediately. As with any type of injection, there is a potential risk of infection where the shot was administered. Other risks are an injection-site reaction, that is a localized reaction that may happen at the site where the study drug is injected. Symptoms related to an injection-site reaction may involve pain, redness, tenderness, warmth, itching, swelling, discomfort, bleeding, hardening of the skin in the area that surrounds where the study medication was given, and severe skin or tissue damage.

Red Blood Cell (RBC) or Platelet Transfusions: The possible risks of having an RBC or platelet transfusion are as follows:

- You may have a mild allergic reaction with skin itching and hives, fever and chills; rarely a serious allergic reaction may happen with severe breathlessness, fast heart rate, chest pain, nausea and vomiting.
- If you have heart or kidney conditions, you may have increased breathing difficulty and a cough; the additional fluid may put further stress called overload on your heart or kidneys.
- If you have undergone multiple RBC transfusions, you can produce antibodies (proteins in your blood) that attack the new red blood cells in your blood or too much iron might accumulate in your body which may need drugs to help your body remove the iron.
- If you have undergone multiple platelet transfusions, you can produce antibodies (proteins in your blood) that attack and destroy platelets in your blood. As a result, you may experience easy bruising, bleeding gums, nosebleeds or blood in your urine or feces for approximately 5-12 days after your transfusion.
- Your immune system can destroy all of the red blood cells (RBCs) in your body if the RBCs in the transfusion are not matching your body's own RBCs. This can cause a rare, but serious, reaction with chest pain, chills and fever, dark urine, lower back pain and nausea.
- If you have a weakened immune system from transplants or other illnesses, you might have an increase in risk of fever, diarrhea and rash because of graft versus host disease when donated white blood cells attack your body tissues.
- In rare cases, donated blood can carry harmful bacteria or viruses which cause blood-borne infection.

What are the risks of the genetic/genomic tests?

When you give your blood or tissue for MDS genetic research, you are sharing genetic information about yourself. As some of your genes are shared by family members, this information may also disclose things about your biological relatives. However, it is very unlikely that the sponsor will find genetic changes that may be passed down in families, as the research will only see genes connected to MDS in diseased (not healthy) tissue. Still, there are some risks to consider. There is a small possibility that information obtained

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from this research may one day be traced back to you. If that occurred, your privacy may be affected by it, and there is a chance—though unlikely—that it could lead to discrimination by employers or insurance companies against you or your family members. To safeguard your identity, your samples will be labeled only with your study number, not your name or other personal details. However, as technology is always changing, we will not be able to predict all possible future uses or risks associated with genetic information.

Pregnancy, contraception, and nursing

Men and females will both be invited to take part in this study, which include females of childbearing potential.

Kindly read the following instructions cautiously, there are some requirements associated with contraception and pregnancy in order to participate in this study. The study doctor will give counselling for appropriate methods of birth control during the study. You will be reminded by the study doctor of the importance of not getting pregnant throughout the study.

For Men

It is unknown whether sperm or an unborn baby will be affected by the study drug. For this reason, to participate in the study you should agree not to father a child throughout the study and for at least 60 days after the last study medication dose.

If you are a male participant and sexually active with a female of who is pregnant, or may become pregnant, irrespective of if you have undergone a vasectomy, you should agree to use condoms with or without spermicide each time you have sex during the study and until at least 60 days after the last study medication dose.

If your partner does get pregnant while you are participating in the study drug treatment, you should inform your study doctor right away who will be able to advise you. In this situation, your partner should be under medical supervision throughout her pregnancy, and the baby must be under supervision after it is born. Your partner can be asked to provide her consent to the collection of information associated with both herself also the baby.

For Females

If you have been surgically sterilized or have been through the menopause (speak about this with your study doctor), you do not require to meet any contraception or pregnancy test requirements to participate in this study. Otherwise, you should consent not to get pregnant or nurse a baby throughout the study and for at least 60 days after the last study medication dose.

If you could become pregnant and are sexually active with a male partner who has not been sterilized, you should consent to use highly effective contraception (mentioned below) from the time of putting a signature on the ICF and until at least 60 days after the last study medication dose:

- Combined (estrogen- and progesterone-containing) hormonal birth control (oral, or in the vagina [intravaginal], or on the skin [transdermal]) related to preventing ovulation
- Progesterone-only hormonal birth control (oral, injectable, implantable) related to the preventing ovulation
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system
- Bilateral tubal ligation (to have both of your uterine tubes tied)

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- Partner with vasectomy, i.e., surgically cut off the supply of sperm (provided that partner is the sole sexual partner of the participant and that the vasectomized partner has obtained medical evaluation of surgical success)
- True sexual abstinence (avoidance) defined as refraining heterosexual intercourse for the study period until at least 60 days after the last study medication dose and only when this is in line with your preferred and normal lifestyle

In order to be suitable for the study, you should have a pregnancy test to confirm that you are not pregnant. This test will be done again just before you begin consuming the study drug and then regularly during the study until at least 60 days after the last study drug dose.

If during the study a pregnancy test indicates that you might be pregnant, the study drug treatment will be discontinued and the treatment will end. By putting a signature on this document, you give consent to the collection of information associated with both yourself and your baby.

You will be asked for the outcome of any tests and procedures conducted during your pregnancy and up to the birth. You might also be asked for the outcome from any assessment of the baby following birth.

What are the potential benefits of participating in this study?

You may or may not benefit as a result of participating in this study. It is not guaranteed that your need to get blood transfusions will reduce; it may even become worse. This study is being performed to gather additional information about a medication that might benefit others in the future.

What will occur if something goes wrong, or I get hurt?

You shall comply with the instructions from your study doctor. If you have an adverse reaction in the study, kindly let your study doctor know right away, and medical management will be given free of cost as long as needed, or till such time it is established that the injury and/or the adverse reaction is not associated with the study drug or the study procedure, whichever is earlier.

In case of any trial-related injury or death (as defined in the applicable Indian regulations) that arise directly from the proper management of the study drug as per the protocol or the accurate performance of the study procedure needed by the protocol, the sponsor or its representative, as the case might be, shall give financial compensation for such injury or death as per the applicable regulations. In case of a study related injury or death (as defined in the applicable Indian regulations) that arise from the violation of the protocol, misconduct or negligence by the study site or your study doctor, the study site, your study doctor or their representative, as the case may be, shall give financial compensation for such injury or death to you.

You will not lose any of your legal rights as by putting a signature on this informed consent form.

What are your alternatives if you do not take part in the study?

You do not need to participate in this study to get treatment for your anemia because of lower-risk myelodysplastic syndrome (LR-MDS).

There are other alternatives like: imetelstat, lenalidomide, luspatercept, or taking part in another clinical trial. There might be benefits and risks associated with these treatments that the study doctor will speak with you.

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This study has a limit on the number of subjects which may be enrolled across all the study sites around the world. So, there is a minor chance that even if you consent to take part and fulfill all entry criteria, after the enrollment limit is reached, you cannot take part in the study. Your study doctor must inform you in advance if this may occur to you.

If you are not permitted to participate in the study for any reason, your treatment options will be discussed with you by the study doctor and might refer you back to your primary care doctor or specialist.

What will occur if new information is available about the study medication or study?

New information regarding the study drug(s) that may affect your decision to remain in the study may get available throughout the study. If this occurs, this information will be shared with you by your study doctor in a timely manner and you will be asked whether you wish to continue taking part in the study. You can decide to stop participating in the study at that time. If you stop participating, the steps you should follow will be discussed by your study doctor. If you decide to continue participating in the study, you might be asked to read and put a signature on a revised consent form that contains the new information.

Can you stop participating in the study?

You may withdraw from the study, at any time, without penalty or loss of benefits to which you are otherwise entitled. It is up to you if you do or do not wish to participate. Your decision will not change the medical care you receive from your doctors now or in the future.

There are a few methods to withdraw from the study. You may withdraw your consent from all participation in the study, including the collection of follow-up data. You may also decide not to continue consuming the study medication (study drug or epoetin alfa) but agree to continue to take part in the non-treatment part of the study and to the continued collection of data. Such continued participation may involve the following:

- An End of Treatment Visit
- Follow-up Visits or Telephone Calls

These options will be discussed with you by your study doctor. Any further participation is voluntary. Even if you agree to continue to take part in the study to gather your data, you may always change your mind and withdraw your consent.

If for any reason, you stop participating in the study the study doctor may carry on to use and distribute any data collected up until that point in the study if it is for the purposes explained in the informed consent form. If you withdraw your consent to take part in the study, then no more information about you will be taken for this study. However, all information you gave before leaving the study can still be used.

Your study doctor may decide that it is best for you to stop participating in the study. If so, they will discuss with you the reasons why you may have to leave the study. For example, you may have to stop taking part in the study against your wishes if you require other treatment, do not comply with the study plan, have a study-related injury, or for any other reason. At any time, the sponsor, regulatory authority, and/or [Ethics Committee](#) may also end the study.

What will occur at the end of the study?

Your study doctor or primary care doctor will discuss with you the options for your continued care at the end of the study.

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If you were allotted to epoetin alfa treatment and had supplies given to you for self-administration, then the needed steps for returning any remaining epoetin alfa supplies to the site will be reviewed by your study doctor.

Do I need access to the study medication after the study stops?

If you were allotted to the study medication, and are still on treatment, then you may be permitted to continue to get elritercept if your study doctor determined that you are still getting clinical benefit from it more than the possible risk of side effects. The Sponsor may carry on to supply study medication through a post study access process. Post study access to study medication might be stopped if the development of study drug has been suspended or discontinued by the sponsor, and/or there is no longer supply available from the sponsor.

If you were allotted to epoetin alfa and are still on treatment, then you may be permitted to continue to get epoetin alfa if your study doctor determined that you are still getting clinical benefit from it more than the possible risk of side effects. The sponsor might continue to supply epoetin alfa via a post-study access process if required.

Will it cost you anything to participate in the study?

There is no cost to you for taking part in this study. The study drug, study-related procedures and tests, and study visit will be given free of cost.

Will you have help with expenses for travel?

Reasonable travel expenses for you and up to one caregiver might also be reimbursed. Also, accommodation and meal costs can be reimbursed if the study needs extended visits or certain procedures. Reimbursement may be given to you for these expenses by your study doctor or his/her staff.

Will payment be given to you if you participate in the study?

Payment will not be given to you for participating in the study.

Reasonable actual [travel costs of up to INR 2000](#) and [meal costs](#) up to INR 435 and [hotel costs](#) up to INR 6000 in total associated with you attending the study clinic for the study will be reimbursed by your study doctor or his or her staff or the site.

Will you have help at home for this study?

If you are allotted to epoetin alfa treatment, your study physician may permit you to get some of the weekly injections at home or at another approved location. If permitted, these injections may be administered by a home healthcare provider. You do not need to agree to home visits for you to take part in this study. If you and your doctor consent to use home healthcare services, a clinician will get in touch with you to schedule the visits. The clinicians that supports this study have obtained specific training on this study and will communicate often with your doctor and the study staff. In order to perform the home visits, the clinician, the clinician's organization, and the home healthcare service provider may have access to your individually identifiable protected health information, like your name, address or phone number. This type of information, which is kept in the United States and might be kept outside the United States, will be used only as needed to schedule and perform the home visits and will not be given to this study sponsor. The data taken during

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a home healthcare visit will be shared with your study staff and filed in your study medical records.

How will your privacy be respected, and the confidentiality of your personal information be kept?

If you consent to participate in the study, the study doctor will collect and keep personal information regarding your health and your treatment. This might involve information that can be used to identify you, like your name, address, phone number, date of birth, racial origin (only to be used for clinical research purposes), new and prevailing medical records, or the types, dates, and results of various tests and procedures, also information in your medical record and information created or taken throughout the study.

Under applicable data protection law including the “Digital Personal Data Protection Act 2023” (DPDPA) both the sponsor and the study doctor/clinic can be solely or jointly be considered data fiduciaries of your personal information in the context of the study (based on the nature of the data) (i.e. they determine how and for what purposes your personal information are used and revealed).

The Sponsor’s Data Protection Officer’s (“DPO”) contact details are as follows: PrivacyOffice@takeda.com

To ensure that the study is being performed accurately, the Sponsor, the Sponsor’s representatives, health authorities and relevant institutional review boards and ethics committees can inspect your medical records, that may involve your name, address and other personal information that could identify you. If needed, some or all of your medical records might be copied during these inspections.

All information about you which leaves the study clinic will be identified by a code number and your initials, without your name and address. Confidentiality will be maintained in accessing, keeping, processing and publication of information associated with your participating in the study.

Your study doctor is responsible for keeping a list of codes to make it possible to connect your code to your name. This list will be kept in a safe place to ensure that in an emergency you may be identified and contacted. The list will be kept for at least 25 years from the completion of the study and then for as long as needed to keep to the legal, regulatory, scientific or other requirements. The list will then be discarded.

Coded information regarding your health and treatment during the study can be used with your consent for the following objectives:

- to perform the research as explained in this informed consent form;
- for scientific meetings, presentations and/or publications regarding the study; and
- to make submissions to Regulatory agencies and other health authorities (for example, the Health Products Regulatory Authority, the European Medicines Agency, and the United States Food and Drug Administration, the Indian Central Drugs Standard Control Organisation).

Your coded personal information may be revealed to other parties, in other countries outside of India, for the objectives explained in this information sheet. Some of these countries do not have data protection or privacy laws that offer the same level of protection as the data protection and privacy laws in this country. However, the Sponsor will do everything possible to keep your coded information confidential. With respect to transfers to its affiliates and business partners located outside of India, Sponsor has put in place appropriate contractual provisions, or is otherwise satisfied that measures are put in place to achieve the level of protection of coded personal information equal to that under Indian law.

The parties that may get the coded information involve the following.

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- The sponsor and other companies and people that act for or with the sponsor, which include the sponsor's business and licensing partners
- Regulatory agencies and other health authorities
- Institutional review boards and ethics committees

You have the right to access, through your study doctor, all the information regarding you and, if applicable, ask for corrections. In certain circumstances, you have the additional rights to object to how your information is being handled, request deletion of your data, restrict aspects of the processing of your information or ask for a copy of your data to be given to you, or a third party, in digital format. However, to ensure that the study is scientifically reliable, you may be unable to review some of your records associated with the study until the study has ended.

You can also have a right to lodge a complaint regarding the your personal information process with your local data protection authority. You may withdraw your consent for data processing at any time by sending written notice to the study doctor at the address indicated on the first page of this information sheet. If you withdraw your consent for data process, you will not be able to participate in the study anymore, and the study doctor will not use or share your information under this consent any more, unless doing so is needed to ensure that the study is scientifically reliable, to record when you withdrew your consent and/or to report any unexpected health concerns that begun before when you withdrew your consent. New information about you will not be added to the study database, but the sponsor may still use and distribute any information it received before you withdrew your consent for the purposes explained in this information sheet.

For additional information about withdrawing this consent, see the section about withdrawal from the study.

This study might only be done by gathering and using personal information on study participants as explained in this form. By putting a signature on the informed consent form, you (or your legal representative) are authorizing the study doctor and sponsor to use and share personal information regarding your health and treatment, as mentioned in the informed consent form. There is no end date for this consent.

If you have any queries, comments or complaints regarding how your information is handled in this study, you must firstly get in touch with your study doctor who will be able to direct your question where appropriate to staff responsible for data protection at the sponsor or site, which include the site Data Protection Officer

Also, in case the sponsor sells study drug to another company performing clinical research, your coded data taken as part of this study might be shared with that company as part of completing that transaction.

An explanation of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as needed by U.S. Law. Information that may identify you will not be included in this web site. Mostly, a summary of the results will be included in the web site. At anytime, you may search this web site.

Also, an explanation of this study will be available on <https://clinicaltrials.takeda.com/> and <https://euclinicaltrials.eu/>.

Is there possible Future Research?

How could your data be used in the future?

Our aim is to advance medical science and improve patient care and, if you agree, we wish to use your coded data taken during this study, for future scientific research. This future research might be done by Takeda and/or researchers who work with Takeda. This future research might be regarding the following:

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- illnesses, conditions, or medications that may, or may not be involved in this study;
- the efficiency, design and methods of future studies.

If you consent to the future use of your coded study data, your data will be held by Takeda for at least 25 years after the completion of this clinical study. The data will be securely stored in various locations and only be identified by a unique code, without your name and personal information.

Study data will also be used by Takeda to create anonymized data that cannot be connected back to you. Independent researchers outside of Takeda may request access to this anonymized data. To use this data, these researchers should meet certain requirements and get approval from Takeda. Takeda will think about the scientific purposes of the request before agreeing to share this anonymized data.

Benefits

In case you agree to the future use of your data, you will not get any direct benefit. However, your data might contribute to research that may help others in the future. As we are not able to identify you, results from any future research will not be shared with you. The use of your data may result in new tests, drugs, devices, or other products or services with commercial value but you will not get payment or share in any financial profits if this happens.

Your decision

If you change your mind regarding your coded data being used for future scientific research, you have the right to withdraw your consent at any time. To withdraw your consent kindly get in touch with your study doctor. If you withdraw your consent after analysis has previously occurred, the results can still be used by Takeda, researchers that work with Takeda, or independent researchers.

How could your biospecimens and images be used in the future?

This study is gathering biospecimens and images from you. Biospecimens involve blood, tissue, and other bodily samples. Images involve images taken from tissue slides and sections from your biopsy. These images might be digitized and analyzed to deepen our knowledge of the disease and effects of your treatment.

Our aim is to advance medical science and make patient care better, and if you agree, we wish to use your biospecimens and images taken during this study for future scientific research. This future research might be regarding the following:

- the illnesses, conditions or medications that may, or may not be involved in this study
- the effectiveness, design and methods of future studies

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Storage of biospecimens and images

In case you agree to the future use of your biospecimens and images, your biospecimens will be kept by Takeda for up to 15 years after the end of this clinical study, and your digitized tissue slide/section images for up to 25 years after the end of this clinical study, unless there are local laws that need a different storage period.

Sharing of biospecimens and images

If you agree to the future use of your biospecimens and images, these might be shared by Takeda with researchers worldwide. To use your biospecimens and images, future researchers should meet certain requirements and get approval from Takeda.

Confidentiality

The confidentiality of your information to the fullest extent possible will be protected by us. Your biospecimens, images, and associated data will be coded to safeguard your identity. The study doctor will only have the key to the code key that may link your biospecimens and images to your identifying information. The key will be stored securely and safeguarded. If your biospecimens are used in future research, additional safeguards will be put in place. These additional safeguards may involve breaking the link with the 'code key.'

Benefits

If you consent to the future use of your biospecimens and images, you will not get any direct benefit. However, your biospecimens and images can contribute to research that may help others in the future. As we are not able to identify you, results from any future research will not be shared with you. The use of your biospecimens and images may result in new tests, medications, devices, or other products or services with commercial value but you will not get payment or share in any financial profits if this happens.

Your decision

It is your choice whether to let Takeda use your biospecimens and images or not for research in the future. If you say "yes," you may later change your mind. If you say "no," you may still fully take part in the main study.

In case you agree but later change your mind and no longer wish to allow us keep, use or share your biospecimens and images for future research purposes, kindly get in touch with your study doctor. We will perform our best to honour your request to discard any of your stored biospecimens and images. However, there might be times we are not able to do this. If the biospecimens and images have previously been used in any future research, the information and results from that research can still be used.

Who do you get in touch with queries?

For additional information kindly get in touch with the following:

Investigator Name:	Dr. Arijit Nag
Daytime telephone number(s):	+91- 033 6605 7622
24-hour contact number(s):	+91- 9051121161
Investigator Email Address:	drarijitnag@gmail.com & arijit.nag@tmckolkata.com

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Ethics Committee Chairperson Name:	Prof. Partha Pratim Majumdar
Ethics Committee address:	Institutional Review Board, Tata Medical Center, 14 Major Arterial Road, EW Rajarhat New Town, Kolkata - 700160, West Bengal, India
Ethics Committee Chairperson telephone number:	+91- 9831004230
Ethics Committee Chairperson Email Address:	Parmaj2023@gmail.com

Has this study been reviewed?

An independent group of people, called a research ethics committee have been reviewed by all research studies to safeguard your safety, rights, health and dignity. This study has been reviewed and a favorable opinion has been given by Ethics Committee.

At any time where there is good reason, the Sponsor, Regulatory Authorities or the Ethics Committee might stop the study.

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Consent Form

By putting a signature below, I confirm that I have read this Participant Information Sheet and Consent Form and know about it, and I voluntarily give consent to participate in this research study and consent to the informed consent form.

Study Protocol:	TAK-226-3001
Study Title:	A Phase 3, Multicenter, Open Label, Randomized Trial to Compare the Efficacy and Safety of Elritercept versus Epoetin Alfa for the Treatment of Anemia Due to IPSS-R Very Low, Low, or Intermediate Risk Myelodysplastic Syndromes in ESA-naïve Adult Participants Who Require Red Blood Cell Transfusions

Study Participant's Name:		Study Participant's Initials:	
Date of Birth/Age:		Study Participant ID:	
Study Participant's Address:			
Qualification			
Occupation (Kindly mark which is appropriate)	Student	Self-Employed	Service
	☐	☐	☐
	☐	☐	☐
	☐	☐	☐
	☐	☐	☐
	☐	☐	☐
	☐	☐	☐
If you select Others in Occupation, kindly add details			
Annual Income of the Study Participant:			

(For the purpose of compensation in the event of trial-related death)

Name of Nominee(s):	
Relation to the Study Participant:	
Address of the Nominee(s):	

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Kindly put initial against each of the following statements to show your agreement

Sr.	Statement	(Study Participant)
(i)	I have read and I know about all the information given in this Participant Information Sheet and Consent Form (this "Form"). I have been given the opportunity to discuss it and ask questions. All my queries have been answered to my satisfaction.	
(ii)	I know that I am participating in this study voluntarily and I may leave the study at any time without being penalized or losing any benefits or medical care I am entitled to.	
(iii)	I know that I may have to withdraw from the study if I need other treatment, do not comply with the study plan, have a study-related injury, or for any other reason.	
(iv)	I agree to permit my body samples/images to be taken, tested, kept and analyzed by the Sponsor or companies who work for the sponsor for the objectives of this study.	
(v)	I authorize people who have a responsibility to verify the conduct of this study (for example, study monitors, auditors, the ethics committee, and applicable regulatory authorities in other countries like United States Food and Drug Administration, Medicines and Health Care Products Regulatory Agency, European Medicines Agency, Pharmaceuticals and Medical Devices Agency and others) direct access to my original medical records that may involve information by which I may be identified.	
(vi)	I know that by putting a signature on this document, I am freely and voluntarily authorizing the collection, use, and disclosure of my coded personal information for medical research objectives, to be shared with Sponsor, its affiliates and business partners, regulatory authorities, and the ethics committee overseeing this study.	
(vii)	I know that by putting a signature on this form I am authorizing the transfer of my coded personal data, including sensitive data, to other countries around the world, including countries where the data protection and privacy laws may not give the same level of data protection as the laws in my home country or the country where I am taking part in the study	
(viii)	I know that I have the liberty to withdraw my consent to the collection, use, and disclosure of my coded personal information at any time without being penalized or loss of benefits to which I am otherwise entitled. However, I cannot continue my participation in the research study after I withdraw consent, and any data about me (which include health information) that has previously been taken may remain part of the study in order to satisfy regulatory requirements and to protect scientific integrity.	
(ix)	I know that I will not lose any of my legal rights by putting a signature on this informed consent form.	

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

(x)	I will get a copy of this form signed and dated.	
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Study Participant's Name (print):	
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Signature (or Thumb impression) of the Study Participant	Date

Name of the Investigator	
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Signature of the Investigator	Date

(* If a Study Participant has limited ability to read and write, a witness must be there during the entire informed consent discussion). In these cases, the study participant will put his/her left thumb impression in the place of the signature.

Study Participant's Legally Acceptable ☐ Not Applicable
Representative's Statement

As the Study Participant's legally acceptable representative, I was present during the consenting procedure and know about the preceding information explaining this study. All of the queries about the study and the study participant's participation in it have been answered to my satisfaction and that of the study participant. I mention that all aspects of the study were clearly presented during the consent procedure. The study participant is willing to take part in the study and I put my signature below on his/her behalf testifying to this effect.

Name of the Legally Acceptable Representative (print):	
Relationship to the Study Participant:	

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Address of the legally acceptable representative:	
Phone Number:	

Signature (or Thumb Impression) of the Legally Acceptable Representative	Date

Witness Declaration of Study Participant's Informed Consent

☐ Not Applicable

By putting a signature on this consent form, I attest that the information was correctly described to the study participant and the legally acceptable representative (if applicable) and apparently understood by them and that informed consent was freely provided by the Study Participant.

Name of the Witness: (print):	
Address of the witness	
Phone Number:	

Signature of the Witness	Date

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Informed Consent Form for Optional Future Research

Kindly put initial against each of the following statements to show your agreement

Sr.	Statement	(Study Participant)
(i)	I have read and I know about all the information regarding the optional future research of my data/samples in this form. I have been given the opportunity to discuss it and ask questions. All my queries have been answered to my satisfaction.	
(ii)	I know that my taking part in this future research is voluntary, and I may withdraw my consent at any time without being penalized or losing any benefits or medical care I am entitled to, and without my participation in the main research study being affected.	
(iii)	I know that I will not lose any of my legal rights by putting a signature on this informed consent form.	
(iv)	I will get a copy of this consent form signed and dated.	

Kindly check the box next to your choice about whether to participate in future research:

(i)	I consent that my coded study data can be used by Takeda and/or researchers who work with Takeda for the future research explained in this informed consent form. ☐ Yes ☐ No
(ii)	I agree that my study data may be anonymized, used and shared by Takeda with independent researchers for the future research explained in this informed consent form. ☐ Yes ☐ No
(iii)	I agree that my remaining biospecimens can be used by Takeda, researchers who work with Takeda and/or independent researchers, for the future research explained in this informed consent form: ☐ Yes ☐ No
(iv)	I agree that my images might be used by Takeda, researchers who work with Takeda and/or independent researchers, for the future research explained in this informed consent form: ☒ Yes ☐ No

Study Participant's Name (print):	
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PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Signature (or Thumb impression) of the Study Participant Date

Name of the Investigator

Signature of the Investigator

Date

(* If a Study Participant has limited ability to read and write, a witness must be there during the entire informed consent discussion). In these cases, the study participant will put his/her left thumb impression in the place of the signature. Also, it shall be clearly shown in the ICF that the content of informed consent is fully presented to the Subject or LAR in oral with the attendance of the witness during the entire informed consent discussion and the subject or LAR know about the content of the informed consent.

Study Participant's Legally Acceptable ☐ Not Applicable
Representative's Statement

As the Study Participant's legally acceptable representative, I was present during the consenting procedure and know about the preceding information explaining this study. All of the queries about the study and the study participant's participation in it have been answered to my satisfaction and that of the Study Participant. I mention that all aspects of the study were clearly presented during the consent procedure. The study participant is willing to take part in the study and I put my signature below on his/her behalf testifying to this effect.

Name of the Legally Acceptable
Representative (print):

Relationship to the Study Participant:

Address of the legally acceptable
representative:

Phone Number:

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

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Signature (or Thumb Impression) of the Legally
Acceptable Representative

Date

Witness Declaration of Study Participant's Informed
Consent

☐

Not Applicable

By putting a signature on this consent form, I attest that the information was correctly described to the study participant and the legally acceptable representative (if applicable) and apparently understood by them and that informed consent was freely provided by the Study Participant.

Name of the Witness: (print):	
Address of the witness	
Phone Number:	

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Signature of the Witness

Date

(The participant information sheet and properly filled consent form copy shall be given to the study participant or his/her attendant)