ForPatients
by Roche

Multiple Myeloma

A PLATFORM STUDY EVALUATING THE SAFETY AND EFFICACY OF MULTIPLE TREATMENTS IN PATIENTS WITH MULTIPLE MYELOMA

A Study Evaluating the Safety and Efficacy of Multiple Treatments in Participants With Multiple Myeloma

Trial Status	Trial Runs In	Trial Identifier
Recruiting	6 Countries	NCT05583617 2023-504484-16-00 CO43923

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Platform Study Evaluating the Safety and Efficacy of Multiple Treatments in Patients With Multiple Myeloma

Trial Summary:

CO43923 is a platform study that will evaluate the safety, efficacy, and pharmacokinetics (PK) of multiple treatment combinations, as monotherapy or in combination, in participants with multiple myeloma (MM). The study is designed with the flexibility to open new treatment substudies as new treatments become available. Information regarding the opened substudies are found below.

Hoffmann-La Roche
Sponsor

Phase 1/Phase 2
Phase

NCT05583617 2023-504484-16-00 CO43923
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

1. Why is the CO43923 SS1 study needed?

Multiple myeloma (MM) is a type of cancer that affects the bone marrow and impacts various parts of the body. Treatments have improved over the years and different types of treatments are now available, helping people to live with MM for longer. But there is no cure for MM at the current time. More research is needed to understand the disease and its treatments. This will help researchers understand where new treatments are needed.

Researchers need more information to understand:

- Which treatments are being prescribed to people for different types of MM, including if they have other health problems
- Which treatments for MM are first prescribed, and how and why treatments are changed over time
- How well prescribed treatments are tolerated – what side effects they cause and how serious they are

The study aims to collect medical information about people with multiple myeloma and the different treatments they are prescribed over time.

2. How does the CO43923 SS1 study work?

This study is recruiting people with MM. People can take part if they are being given routine treatment for MM at a clinical trial site for a Roche-sponsored trial known as ‘CO43923’.

People who take part in this study (participants) will not be given clinical trial treatment. Participants will receive standard treatment for their MM and will be followed-up regularly, in the usual way outside of a clinical study, by their doctor. Information on the participant and their disease will be collected, including blood and bone marrow tests, scan results (imaging), genetic test results, treatments given and side effects. The total time of participation in the study will be up to 20 years. Participants can leave the study at any time, and their routine medical care will not be affected.

3. What are the main endpoints of the study?

The main study endpoints (the main results measured in the study) are to understand:

- Which treatments are prescribed for MM and in what order, over time
- How well prescribed treatments work, measured by:
    - the number of participants with no detectable cancer, or at least a 90% or 50% reduction in cancer after starting routine treatment
    - the amount of time between the start of treatment and participants cancer worsening
    - the amount of time taken to first respond to treatment and to the best response seen to treatment in participants with at least a 50% reduction in cancer

  - the number of participants with no detectable MM in bone marrow (and which test is used)
  - how long participants live
- The number and seriousness of side effects

Other information that will be collected in the study includes:

- Participants' age, sex, race/ethnicity
- Other medical conditions and medicines being taken
- Past and current blood test and scan results
- Genetic information on their MM

4. Who can take part in this study?

People can take part in this trial if they have been diagnosed with MM and are under the care of a doctor at a site where the clinical trial CO43923 is taking place.

People may not be able to take part in this trial if they do not agree for their information to be stored and used (processed) for research purposes.

5. What treatment will participants be given in this study?

Everyone who joins this clinical trial will be given routine medical care for their MM. No experimental treatments will be given in this study.

6. Are there any risks or benefits in taking part in this study?

People who would like to participate will be told about any risks and benefits of routine medical care. In addition, people will be told how their information and medical samples will be used, how long they will be kept for, and how their personal information will be protected. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the study

Participants' personal and medical information will be securely stored to minimise the risk of it being seen by unauthorised people.

Potential benefits associated with the study

Participants will not be given clinical trial treatment beyond their usual MM treatment; people will be treated for MM in the same way if they take part in the study or not – so participants' health will not improve from participation in the study. Still, the information

collected may help other people with similar medical conditions in the future by helping researchers understand MM better.

1. Why is the CO43923 SS2 clinical trial needed?

Multiple myeloma (MM) is a cancer that forms in plasma cells (a type of white blood cell that is made in the bone marrow). People diagnosed with MM are first treated with a combination of anti-cancer drugs. This is often followed by a stem cell transplant that aims to replace the abnormal bone marrow. After the stem cell transplant, maintenance therapy (to help stop cancer coming back) with lenalidomide is considered the standard treatment for most people diagnosed with MM. However, new treatments are needed for when the MM is difficult to remove completely (high-risk MM) because lenalidomide does not work as well in these situations.

Cevostamab is a type of drug called a bispecific antibody. It works by binding to certain proteins on the cancer cells and cells of the immune system to bring them closer together, which helps the body destroy the cancer. Drugs like cevostamab, a type of immunotherapy, help a person's own immune system target cancer cells. Researchers hope that they will provide better health outcomes for people with high-risk MM after a transplant.

This clinical trial aims to test how safe and how well cevostamab in combination with lenalidomide works, and how the body processes these drugs.

2. How does the CO43923 SS2 clinical trial work?

This clinical trial is recruiting people with MM. People can take part if they have been diagnosed with high-risk MM that has previously responded to treatment and have received a transplant.

People who take part in this clinical trial (participants) will be given the clinical trial treatment cevostamab in a hospital for 14 treatment 'cycles' – a treatment cycle is the period of treatment and recovery time before the next dose of treatment is given. Participants will also be given lenalidomide until their disease worsens or until they stop treatment due to side effects. The clinical trial doctor will see them regularly; these hospital visits will include checks to see how the participant responds to the treatment and any side effects they may have. After their final dose, participants will be seen by the clinical trial doctor around every 3 months at the hospital or by telephone for as long as they agree. The total time of participation in the clinical trial will be about 1 year or more. Participants are free to stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the CO43923 SS2 clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see how safe treatment is) are the number, type and seriousness of side effects and the maximum dose of cevostamab that can be given with lenalidomide before participants have unacceptable side effects.

The other clinical trial endpoints include:

- The number of participants whose response to treatment improves
- The amount of time between the start of the trial treatment and participants' cancer worsening
- The number of participants who have no detectable cancer in bone marrow or on blood tests, or at least 90% reduction in cancer on blood tests
- How long participants live
- How the body processes and gets rid of cevostamab and lenalidomide

4. Who can take part in this clinical trial?

People can take part in this trial if they are at least 18 years old, have been diagnosed with high-risk MM, have previously received a transplant within the past 100 days and have not yet started maintenance treatment.

People may not be able to take part in this trial if they have certain other medical conditions, such as autoimmune, heart or lung disease, or certain infections, have previously received certain treatments, including cevostamab, are pregnant or breastfeeding, or are planning to become pregnant during or within 5 months of treatment.

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be given cevostamab and lenalidomide. To begin, participants will be given step-up (increasing) doses of cevostamab over 2 weeks; as an infusion into the vein on Days 1 and 4, with the target dose given on Day 8. Step-up dosing aims to prevent and/or reduce side effects.

Treatment will then be provided in 28-day treatment cycles, where participants will be given:

- Cevostamab, as an infusion into the vein on Days 1 and 15 in Cycles 1#6, then on Day 1 only in Cycles 7#13
- Lenalidomide, as a capsule to be swallowed once a day on Days 1#21 of every cycle

Participants may also receive tocilizumab as an infusion into the vein if they experience certain side effects during the clinical trial.

This is an open-label trial, which means everyone involved, including the participants and the doctors, know which clinical trial drug is being used.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical trial. Side effects can be mild to severe and even life-threatening and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly. Potential participants will be told about the known side effects of cevostamab, tocilizumab and lenalidomide and, where relevant, also potential side effects based on human and laboratory studies or knowledge of similar drugs. Participants will be told about any known side effects of infusions into the vein (intravenous infusions) or of swallowing capsules.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial, but the information that is collected may help other people who have a similar medical condition in the future.

1. Why is the CO43923 SS4 clinical trial needed?

Multiple myeloma (MM) is a cancer that forms in plasma cells – a type of white blood cell that is made in the bone marrow. Different types of medicines are given as standard-of-care treatment depending on the type of MM a person has. This includes protease inhibitors (PIs) or medicines that help a person’s own immune system target and destroy cancer cells – known as ‘immunotherapy’ (such as IMiDs or anti-CD38 drugs). But for most people, MM eventually comes back after treatment or does not respond to treatment (known as ‘relapsed/refractory’ or ‘R/R’ MM).

Cevostamab and iberdomide are new experimental drugs against MM – this means that health authorities have not approved cevostamab or iberdomide for the treatment of R/R MM, alone or in combination with each other. Although cevostamab and iberdomide have not been given together to people before, researchers hope that combined cevostamab and iberdomide treatment will improve health outcomes for people with R/R MM.

This clinical trial aims to see how safe and how well cevostamab in combination with iberdomide works, and how the body processes these drugs.

2. How does the CO43923 SS4 clinical trial work?

This clinical trial is recruiting people with R/R MM. People can take part if they have previously received a PI, an IMiD and an anti-CD38 medicine, and have no standard-of-care treatment options available to them.

People who take part in this clinical trial (participants) will be given the clinical trial treatment cevostamab in a hospital at different intervals throughout the trial for 18 treatment ‘cycles’ – a treatment cycle is the period of treatment and recovery time before the next dose of treatment is given. Participants will also be given iberdomide. Treatment will be stopped if MM worsens or if participants have unacceptable side effects. If their MM worsens after 18 cycles, participants who benefitted from treatment may be given up to 17 more cycles of treatment.

The clinical trial doctor will see participants regularly. These hospital visits will include checks to see how the participant responds to the treatment and any side effects they may have. After their final dose, participants will be seen by the clinical trial doctor around every 3 months at the hospital or by telephone for as long as they agree. The total time of participation in the clinical trial will depend on how the participant responds to treatment and could be more than 3 years. Participants are free to stop trial treatment and leave the clinical trial at any time.

3. What are the main endpoints of the CO43923 SS4 clinical trial?

The main clinical trial endpoints (the main results measured in the trial to see how safe treatment is) are the number, type and seriousness of side effects and the maximum doses of cevostamab and iberdomide that can be given together before participants have unacceptable side effects.

The other clinical trial endpoints include:

- The number of participants whose tumours shrink with trial treatment and the amount of time this lasts if disease progresses
- The number of participants who have no detectable cancer in bone marrow or on blood tests, or at least 90% reduction in cancer on blood tests
- The amount of time between the start of the trial treatment and participants’ cancer worsening
- The amount of time taken to first respond to treatment and to the best response seen to treatment in participants with at least a 50% reduction in cancer
- How long participants live
- How the body processes and gets rid of trial treatment

4. Who can take part in this clinical trial?

People with R/R MM can take part in this trial if they are at least 18 years old. People may not be able to take part in this trial if they have certain other medical conditions, such as autoimmune, heart or lung disease, uncontrolled high blood pressure or diabetes, or certain infections.

People who have previously received certain treatments including cevostamab, who are pregnant or breastfeeding, or who are planning to become pregnant during or shortly after the trial, will also not be able to take part.

5. What treatment will participants be given in this clinical trial?

Everyone who joins this clinical trial will be given cevostamab and iberdomide. To begin, participants will be given step-up (increasing) doses of cevostamab over 2 weeks as an infusion into the vein on Days 1 and 4, with the target dose given on Day 8. Step-up dosing aims to prevent and/or reduce side effects. Treatment will then be provided in 21-day cycles, where participants will be given:

- Cevostamab, as an infusion into the vein on Day 1, AND
- Iberdomide, as a capsule to be swallowed once a day on Days 1#14 of each cycle

Participants may also receive tocilizumab as an infusion into the vein if they experience certain side effects during the clinical trial. This is an open-label trial, which means everyone involved, including the participants and the doctors, know which clinical trial drug is being used.

6. Are there any risks or benefits in taking part in this clinical trial?

The safety or effectiveness of the experimental treatment or use may not be fully known at the time of the trial. Most trials involve some risks to the participant. However, it may not be greater than the risks related to routine medical care or the natural progression of the health condition. People who would like to participate will be told about any risks and benefits of taking part in the clinical trial, as well as any additional procedures, tests or assessments they will be asked to undergo. All of these will be described in an informed consent document (a document that provides people with the information they need to decide to volunteer for the clinical trial).

Risks associated with the clinical trial drugs

Participants may have side effects (an unwanted effect of a drug or medical treatment) from the drugs used in this clinical trial. Side effects can be mild to severe and even life-threatening and vary from person to person. Participants will be closely monitored during the clinical trial; safety assessments will be performed regularly. Potential participants will be told about the known side effects of cevostamab, iberdomide and tocilizumab

and, where relevant, also potential side effects based on human and laboratory studies or knowledge of similar drugs. Participants will be told about any known side effects of infusions into the vein (intravenous infusions) or of swallowing capsules.

Potential benefits associated with the clinical trial

Participants' health may or may not improve from participation in the clinical trial, but the information that is collected may help other people who have a similar medical condition in the future.

Inclusion Criteria:

- Diagnosed with MM per International Myeloma Working Group (IMWG) criteria
- Eastern Cooperative Oncology Group Performance Status of 0, or 1, or 2
- Resolution of AEs from prior anti-cancer therapy to Grade <=1
- Agreement to undergo scheduled assessments and procedures

Additional Inclusion Criteria for SS2:

- Completion of planned induction therapy and achievement of at least a partial response (PR)
- Autologous Stem Cell Transplant (SCT) within 100 days prior to first study treatment and the absence of progressive disease
- Cytogenetic high-risk features at diagnosis
- Treatment with any investigational medicinal products, systemic cancer therapies, immunotherapies received previously in CO43923 (any arms) within 5 half-lives or 3 weeks whichever is the shortest
- Agreement to comply with all local requirements of the lenalidomide risk minimization plan, which includes the global pregnancy prevention program
- For female participants of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception
- For male participants: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom even if they have had a prior vasectomy, and agreement to refrain from donating sperm

Additional Inclusion Criteria for SS4:

- Previously exposed to at least a PI, an IMiD, and an anti-CD38 antibody for the treatment of R/R MM for whom no suitable SOC therapy options are available

Exclusion Criteria:

- Inability to comply with protocol-mandated hospitalization and procedures
- History of confirmed progressive multifocal leukoencephalopathy
- History of other malignancy within 2 years prior to screening
- Current or past history of central nervous system (CNS) disease
- Significant cardiovascular disease that may limit a participant's ability to adequately respond to a CRS event
- Symptomatic active pulmonary disease or requiring supplemental oxygen
- Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection at study enrollment, or any major episode of infection requiring treatment with IV antibiotics where the last dose of IV antibiotics was given within 14 days prior to first study treatment

- Known or suspected chronic active Epstein-Barr virus (EBV) infection
- Positive serologic or PCR test results for acute or chronic hepatitis B virus (HBV) infection
- Acute or chronic hepatitis C virus (HCV) infection
- Known history of HIV seropositivity
- Administration of a live, attenuated vaccine within 4 weeks prior to initiation of study treatment or anticipation that such a live, attenuated vaccine will be required during the study
- Any medical condition or abnormality in clinical laboratory tests that, in the investigator's judgment, precludes the participant's safe participation in and completion of the study, or which could affect compliance with the protocol or interpretation of results

Additional Exclusion Criteria for SS2:

- Hypersensitivity reactions to lenalidomide or other immunomodulatory drugs
- Harbor lesions at proximity of vital organs that may develop sudden decompensation/deterioration in the setting of a tumor flare
- Prior treatment with any investigational medicinal product, systemic cancer therapy, or immunotherapies in any arm of study CO43923 within 5 half-lives or 3 weeks, whichever is shorter
- Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection (excluding fungal infections of nail beds) at study enrollment, or any major episode of infection requiring treatment with IV antimicrobials where the last dose of IV antimicrobial was given within 14 days prior to first study treatment
- History of erythema multiforme, Grade >=3 rash, or blistering following prior treatment with immunomodulatory derivatives
- Pregnant or breastfeeding, or intending to become pregnant during the study or within 5 months after the final dose of study treatment Exlcusion Criteria Applicable to SS2 and SS4
- History of autoimmune disease
- Known history of hemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)
- History of severe allergic or anaphylactic reactions to monoclonal antibody therapy (or recombinant antibody-related fusion proteins)
- Received a cumulative dose of corticosteroids equivalent to >=140 mg of prednisone within the 14-day period before the first dose of the study drug (does not include pretreatment medication)
- Active symptomatic COVID-19 infection at study enrollment or requiring treatment with IV antiviral where the last dose of IV antiviral treatment was given within 14 days prior to first study treatment. Participants with active COVID-19 infection must have clinical recovery and two negative antigen tests at least 24 hours apart prior to first study treatment.
- Positive and quantifiable EBV PCR or CMV PCR prior to first study treatment

Additional Exclusion Criteria for SS4:

- Treatment with any investigational medicinal products, systemic cancer therapies, immunotherapies within 5 half-lives or 12 weeks before starting pre-phase
- History of anaphylaxis or hypersensitivity, including >=Grade 3 rash, during prior treatment with IMiDs, dexamethasone, any CELMoDs, or the excipients contained in the formulations
- Known anaphylaxis, allergies, hypersensitivity, or intolerance to boron or mannitol, hyaluronidase, sorbitol, corticosteroids, monoclonal antibodies (or recombinant antibody-related fusion proteins), or human proteins, CRBN modulating agents or their excipients, or known sensitivity to mammalian-derived products
- Administration of strong CYP3A modulators; administration of proton-pump inhibitors within 2 weeks of starting study treatment
- Uncontrolled hypertension or uncontrolled diabetes within 14 days prior to enrollment
- Concurrent administration of a strong inhibitor, modulator or inducer of cytochrome P450 (CYP3A4/5) (including within 14 days of initiating study treatment)

- History of malignancies, other than MM, unless the subject has been free of the disease for >=5 years
- Peripheral neuropathy >Grade 2
- Prior treatment with cevostamab or another agent targeting FcRH5 or iberdomide
- Pregnant or breastfeeding, or intending to become pregnant during the study or within 5 months after the final dose of study treatment
- History of Stevens-Johnson syndrome, toxic epidermal necrolysis, or drug rash with eosinophilia and systemic symptoms
- Treatment with systemic immunosuppressive medications
- Prior treatment with CAR T-cell therapy (autologous or allogeneic) within 12 weeks before starting pre-phase
- Autologous SCT within 100 days prior to starting pre-phase
- Prior allogeneic SCT
- Plasmacytoma in proximity of vital organs that may develop sudden decompensation/deterioration in the setting of a tumor flare