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A study to evaluate preventive treatments for talquetamab-related oral toxicity

Submission date 11/05/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 14/08/2024	**Overall study status** Ongoing	
Last Edited 06/06/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Relapsed or refractory multiple myeloma (MM) is a blood cancer that forms in a type of white blood cells (WBC) called plasma cells. Drugs that activate T-cells (a type of WBC) to attack cancer cells may be an effective way to destroy them. Cancer is called relapsed if it comes back after treatment and is called 'refractory' if does not respond to treatment. Talquetamab (JNJ-64407564) binds to proteins called cluster of differentiation 3 (CD3) receptor, found on T-cells and G protein-coupled receptor family C group 5 member D (GPRC5D), found on myeloma cells. This activates the T-cells and leads to the killing of myeloma cells. In this study, researchers want to learn how preventive measures started before the first dose of talquetamab and continued throughout the treatment phase may reduce the number, intensity, or length of time for oral taste changes incidents related to talquetamab compared to no preventive measures for oral taste changes. This study aims to assess preventive measures for the side effects of an approved myeloma therapy (talquetamab).

Who can participate?
Male and female healthy participants 18 years or older with relapsed or refractory MM who have disease progression after receiving at least 1 of each of the following medication classes. PI, IMIDs, and anti-CD38 mAb.

What does the study involve?
The study will be conducted as:
1. Screening (Up to 28 days): Confirm if the participants can take part in the study.
2. Treatment Phase (Up to 12 months)*: Participants will be divided into either of the 4 treatment groups in a random way to receive the treatment:
• Cohort A (control): Talquetamab as an injection under the skin
• Cohort B: Prophylaxis mouth wash plus talquetamab
• Cohort C: Prophylaxis by mouth plus talquetamab
• Cohort D: Prophylaxis by mouth plus talquetamab
*Prophylaxis Treatment Phase duration could be longer than 12 months, if there are clinical benefits relevant to the participant and part of the objectives of the study, at treating physician' s discretion.

Talquetamab Treatment Phase: Until disease progression, death, talquetamab treatment discontinuation for any other reason (e.g. unacceptable toxicity, withdrawal of consent), or end of study, whichever occurs first.

3. Follow-up Phase (Up to approximately 12 months): Participants will be followed up for their overall health throughout the study.
During the study, some tests such as blood and urine tests, neurological examination, and physical examination will be performed. Side effects will be recorded until the study ends (Up to 12 to 30 months).

What are the possible benefits and risks of participating?
Taking talquetamab may or may not improve multiple myeloma. The benefit to study participants receiving talquetamab in this study cannot be guaranteed.
Participants may experience some benefit from participation in the study that is not due to receiving talquetamab but rather is due to regular visits and assessments monitoring overall health. Participation in the study may help other people with multiple myeloma in the future.

Participants may have side effects from the drug(s) or procedures used in this study that may be mild to severe and even life-threatening, and they can vary from person to person. The most common, known risks are getting symptoms such as cytokine release syndrome (CRS), cytopenias, skin and nail changes, oral side-effects, infection, injection-site reactions, and increased risk for immune effector cell-associated neurotoxicity syndrome (ICANS). The participant information sheet and informed consent form, which will be signed by every participant agreeing to participate in the study, includes a detailed section outlining the known risks of participating in the study. Not all possible side effects and risks related to talquetamab are known at this moment. During the study, the sponsor may learn new information about talquetamab. The study doctor will tell participants as soon as possible about any new information that might make them change their minds about being in the study, such as new risks.
To minimise the risk associated with taking part in the study, participants are frequently looked at and asked about any side effects and other medical events. Participants are educated to report any such events to the study doctor who will provide appropriate medical care. Any serious side effects that are reported to the sponsor are thoroughly reviewed by a safety team.
There are no costs to participants to be in the study. The sponsor will pay for the study drug and tests that are part of the study. The participant will receive reasonable reimbursement for study-related costs (for example, travel/parking costs).

Where is the study run from?
Janssen-Cilag International NV

When is the study starting and how long is it expected to run for?
May 2024 to January 2027

Who is funding the study?
Janssen-Cilag International NV

Who is the main contact?
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Contact information

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1009729

ClinicalTrials.gov (NCT)
NCT06500884

Protocol serial number
64407564MMY2006, IRAS 1009729, CPMS 61163

Study information

Scientific Title
A phase II, open-label, randomized study to evaluate prophylactic interventions on talquetamab-related oral toxicity

Acronym
TALISMAN

Study objectives
Primary objectives:
1. To find preventive measures that can reduce number, intensity, and length of time for taste change incidents related to talquetamab during treatment phase.
2. To better understand the signs and symptoms of taste changes related to talquetamab.

Secondary objectives:
1. To find out the impact of preventive measures on problems with sense of taste.
2. To assess harmful effects in the mouth due to treatment-related side effects.
3. To assess quality of life parameters related to overall health and specific impact of taste changes, xerostomia (dry mouth), dysphagia (difficulty swallowing), oral mucositis (mouth ulcers), and other harmful effects in mouth.
4. To assess the impact of preventive measures on change in body weight.
5. To assess participants' ability to follow the talquetamab treatment schedule.
6. To assess the impact of preventive measures on smell function.
7. To determine how well (efficacy) talquetamab works.
8. To determine safety of talquetamab and preventive measures.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 01/08/2024, North East - Tyne & Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive , Newcastle upon Tyne , NE2 4NQ, United Kingdom; +44 (0)20 710 48120; tyneandwearsouth.rec@hra.nhs.uk), ref: 24/NE/0099

Study design
Multi-centre randomized controlled open-label parallel-group study

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Multiple myeloma

Interventions
Cohort A: Talquetamab. Participants with relapsed or refractory multiple myeloma (RRMM) (previously exposed to at least 1 proteasome inhibitor (PI), 1 immunomodulatory drug(s) [IMiD]), and an anti-CD38 monoclonal antibody [mAb]) will be treated with talquetamab subcutaneously until progressive disease, death, lost to follow-up, withdrawal of consent, discontinuation because of toxicity, or until 12 months after the start of talquetamab treatment, whichever occurs first.

Cohort B: Prophylaxis A and Talquetamab. Participants with RRMM (previously exposed to at least 1 PI, 1 IMiD, and an anti-CD38 mAb) will receive prophylaxis A along with talquetamab therapy. Participants will start the assigned prophylaxis 1 week before starting talquetamab treatment. After step-up dosing of talquetamab therapy, participants will be treated with talquetamab until progressive disease, death, lost to follow-up, withdrawal of consent,

discontinuation because of toxicity, or until 12 months after the start of talquetamab treatment, whichever occurs first.

Cohort C: Prophylaxis B and Talquetamab. Participants with RRMM (previously exposed to at least 1 PI, 1 IMiD, and an anti-CD38 mAb) will receive prophylaxis B along with talquetamab therapy. Participants will start the assigned prophylaxis 1 week before starting talquetamab treatment. After step-up dosing of talquetamab therapy, participants will be treated with talquetamab until progressive disease, death, lost to follow-up, withdrawal of consent, discontinuation because of toxicity, or until 12 months after the start of talquetamab treatment, whichever occurs first.

Cohort D: Prophylaxis C and Talquetamab. Participants with RRMM (previously exposed to at least 1 PI, 1 IMiD, and an anti-CD38 mAb) will receive prophylaxis C along with talquetamab therapy. Participants will start the assigned prophylaxis 1 week before starting talquetamab treatment. After step-up dosing of talquetamab therapy, participants will be treated with talquetamab until progressive disease, death, lost to follow-up, withdrawal of consent, discontinuation because of toxicity, or until 12 months after the start of talquetamab treatment, whichever occurs first.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Talquetamab, prophylaxis A, prophylaxis B, prophylaxis C

Primary outcome(s)
1. Percentage of participants with the occurrence of taste dysfunction (hypogeusia) measured using the Total Waterless Empirical Taste Test (WETT) score up to 12 months
2. Percentage of participants with the occurrence of severe hypogeusia measured using the WETT score up to 12 months
3. Time to first onset of severe hypogeusia measured using the WETT score up to 12 months
4. Percentage of participants who report resolution/improvement of hypogeusia/ageusia measured using the WETT score at months 3 and 6

Key secondary outcome(s))
1. Change from baseline in WETT testing score over time up to 30 months
2. Percentage of time with hypogeusia up to 12 months
3. Number of participants with treatment-emergent oral toxicities (dysgeusia, oral mucositis, dysphagia, and xerostomia) up to 30 months
4. Time to the first onset of treatment-emergent oral toxicities (dysgeusia, oral mucositis, dysphagia, and xerostomia) up to 30 months
5. Duration of treatment-emergent oral toxicities (dysgeusia, oral mucositis, dysphagia, and xerostomia) up to 30 months
6. Change from baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 items (EORTC-QLQ-C30) domains scores up to 30 months
7. Change from baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Oral Health (EORTC-QLQ-OH15) domains scores up to 30 months
8. Percentage of participants reporting oral toxicity symptoms using the Patient-reported

Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) up to 12 months
9. Percentage of participants reporting oral toxicity symptoms using the Short Xerostomia Inventory (SXI) score up to 30 months
10. Percentage of participants reporting oral toxicity symptoms using the Epstein Taste Survey (ETS) up to 30 months
11. Percentage of participants reporting oral toxicity symptoms using the Scale of Subjective Total Taste Acuity (STTA) up to 12 months
12. Change from baseline in body weight over time up to 30 months
13. Change from baseline in Body Mass Index (BMI) over time up to 30 months
14. Percentage of participants with dose reductions, interruptions, and discontinuations up to 12 months
15. Change from baseline in Smell Identification Test Score at day 1 cycles 1, 4, 8 and 12
16. Change from baseline in Smell Detection Threshold Test Score at day 1 cycles 1, 4, 8 and 12
17. Percentage of participants with Overall Response Rate up to 30 months
18. Percentage of participants with Complete Response (CR) or Better Response up to 30 months
19. Percentage of participants with Very Good Partial Response (VGPR) or Better Response up to 30 months
20. Duration of Response (DOR) up to 30 months
21. Time to Response (TTR) up to 30 months
22. Number of participants with Treatment-emergent Adverse Events (TEAEs) up to 30 months

Completion date
18/10/2027

Eligibility

Key inclusion criteria
1. Multiple myeloma (MM) according to IMWG diagnostic criteria
2. Were triple-class exposed (received prior treatment with a PI, an IMiD, and anti-CD38 mAb)
3. Documented evidence of progressive disease based on the investigator’s determination of response by IMWG criteria on or after their last regimen
4. Have an Eastern Cooperative Oncology Group performance status (ECOG-PS) of 0 or 1 at screening. Participants with ECOG PS 2 or 3 are eligible for the study if the ECOG-PS score is related to stable physical limitations (e.g., wheelchair-bound due to prior spinal cord injury) and not related to multiple myeloma or associated therapy
5. Be willing and able to adhere to the lifestyle restrictions specified in the protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Contraindications or life-threatening known allergies, hypersensitivity, or intolerance to any study drug or its excipients
2. Stroke, transient ischemic attack, or seizure within 6 months prior to enrollment
3. Any of the following within 6 months prior to the first dose of study treatment: severe or unstable angina, myocardial infarction; major thromboembolytic event (e.g., pulmonary embolism, cerebrovascular accident), clinically significant ventricular arrythmia or heart failure New York Heart Association functional classification Class III or IV. Uncomplicated deep vein thrombosis is not considered exclusionary
4. Major surgery or had significant traumatic injury within 2 weeks prior to the start of administration of study treatment, or will not have fully recovered from surgery, or has major surgery planned during the time the participant is expected to be treated in the study or within 2 weeks after administration of the last dose of study treatment
5. A WETT score suggesting severe hypogeusia or ageusia at screening. Also, unresolved/severe dysgeusia referred by the participant or a finding in the physical examination/oral cavity inspection. Some examples include leukoplakia, prior mouth cancers, extensive dental caries, severe periodontitis, active oral infections, candidiasis, parotic gland removal, or radiotherapy with resultant xerostomia

Date of first enrolment
16/04/2025

Date of final enrolment
17/10/2026

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Brazil

Korea, South

Netherlands

Spain

United States of America

Study participating centre

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Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen Research & Development, LLC

Results and Publications

Individual participant data (IPD) sharing plan
The Janssen Pharmaceutical Companies of Johnson & Johnson data sharing policy is available at www.janssen.com/clinicaltrials/transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access (YODA) Project site at https://yoda.yale.edu/.

IPD sharing plan summary
Stored in non-publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes