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A study comparing talquetamab plus pomalidomide, talquetamab plus teclistamab, and elotuzumab, pomalidomide, and dexamethasone or pomalidomide, bortezomib, and dexamethasone in participants with relapsed or refractory myeloma who have received an Anti-CD38 antibody and lenalidomide

Submission date 12/10/2023	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol
Registration date 15/12/2023	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 03/03/2025	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

Multiple myeloma is a blood cancer that affects certain types of white blood cells called plasma cells. Although treatments are available, multiple myeloma can come back after treatment or be resistant to standard treatment. Drugs that redirect T cells (a type of white blood cell) to attack cancer cells may be an effective means to destroy cancer cells leading to a long-term treatment response. Talquetamab (also known as JNJ-64407564 or Tal or Talvey) and teclistamab (JNJ-64007957 or Tec or Tecvayli) are modified antibodies* that bind to proteins on the surface of multiple myeloma cells and T cells, which activates T cells and kills tumor cells. *Antibody is a protein that helps protect the body against foreign matter, such as bacteria and viruses. In this study, researchers want to learn about the effectiveness of Tal-pomalidomide (Tal-P) or Tal-Tec compared to elotuzumab, pomalidomide, and dexamethasone (EPd) or pomalidomide, bortezomib, and dexamethasone (PVd). One way to see how well a new treatment works is to measure the time it takes for the disease to come back or get worse. Participants will have an equal chance of receiving either Tal-P or Tal-Tec in addition to EPd or PVd treatment chosen by the study doctor. This is an open-label study, which means that the participant, caregiver, and the study doctor will know about the study drug received.

Who can participate?
Patients aged 18 years old and over, diagnosed with multiple myeloma who have been previously treated with 1 to 4 lines of treatments in the past, to which they either did not respond or after which their multiple myeloma has come back.

What does the study involve?
The study will be conducted in 3 phases:
1. Screening Phase: Participants will be screened and enrolled into the study.
2. Treatment Phase: Participants will be randomly divided into 3 groups:
Arm A: Participants will receive Tal-P
Arm B: Participants will receive Tal-Tec
Arm C: Participants will receive either EPd or PVd as per the investigator's choice
3. Follow-up: Participants will be monitored for their health for up to 8 weeks after the last dose of study treatment.

Participants will undergo a safety assessment which includes adverse events, laboratory test results, physical examination findings, assessment of the Eastern Cooperative Oncology Group (ECOG) performance status grade, pharmacokinetics (body does to a drug), and immunogenicity (ability of a foreign substance to enter a person's body and cause an immune response), and biomarkers (an objective measure that captures what is happening in a cell or an organism) will be assessed at specified time points. The overall duration of study is approximately 6 years 5 months.

What are the possible benefits and risks of participating?
There is no established benefit to participants of this study. Based on scientific theory and clinical data, taking talquetamab and teclistamab may improve relapsed or refractory multiple myeloma. However, this cannot be guaranteed because talquetamab and teclistamab are still under investigation as a treatment and it is not known whether talquetamab and teclistamab will work. If participants are put in the comparator group, they will not receive talquetamab and teclistamab.
Participants may experience some benefit from participation in the study that is not due to receiving study drug, but due to regular visits and assessments monitoring overall health. Participation may help other people with relapsed or refractory myeloma in the future.
Participants may have side effects from the drugs 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, immune effector cell-associated neurotoxicity syndrome, skin and nail changes, weight loss, systemic administration-related reaction, cytopenias, infections, injection-site reaction, immune-related adverse events, neurological side effects such as
co-ordination, balance and speech disorders and hypogammaglobulinemia after getting the study drug or not. There are other, less frequent risks. 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 and teclistamab are known at this moment. During the study, the sponsor may learn new information about talquetamab and teclistamab. 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 reviewed for 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 specialist drug 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 (e.g., travel/parking costs).

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

When is the study starting and how long is it expected to run for?
October 2023 to June 2027

Who is funding the study?
Janssen-Cilag International NV (Netherlands)

Who is the main contact?
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Scientific

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Additional identifiers

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IRAS number
1008541

ClinicalTrials.gov number
NCT06208150

Secondary identifying numbers
64407564MMY3009, CPMS 57469, IRAS 1008541

Study information

Scientific Title
A phase III randomized study comparing talquetamab in combination with pomalidomide (Tal-P), talquetamab in combination with teclistamab (Tal-Tec), and investigator's choice of either elotuzumab, pomalidomide, and dexamethasone (EPd) or pomalidomide, bortezomib, and dexamethasone (PVd) in participants with relapsed or refractory myeloma who have received 1 to 4 prior lines of therapy including an Anti-CD38 antibody and lenalidomide

Acronym
MonumenTAL-6

Study objectives
The purpose of this study is to compare the effectiveness of either talquetamab plus pomalidomide (Tal-P) or talquetamab plus teclistamab (Tal-Tec) with elotuzumab, pomalidomide, and dexamethasone (EPd) or pomalidomide, bortezomib, and dexamethasone (PVd).

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 07/12/2023, East Midlands - Derby Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; None available; derby.rec@hra.nhs.uk), ref: 23/EM/0251

Study design

Randomized controlled open-label parallel-group study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Relapsed or refractory myeloma

Interventions
Arm A: Talquetamab + Pomalidomide (Tal-P) Participants will receive talquetamab as subcutaneous (SC) injections; pomalidomide will be self-administered as a single dose orally; dexamethasone may be given orally or intravenously as a pretreatment medication and study drug.
Arm B: Talquetamab + Teclistamab (Tal-Tec)- Participants will receive teclistamab in combination with talquetamab both as SC injection; dexamethasone may be given orally or intravenously as a pretreatment medication and study drug.

Arm C: Elotuzumab+ Pomalidomide+Dexamethasone (EPd) or Pomalidomide+Bortezomib+Dexamethasone (PVd)- Participants will either receive elotuzumab intravenous (IV) injection in combination with pomalidomide and dexamethasone orally; or pomalidomide orally in combination with bortezomib SC injection and dexamethasone orally as per investigator choice. Dexamethasone will be administered as a pretreatment medication.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Therapy, Others (Immunogenicity)

Phase
Phase III

Drug/device/biological/vaccine name(s)
Talquetamab, teclistamab, pomalidomide, dexamethasone, bortezomib, elotuzumab

Primary outcome measure
Progression-free survival defined as the duration from the date of randomization to either progressive disease or death, whichever comes first, measured up to 7 years and 2 months.

Secondary outcome measures

1. Overall response is defined as the percentage of participants with the best overall response of partial response (PR) or better according to international myeloma working group (IMWG) response criteria, measured up to 7 years 2 months.
2. Complete Response (CR) or better is defined as the percentage of participants with the best overall response of CR or better according to IMWG response criteria, measured up to 7 years 2 months.
3. Very Good Partial Response or better is defined as the percentage of participants with best overall response of VGPR or better rate according to IMWG response criteria, measured up to 7 years 2 months.
4. Minimal Residual Disease-negative CR is defined as the percentage of participants who achieve both CR or better and MRD negativity at a threshold of 10^-5 at any timepoint after the date of randomization and before disease progression or start of subsequent antimyeloma therapy (SST), measured up to 7 years 2 months.
5. Overall Survival (OS) is defined as the time from randomization to the date of participant's death, measured up to 7 years 2 months.
6. Progression Free Survival on Next-line Therapy (PFS2) is defined as time from randomization to progression on the next line of therapy or death, whichever comes first, measured up to 7 years 2 months.
7. Time To Next Treatment (TTNT) is defined as the time from randomization to the start of SST, measured up to 7 years 2 months.
8. Serum concentrations Talquetamab and teclistamab will be reported, measured up to 7 years 2 months.
9. Number of Participants with Anti-drug Antibodies (ADAs) to Talquetamab and Teclistamab will be reported, measured up to 7 years 2 months.
10. Time to Sustained Worsening in Symptoms, Functioning, and Health-related Quality of Life (HRQoL) as Assessed by Multiple Myeloma Symptom and Impact Questionnaire (MySIm- Q). Time to sustained worsening in symptoms, functioning and HRQoL is defined as the interval from the date of randomization to the start date of meaningful change. The MySIm-Q is a disease-specific patient-reported outcome (PRO) assessment complementary to the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 item (EORTC-QLQ-C30). It includes 17 items resulting in a symptom subscale and an impact subscale. This will be measured up to 7 years 2 months.
11. Time to Sustained Worsening in Symptoms, Functioning, and Health-related Quality of Life (HRQoL) as Assessed by EORTC-QLQ-C30. Time to sustained worsening in symptoms, functioning and HRQoL is defined as the interval from the date of randomization to the start date of meaningful change. EORTC-QLQ-C30 Version 3 includes 30 items that make up 5 functional scales (physical, role, emotional, cognitive, and social), 1 global health status scale, 3 symptom scales (pain, fatigue, and nausea or vomiting), and 5 single symptom items (dyspnea, insomnia, appetite loss, constipation, and diarrhea) and a single impact item (financial difficulties). The recall period is 7 days ("past week"), and responses are reported using a verbal and numeric rating scales. The item and scale scores are transformed to a 0 to 100 scale. A high scale score represents a higher response level. This will be measured up to 7 years 2 months.
12. Time to Sustained Worsening in Symptoms, Functioning, and Health-related Quality of Life (HRQoL) as Assessed by EuroQol Five Dimension Questionnaire 5-Level (EQ-5D-5L). Time to sustained worsening in symptoms, functioning and HRQoL is defined as the interval from the date of randomization to the start date of meaningful change. The EQ-5D-5L is a 5-item questionnaire that assesses 5 domains including mobility, self-care, usual activities, pain or discomfort, and anxiety or depression plus a visual analog scale rating "health today" with anchors ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). This will be measured up to 7 years 2 months.
13. Time to Sustained Worsening in Symptoms, Functioning, and Health-related Quality of Life (HRQoL) as Assessed by Patient Global Impression –Severity (PGI- S). Time to sustained

worsening in symptoms, functioning and HRQoL is defined as the interval from the date of randomization to the start date of meaningful change. The PGI-S will be used as an anchor, external criterion, to determine meaningful change in scores for the MySIm-Q and EORTC-QLQ-C30 in this population. The response options are presented as a 5-point verbal rating scale from “none” to “very severe.” This will be measured up to 7 years 2 months.
14. Time to Sustained Worsening in Symptoms, Functioning, and Health-related Quality of Life (HRQoL) as Assessed by Epstein Taste Survey. Time to sustained worsening in symptoms, functioning and HRQoL is defined as the interval from the date of randomization to the start date of meaningful change. The epstein taste survey consists of 17 items from the full 71 item PRO instrument, specific to taste changes. developed for use in patients with head and neck cancer as a composite of the Vanderbilt Head and Neck Symptom Survey. This will be measured up to 7 years 2 months.
15. Change from Baseline in Symptoms, Functioning, and Health-related Quality of Life (HRQoL) as Assessed by MySIm-Q. Change from baseline in symptoms, functioning, and HRQoL as assessed by MySIm-Q will be reported. The MySIm-Q is a disease-specific patient-reported outcome (PRO) assessment complementary to the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 item (EORTC-QLQ-C30). It includes 17 items resulting in a symptom subscale and an impact subscale. This will be measured up to 7 years 2 months.
16. Change from Baseline in Symptoms, Functioning, and Health-related Quality of Life (HRQoL) as Assessed by EORTC-QLQ- C30. Change from baseline in symptoms, functioning, and HRQoL as assessed by EORTC-QLQ-C30 will be reported. The EORTC-QLQ-C30 Version 3 includes 30 items that make up 5 functional scales (physical, role, emotional, cognitive, and social), 1 global health status scale, 3 symptom scales (pain, fatigue, and nausea or vomiting), and 5 single symptom items (dyspnea, insomnia, appetite loss, constipation, and diarrhea) and a single impact item (financial difficulties). The recall period is 7 days ("past week"), and responses are reported using a verbal and numeric rating scales. The item and scale scores are transformed to a 0 to 100 scale. A high scale score represents a higher response level. Thus, a high score for a functional scale represents a high or healthy level of functioning and a high score for the global health status represents high HRQoL, but a high score for a symptom scale or item represents a high level of symptomatology or problems. This will be measured up to 7 years 2 months.
17. Change from Baseline in Symptoms, Functioning, and Health-related Quality of Life (HRQoL) as Assessed by EQ-5D-5L. Change from baseline in symptoms, functioning, and HRQoL as assessed by EQ-5D-5L will be reported. The EQ-5D-5L is a 5-item questionnaire that assesses 5 domains including mobility, self-care, usual activities, pain or discomfort, and anxiety or depression plus a visual analog scale rating "health today" with anchors ranging from 0 (worst imaginable health state) to 100 (best imaginable health state). This will be measured up to 7 years 2 months.
18. Change from Baseline in Symptoms, Functioning, and Health- related Quality of Life (HRQoL) as Assessed by PGI-S. Change from baseline in symptoms, functioning, and HRQoL as assessed by PGI-S will be reported. The PGI-S will be used as an anchor, external criterion, to determine meaningful change in scores for the MySIm-Q and EORTC-QLQ-C30 in this population. The response options are presented as a 5-point verbal rating scale from “none” to “very severe." This will be measured up to 7 years 2 months.
19. Change from Baseline in Symptoms, Functioning, and Health-related Quality of Life (HRQoL) as Assessed by Epstein Taste Survey. Change from baseline in symptoms, functioning, and HRQoL as assessed by epstein taste survey will be reported. The epstein taste survey consists of 17 items from the full 71 item PRO instrument, specific to taste changes. developed for use in patients with head and neck cancer as a composite of the Vanderbilt Head and Neck Symptom Survey. This will be measured up to 7 years 2 months.
20. Percentage of Participants With Meaningful Improvement in HRQoL as Assessed by EORTC-QLQ- C30. Percentage of participants with meaningful improvement in HRQol as assessed by

EORTC-QLQ-C30 will be reported. The EORTC-QLQ-C30 Version 3 includes 30 items that make up 5 functional scales (physical, role, emotional, cognitive, and social), 1 global health status scale, 3 symptom scales (pain, fatigue, and nausea or vomiting), and 5 single symptom items (dyspnea, insomnia, appetite loss, constipation, and diarrhea) and a single impact item (financial difficulties). The recall period is 7 days ("past week"), and responses are reported using a verbal and numeric rating scales. The item and scale scores are transformed to a 0 to 100 scale. A high scale score represents a higher response level. Thus, a high score for a functional scale represents a high or healthy level of functioning and a high score for the global health status represents high HRQoL, but a high score for a symptom scale or item represents a high level of symptomatology or problems. This will be measured up to 7 years 2 months.

Overall study start date
10/10/2023

Completion date
14/06/2027

Eligibility

Key inclusion criteria
1. Documented multiple myeloma as defined by the criteria below:
1.1. Multiple myeloma diagnosis according to the International Myeloma Working Group (IMWG) diagnostic criteria
1.2. Measurable disease at screening as assessed by the central laboratory, defined by any of the following:
1.2.1. Serum M-protein level greater than or equal to (>=) 0.5 gram per deciliter (g/dL); or
1.2.2. Urine M-protein level >= 200 milligrams (mg) per 24 hours; or
1.2.3. Light chain multiple myeloma without measurable M-protein in the serum or the urine: serum immunoglobulin (Ig) free light chain (FLC) >= 10 milligrams per deciliter (mg/dL) and abnormal serum Ig kappa lambda FLC ratio
2. Relapsed or refractory disease as defined below:
2.1. Relapsed disease is defined as an initial response to prior treatment, followed by confirmed progressive disease (PD) by IMWG criteria greater than (>) 60 days after cessation of treatment
2.2. Refractory disease is defined as less than (<) 25 percent (%) reduction in M-protein or confirmed PD by IMWG criteria during previous treatment or less than or equal to (<=) 60 days after cessation of treatment
3. Documented evidence of PD or failure to achieve a minimal response to the last line of therapy based on the investigator’s determination of response by IMWG criteria on or after their last regimen
4. Have an Eastern Cooperative Oncology Group (ECOG) performance status score of 0, 1, or 2 at screening and immediately prior to the start of administration of study treatment
5. A participant must agree not to be pregnant, breastfeeding, or planning to become pregnant while enrolled in this study or within 6months after the last dose of study treatment

Participant type(s)
Patient

Age group
Mixed

Lower age limit

18 Years

Sex
Both

Target number of participants
795

Key exclusion criteria
1. Contraindications or life-threatening allergies, hypersensitivity, or intolerance to any study drug or its excipients
2. Stroke, transient ischemic attack, or seizure within 6 months prior to signing the informed consent form (ICF)
3. 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
4. A maximum cumulative dose of corticosteroids of >=140 mg of prednisone or equivalent within the 14-day period before the first dose of the study drug
Known active central nervous system (CNS) involvement or exhibits clinical signs of meningeal involvement of multiple myeloma. If either is suspected, negative whole-brain magnetic resonance imaging (MRI) and lumbar cytology are required.

Date of first enrolment
29/01/2024

Date of final enrolment
29/09/2025

Locations

Countries of recruitment
Argentina

Australia

Austria

Belgium

Brazil

Canada

China

Czech Republic

Denmark

England

France

Germany

Greece

Hungary

India

Israel

Italy

Japan

Korea, South

Netherlands

Poland

Saudi Arabia

Scotland

Spain

Sweden

Türkiye

United Kingdom

United States of America

Wales

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Janssen Research and Development

Alternative Name(s)
Janssen R&D, Janssen Research & Development, Janssen Research & Development, LLC, Janssen Research & Development LLC, Janssen Pharmaceutical Companies of Johnson & Johnson, Research & Development at Janssen, JRD, J&J PRD

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
1. Peer reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website
5. Submission to regulatory authorities
6. Other

Intention to publish date
14/06/2028

Individual participant data (IPD) sharing plan
Study results will be available via publication in scientific journals, the EudraCT database & presentation at scientific meetings. Results will be made available to participants via a Plain Language Summary a year after the end of the study. The summary will describe the results regardless of study outcome in language that is understandable to the general public. It will not contain individual participant results or their personal information. A copy of the Summary will be provided to the REC.

The data sharing policy of the Janssen Pharmaceutical Companies of Johnson and Johnson is available at www.janssen.com/clinical-trials/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 yoda.yale.edu.

IPD sharing plan summary
Available on request