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A clinical study to compare teclistamab monotherapy versus pomalidomide, bortezomib, dexamethasone (PVd) or carfilzomib, dexamethasone (Kd) in participants with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy, including an anti-CD38 monoclonal antibody and lenalidomide

Submission date 30/12/2022	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 18/08/2023	**Overall study status** Ongoing	
Last Edited 28/11/2024	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Multiple myeloma (MM) is a blood cancer that affects certain types of white blood cells called plasma cells. Although treatments are available, MM can reoccur or be resistant to standard treatment. Teclistamab (JNJ-64007957) is a modified antibody* that binds to T cells and BCMA (B cell maturation antigen**) present on plasma cells resulting in T cell activation and breakdown of BCMA cells, leading to cell death. The study is designed to assess if treatment with teclistamab as single therapy will keep participants' cancer from getting worse for a longer period as compared to combination therapy of pomalidomide, bortezomib, dexamethasone (PVd) or carfilzomib, dexamethasone (Kd).

*a protein that helps protect the body against foreign matter, such as bacteria and viruses.
**a protein on the cell surface

Who can participate?
This study will include male and female participants who are 18 years or older, have MM that has reoccurred or resistant to standard treatment, have received 1 to 3 prior lines of therapy and have been exposed to anti-cluster of differentiation 38 (CD38) monoclonal antibody*** therapy and lenalidomide.

***protein that binds to certain targets in the body, such as antigens on the surface of cancer cells.

What does the study involve?
Participants will be screened if they can take part in the study. They will be divided into two groups and will receive:
1. Group A: Teclistamab as an injection under the skin
2. Group B: Either PVd (P and D orally, V as injection under skin) or Kd (K as injection into vein, D orally/ injection into vein) based on physician's choice.
Participants will be followed-up to monitor their health until death, withdrawal of consent, lost to follow-up, or end of the study, whichever occurs first.
During the study, tests such as blood and urine tests, physical examination, vital signs, neurologic examinations, Eastern Cooperative Oncology Group status, and questionnaires will be performed. Side effects will be recorded until 30 days after the last dose or if they start the next therapy. The overall duration of the study will be up to 9 years.

What are the possible benefits and risks of participating?
Teclistamab has shown benefit in patients with MM who have received at least 3 prior therapies. Based on scientific theory, participants who have received 1 to 3 prior therapies may benefit from teclistamab, however, this benefit cannot be guaranteed.
If participants are put in the comparator group, they will not receive teclistamab but will receive treatment already on the market.
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 multiple 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. Some of the potential risks associated with teclistamab include cytokine release syndrome (which may cause symptoms and signs including fever, low blood pressure, nausea and fatigue), neurological side effects, infections, injection site reactions and lowered number of white cells or antibodies in the blood. Some of the most common risks of PVd include a reduction of white blood cells in the blood and problems with nerves causing pain, tingling or weakness. Other potential risks include formation of blood clots in the blood vessels and infections. The most common risks with carfilzomib in the Kd arm include lowered number of white and red blood cells, nausea and fatigue Some other potential risks include heart problems, high blood pressure, shortness of breath and infusion reactions. For a complete list of known risks to participating in the study, refer to the participant information sheet and informed consent form, which will be signed by every participant agreeing to participate in the study.
Not all possible side effects and risks related to teclistamab are known at this moment. During the study, the sponsor may learn new information about teclistamab. The study doctor will tell participants as soon as possible about any new information that might make them change their mind about being in the study, such as new risks.
In addition, participants will be provided with and asked to carry a 'patient safety card' with them at all times. This has the contact details of the study team and a 24-hour emergency number should a participant need emergency treatment out of hours.
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. The sponsor has also implemented an Independent Data Review Committee who will perform a safety review of study data at predetermined timepoints and make recommendations regarding the continuation of the study as needed.

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?
January 2023 to November 2031

Who is funding the study?
Janssen Research and Development (Netherlands)

Who is the main contact?
Local Trial Manager, JanssenUKRegistryQueries@its.jnj.com

Contact information

Type(s)
Scientific

Contact name
Miss Ana Moreno

Contact details
Medical Information and Product Information Enquiry
High Wycombe
United Kingdom
HP12 4DP
+44 (0)1494 567 444
medinfo@its.jnj.com

Type(s)
Principal Investigator

Contact name
Dr Stephen Hawkins

Contact details
Clatterbridge Rd
Wirral
United Kingdom
CH63 4JY

Additional identifiers

EudraCT/CTIS number
2022-000928-37

IRAS number

1006875

ClinicalTrials.gov number
NCT05572515

Secondary identifying numbers
64007957MMY3006, IRAS 1006875, CPMS 54402

Study information

Scientific Title
A Phase III randomized study comparing teclistamab monotherapy versus pomalidomide, bortezomib, dexamethasone (PVd) or carfilzomib, dexamethasone (Kd) in participants with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy, including an anti-CD38 monoclonal antibody and lenalidomide

Acronym
MajesTEC-9

Study objectives
Main objectives:
1. To compare how well teclistamab works compared to a combination of pomalidomide, bortezomib, and dexamethasone (PVd) or carfilzomib and dexamethasone (Kd)

Secondary objectives:
1. To further compare how well teclistamab works as compared to a treatment combination of PVd/Kd
2. To assess the safety profile of teclistamab
3. To evaluate the pharmacokinetics (what the body does to the drug) of teclistamab
4. To evaluate the immunogenicity (immune response against the drug) of teclistamab
5. To assess participant’s symptoms, functioning, and health-related quality of life (HRQoL) with teclistamab versus PVd/Kd
6. To evaluate how well teclistamab works in participants with high-risk disease

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 11/07/2023, East of England - Cambridge Central Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048285; cambridgecentral.rec@hra.nhs.uk), ref: 23/EE/0030

Study design
Open randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

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

Interventions
Participants will receive either Teclistamab or Pomalidomide, Bortezomib and Dexamethasone (PVd)/ Carfilzomib and Dexamethasone (Kd), as described below. Central randomisation will be implemented in this study. Participants will be randomly assigned to 1 of 2 treatment groups based on a computer-generated randomisation schedule prepared before the study by or under the supervision of the sponsor.

Experimental: Arm A: Teclistamab
Participants will receive teclistamab monotherapy.

Drug: Teclistamab
Teclistamab will be administered subcutaneously.
Other Names: JNJ-64007957

Experimental: Arm B: Pomalidomide, Bortezomib and Dexamethasone (PVd) or Carfilzomib and Dexamethasone (Kd)
Participants will receive either PVd or Kd based on the principal investigator’s choice.

Pomalidomide, Bortezomib and Dexamethasone (PVd):
Drug: Pomalidomide
Pomalidomide will be administered orally.

Drug: Bortezomib
Bortezomib will be administered subcutaneously.

Drug: Dexamethasone
Dexamethasone will be administered orally.

Carfilzomib and Dexamethasone (Kd):
Drug: Carfilzomib
Carfilzomib will be administered intravenously.

Drug: Dexamethasone
Dexamethasone will be administered intravenously or orally.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Teclistamab, pomalidomide, bortezomib, dexamethasone, carfilzomib

Primary outcome measure
Progression-free survival (PFS), defined as the time from the date of randomisation to the date of first documented disease progression, as defined in the International myeloma working group (IMWG) 2016 response criteria, or death due to any cause, whichever occurs first.

Secondary outcome measures
1. Overall response (partial response [PR] or better), defined as participants who have a PR or better prior to subsequent antimyeloma therapy in accordance with the IMWG 2016 criteria - measured up to 9 years.
2. Very good partial response (VGPR) or better response (stringent complete response [sCR] +complete response [CR]+VGPR), defined as participants who achieve a VGPR or better response prior to subsequent antimyeloma therapy in accordance with the IMWG 2016 criteria - measured up to 9 years.
3. Complete response (CR) or better response, defined as participants who achieve a CR or better response prior to subsequent antimyeloma therapy in accordance with the IMWG 2016 criteria - measured up to 9 years.
4. Minimal residual disease (MRD) negativity, defined as participants who achieve MRD negativity at a threshold of 10^-5 at any timepoint after the date of randomisation and before disease progression or start of subsequent antimyeloma therapy - measured up to 9 years.
5. Duration of response (DOR), defined as the time interval between the date of initial documentation of a response (PR or better) to the date of first documented evidence of progressive disease according to the IMWG 2016 response criteria or death due to any cause, whichever occurs first - measured up to 9 years.
6. Time to next treatment (TTNT), defined as the time from randomisation to the start of subsequent antimyeloma treatment - measured up to 9 years.
7. Progression-free survival on next-line therapy (PFS2), defined as the time interval between the date of randomisation and date of event, which is defined as progressive disease as assessed by the investigator on the first subsequent line of antimyeloma therapy, or death from any cause, whichever occurs first - measured up to 9 years.
8. Overall survival (OS), defined as the time from the date of randomisation to the date of the participant’s death due to any cause - measured up to 9 years.
9. Number of participants with adverse events (AEs) by severity, reported up to 9 years.
10. Number of participants with serious adverse events (SAEs) by Severity, reported up to 9 years.
11. Number of participants with abnormal laboratory results, such as hematology and chemistry, reported up to 9 years.
12. Serum concentrations of teclistamab, reported up to 9 years.
13. Number of participants with anti-drug antibodies (ADAs) to teclistamab, reported up to 9 years.
14. Change from Baseline in Symptoms, Functioning, and Overall Health-related Quality of Life (HRQoL) as Assessed by European Organisation for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30 (EORTC-QLQ-C30) determined from baseline up to 9 years. 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/vomiting), and 6 single symptom items (dyspnea, insomnia, appetite loss,

constipation, diarrhea, and financial difficulties). 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/healthy level of functioning and a high score for the global health status represents high HRQoL, but a high score for a symptom scale/item represents a high level of symptomatology/problems.
15. Change from Baseline in Symptoms, Functioning, and Overall HRQoL as Assessed by Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q) Scale Score determined from baseline up to 9 years. The MySIm-Q is a disease-specific PRO assessment complementary to the EORTC-QLQ-C30. It includes 17 items resulting in a symptom subscale and an impact subscale. The recall period is the "past 7 days", and responses are reported on a 5-point verbal rating scale.
16. Change from Baseline in Symptoms, Functioning, and Overall HRQoL as Assessed by Patient-reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) determined from baseline up to 6 months. The National Cancer Institute's (NCI's) PRO-CTCAE is an item library of common adverse events experienced by people with cancer that are appropriate for self-reporting of treatment tolerability. Each symptom selected for inclusion can be rated by up to 3 attributes characterising the presence/frequency, severity, and/or interference of the AEs. It ranges from 0 to 4 with higher scores indicating higher frequency or greater severity/impact.
17. Change from Baseline in Symptoms, Functioning, and Overall HRQoL as Assessed by EuroQol Five Dimension Questionnaire 5-Level (EQ-5D-5L) determined from baseline up to 9 years. The EQ-5D-5L is a generic measure of health status. The EQ-5D-5L is a 5-item questionnaire that assesses 5 domains including mobility, self-care, usual activities, pain/discomfort, and anxiety /depression plus a visual analog scale rating "health today" with anchors ranging from 0 (worst imaginable health state) to 100 (best imaginable health state).
18. Time to worsening in symptoms, functioning, and overall HRQoL, measured as the interval from the date of randomisation to the start date of meaningful change, up to 9 years.
19. PFS in participants in high-risk molecular features, defined as the time from the date of randomisation to the date of first documented disease progression, as defined in the IMWG 2016 response criteria, or death due to any cause, whichever occurs first – measured up to 9 years.
20. Depth of response in participants in high-risk molecular features, measured up to 9 years.

Overall study start date
23/01/2023

Completion date
30/11/2031

Eligibility

Key inclusion criteria
1. Documented diagnosis of multiple myeloma as defined by the criteria below:
1.1. Multiple myeloma diagnosis according to International Myeloma Working Group (IMWG) diagnostic criteria.
1.2. Measurable disease at screening as defined by any of the following:
1.2.1. Serum M-protein level ≥0.5 grams per deciliter (g/dL) (central laboratory)
1.2.2. Urine M-protein level ≥200 milligrams (mg)/24 hours (central laboratory)
1.2.3. Serum immunoglobulin free light chain ≥10 milligrams per deciliter (mg/dL) (central laboratory) and abnormal serum immunoglobulin kappa lambda free light chain ratio
2. Received 1 to 3 prior lines of antimyeloma therapy including a minimum of 2 consecutive cycles of an anti-cluster of differentiation 38 (CD38) monoclonal antibody at the approved

dosing regimen in any prior line and 2 consecutive cycles of lenalidomide in any prior line.
3. Documented evidence of progressive disease or failure to achieve a response to the last line of therapy based on the investigator's determination of response by International myeloma working group (IMWG) criteria.
4. Have an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 to 2.
5. A female participant must agree not to be pregnant, breastfeeding, or plan to become pregnant while enrolled in this study or within 6 months after the last dose of study treatment.
6. Must be willing and able to adhere to the lifestyle restrictions specified in this protocol.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
590

Key exclusion criteria
1. Received any prior B cell maturation antigen (BCMA)-directed therapy
2. A participant is not eligible to receive PVd as control therapy if any of the following are present:
2.1. Received prior pomalidomide therapy,
2.2. Does not meet criteria for bortezomib retreatment,
2.3. Contraindications or life-threatening allergies, hypersensitivity, or intolerance to pomalidomide or bortezomib,
2.4. Grade 1 peripheral neuropathy with pain or Grade ≥2 peripheral neuropathy as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0,
2.5. Received a strong cytochrome P (CYP) 3A4 inducer within 5 half-lives prior to randomisation
3. A participant is not eligible to receive Kd as control therapy if any of the following are present:
3.1. Received prior carfilzomib therapy,
3.2. Uncontrolled hypertension, defined as an average systolic blood pressure greater than (>) 159 millimeters of mercury (mmHg) or diastolic blood pressure >99 mmHg despite optimal treatment,
3.3. Grade 2 peripheral neuropathy with pain or Grade ≥3 peripheral neuropathy as defined by NCI-CTCAE Version 5.0,
3.4. Contraindications or life-threatening allergies, hypersensitivity, or intolerance to carfilzomib (intolerance defined as prior therapy discontinued due to any adverse event [AE] related to carfilzomib)
4. Central nervous system (CNS) involvement or clinical signs of meningeal involvement of multiple myeloma.
5. Received a live, attenuated vaccine within 4 weeks before randomisation
6. Plasma cell leukaemia at the time of screening, Waldenstrom's macroglobulinemia, polyneuropathy, organomegaly, endocrinopathy, M-protein (POEMS) syndrome and skin changes, or primary amyloid light chain amyloidosis
7. Received a maximum cumulative dose of corticosteroids of ≥140 mg of prednisone or equivalent within 14 days prior to randomisation

Date of first enrolment
29/03/2023

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
Australia

Austria

Belgium

Brazil

Canada

China

Denmark

France

Germany

Greece

India

Israel

Italy

Japan

Malaysia

Netherlands

Poland

Portugal

Spain

Sweden

Türkiye

United Kingdom

Study participating centre
The Clatterbridge Cancer Centre
Wirral
United Kingdom
CH63 4JY

Sponsor information

Organisation
Janssen-Cilag International NV

Sponsor details
Archimedesweg 29
Leiden
Netherlands
2333 CM
+31 (0)71 524 21 06
ClinicalTrialsEU@its.jnj.com

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

Results of the study will be available to the wider scientific community via publication in scientific journals and presentation at scientific meetings. Study results will be available to participants via provision of a Plain Language Summary at the end of the study and in addition results will be published in the EudraCT database.

Intention to publish date
16/05/2032

Individual participant data (IPD) sharing plan
The data sharing policy of the Janssen Pharmaceutical Companies of Johnson and Johnson is available at https://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