ISRCTN15262649 https://doi.org/10.1186/ISRCTN15262649

A study of ramantamig plus daratumumab versus investigator's choice in participants with newly diagnosed multiple myeloma

Submission date 02/07/2026	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol
Registration date 24/08/2026	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 27/10/2026	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Newly diagnosed multiple myeloma (NDMM) is a blood cancer that forms in a type of white blood cells (WBCs) called plasma cells. Although treatment options are available, but either cancer can come back, it can cause harmful side effects or spread to other parts of body. Hence, there is a need for better treatment options. JNJ-79635322 (Ramantamig) binds to proteins called B-cell maturation antigen* and G protein-coupled receptor family C Group 5 member D* found mainly on cancer cells, and cluster of differentiation 3 (CD3) found on T-cells. Upon binding, it activates T-cells and leads to killing of cancer cells. *Protein found on cancer cells that new treatments can target to help fight the disease.

Who can participate?
Participants aged 18 years or older with NDMM who are not suitable for or not planned to receive a stem cell transplant.

What does the study involve?
1.Screening phase (up to 28 days)
2.Treatment phase (Start of treatment until treatment completion or discontinuation):
Participants will be randomly (by chance) assigned to either:
•Arm A: Ramantamig-D
•Arm B: Either DVRd or DRd (investigator's choice)
3.Follow-up phase: Until death, withdrawal of consent, lost to follow-up, or end of the trial, whichever occurs first.

Safety assessments include adverse events, physical examinations, vital signs, electrocardiogram, clinical laboratory tests, suicide assessments, and tuberculosis screening. The overall duration of the study will be approximately 5 years

What are the possible benefits and risks of participating?
There is no established benefit to participants of this study. Based on scientific theory, taking Ramantamig-D may improve NDMM. However, this cannot be guaranteed because Ramantamig-

D is still under investigation as a treatment and it is not known whether Ramantamig -D will work.
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 NDMM 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. Potential risks include cytokine release syndrome (CRS; inflammation condition that may occur after treatment with some types of immunotherapy), immune effector cell-associated neurotoxicity syndrome (ICANS; neurological side effects may occur that include headaches or a condition of brain), infections, Hypogammaglobulinemia (low protein in blood that fights infection), immune-mediated toxicity (hyperactive immune system attacks healthy tissues), harm to mouth, skin and nails, systemic administration-related reaction (sARRs; side effects caused due to administration of drug into the vein), injection site reactions, tumor lysis syndrome (TLS; large numbers of cancer cells die rapidly releasing their contents in to the blood stream), cytopenias (abnormally low number of blood cells). 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 to participating in the study.
Not all possible side effects and risks related to Ramantamig-D are known at this moment. During the study, the sponsor may learn new information about Ramantamig-D. 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.
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 their 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?
September 2026 to February 2035

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

Who is the main contact?
medinfo@its.jnj.com

Contact information

Type(s)
Scientific, Public

Contact name
None - Medical Information and Product Information Enquiry

Contact details
Janssen Research & Development (Janssen-Cilag Ltd), 20 Grenfell Road
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SL6 1EH
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medinfo@its.jnj.com

Type(s)
Principal investigator

Contact name
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United Kingdom
CT1 3NG

Additional identifiers

ClinicalTrials.gov (NCT)
NCT07665450

Clinical Trials Information System (CTIS)
2026-526654-14

Integrated Research Application System (IRAS)
1014316

Central Portfolio Management System (CPMS)
73944

Sponsor's protocol code number
79635322MMY3004

Study information

Scientific Title
A phase 3 randomized study comparing ramantamig plus daratumumab versus investigator’s choice of daratumumab, bortezomib, lenalidomide, and dexamethasone (DVRd) or daratumumab, lenalidomide, and dexamethasone (DRd) in participants with newly diagnosed multiple myeloma for whom hematopoietic stem cell transplant is not planned as initial therapy

Acronym
TRIlogy-7

Study objectives

Main objectives:
To find out whether using ramantamig along with daratumumab can- help participants with NDMM live longer without the disease getting worse and- have no signs of cancer after 12 months of treatment, compared to standard treatment of DVRd or DRd in participants who are not suitable for or not planned to receive a stem cell transplant
Secondary objectives:
1.To assess whether ramantamig-D can help patients with newly diagnosed multiple myeloma live longer (overall survival) compared to standard treatment of DVRd or DRd in participants who are not suitable for or not planned to receive a stem cell transplant
2.To find out whether ramantamig-D will improve 24-month sustained minimal residual disease (MRD) negative complete response rate. MRD is a situation where there are no detectable signs of remaining cancer cells for at least 24 months
3. To compare how well ramantamig-D works compared to standard treatments (DVRd or DRd)
4. To further understand how safe ramantamig-D is
5. To learn how participants feel and function during treatment, including their overall well-being (health-related quality of life), using participant questionnaires
6. To understand how well participants are able to tolerate (manage) treatment with ramantamig-D

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 18/08/2026, North West – Haydock REC (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; haydock.rec@hra.nhs.uk), ref: 26/NW/0213

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Safety

Study type(s)

Health condition(s) or problem(s) studied
Newly diagnosed multiple myeloma

Interventions

Experimental: Arm A: Ramantamig plus Daratumumab (Ramantamig-D)
Participants will receive ramantamig D subcutaneous injection.

Active Comparator: Arm B: Investigator's Choice (DVRd or DRd)
Participants will receive either daratumumab, bortezomib, lenalidomide, dexamethasone (DVRd) or daratumumab, lenalidomide, dexamethasone (DRd) as per investigator's choice.
Daratumumab will be administered subcutaneously.
Lenalidomide will be administered orally.
Bortezomib will be administered subcutaneously or intravenously.
Dexamethasone will be administered orally or intravenously.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Ramantamig, daratumumab, lenolidomide, bortezomib, dexamethosone

Primary outcome(s)
Current primary outcome(s) as of 27/10/2026:

1. Progression-Free Survival (PFS)
PFS is defined as the duration from randomization to either confirmed progression of disease (PD) or death, whichever occurs first up to 62 months
2. Percentage of Participants Achieving 12-Month Minimal Residual Disease (MRD)-Negative Complete Response (CR) 12-month MRD-negative CR rate is defined as participants who achieve MRD-negative status at 12 months (+/-3 months) from randomization, as determined by next-generation sequencing (NGS), prior to PD or subsequent antimyeloma therapy (including ASCT). Additionally, participant must achieve CR or better any time from randomization up to and including 12+3 months prior to PD or subsequent antimyeloma therapy, according to international myeloma working group (IMWG) criteria up to 12 months

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Previous primary outcome(s):

1. Progression-Free Survival (PFS). PFS is defined as the time from treatment assignment (that is, randomisation in the trial) to confirmed progression of disease (PD) or death, whichever occurs first up to approx 62 months
2. Percentage of Participants Achieving 12-Month Minimal Residual Disease (MRD)-Negative Complete Response CR 12-month MRD-negative CR rate is defined as achieving MRD-negative status at the analysis time window of 12 months (+/-3 months), as determined by next-generation sequencing (NGS) with sensitivity of 10^-5, prior to PD or subsequent antimyeloma therapy (including ASCT). Additionally, CR or better must be achieved any time from randomisation up to and including 12+3 months, according to international myeloma working group (IMWG) criteria up to 12 months

Key secondary outcome(s)
Current key secondary outcome(s) as of 27/10/2026:

1. Overall survival (OS): Overall survival is defined as the time from treatment assignment (that is, randomization in the trial) to death from any cause. Assessed up to approximately 100 months
2. Percentage of Participants Achieving 24-Month Sustained MRD-Negative CR
24-month sustained MRD-negative CR is defined as participants who achieve MRD-negative CR status, as determined by NGS for at least 24 months without any examination showing MRD positive status or PD in between up to 5 years
3. Percentage of participants with very good partial response (VGPR) or better: Percentage of participants achieving VGPR, CR, or stringent complete response (sCR) before receiving subsequent antimyeloma therapy, in accordance with International Myeloma Working Group (IMWG) criteria, during or after the trial intervention. Assessed up to 5 years
4. Percentage of participants achieving CR or sCR: Percentage of participants achieving CR or sCR before receiving subsequent antimyeloma therapy, in accordance with IMWG criteria, during or after the trial intervention. Assessed up to 5 years
5. Percentage of participants with overall response: Percentage of participants achieving partial response (PR) or better before receiving subsequent antimyeloma therapy, in accordance with IMWG criteria, during or after the trial intervention. Assessed up to 5 years
6. Percentage of participants with overall MRD-negative CR: Percentage of participants who achieve MRD-negative status, as determined by next-generation sequencing (NGS), at any time after randomization and before PD or subsequent antimyeloma therapy, and who achieve CR or better. Assessed up to 5 years
7. Percentage of Participants with 12-Month Sustained MRD-Negative CR
Percentage of participants who achieve MRD-negative CR status, as determined by NGS, for at least 12 months without any examination showing MRD-positive status or PD in between will be reported up to 5 years
8. Progression-free survival 2 (PFS2): PFS2 is defined as the time from randomization to PD on the first subsequent line of antimyeloma therapy, as assessed by the investigator, or death from any cause, whichever occurs first. Assessed up to approximately 100 months
9. Number of participants with adverse events (AEs): An adverse event is any untoward medical occurrence in a participant receiving a pharmaceutical product, whether investigational or non-investigational, and does not necessarily have a causal relationship with the intervention. Assessed up to approximately 100 months
10. Change from baseline in health-related quality of life (HRQoL) assessed by the Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q): The MySIm-Q is a disease-specific patient-reported outcome measure complementary to the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30). It contains 17 items with a 7-day recall period and responses scored from 0 to 4, with higher scores indicating greater symptom severity or impact. Assessed up to approximately 100 months
11. Change from baseline in HRQoL assessed by the EORTC QLQ-C30: The EORTC QLQ-C30 Version 3 contains 30 items covering functional scales, global health status, symptom scales, and individual symptom items. Scores are transformed to a 0 to 100 scale. Higher scores represent better HRQoL and functioning, and more severe symptoms where applicable. Assessed up to approximately 100 months
12. Change from baseline in HRQoL assessed by the EuroQol 5 Dimensions 5 Levels (EQ-5D-5L): The EQ-5D-5L is a self-administered generic health status measure comprising a descriptive system and a visual analogue scale. It assesses mobility, self-care, usual activities, pain /discomfort, and anxiety/depression. Higher scores indicate worse HRQoL. Assessed up to approximately 100 months
13. Change from baseline in HRQoL assessed by the Patient Global Impression of Symptom Severity (PGIS): The PGIS is a 2-item questionnaire assessing symptom severity and the impact of symptoms on a 5-point verbal rating scale. Scores range from 1 (none) to 5 (very severe), with higher scores indicating greater symptom severity. Assessed up to approximately 100 months

14. Change from baseline in HRQoL assessed by the European Organisation for Research and Treatment of Cancer Item List 46 (EORTC IL46): The EORTC IL46 consists of a single question measuring the overall burden of treatment-related symptoms. Responses range from "not at all" to "very much" on a 4-point scale, with higher scores indicating greater symptom burden. Assessed up to approximately 100 months
15. Percentage of participants with tolerability to ramantamig-D measured through patient-reported outcomes (PROs): Percentage of participants with tolerability to ramantamig-D as measured through patient-reported outcomes. Assessed up to approximately 100 months

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Previous key secondary outcome(s):

1. Overall survival (OS): Overall survival is defined as the time from treatment assignment (that is, randomization in the trial) to death from any cause. Assessed up to approximately 100 months
2. Percentage of participants achieving 24-month sustained MRD-negative complete response (CR): 24-month sustained MRD-negative CR is defined as achieving confirmed CR or better while maintaining MRD-negative status for at least 24 months without any examination showing MRD-positive status or progressive disease (PD) in between. Assessed up to 5 years
3. Percentage of participants with very good partial response (VGPR) or better: Percentage of participants achieving VGPR, CR, or stringent complete response (sCR) before receiving subsequent antimyeloma therapy, in accordance with International Myeloma Working Group (IMWG) criteria, during or after the trial intervention. Assessed up to 5 years
4. Percentage of participants achieving CR or sCR: Percentage of participants achieving CR or sCR before receiving subsequent antimyeloma therapy, in accordance with IMWG criteria, during or after the trial intervention. Assessed up to 5 years
5. Percentage of participants with overall response: Percentage of participants achieving partial response (PR) or better before receiving subsequent antimyeloma therapy, in accordance with IMWG criteria, during or after the trial intervention. Assessed up to 5 years
6. Percentage of participants with overall MRD-negative CR: Percentage of participants who achieve MRD-negative status, as determined by next-generation sequencing (NGS), at any time after randomization and before PD or subsequent antimyeloma therapy, and who achieve CR or better. Assessed up to 5 years
7. Percentage of participants with 12-month sustained MRD-negative CR: Percentage of participants with confirmed CR or better who maintain MRD-negative status, as determined by NGS, for at least 12 months without any examination showing MRD-positive status or PD in between. Assessed up to 5 years
8. Progression-free survival 2 (PFS2): PFS2 is defined as the time from randomization to PD on the first subsequent line of antimyeloma therapy, as assessed by the investigator, or death from any cause, whichever occurs first. Assessed up to approximately 100 months
9. Number of participants with adverse events (AEs): An adverse event is any untoward medical occurrence in a participant receiving a pharmaceutical product, whether investigational or non-investigational, and does not necessarily have a causal relationship with the intervention. Assessed up to approximately 100 months
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Completion date
02/02/2035

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 27/10/2026:

1. Documented diagnosis of multiple myeloma (MM) according to the IMWG diagnostic criteria
2. Not considered for high-dose chemotherapy with autologous stem cell transplantation (ASCT) due to:
i. ineligible due to advanced age; or
ii. ineligible due to presence of comorbid condition(s) likely to have a negative impact on tolerability of high-dose chemotherapy with ASCT
3. Have an eastern cooperative oncology status (ECOG) performance status of 0 to 2
4. Must sign an informed consent form (ICF)
5. Measurable disease at screening as assessed by central laboratory as defined in the protocol

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Previous key inclusion criteria:

1. Documented diagnosis of multiple myeloma (MM) according to the IMWG diagnostic criteria
2. Not considered for high-dose chemotherapy with autologous stem cell transplantation (ASCT) due to:
i. ineligible due to advanced age; or
ii. ineligible due to presence of comorbid condition(s) likely to have a negative impact on tolerability of high-dose chemotherapy with ASCT; or
iii. deferral of high-dose chemotherapy with ASCT as initial treatment

3. Have an eastern cooperative oncology status (ECOG) performance status of 0 to 2
4. Must sign an informed consent form (ICF)
5. Measurable disease at screening as assessed by central laboratory as defined in the protocol

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current key exclusion criteria as of 27/10/2026:

1. Myeloma Frailty Score of greater than or equal to (>=) 2 with the exception of participants who have a score of 2 based on age alone
2. Suspected or known allergies, hypersensitivity, intolerance or other contraindications to any trial intervention or its excipients
3. Had major surgery (for example, requiring general anesthesia) or had significant traumatic injury within 2 weeks prior to first dose of trial intervention or will not have fully recovered from surgery, or has surgery planned during the time the participant is expected to participate in the trial
4. Known active or prior CNS involvement or exhibits clinical signs of meningeal involvement of MM
5. Received any prior therapy(ies) for treatment of MM or smoldering myeloma, with the exception of emergency use of a short course of corticosteroids

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1. Myeloma Frailty Score of greater than or equal to (>=) 2 with the exception of participants who have a score of 2 based on age alone
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4. Known active or prior CNS involvement or exhibits clinical signs of meningeal involvement of MM

5. Received any prior therapy(ies) for treatment of MM or smoldering myeloma, with the exception of emergency use of a short course of corticosteroids

Date of first enrolment
23/09/2026

Date of final enrolment
15/08/2028

Locations

Countries of recruitment
United Kingdom

England

Scotland

Australia

Brazil

China

Czech Republic

France

Germany

Greece

Israel

Italy

Japan

Netherlands

Poland

Portugal

Spain

United States of America

Study participating centre

Kent and Canterbury Hospital
Ethelbert Road
Canterbury
England
CT1 3NG

Study participating centre
Blackpool Victoria Hospital
Whinney Heys Road
Blackpool
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FY3 8NR

Study participating centre
New Cross Hospital
Wolverhampton Road
Heath Town
Wolverhampton
England
WV10 0QP

Study participating centre
Addenbrookes Hospital
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
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Scotland
EH4 2XU

Study participating centre
University Hospital Bristol and Weston, Bristol Haematology and Oncology Centre
Horfield Road

Bristol
England
BS2 8ED

Study participating centre
University College Hospital, Cancer Clinical Trials Unit
250 Euston Road
London
England
NW1 2PG

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
England
B15 2GW

Study participating centre
Colchester General Hospital
Turner Road
Colchester
England
CO4 5JL

Sponsor information

Organisation
Janssen-Cilag International N.V.

Funder(s)

Funder type

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

Individual participant data (IPD) sharing plan
The data sharing policy of Johnson & Johnson Innovative Medicine is available at www.jnj.com /innovativemedicine/our-innovation/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at yoda.yale.edu

IPD sharing plan summary
Available on request