Phase 1, First-in-Human, Dose Escalation Study of JNJ-79635322, a Trispecific Antibody, in Participants with Relapsed or Refractory Multiple Myeloma

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This study has been transitioned to CTIS with ID 2023-503679-12-00 check the CTIS register for the current data. Part 1 (Dose Escalation) - to identify the recommended Phase 2 dose(s) and schedule(s) to be safe for JNJ-79635322. Part 2 (Dose...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haematopoietic neoplasms (excl leukaemias and lymphomas)
Study type	Interventional

Summary

ID

NL-OMON53500

Source
ToetsingOnline

Brief title
79635322MMY1001

Condition

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
disease of Kahler, multiple myeloma

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag

Source(s) of monetary or material Support: the sponsor of the study

Intervention

Keyword: dose finding, first in human, safety, tolerability

Outcome measures

Primary outcome

Part 1 (Dose Escalation): Frequency and type of DLTs; incidence and

severity of AEs

Part 2 (Dose Expansion): Frequency and severity of AEs and assessment

of laboratory values

Secondary outcome

- Serum concentrations and PK parameters of JNJ-79635322

- Presence of antidrug antibodies to JNJ-79635322

- Response as defined by IMWG 2016 response criteria

- DOR and TTR where response is defined by IMWG 2016 criteria

Study description

Background summary

See section 2.2 of the protocol
Multiple myeloma is a malignant plasma cell disorder that accounts for approximately 10% of all
hematologic cancers, making it the second most common hematologic malignancy. There has been remarkable progress in the treatment of MM in the last 30 years resulting in marked
survival improvements. Therapies include agents such as proteasome inhibitors (bortezomib,
carfilzomib, ixazomib), immunomodulatory drugs (eg, lenalidomide, thalidomide, pomalidomide), monoclonal antibodies (eg, daratumumab, elotuzumab), high-dose chemotherapy
(cyclophosphamide, melphalan), anthracyclines (eg, doxorubicin), a selective

inhibitor of nuclear
export (selinexor), an antibody-drug conjugate (belantamab mafodotin), or a combination of such
drugs, and consideration of SCT for those patients that qualify. However, despite these
improvements, MM remains incurable.

Study objective

This study has been transitioned to CTIS with ID 2023-503679-12-00 check the CTIS register for the current data.

Part 1 (Dose Escalation) - to identify the recommended Phase 2 dose(s) and schedule(s) to be safe for JNJ-79635322. Part 2 (Dose Expansion) is to characterize the safety and tolerability of JNJ-79635322 at the RP2D(s).

Study design

Study Type:Interventional
Primary Purpose: Treatment
Study Phase: Phase 1
Intervention Study Model: Sequential Assignment
Number of Arms: 2

The study consists of a Screening Period, a Treatment Period, and a Posttreatment Follow-up
Period. The study treatment will
be administered in the hospital or at the study site, as described in Section 6.1 in the protocol and in accordance
with institutional standards. Study procedures and laboratory assessments will be performed to
monitor safety, evaluate anticancer activity, and collect data for PK and PD endpoints. The
Treatment Period will extend from the start of study treatment administration until the study
treatment is discontinued. Participants may continue to receive study treatment until confirmed
disease progression (according to IMWG 2016 criteria), unacceptable toxicity, withdrawal of consent, or investigator or sponsor decision to discontinue treatment (see
Section 7.1 in the protocol). After treatment discontinuation, participants will have an EOT Visit. The
Posttreatment Follow-up Period will begin when a participant discontinues study treatment and
will continue for up to 16 weeks or until death, loss to follow-up, or discontinuation of the study,

whichever occurs first.

Intervention

Intervention Name: JNJ-79635322
Type: Drug
Associated Arms: Part 1: Dose Escalation; Part 2: Dose Expansion
Description: JNJ-79635322 will be administered as SC injection.

Study burden and risks

Any drug has risks and side effects which may vary from person to person. Side effects may be mild to very severe. Most side effects will go away after treatment is stopped, but some may be long lasting. Side effects seen in research studies can result from a patient*s disease, the study drug, other drugs, other diseases, or a combination of these.

As of 25 May 2022, no clinical study patients have been treated with JNJ-79635322. This section gives you the information known so far about possible side effects of JNJ-79635322 based on clinical experience with other therapies that work in a similar way.
- CRS
- Neurological Side Effects: ICANS
- Infections: Upper respiratory tract infrections
- hypogammaglobulinemia
- immune related effects
- oral side effects: dry mouth, altered taste, loss of taste, difficulty swallowing, weight loss
- skin and nail problems: dry skin, skin peeling, itching, rash, PPE
- systemic administration related reactions
- injection site reactions
- tumor lysis syndrome
- blood cell effects

Collection of blood: the subject may experience bruising or irritation at the site where the needle enters the skin. Some patients may faint and, in rare cases, get an infection.
Ecg (electrocardiogram): There is usually no risk associated with undergoing an ecg. The stickers may pull on the subject's skin or cause redness or itching.
Bone marrow aspirate: During and after the procedure, the subject may experience pain and discomfort. There is also a risk of infection and bleeding at that site. The subject may also have an allergic reaction to the anesthetic.
MRI scan: There are no known risks or side effects of an MRI scan. If a contrast agent is used, the investigator will inform the subject of possible side effects or an allergic reaction.
CT scan: CT scans emit some radiation, so there is a small risk of causing

cancer and other conditions. Each individual scan carries a small risk.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1) >=18 years of age (or the legal age of consent in the jurisdiction in which the study is taking place) at the time of informed consent.
2) Have documented initial diagnosis of multiple myeloma according to IMWG diagnostic criteria (Appendix 10.9)
3) Have relapsed or refractory disease and have been treated with a proteasome inhibitor, IMiD agent, and an anti-CD38-based therapy for the treatment of MM
4) Have measurable disease at screening as defined by at least 1 of the following:

a. Serum M-protein level >=0.5 g/dL; or
b. Urine M-protein level >=200 mg/24 hours; or
c. Light chain multiple myeloma: Serum Ig FLC >=10 mg/dL and abnormal serum Ig kappa lambda FLC ratio.
d. For participants without measurable disease in the serum, urine, or involved FLC, presence of plasmacytomas (>=2 cm).
5) Clinical laboratory values meeting the following criteria prior to treatment (see protocol pages 32 - 33)
6) Must have an ECOG status of 0 or 1
7) A female participant of childbearing potential must have a negative
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highly sensitive serum ß hCG test at screening and a negative urine or serum pregnancy test within 72 hours before the start of study treatment administration and must agree to further serum or urine pregnancy tests during the study
8) A female participant must be
a. Not of childbearing potential, or
b. Of childbearing potential and practicing at least 1 highly effective method of contraception and agrees to remain on a highly effective method while receiving study drug and until 6 months after last dose. The investigator should evaluate the potential for contraceptive method failure (eg, noncompliance, recently initiated) in relationship to the first dose of study drug.
Note: If a female participant becomes of childbearing potential after the start of the study, the female participant must comply with (b.).
9) A female participant must agree not to donate eggs (ova, oocytes) or freeze for future use for the purposes of assisted reproduction during the study and for a period of 6 months after last dose of study treatment. Female participants should consider preservation of eggs prior to study treatment as anticancer treatments may impair fertility
10) A male participant must wear a condom when engaging in any activity that allows for passage of ejaculate to another person during the study and for 3 months after receiving the last dose of study treatment. If partner is a female person of childbearing potential, the male participant must use condom (with or without spermicide) and the partner must also be practicing a highly effective method of contraception (see Appendix 10.5). A male participant who is vasectomized must still use a condom (with or without spermicide), but the partner is not required to use contraception.
11) A male participant must agree not to donate sperm for the purpose of reproduction during the study and for a minimum of 3 months after receiving the last dose of study drug. Male participants should consider preservation of sperm prior to study treatment as anticancer treatments may impair fertility
Informed Consent
12) Must sign an ICF (or their legally acceptable representative must

sign) indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study
13) Be willing and able to adhere to the lifestyle restrictions specified in this protocol

Exclusion criteria

1) Central nervous system involvement or clinical signs of meningeal involvement of multiple myeloma. If either is suspected, whole brain MRI and lumbar cytology are required during screening
2) Active plasma cell leukemia, Waldenström's macroglobulinemia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, Mprotein, and skin changes), or primary light chain amyloidosis.
3) Pulmonary compromise requiring supplemental oxygen used to maintain adequate oxygenation
4) Any serious underlying medical conditions, such as:
a. Evidence of active viral, bacterial, or systemic fungal infection requiring ongoing antiviral, antibacterial, or antifungal treatment.
b. Active autoimmune disease requiring systemic immunosuppressive therapy within 6 months before start of study treatment. EXCEPTION: Participants with vitiligo, type I diabetes, and prior autoimmune thyroiditis that is currently euthyroid based on clinical symptoms and laboratory testing are eligible regardless of when these conditions were diagnosed.
c. Disabling psychiatric conditions, substance abuse (eg, alcohol or drug abuse), severe dementia, or altered mental status
d. Any other issue that would impair the ability of the participant to receive or tolerate the planned treatment at the investigational site, to understand the informed consent, or any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (eg, compromise the well-being of the participant) or that could prevent, limit, or confound the protocolspecified assessments.
5) Have a prior or concurrent second malignancy (other than the disease under study) which natural history or treatment is likely to interfere with any study endpoints of safety or the efficacy of the study treatment(s)
6) History of stroke or seizure within 6 months prior to the first dose of study treatment
7) History of any of the following cardiac conditions
a. New York Heart Association stage III or IV congestive heart failure.
b. Myocardial infarction, unstable angina, or coronary artery bypass graft <=6 months prior to enrollment.

c. History of clinically significant ventricular arrhythmia or unexplained syncope not believed to be vasovagal in nature or due to dehydration.
d. History of severe nonischemic cardiomyopathy.
e. Screening 12-lead triplicate ECG showing an average baseline QTc interval of >470 msec
8) Known allergies, hypersensitivity, or intolerance to excipients of JNJ-79635322
Prior/Concomitant Therapy or Clinical Study Experience
9) Prior antitumor therapy as follows, in the specified time frame prior to the first dose of study treatment:
a. Targeted therapy, epigenetic therapy, mAb treatment, or treatment with an investigational drug or an invasive investigational medical device within 21 days or at least 5 half-lives, whichever is less.
b. Gene-modified adoptive cell therapy (eg, CAR modified T cells, natural killer cells) within 90 days.
c. Prior treatment with CD3-redirecting therapy within 21 days prior to first dose of study treatment.
Note: Prior exposure to BCMA or GPRC5D targeting agents may be allowed after discussion with the sponsor.
d. Conventional chemotherapy within 21 days.
e. PI therapy within 14 days.
f. Immunomodulatory agent therapy within 7 days.
g. Radiotherapy within 14 days. However, if palliative focal radiation was used, the participant is eligible irrespective of the end date of radiotherapy.
10) Received a cumulative dose of corticosteroids equivalent to >140 mg of prednisone within the 14-day period before the start of study treatment administration
11) Nonhematologic toxicity from prior anticancer therapy that has not resolved to baseline level or to less than or equal to Grade 1 (except alopecia, tissue post-RT fibrosis [any grade] or peripheral neuropathy<= 3)
12) Stem cell transplantation:
a. Allogeneic stem cell transplant within 6 months before the start of study treatment administration. Participants who
received an allogeneic transplant must be off all immunosuppressive medications for >=42 days without signs of graft-versus-host disease.
b. Received an autologous stem cell transplant <=12 weeks before the start of study treatment administration.
13) Trauma or major surgery (eg, requiring general anesthesia) within 2 weeks, or participant will not have fully recovered from surgery, or participant has surgery planned during the time he or she is expected to participate in the study. Participants with planned surgical procedures to be conducted under local anesthesia may participate.
14) Pregnant, breastfeeding, or planning to become pregnant while enrolled in this study or within 6 months after the last dose of study drug

15) Plans to father a child while enrolled in this study or within 3 months after the last dose of study drug
16) Known history of HIV infection
17)Active hepatitis B and hepatitis C infection
18) Received live attenuated vaccine within 4 weeks before first dose of treatment
19) Body weight <40kg at screening or at the time of the first administration of study drug

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-07-2023
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	JNJ-79635322
Generic name:	JNJ-79635322

Ethics review

Approved WMO

Date:	13-10-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	28-03-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-05-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-503679-12-00
EudraCT	EUCTR2022-001465-12-NL
CCMO	NL82103.029.22