A phase 2 study of Belantamab Mafodotin in patients with relapsed or refractory AL amyloidosis

Published: 01-02-2021
Last updated: 10-01-2025

This study has been transitioned to CTIS with ID 2024-513075-40-00 check the CTIS register for the current data. To evaluate the efficacy of blmf in patients with relapsed or refractory AL amyloidosis.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Plasma cell neoplasms
Study type	Interventional

Summary

ID

NL-OMON54340

Source
ToetsingOnline

Brief title
EMN27

Condition

- Plasma cell neoplasms

Synonym
AL amyloidosis; primary amyloidosis

Research involving
Human

Sponsors and support

Primary sponsor: Stichting European Myeloma Network (EMN)
Source(s) of monetary or material Support: GlaxoSmithKline,Stichting European Myeloma Network - EMN

Intervention

Keyword: Belantamab Mafodotin, relapsed or refractory AL amyloidosis

Outcome measures

Primary outcome

Primary Endpoint: The primary end point of the study is the CR/VGPR/low-dFLC response rate at 6 months/4 cycles from start of therapy with blmf, according to consensus response criteria.

Stratification Factors: This is a single arm study; no stratification is required for disposition to treatment arms

Secondary outcome

Secondary Endpoints

Safety

1. Rates of grade 3 or higher AEs related to blmf therapy,

2. Rates of treatment discontinuation due to toxicity related to blmf,

3. Dose reduction due to toxicity of blmf therapy,

4. Any grade hematologic AEs,

5. Any grade non-hematologic AEs,

6. Rates of AEs of special interest (Ocular toxicity)

Efficacy

1. Overall hematologic response rates at 3 and at 6 months (CR + VGPR + low-dFLC response + PR),

2. Organ response rates per individual organ (heart, kidney, liver) at 3, 6, 12, 18 and 24 months from start of therapy,

3. Time to first hematologic response (CR/VGPR/low-dFLC response/PR),

4. Time to at least a very good hematologic response (VGPR or better),

5. Time to at least a low-dFLC response (low-dFLC response or CR),

6. Duration of hematologic response (time from first response to hematologic

progression, for those who achieved at least a hemPR or low-dFLC response)

7. Time to a subsequent therapy, either due to progression or inadequate

response,

8. Time to hematologic progression or major organ deterioration or death,

9. Overall survival,

10. Quality of life

Study description

Background summary

AL Amyloidosis is considered a rare disease, for which no specific standard of care therapies exist. Therefore, we continue to seek better treatment results by means of new medicines for patients who are diagnosed with this disease. Belantamab mafodotin is a type of monoclonal antibody (protein) that targets and destroys a specific type of immune cells (plasma cells) in the body. These plasma cells produce the abnormal proteins (the light chains) which form amyloid in AL Amyloidosis.
Doctors cannot prescribe belantamab mafodotin yet (outside of a study). However, belantamab mafodotin has been evaluated (and continues to be evaluated) for its efficacy in patients with multiple myeloma (another disorder of plasma cells), however, it does not have an approved indication for AL Amyloidosis.

Study objective

This study has been transitioned to CTIS with ID 2024-513075-40-00 check the CTIS register for the current data.

To evaluate the efficacy of blmf in patients with relapsed or refractory AL amyloidosis.

Study design

•This is an open-label, multicenter, Phase 2 study in patients with light chain (AL) amyloidosis, previously treated, and requiring therapy.
•Approximately 35 patients will receive therapy with belantamab mafodotin (blmf).
•The study has four phases: Screening Phase, Treatment Phase, Post-Treatment Observation Phase, and Long-term Follow-up Phase
•A safety run-in will be conducted in six patients treated with blmf for at least one cycle.
Dosing of these six patients will be staggered so that no patient receives their first dose earlier than 48 hours after the previously enrolled patient. Safety evaluation will be performed by the sponsor after all six patients complete at least one therapy cycle. A Data Monitoring Committee (DMC), consisting of two clinicians and one statistician, will be established to review safety results. The evaluation of the safety run-in will not include patients who will not have completed the first cycle of treatment for reasons unrelated to the study treatment. More specifically, this refers to patients who die, withdraw from the study, or discontinue study treatment for reasons other than toxicity, i.e., disease progression, patient choice, patient lost to follow-up. If a safety signal is detected and the DMC deems, in the recommendation sent to the Sponsor, that the safety profile of the study treatment is unfavorable, recruitment will be temporarily interrupted, and dose and schedule of the drug will be re-evaluated. If no safety signal is observed, enrollment will resume.
•Patients in the safety run-in will continue all scheduled assessments as specified in the Time and Events Schedule in the protocol, and contribute to the overall safety evaluation.

Intervention

Treatment will be given in 42 day Cycles for a maximum of 1 year (8 cycles), on day 1 of every cycle.

Study burden and risks

As with all research studies, the study treatment and study procedures may involve unknown risks. Any medication can have temporary or permanent side effects that may or may not be expected.

The most common side effects occurring in more than 10% of subjects (10 or more out of 100 patients) were:
o Eye problems: blurred vision, dry/itchy eyes, changes in vision, eye discomfort, , difficulty seeing at night, inflammation or other changes of front part of eye.
o Low number of blood cells called platelets (thrombocytopenia), which may cause bleeding and easy bruising. Bleeding may be serious, or life threatening and may require a transfusion.

o Feeling tired (fatigue)
o Having fewer red blood cells than normal (anemia).
o Feeling sick to your stomach (nausea)
o Abnormal liver tests
o Fever (if you have a fever, please contact your trial doctor immediately)
o Pneumonia, or other lung infections
o Cold or cold-like symptoms (upper respiratory tract infection)
o Low number of certain types of white blood cells called neutrophils (neutropenia) and lymphocytes (lymphopenia), which could increase the risk of infection. If you have a fever, please contact your trial doctor immediately
o Diarrhoea
o Reactions from the infusion of belantamab mafodotin, usually happen within the first 24 hrs after the infusion. Symptoms may include: flushing, chills, fever, difficulty breathing, rapid heartbeat or a drop-in blood pressure (feeling light-headed).

Other common side effects seen in 1% to 10% of subjects (between 1 to 10 out of 100 people) were:
o Other eye problems: eye irritation, abnormal sensitivity of the eyes to light, and sores on the eyes possibly with infection.
o Increased albumin, a type of protein, in the urine (albuminuria)
o An increase in an enzyme released into the blood when muscle is damaged (creatine phosphokinase)
o Vomiting

In another study which is testing belantamab mafodotin in combination with two medicines already approved for the treatment of Relapsed/Refractory Multiple Myeloma (RRMM), called lenalidomide and dexamethasone, two patients who had low neutrophil counts developed serious infections which led to death.
If you have fever at any point while you are in this study, please contact your study doctor immediately.

Possible Side effects from tests
•Blood draw: Taking blood may cause bruising at the place where the needle goes into the skin. Fainting, and in rare cases infection, may occur.
•X-Ray Risks: The radiation dose that is in the x-ray(s) taken for this study is small. There is no significant risk from this amount of radiation.
•ECG Risk: There is generally no risk with having an ECG. The sticky patches may pull your skin or cause redness or itching.
•CT scan Risk: CT scans do create low levels of radiation, which has a small potential to cause cancer and other defects. However, the risk associated with any one scan is small.
•MRI Risk: There are no known risks or side effects with having an MRI. If a contrast material is used, your study doctor will tell you about possible side effects or allergic reaction.
•Risk of bone marrow investigations (biopsy/aspirate): The area around where

the aspirate and/or biopsy are taken is numbed using an injection of numbing medication. You may experience pain and discomfort during and after the procedure. There is also a risk of infection and of bleeding from the biopsy site. You could also have an allergic reaction to the numbing medication. If you have a prior history of allergies, you should inform your study doctor.

Embryo-fetal toxicity: belantamab mafodotin may harm an unborn baby.
Fertility: belantamab mafodotin treatment may affect men and women*s ability to have children.

Contacts

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Stichting European Myeloma Network (EMN)

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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.Diagnosis of AL amyloidosis, confirmed by histology and typed with

immunohistochemistry, immunoelectron microscopy or mass spectrometry, or if not available, for patients with biopsy confirmed amyloidosis and cardiac involvement alone, if they also have a negative PYP- or DPD-Tc99m bone scan. 2..Patients must have had at least two cycles of therapy directed against plasma cell clone. However, patients that have received high dose therapy with melphalan as their only therapy are also eligible. 3.Patients must be 18 years of age or above. 4.ECOG performance status 0, 1 or 2. 5.Mayo stage 1 or Mayo stage 2 or Mayo stage 3A1-3 defined as both cTnT < 0.035 ng/mL (or in place of cTnT the cTnI < 0.10 ng/mL or high sensitivity Troponin T < 54 ng/L) AND simultaneous NT-proBNP <= 332 ng/L, OR EITHER above threshold, or BOTH above threshold but with NTproBNP < 8500 ng/L (stage 3A disease) 6.Supine systolic blood pressure >= 90 mmHg. 7.Measurable disease defined by at least one of the following: a.serum free light chain (FLC) >=2.0 mg/dL (20 mg/L) with an abnormal kappa:lambda ratio or the difference between involved and uninvolved free light chains (dFLC) >=2mg/dL (20 mg/L). b.presence of a monoclonal spike that is >=0.5 g/dl. 8.Symptomatic organ involvement (heart, kidney, liver/GI tract, peripheral nervous system). 9.Written informed consent in accordance with local and institutional guidelines. 10.Female patients: contraceptive use should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies. A female patient is eligible to participate if she is not pregnant or breast-feeding, and at least one of the following conditions applies: a.She is not of childbearing potential (WOCBP) OR b.She is a WOCBP and using, during the intervention period and for at least 4 months after the last dose of the trial, a contraceptive method that is highly effective (failure rate <1% per year), preferably with low user dependency (as described in Appendix 3). Patient agrees not to donate eggs (ova, oocytes) for the purpose of reproduction during this period. The investigator should evaluate the effectiveness of the contraceptive method in relationship to the first dose of trial intervention. A WOCBP must have a negative highly sensitive serum-pregnancy test (as required by local regulations) 72 hours before the first dose of the trial intervention. The investigator is responsible for reviewing the medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with a nearly undetected pregnancy. Nonchildbearing potential is defined as follows (by other than medical reasons): a.>=45 years of age and has not had menses for >1 year b.Patients who have been amenorrhoeic for <2 years without a history of hysterectomy and oophorectomy must have a follicle stimulating hormone value in the postmenopausal range after screening evaluation c.Post-hysterectomy, post-bilateral oophorectomy, or post-tubal ligation. Documented hysterectomy or oophorectomy must be confirmed with medical records of the actual procedure or confirmed by an ultrasound. Tubal ligation must be confirmed with medical records of the actual procedure. 12. Male patients: contraceptive use should be consistent with local regulations regarding the methods of contraception for those participating in clinical studies. Male patients are eligible to participate if they agree to the following during the intervention period and for 6 months after the last dose of trial treatment to allow for clearance of any altered sperm: a.Refrain from donating sperm PLUS, either: b.Be abstinent

from heterosexual intercourse as their preferred and usual lifestyle (abstinent on a long term and persistent basis) and agree to remain abstinent. OR c.Must agree to use contraception/barrier as detailed below: Agree to use a male condom, even if they have undergone a successful vasectomy, and female partner agrees to use an additional highly effective contraceptive method with a failure rate of <1% per year as when having sexual intercourse with a woman of childbearing potential who is not pregnant. 13. All toxicities related to previous treatment (defined by National Cancer Institute- Common Toxicity Criteria for Adverse Events [NCI-CTCAE], version 5, corneal toxicities are defined according to the Keratopathy Visual Activity [KVA] scale), must be <= Grade 1 at the time of enrolment except for alopecia. 14. Patient must be able to understand the trial procedures and agree to participate in the trial by providing written informed consent.

Exclusion criteria

1.Presence of non-AL amyloidosis. 2.Presence of lytic bone lesions or active myeloma with hypercalcemia, cast nephropathy, anemia due to marrow infiltration or extramedullary disease > 60% plasma cells in bone marrow. 3.Previous exposure to anti-BCMA agents 4.Cardiac stage IIIB disease: both cTnT > 0.035 ng/mL (or in place of cTnT the cTnI > 0.10 ng/mL or high sensitivity Troponin T > 54 ng/L) AND simultaneous NT-proBNP >8500 ng/L. 5.Known repetitive ventricular arrhythmias on 24h Holter Electrocardiograms (ECG) despite anti-arrhythmic treatment. Patient must not have evidence of cardiovascular risk including any of the following: •Evidence of current clinically significant uncontrolled arrhythmias, including clinically significant ECG abnormalities such as 2nd degree (Mobitz Type II) or 3rd degree atrioventricular (AV) block. •History of myocardial infarction, acute coronary syndromes (including unstable or uncontrolled angina), coronary angioplasty, or stenting or bypass grafting within three (3) months of screening. •Class III or IV heart failure as defined by the New York Heart Association functional classification system (NYHA, 1994). •Severe uncontrolled ventricular arrhythmias, sick sinus syndrome, electrocardiographic evidence of acute ischemia or Grade 3 conduction system abnormalities (unless patient has a pacemaker). •Uncontrolled hypertension or hypotension (i.e., supine SBP< 90 mmHg despite supportive therapy with midodrine) 6.Significant neuropathy (Grades 3-4, or Grade 2 with pain) within 14 days prior to Cycle 1 Day 1. 7.Pleural effusions requiring thoracentesis or ascites requiring paracentesis within 14 days prior to Cycle 1 Day 1. 8.Ongoing corneal epithelial disease except mild changes in corneal epithelium (mild punctate keratopathy). 9.Current unstable liver or biliary disease defined by the presence of ascites, encephalopathy, coagulopathy, hypoalbuminemia (except due to related nephrotic syndrome), esophageal or gastric varices, persistent jaundice, or cirrhosis. Note: Stable non-cirrhotic chronic liver disease (including Gilbert*s syndrome or asymptomatic gallstones) or hepatobiliary involvement of malignancy is

acceptable if otherwise meets entry criteria. 10.Active renal condition (infection, requirement for dialysis or any other condition that could affect the patient*s safety) unrelated to AL amyloidosis. Patients with isolated proteinuria resulting from AL are eligible, provided they fulfil other inclusion criteria. 11.Patient must not use contact lenses while participating in this trial. 12.Patient must not be simultaneously enrolled in any interventional clinical trial. 13.Use of an investigational drug or approved systemic anti-myeloma therapy (including systemic steroids) within 14 days or five half-lives, whichever is shorter, prior to the first dose of trial drug. 14.Plasmapheresis within seven days prior to the first dose of the trial treatment. Serious conditions unrelated to AL, such as SARS-CoV-2, may be permitted but need to be discussed with the medical doctor and trial-site personnel. 15.Treatment with a monoclonal antibody within 30 days prior to the first dose of the trial treatment 16.Major surgery <= 4 weeks prior to initiating trial treatment. 17.Evidence of active mucosal or internal bleeding 18.Known immediate or delayed hypersensitivity reaction or idiosyncratic reactions to blmf or drugs chemically related to blmf, or any of the components of the trial treatment. 19.Active infection requiring treatment. 20.Known HIV infection (defined as positive testing for human immunodeficiency virus [HIV] antibodies). 21.Positive test for hepatitis B surface antigen (HBsAg), or hepatitis B core antibody (HBcAb) at screening or within 3 months prior to the first dose of trial treatment. 22.Positive test for hepatitis C antibody hepatitis C RNA at screening or within 3 months prior to the first dose of the trial treatment. 23.Invasive malignancies other than the disease under study, unless the second malignancy has been medically stable for at least 2 years and, in the opinion of the principal investigators, will not affect the evaluation of the effects of the clinical trial treatments of the currently targeted malignancy. Patients with curatively treated non-melanoma skin cancer may be enrolled without a 2-year restriction. 24.Any serious and/or unstable pre-existing medical, psychiatric disorder, or other conditions (including lab abnormalities) that could interfere with the patient*s safety, informed consent or compliance to the trial procedures. 25.Patients must not be pregnant or breast-feeding. 26. Participant must not have received a live or live-attenuated vaccine within 30 days prior to first dose of belantamab mafodotin.

Study design

Design

Study phase:	2
Study type:	Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-06-2022
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Blenrep
Generic name:	Belantamab mafodotin

Ethics review

Approved WMO Date:	01-02-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-06-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-11-2021
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-03-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	CTIS2024-513075-40-00
EudraCT	EUCTR2020-004001-32-NL
CCMO	NL75978.056.20