A Randomized, Open-Label, Phase 3 Trial of Epcoritamab vs Investigator*s Choice Chemotherapy in Relapsed/Refractory Diffuse Large B-cell Lymphoma

Published: 07-10-2020
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This study has been transitioned to CTIS with ID 2023-504830-23-00 check the CTIS register for the current data. Compare the clinical efficacy of Epcoritamab to SOC (R-GemOx or BR)

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lymphomas non-Hodgkin's B-cell
Study type	Interventional

Summary

ID

NL-OMON54027

Source
ToetsingOnline

Brief title
GCT3013-05

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
lymphoma, non-hodgkin lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Genmab
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: Bispecific antibody, Epcoritamab, Relapsed/Refractory Diffuse Large B-Cell Lyphoma

Outcome measures

Primary outcome

Overall survival

Secondary outcome

- Progression-free survival (PFS) determined by Lugano criteria per independent

review committee (IRC) assessment and investigator assessment

- Overall response rate (ORR) determined by Lugano criteria per IRC assessment

and investigator assessment

- Complete response (CR) rate, determined by Lugano criteria per IRC assessment

and investigator assessment

- Duration of response (DOR) determined by Lugano criteria per IRC assessment

and investigator assessment

Study description

Background summary

30-40% of the patients diagnosed with diffuse large B-cell lymphoma (DLBCL) will have R/R (relapse/refractory) disease. DLBCL is the most common type of non- Hodgkin lymphoma (NHL). The cure rate for R/R patients is less than 10%. Current therapies for R/R patients are limited, hence there is a need for novel therapies.
Epcoritamab is a fully human IgG1-bispecific antibody targeting CD3+ T-cells and CD20+ B cells; the mechanism of action is engagement of T cells as effector cells to induce killing of CD20- expressing B cells and tumor cells. CD20 is a clinically validated target for treatment of B-cell malignancies. This mechanism of action is different compared to chemotherapy or a conventional CD20- targeting mAb.

Subjects with R/R DLBCL may benefit from treatment with Epcoritamab in terms of disease reduction or control.

Study objective

This study has been transitioned to CTIS with ID 2023-504830-23-00 check the CTIS register for the current data.

Compare the clinical efficacy of Epcoritamab to SOC (R-GemOx or BR)

Study design

A randomized, open-label, phase 3 study

Intervention

Eligible subjects will be randomized to either epcoritamab or investigators choice chemotherapy (i.e., sites will a priori choose either R-GemOx or BR) (SOC).

Epcoritamab arm:
Epcoritamab will be administered as a SC injection in 28- day cycles as follows:
• Cycle 1: 0.16 mg SC on Day 1 (priming dose), 0.8 mg SC on Day 8 (intermediate dose), 48 mg (full dose) SC on Days 15 and 22 (once weekly)
• Cycles 2 and 3: 48 mg SC on Days 1, 8, 15, 22 (once weekly)
• Cycles 4 through 9: 48 mg SC on Days 1 and 15 (every 2 weeks)
• Cycle 10 onward: 48 mg SC on Day 1 (every 4 weeks)

Investigators choice chemotherapy arm:
Subjects will receive 1 of the 2 chemotherapy options below:
- Bendamustine and rituximab (BR): rituximab 375 mg/m2 IV on Day 1 and bendamustine 90 mg/m2 IV on Days 1 and 2 of each 21-day cycle for up to 6 cycles.
- Rituximab, gemcitabine and oxaliplatin (R-GemOx): rituximab 375 mg/m2 IV on Days 1 and 15 and gemcitabine 1000 mg/m2 IV followed by oxaliplatin 100 mg/m2 IV on Days 2 and 16 of each 28-day cycle for up to 4 cycles.

Study burden and risks

Treatment with epcoritamab involves subcutaneous injection (the first 4 visits followed by hospitalization and premedication). Risks associated with participation are side effects, among which tumor lysis syndrome, cytokine release syndrome and neurological
symptoms (ICANS).

The risk to subjects in this trial should be minimized by compliance with the eligibility criteria, trial procedures, close monitoring, and proper/prompt management of TEAEs.

The patients will need to follow appointments for visits and will undergo physical examination, ECOG, neurological evaluation (ICANS), ECG, venapunctions, scans and biopsies. Patients will be interviewed on past and present medical conditions, diseases,
surgeries, allergies and previous medicines. Also, patients should not become pregnant, breastfeed a baby, father a child or donate sperm or eggs while participating in this trial and must agree to use a highly effective method of birth control from the time of screening until 12 months after the last dose of epcoritamab. Patients will be tested for hepatitis B, C and cytomegalovirus, HIV.

Subjects with R/R DLBCL may benefit from treatment with epcoritamab in terms of disease reduction or control, as epcoritamab has a different mode of action from chemotherapy and direct CD20-targeting monoclonal antibodies. It is expected that toxicities can be managed with standard supportive care. The potential benefit of therapy with epcoritamab is expected to outweigh the treatment-related risks. Treatment with investigator*s choice immunochemotherapy regimens is according to local guidelines and represents standard of care treatment with established benefit-risk profiles.
With safety precautions and a close monitoring plan in place, the described risks are outweighed by the potential benefit subjects might receive from epcoritamab.
More detailed information about the known and expected benefits and risks and reasonably expected AEs of epcoritamab are found in the IB

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Must be at least 18 years of age (>=20 years of age in Japan);
2. ECOG PS score of 0-2;
3. One of the confirmed histologies below with CD20 positivity:
a. DLBCL, NOS (according to the WHO 2016 classification) and including de novo or histologically transformed from follicular lymphoma (FL).
b. "Double-hit" or "triple-hit" DLBCL with MYC and BCL2 and / or BCL6 traslocations
c. FL Grade 3B
d. T-cell/histiocyte-rich large B-cell lymphoma
4. CD20-positivity at representative tumor biopsy based on the pathology report;
5. Relapsed or refractory disease and previously treated with at least 1 line of systemic antineoplastic therapy including anti-CD20 mAb containing combination chemotherapy since lymphoma diagnosis (ie, having received R-CHOP or an equivalent regimen that would be considered adequate first-line treatment for DLBCL);
6. Failed previous HDT-ASCT or not eligible for HDT-ASCT at screening. If ineligible for HDT-ASCT, the decision must have been based on age, performance status, comorbidity, and/or insufficient response to prior treatment;
7. Has measurable disease:
a. A fluorodeoxyglucose-positron emission tomography (FDG- PET) scan demonstrating positive lesion(s) compatible with computed tomography (CT) or magnetic resoncance imagining (MRI)-defined anatomical tumor sites
b. >=1 measurable nodal lesion (long axis >1.5 cm and short axis >1.0 cm) and/or >=1 measurable extra-nodal lesion (long axis >1.0 cm) on CT scan or MRI;
8. Absolute neutrophil count >=1.0 x 10e9/L (growth factor permitted);
9. Platelet count >75 x 10e9/L (or >50 x 10e9/L if bone marrow involvement or splenomegaly);
10. Alanine aminotransferase level <=3 times the upper limit of normal (xULN), unless enzyme elevation is due to a nonhepatic origin or lymphoma involvement

of the liver and ALAT and ASAT levels are =5 xULN;
11. Total bilirubin level <=2 xULN, unless bilirubin rise is due to Gilbert's syndrome or of non-hepatic origin or lymphoma involvement of the liver and total bilirubin is =5xULN;
12. Estimated glomerular filtration rate (eGFR) >=50 mL/min/1.73m2 as calculated by Cockcroft-Gault;
13. PT/INR/aPTT =1.5 xULN, unless receiving anticoagulation;
14. A female subject with reproductive potential must agree to use adequate contraception during the trial, and for 12 months after the last administration of trial treatment. Adequate contraception is defined as highly effective methods of contraception;
15. A female subject of childbearing potential must have a negative serum (beta-hCG) pregnancy test at screening and a negative serum or urine pregnancy test before treatment administration on Day 1 of Cycle 1;
16. A male subject who is sexually active with a female of reproductive potential and has not had a vasectomy must agree to use a barrier method of birth control and must agree not to donate sperm during the trial and for 12 months after receiving the last administration of trial treatment.
17. Life expectancy >2 months on SOC treatment.
18. Able to provide baseline fresh or archival tumor biopsies.

Exclusion criteria

1. Primary CNS tumor or known CNS involvement as assessed by brain MRI at screening or by CT and lumbar puncture (if MRI contraindicated);
2. Any prior therapy with a bispecific antibody targeting CD3 and CD20;
3. History of severe allergic or anaphylactic reactions to anti-CD20 antibody therapy;
4. Contraindication to any component of SOC regimen selected by site;
5. Major surgery within 4 weeks prior to randomization;
6. Chemotherapy and other non-investigational antineoplastic agents (except CD20 mAbs) within 4 weeks or 5 half-lives (whichever is shorter) prior to randomization;
7. ASCT within 100 days of randomization;
8. Treatment with CAR-T therapy within 100 days prior to randomization;
9. Receiving immunosuppresive therapy, including more than the equivalent of >=20 mg of prednisolone daily, unless for disease control;
10. Seizure disorder requiring anti-epileptic therapy;
11. Vaccination with live vaccines within 28 days prior to randomization. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette-Guérin, and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (eg, FluMist®) are live attenuated vaccines and are not allowed. Experimental and/or non

authorized severe acute respiratory syndrome coronavirus 2 (SARS-CoV- 2) vaccinations are not allowed;
12. Clinically significant cardiac disease
13. Screening 12-lead ECG showing a baseline QT interval as corrected by Fridericia's formula (QTcF) >470 msec;
14. Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results;
15. Known active bacterial, viral, fungal, mycobacterial, parasitic, or other infection requiring systemic treatment at time of randomization;
16. Known history of positivity for human immunodeficiency virus (HIV) infection. Note: HIV testing is required at screening only if required per local health authorities or institutional standards.
17. Active hepatitis B virus (HBV) (DNA polymerase chain reaction [PCR]-positive) or hepatitis C (RNA PCR-positive infection). Subjects with evidence of prior HBV but who are PCR-negative are permitted in the trial but should receive prophylactic antiviral therapy. Subjects who received treatment for hepatitis C that was intended to eradicate the virus may participate if hepatitis C RNA levels are undetectable;
18. Has known past or current malignancy other than inclusion diagnosis, except for:
a. Cervical carcinoma of Stage 1B or less
b. Non-invasive basal cell or squamous cell skin carcinoma
c. Non-invasive, superficial bladder cancer
d. Prostate cancer with a current PSA level <0.1 ng/mL
e. Any curable cancer with a complete response of >2 years duration;
19. Contraindication to all uric acid lowering agents;
20. A woman of childbearing potential with a positive serum or urine pregnancy test at screening or lactating females;
21. Clinically significant liver disease, including active hepatitis, current alcohol abuse, or cirrhosis;
22. Active tuberculosis or history of completed treatment for active tuberculosis within the past 12 months;
23. Receiving immunostimulatory agent;
24. Prior allogeneic hematopoietic stem cell transplantation.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-01-2022
Enrollment:	17
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bendamustine / Levact
Generic name:	Bendamustine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Gemcitabine
Generic name:	Gemcitabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	MabThera / Rixathon / Ruxience / Truxima
Generic name:	Rituximab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	N/A
Generic name:	Epcoritamab
Product type:	Medicine
Brand name:	Oxaliplatin / Oxalisin
Generic name:	Oxaliplatin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-10-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-02-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	08-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-11-2023
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	CTIS2023-504830-23-00
EudraCT	EUCTR2020-003016-27-NL
CCMO	NL75079.056.20