The Phase 1b/2, Open-Label Trial to Assess the Safety and Preliminary Efficacy of Epcoritamab (GEN3013; DuoBody®-CD3xCD20) in Combination with Other Agents in Subjects with B-cell Non-Hodgkin Lymphoma

Published: 15-06-2020
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This study has been transitioned to CTIS with ID 2023-504805-35-00 check the CTIS register for the current data. Dose Escalation PhasePrimary - Evaluate the safety and tolerability of epcoritamab in combination with other agents Secondary-...

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

Summary

ID

NL-OMON54276

Source
ToetsingOnline

Brief title
GCT3013-02 / EPCORE* NHL-2

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
B-cell Non-Hodgkin Lymphoma, B-cell Non-Hodgkin Lymphoma cancer

Research involving

Human

Sponsors and support

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

Intervention

Keyword: B-Cell Non-Hodgkin Lymphoma, Combination, Epcoritamab, Phase 1b/2

Outcome measures

Primary outcome

Dose Escalation Phase

- Incidence of dose-limiting toxicities

- Incidence and severity of adverse events (AEs)

- Incidence and severity of changes in laboratory values

- Incidence of dose interruptions and delays

Expansion Phase:

Arms 1-6 and 8-10:

- ORR determined by Lugano criteria

Arm 7:

- Incidence and severity of AEs

- Incidence and severity of changes in laboratory values

- Incidence of dose interruptions and delays

Secondary outcome

Dose Escalation Phase

-PK parameters (clearance, volume of distribution, area

under-the-concentration-time curve (AUC0-last and AUC0-*), maximum

concentration (Cmax), time of Cmax (Tmax), predose values, and half-life)

-Pharmacodynamic markers in blood samples and within tumor (on-treatment biopsy)

-Incidence of anti-drug antibodies (ADAs) to epcoritamab

-ORR determined by Lugano criteria

-Duration of response (DOR) determined by Lugano criteria

-Time to response (TTR) determined by Lugano criteria

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

-Overall survival (OS)

-Time to next anti-lymphoma therapy (TTNT)

-Rate and duration of minimal residual disease (MRD) negativity

Expansion Phase:

-DOR determined by Lugano criteria (Arms 1-6 and 8-10)

-TTR determined by Lugano criteria (Arms 1-6 and 8-10)

-PFS determined by Lugano criteria (Arms 1-6 and 8-10)

-CR rate (Arm 1-10 except Arm 7 subjects in CR at baseline)

-OS (Arms 1-10)

-TTNT (Arms 1-10)

-Rate and duration of MRD negativity (Arms 1-10)

-Rate of conversion from MRD positivity to MRD negativity (Arm 7)

-CR rate (Arm 7 subjects in PR at baseline)

-TTCR (Arms 1-10, except Arm 7 subjects in CR at baseline)

-DoCR (Arms 1-10)

-Incidence and severity of AEs (Arms 1-6, and 8-10)

-Incidence and severity of changes in laboratory values (Arms 1-6, and 8-10)

-Incidence of dose interruptions and delays (Arms 1-6, and 8-10)

-PK parameters

-Pharmacodynamic markers in blood samples and within tumor (ontreatment biopsy)

-Incidence of ADAs to epcoritamab

Study description

Background summary

There is an unmet medical need for new efficacious therapies for patients with B-cell non-Hodgkin lymphoma (B-NHL). Epcoritamab demonstrated a favorable safety profile and overall response rate (ORR) in a monotherapy trial. Combining epcoritamab with chemotherapeutic agents with different mechanisms of action may improve efficacy with a low potential for overlapping toxicities

Study objective

This study has been transitioned to CTIS with ID 2023-504805-35-00 check the CTIS register for the current data.

Dose Escalation Phase
Primary
- Evaluate the safety and tolerability of epcoritamab in combination with other agents

Secondary
- Characterize the PK properties of epcoritamab
- To evaluate pharmacodynamic markers linked to efficacy and mechanism of action of epcoritamab
- Evaluate immunogenicity
- Assess the preliminary anti-tumor activity of epcoritamab in combination with other agents

Expansion Phase:
Arms 1-6 and 8-10: Assess the preliminary anti-tumor activity of epcoritamab in combination with other agents
Arm 7: Evaluate the safety and tolerability of epcoritamab following standard

of care (SOC)

Secondary
- Further assess the preliminary anti-tumor activity of epcoritamab in combination with other agents
- Further evaluate the safety and tolerability of epcoritamab in combination with other agents
- Characterize the PK properties of Epcoritamab
- To evaluate pharmacodynamic markers linked to efficacy and mechanism of action of epcoritamab
- Evaluate immunogenicity

Study design

This is a phase 1b/2, open-label, multinational, multicenter, interventional trial to evaluate the safety, tolerability, PK, pharmacodynamics/biomarkers, immunogenicity, and preliminary efficacy of epcoritamab in combination with other standard of care (SOC) agents in subjects with B-NHL.

Intervention

Epcoritamab (the investigational medicinal product [IMP]) will be administered as a
subcutaneous injection. The schedules of administration are as follows:
Arm 1: epcoritamab + R-CHOP for 8 cycles (21-day cycles; 6 cycles of epcoritamab in combination with SOC followed by 2 cycles of epcoritamab monotherapy)
Arm 2: epcoritamab + rituximab + lenalidomide until progression (28-day cycles; 12 cycles of epcoritamab in combination with SOC followed by epcoritamab monotherapy until progression or unacceptable toxicity)
Arm 3: epcoritamab + BR for 8 cycles (21-day cycles; 6 cycles in combination with SOC followed by 2 cycles of epcoritamab monotherapy)
Arm 4: epcoritamab + R-DHAP until high-dose therapy with autologous stem cell transplant (HDT-ASCT) (21-day cycles; 3 cycles of epcoritamab in combination with SOC followed by epcoritamab monotherapy until conditioning for transplant)
Arm 5: epcoritamab + GemOx until progression (28-day cycles; 4 cycles in combination with SOC followed by epcoritamab monotherapy until progression or unacceptable toxicity)
Arm 6: epcoritamab + rituximab + lenalidomide, 12 cycles in combination followed by epcoritamab monotherapy Q4W for total of 2 yrs.
Arm 7: epcoritamab maintenance, step-up dosing in C1, followed by Q8W for a total of 2 yrs
Arm 8: epcoritamab + R- mini-CHOP for up to 6 cycles (21 day cycles) followed by 2 cycles of epcoritamab (28 day cycles)

Study burden and risks

Subjects will need to follow appointments for visits. They will have physical examinations, blood samples, ECGs, scans and biopsies taken, they will be questioned about their medical condition and history, race, ethnicity and they will be tested for HIV, hepatitis B, C, and cytomegalovirus. Pregnancy must be avoided by using a highly effective method of birth control from the time of screening until 12 months after the last dose of epcoritamab.Treatment with Epcoritamab involves subcutaneous injection (the first injection is followed by at least 24h hospitalization) and premedication. Risks associated with participation are side effects, such as B cell depletion, cytokine release syndrome and neurological symptoms, local reaction to injection site, clinical tumor lysis syndrome, drug-drug interactions, risks associated with blood sampling, obtaining a biopt or aspirate, ECG and imaging procedures. CD20 targeting drugs also have known side effects which may occur.

There is an unmet medical need for new efficacious therapies for patients with B-cell
non-Hodgkin lymphoma (B-NHL).Safety precautions and close monitoring will be done in this trial to facilitate a positive benefit-risk ratio for each
subject. Subjects with B-cell NHL may benefit from treatment with epcoritamab combined with SOC therapy in terms of additional disease reduction, as epcoritamab has a different mode of action from chemotherapy and direct CD20-targeting monoclonal antibodies. It is expected that there will be minimal overlapping toxicity with the SOC agents, and that this can be managed with standard supportive care. The potential benefit of therapy with epcoritamab is expected to outweigh the treatment-related risks.

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. Subject must sign an ICF
2. At least 18 years of age
3. Measurable disease defined as >=1 measurable nodal lesion (long axis >1.5 cm and short axis >1.0 cm) or >=1 measurable extra-nodal lesion (long axis >1.0 cm) on CT or MRI
4. ECOG PS score of 0, 1 or 2
5. Acceptable organ function at screening
6. CD20-positive NHL at representative (previous or current) tumor biopsy
7. If of childbearing potential subject must practicing a highly effective method of birth control
8. A man who is sexually active with a woman of childbearing potential must agree to use a barrier method of birth control
9. Life expectancy > 2 months with SoC treatment

Arm 1: One of these confirmed histologies:
- DLBCL, NOS
- T-cell / histiocyte rich DLBCL
- "double-hit" or "triple-hit" DLBCL
- FL Grade 3B

Arm 2 and Arm 9: R/R FL

Arm 3: Newly diagnosed, previously untreated FL grade 1-3A

Arm 4 and arm 10: One of these confirmed histologies and eligible for HDT-ASCT:
- DLBCL, NOS
- T-cell / histiocyte rich DLBCL
- "double-hit" or "triple-hit" DLBCL
- FL Grade 3B

Arm 5: One of these confirmed histologies and ineligible for HDT-ASCT:
- DLBCL, NOS
- T-cell / histiocyte rich DLBCL
- "double-hit" or "triple-hit" DLBCL
- FL Grade 3B

Arm 6: previously untreated CD20+ FL

Arm 7: FL and in CR or PR per Lugano criteria following first-line or second-line treatment with SOC regiment and last dose of SOC within 6 months prior to enrollment

Arm 8: One of these confirmed histologies:
- DLBCL, NOS
- T-cell/histiocyte rich DLBCL
- "double-hit" or "triple-hit" DLBCL
- FL Grade 3B
For Arm 8, subjects must be ineligible to receive full-dose anthracycline (as part of R-CHOP) per eligibility criteria

Arm 9: Must have received only 1 prior line of therapy. This first-line therapy must have included an anti-CD20 antibody in combination with chemotherapy. Progressed within 24 months of initiating first-line treatment

Exclusion criteria

1. Chemotherapy, radiation therapy, or major surgery within 4 weeks prior to the first dose of epcoritamab
2. Any prior treatment with a bispecific antibody targeting CD3 and CD20
3. Treatment with CAR-T therapy within 100 days prior to first dose of epcoritamab
4. Clinically significant cardiac disease
5. Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results
6. CNS lymphoma or known CNS involvement by lymphoma at screening as confirmed by MRI/CT scan of the brain and, if clinically indicated, by lumbar puncture
7. Active HBV or HBC (DNA PCR positive infection)
8. Known history of seropositivity of human immunodeficiency virus (HIV)
9. Active tuberculosis or history of completed treatment for active tuberculosis within the past 12 months
10. Subject has current seizure disorder requiring anti-epileptic therapy

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-10-2020
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	GEN3013; DuoBody®-CD3xCD20
Generic name:	Epcoritamab

Ethics review

Approved WMO Date:	15-06-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-08-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	12-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-01-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-02-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-06-2021
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-03-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	11-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-10-2023
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	CTIS2023-504805-35-00
EudraCT	EUCTR2020-000845-15-NL
CCMO	NL74222.056.20