A Phase 3, Randomized, Open-Label Study to Evaluate Safety and Efficacy of Epcoritamab in Combination with R-CHOP compared to R-CHOP in Subjects with Newly Diagnosed Diffuse Large B-Cell Lymphoma (DLBCL)

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This study has been transitioned to CTIS with ID 2023-505277-32-00 check the CTIS register for the current data. The primary objective of this study is to evaluate whether the addition of epcoritamab to 6 cycles of standard R-CHOP followed by 2…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haematological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON53434

Source
ToetsingOnline

Brief title
M20-621

Condition

- Haematological disorders NEC

Synonym
Diffuse Large B Cell Lymphoma, Lymphoma

Research involving

Human

Sponsors and support

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

Intervention

Keyword: DLBCL, Epcoritamab, First-line, R-CHOP

Outcome measures

Primary outcome

The number of participants with progression-free survival (PFS) with IPI of

3-5.

Secondary outcome

Number of participants with event-free survival (EFS)

Percentage of participants with complete remission (CR)

Overall survival (OS)

Percentage of participants with minimal residual disease (MRD) negativity

Number of participants with PFS

Study description

Background summary

B-cell Lymphoma is an aggressive and rare cancer of a typeof immune cells (a white blood cell responsible for fightinginfections). The purpose of this study is to assess thechange in disease activity of epcoritamab when combinedwith intravenous and oral rituximab, cyclophosphamide,doxorubicin hydrochloride, vincristine, and prednisone(R-CHOP) or R-CHOP in adult participants globally withdiffuse large b-cell lymphoma (DLBCL). Change in diseaseactivity will be assessed.

Study objective

This study has been transitioned to CTIS with ID 2023-505277-32-00 check the CTIS register for the current data.

The primary objective of this study is to evaluate whether the addition of epcoritamab to 6 cycles of standard R-CHOP followed by 2 cycles of epcoritamab (E + R-CHOP) can prolong progression-free survival (PFS) compared with 6 cycles of standard R-CHOP followed by 2 cycles of rituximab (R-CHOP) in subjects with newly diagnosed DLBCLwith an IPI of 3-5.

The secondary objective of this study is to evaluate and compare PFS between the two treatment arms in participants with newly diagnosed DLBCL with an IPI of 2-5. - To evaluate and compare each key secondary endpoint for both the subset of participants with an IPI of 3-5 and all randomized participants per the hierarchical order specified in the protocol.

Study design

Randomized, open label,parallel group study.

Intervention

In the Arm 1, participants will receive subcutaneousepcoritamab combined with intravenous and oral R-CHOPfollowed by subcutaneous epcoritamab in 21-day cycles. Inthe Arm 2, participants will receive intravenous and oralR-CHOP followed by intravenous rituximab in 21-daycycles.

Study burden and risks

There may be higher treatment burden for participants inthis trial compared to their standard of care. Participantswill attend regular visits during the study at an approvedinstitution (hospital or clinic). The effect of the treatmentwill be frequently checked by medical assessments, bloodtests, questionnaires and side effects.

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.Adult male or female, >= 18 years old and < 80 years old, with a life expectancy of >= 12 months.
2.Subject is planned to receive treatment with 6 cycles of standard R CHOP per investigator determination.
3.Subject must have newly diagnosed, histologically confirmed CD20+ DLBCL (de novo or histologically transformed from a diagnosis of follicular lymphoma) at most recent representative tumor biopsy based on the pathology report, with a World Health Organization (WHO) 2016 classification and including:
- DLBCL, Not Otherwise Specified (NOS).
- High grade B-cell lymphoma with MYC and BCL-2 and/or BCL-6 rearrangement with DLBCL morphology.
- T-cell/histiocyte-rich large B-cell lymphoma.
- Epstein Barr virus-positive DLBCL, NOS.
- Follicular lymphoma Grade 3b.
4.Availability of archival or freshly collected tumor tissue at Screening. Archival paraffin-embedded tissue must be obtained within 8 weeks prior to Cycle 1 Day 1.
5.Subject must have an IPI score of 2-5. The number of subjects with IPI 2 will be capped at 30% of the overall sample size.
6.Subject must have an Eastern Cooperative Oncology Group (ECOG) performance status score of 0-2 prior to initiating R-CHOP treatment. Note that subject with an initial ECOG performance status >= 3 may be screened if pre-phase treatment is planned. Subject may be eligible if ECOG performance status were to improve to 0-2 during pre phase treatment.

7.Subject has at least one target lesion defined as:
- >= 1 measurable nodal lesion (long axis > 1.5 cm) or >= 1 measurable extra-nodal lesion (long axis > 1 cm) on CT scan or MRI.
AND
- PET-positive on PET-CT scan.
8.Laboratory values meeting the following criteria within the screening period prior to the first dose of study drug:
- Absolute neutrophil count (ANC) >= 0.5 × 109/L. (antibacterial prophylaxis per institutional standard practice should be considered for participants with ANC 1.0 x 109/L).
- Hemoglobin >= 8 g/dL.
- Platelet count >= 75 × 109/L, or >= 25 × 109/L in the presence of bone marrow involvement or splenomegaly
- Serum aspartate aminotransferase or serum alanine aminotransferase <= 3.0 × upper limit of normal (ULN) unless due to hepatic involvement of disease or non-hepatic origin.
- Total bilirubin level <= 1.5 × ULN, ULN, unless the bilirubin rise is due to Gilbert*s syndrome or lymphoma hepatobiliary involvement. Participants with Gilbert*s syndrome must have a direct bilirubin of < 2 x ULN. Participants with hepatobiliary involvement must have a total bilirubin of < 5 x ULN and without a percutaneous biliary drain.
- Estimated creatinine clearance >= 40 mL/min, as calculated by the Cockcroft-Gault formula with considerations for body weight.
- Prothrombin time/international normalized ratio/activated partial thromboplastin time <= 1.5 × ULN, unless receiving anticoagulation.
9. Left ventricular ejection fraction must be >= 50% by multi gated acquisition or transthoracic echocardiography at Screening.

Exclusion criteria

1. Subject with history of prior systemic anti-lymphoma therapy for DLBCL (including any definitive radiotherapy with curative intent) other than corticosteroids with or without vincristine during pre-phase treatment, or non-curative intent palliative radiotherapy with the stipulation that radiated lesions cannot be selected as target lesion for response assessment.
2. Subject has clinically significant cardiovascular disease, including:
• Myocardial infarction or stroke within 6 months prior to enrollment.
OR
• The following conditions within 3 months prior to enrollment: unstable or uncontrolled disease/condition related to or affecting cardiac function (e.g., unstable angina, congestive heart failure, New York Heart Association Class III IV), uncontrolled cardiac arrhythmia
OR
• Screening 12-lead electrocardiogram (ECG) showing a baseline QT interval as corrected by Fridericia*s formula (QTcF) > 470 msec (male) or > 480 sec

(female)
OR
• Other clinically significant electrocardiogram abnormalities within 6 months prior to enrollment unless deemed stable and appropriately treated .

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):	03-05-2023
Enrollment:	111
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cyclophosphamide
Generic name:	Cyclophosphamide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Doxorubicin
Generic name:	Doxorubicin
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	Epcoritamab
Generic name:	Epcoritamab
Product type:	Medicine
Brand name:	Rituximab
Generic name:	Rituximab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vincristine
Generic name:	Vincristine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	26-10-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-01-2023
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-04-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	10-05-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-08-2023

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	CTIS2023-505277-32-00
EudraCT	EUCTR2021-000168-31-NL
CCMO	NL82498.028.22