A Randomized, Multicenter, Open-Label, Phase 3 Study to Compare the Efficacy and Safety of Acalabrutinib (ACP-196) in Combination with Venetoclax with and without Obinutuzumab Compared to Investigator*s Choice of Chemoimmunotherapy in Subjects with Previously Untreated Chronic Lymphocytic Leukemia Without del(17p) or TP53 Mutation

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This study has been transitioned to CTIS with ID 2023-509349-11-00 check the CTIS register for the current data. Primary objective: To determine the efficacy of the combination of acalabrutinib and venetoclax without obinutuzumab (AV; Arm A), or...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON52519

Source
ToetsingOnline

Brief title
ACE-CL-311

Condition

- Leukaemias

Synonym
Chronic B-Cell Leukemia, CLL, Leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Acerta Pharma BV

Intervention

Keyword: Acalabrutinib, CLL (Chronic Lymphocytic Leukemia)

Outcome measures

Primary outcome

To evaluate the efficacy of AV (Arm A) compared with chemoimmunotherapy (FCR/BR; Arm C) on the basis of the following endpoint:

- PFS after randomization, defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the Independent Review Committee (IRC) according to the IWCLL 2018 criteria

Secondary outcome

To evaluate the efficacy of AVG (Arm B) versus FCR/BR (Arm C) based on the following endpoint:

- PFS after randomization, defined as the time from randomization to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the IRC assessment according to the IWCLL 2018

criteria

Study description

Background summary

This randomized, global, multicenter, open-label, Phase 3 study will evaluate the efficacy and safety of AV and AVG versus chemoimmunotherapy (FCR or BR) in subjects with previously untreated CLL without del(17p) or TP53. Subjects will be randomized in a 1:1:1 ratio into 3 arms through a block stratified randomization procedure.

Study objective

This study has been transitioned to CTIS with ID 2023-509349-11-00 check the CTIS register for the current data.

Primary objective: To determine the efficacy of the combination of acalabrutinib and venetoclax without obinutuzumab (AV; Arm A), or with obinutuzumab (AVG; Arm B) compared with chemoimmunotherapy (fludarabine/cyclophosphamide/rituximab [FCR]/bendamustine/rituximab [BR]; Arm C) by assessment of PFS (progression-free survival) in patients with previously untreated Chronic Lymphocytic Leukemia without del(17p) or tp53 mutation.

Study design

Randomized, Phase III, open-label study. Randomisation 1:1:1 to:
- Acalabrutinib and venetoclax
- Acalabrutinib, venetoclax and obinutuzumab
- Chemoimmunotherapy; fludarabine/cyclophosphamide/rituximab (FCR) or bendamustine/rituximab (BR) (investigator*s choice).

Approximately 780 subjects will receive treatment for a set period of time. The study includes screening (30 days), treatment (from randomization until study drug discontinuation) and follow-up phase.

Intervention

- Acalabrutinib (Calquence)
- Venetoclax (Venclyxto)
- Obinutuzumab (Gazyvaro)
- Chemoimmunotherapy: fludarabine/cyclophosphamide/rituximab (FCR), bendamustine/rituximab (BR)

Study burden and risks

Patients in arm A and B will visit the hospital more often compared to standard of care. During the study visit additional blood, CT scans and bone marrow aspirate/biopsies will be taken compared to standard of care. The patients are also asked to complete questionnaires and diaries and to provide an optional sputum sample.
The study drugs may reduce the CLL, but this is not sure. The study drugs may cause 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

- Men and women >=18 years of age.
- Eastern Cooperative Oncology Group (ECOG) performance status of 0-2.
- Diagnosis of CLL and active disease requiring treatment per iwCLL 2018 criteria
- *Adequate bone marrow function within 1 week of Screening
o ANC >=750 cells/ µL (0.75x10^9 /L); ANC >=500 µL (0.50x10^9 /L) in subjects with documented bone marrow involvement of CLL
o Platelet count >=50,000 cells/ µL (50x10^9 /L); platelet count >=30,000 µL (30x10^9 /L) in subjects with documented bone marrow involvement of CLL
- Serum AST and ALT <=2.5xULN
- Total bilirubin <=2xULN
- Estimated creatinine clearance of >=50 mL/min; >=70 mL/min for FCR (Arm C)

Exclusion criteria

- Any prior CLL-specific therapies.
- Detected del(17p) or TP53 mutation.
- Transformation of CLL to aggressive non-Hodgkin lymphoma (NHL) (e.g., Richter's transformation, prolymphocytic leukemia [PLL], or diffuse large B cell lymphoma [DLBCL]), or central nervous system (CNS) involvement by leukemia.
- History of confirmed progressive multifocal leukoencephalopathy (PML).
- Major surgical procedure within 30 days before the first dose of study drug.
- Significant cardiovascular disease such as symptomatic arrhythmias, congestive heart failure, or myocardial infarction within 6 months of Screening, or any Class 3 or 4 cardiac disease. Note: Subjects with controlled, asymptomatic atrial fibrillation are allowed to enroll on study.
- History of stroke or intracranial hemorrhage within 6 months before first dose of study drug.
- Requires or receiving anticoagulation with warfarin or equivalent vitamin K antagonists.

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):	13-05-2020
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Calquence
Generic name:	acalabrutinib
Product type:	Medicine
Brand name:	Cyclophosphamide
Generic name:	cyclophosphamide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Fludarabine
Generic name:	fludarabine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Gazyvaro
Generic name:	obinutuzumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Venclyxto
Generic name:	venetoclax
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	16-07-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-03-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-05-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	15-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-09-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	25-10-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214

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Approved WMO Date:	08-12-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	04-01-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	CTIS2023-509349-11-00
EudraCT	EUCTR2018-002443-28-NL
ClinicalTrials.gov	NCT03836261
CCMO	NL70443.018.19