A Phase 3b, Multicenter, Open-Label, Single-Arm Study of Acalabrutinib (ACP-196) in Subjects with Chronic Lymphocytic Leukemia

Published: 03-10-2019
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This study has been transitioned to CTIS with ID 2023-507669-24-00 check the CTIS register for the current data. To evaluate the safety and tolerability of acalabrutinib monotherapy in subjects with treatment-naive or relapsed/refractory chronic…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON54635

Source
ToetsingOnline

Brief title
ASSURE

Condition

- Leukaemias

Synonym
Bloodcancer, leukemia

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca

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

Intervention

Keyword: Acalabrutinib (ACP-196), Chronic Lymphocytic Leukemia, Phase 3b

Outcome measures

Primary outcome

Frequency and relatedness of all adverse events, which will also include: Grade >=3 adverse events, serious adverse events, adverse events that lead to discontinuation of treatment, events of clinical interest defined as cardiac rhythm disorders, opportunistic infections, interstitial lung disease, major hemorrhage, and cytopenias

Secondary outcome

Objective response rate, duration of response and progression-free survival

Study description

Background summary

Chemoimmunotherapy is considered standard of care for previously untreated subjects with chronic
lymphocytic leukemia (CLL) who do not have significant comorbidities; however, chemoimmunotherapy is associated with significant toxicities. Furthermore, chemoimmunotherapy is not recommended in subjects with del(17p) or TP53 mutation because of inferior response and outcome. In this population, available options are limited and include obinutuzumab or ibrutinib. Acalabrutinib has shown significant efficacy and tolerability in subjects with treatment-naïve (TN) or relapsed/refractory (R/R) CLL and is currently being studied in randomized Phase 3 studies comparing it with standard of care treatments (Studies ACE-CL-006, ACE-CL-007, and ACE-CL-309). Additional safety data are needed to further characterize less common associated adverse events (AEs) and management of common AEs. Data collected in a setting more reflective of real-world practice may further inform subject management.

Study objective

This study has been transitioned to CTIS with ID 2023-507669-24-00 check the CTIS register for the current data.

To evaluate the safety and tolerability of acalabrutinib monotherapy in subjects with treatment-naive or relapsed/refractory chronic lymphocytic leukemia.

Study design

This global, Phase 3b, multicenter, open-label, single-arm study will evaluate the safety and
efficacy of acalabrutinib 100 mg twice daily (bid) in approximately 600 subjects with chronic
lymphocytic leukemia (CLL). Subjects will be enrolled into 3 cohorts: treatment-naive (TN),
relapsed/refractory (R/R), prior Bruton tyrosine kinase inhibitor (BTKi) therapy.

Intervention

Study treatment (acalabrutinib 100 mg) will be provided as hard, gelatin capsules for twicedaily oral administration until completion of 48 cycles, disease progression, toxicity requiring discontinuation, withdrawal of consent, lost to follow-up, death, or study termination by the sponsor.

Study burden and risks

Acalabrutinib is an approved drug for the treatment of adult subjects with mantle cell lymphoma. As with any drug, there may be unknown and potentially serious or life-threatening side effects that could occur with acalabrutinib. The full side-effect profile of acalabrutinib is not yet known. Side effects can vary from mild to very serious and may vary from person to person. Participating subjects may have some or no side effects. Everyone taking part in the study will be watched carefully for any side effects. Taking part in this research study may not help the participation subject but will help AstraZeneca to answer certain research questions. Information from this research study may help cancer subjects in the future.

Contacts

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Scientific
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Gartunavagen 1
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Men and women >=18 years of age; 2. Diagnosis of CLL that meets published diagnostic criteria: a. Monoclonal B-cells (either kappa or lambda light chain restricted) that are clonally co-expressing >=1 B-cell marker (CD19, CD20, and CD23) and CD5; b. Prolymphocytes may comprise <55% of blood lymphocytes; c. Presence of >=5 × 10^9 B lymphocytes/L (5000/µL) in the peripheral blood (at any point since the initial diagnosis); 3. Active disease per IWCLL 2018 criteria that requires treatment: a. Evidence of progressive marrow failure as manifested by the development of, or worsening of, anemia (hemoglobin <10 g/dL) and/or thrombocytopenia (platelets <100,000/µL). b. Massive (i.e., >=6 cm below the left costal margin), progressive, or symptomatic splenomegaly. c. Massive nodes (i.e., >=10 cm in the longest diameter), progressive, or symptomatic lymphadenopathy. d. Progressive lymphocytosis with an increase of >50% over a 2-month period or a LDT of <6 months. Lymphocyte doubling time may be obtained by linear regression extrapolation of absolute lymphocyte count obtained at intervals of 2 weeks over an observation period of 2 to 3 months. In participants with initial blood lymphocyte counts of <30x109/L (30,000/µL), LDT should not be used as a single parameter to define indication for treatment. In addition, factors contributing to lymphocytosis or lymphadenopathy other than CLL (e.g., infections) should be excluded. e. Autoimmune anemia and/or thrombocytopenia that is poorly responsive to standard therapy. f. B-symptoms

documented in the participants chart with supportive objective measures, as appropriate, defined as >=1 of the following disease-related symptoms or signs (please refer to protocol for related symptoms); 4. Must meet 1 of the following criteria: a. Have received no prior therapy for treatment of CLL and meets 1 of the following criteria: i. A score of >6 on the Cumulative Illness Rating Scale (CIRS). ii. Creatinine clearance of 30 to 69 ml/min using the Cockcroft-Gault equation. b. Have previously received therapy for CLL and have either refractory or relapsed CLL. c. Have received prior BTKi therapy (i.e., defined as a participant who discontinued a BTKi for any reason except disease progression) for CLL. d. Have either TN or R/R CLL and are receiving concomitant vitamin K antagonists (e.g., coumadin). 5. ECOG performance status of <=2; 6. Female subjects of childbearing potential (i.e., not surgically sterile or postmenopausal) who are sexually active with a non-sterilized male partner must use >=1 highly effective method of contraception from the time of screening and must agree to continue using such precautions for 2 days after the last dose of study treatment. Non-sterilized male participants who are sexually active with a female partner of childbearing potential must use a male condom plus spermicide during the study. 7. Fluorescence in situ hybridization (FISH) results within 60 days before screening reflecting the presence or absence of del(17p), del(13q), del(11q), and trisomy of chromosome 12 along with the percentage of cells with the deletion, along with TP53 sequencing. Participants must also have molecular analysis to detect IGHV mutation status at any time point since diagnosis. 8. Participants must be willing and able to adhere to the study visit schedule, understand and comply with other protocol requirements, and provide written informed consent and authorization to use protected health information.

Exclusion criteria

1. Participants who have had disease progression while on a BTKi for any malignant or nonmalignant condition. 2. Prior malignancy (other than CLL), except for adequately treated basal cell or squamous cell skin cancer, in situ cancer, early stage prostate cancer, or other cancer from which the participant has been disease-free for >=2 years. 3. History of confirmed progressive multifocal leukoencephalopathy. 4. Significant cardiovascular disease such as symptomatic arrhythmias, congestive heart failure, or myocardial infarction within 6 months before screening, or any Class 3 or 4 cardiac disease as defined by the NYHA Functional Classification, or QTcF >480 msec at screening. Note: participants with rate-controlled, asymptomatic atrial fibrillation are allowed to enroll in the study. 5. Malabsorption syndrome, disease significantly affecting gastrointestinal function, resection of the stomach, extensive small bowel resection that is likely to affect absorption, symptomatic inflammatory bowel disease, partial or complete bowel obstruction, or gastric restrictions and bariatric surgery, such as gastric bypass. 6. Evidence of active Richter's transformation. If Richter*s transformation is

suspected (i.e., LDH increased, asymmetric fast LN growth or clinical suspicion), it should be ruled out with positron emission tomography-computed tomography (PET-CT) and/or biopsy according to guidelines. 7. Central nervous system (CNS) involvement by CLL. 8. Known history of human immunodeficiency virus, serologic status reflecting active HBV or HCV infection, any uncontrolled active systemic infection along with participants who are on ongoing anti-infective treatment and participants who have received vaccination with a live attenuated vaccine within 4 weeks before the first dose of study intervention. a. Participants who are anti-HBc positive and who are anti-HBs negative will need to have a negative hepatitis B virus PCR result before enrollment. Those who are HBsAg positive or hepatitis B virus PCR positive will be excluded. b. Participants who are HCV antibody positive will need to have a negative HCV PCR result before enrollment. Those who are HCV PCR positive will be excluded. 9. Uncontrolled autoimmune hemolytic anemia or idiopathic thrombocytopenic purpura defined as declining hemoglobin or platelet count secondary to autoimmune destruction within the screening period or requirement for high doses of steroids (>20 mg daily of prednisone or equivalent for longer than 2 weeks). 10. History of stroke or intracranial hemorrhage within 6 months before the first dose of study intervention. 11. History of bleeding diathesis (e.g., hemophilia or von Willebrand disease). 12. Presence of a gastrointestinal ulcer diagnosed by endoscopy within 3 months before Screening. 13. Major surgical procedure within 4 weeks before first dose of study treatment. Note: Participants who have had major surgery, must have recovered adequately from any toxicity and/or complications from the intervention before the first dose of study treatment. 14. Requires treatment with proton-pump inhibitors (e.g., omeprazole, esomeprazole, lansoprazole, dexlansoprazole, rabeprazole, or pantoprazole). Subjects receiving proton-pump inhibitors who switch to H2-receptor antagonists or antacids are eligible for enrollment in this study. 15. All participants requiring or receiving anticoagulation with warfarin or equivalent vitamin K antagonists (e.g., phenprocoumon) within 7 days before first dose of study treatment except those participants who will be enrolled into the vitamin K antagonist cohort. 16. Absolute neutrophil count <0.50 x 109/L or platelet count <30 x 109/L, unless proven due to CLL and raised above the limits by granulocyte colony-stimulating factor therapy and/or pooled platelet transfusion. 17. Total bilirubin >3.0 ULN; or AST or ALT >3.0 x ULN. Exception will be for Gilbert syndrome; if an investigator feels that a participants total bilirubin is elevated secondary to Gilbert*s, the participant must have a documented unconjugated bilirubin being >80% of the total bilirubin number. The investigator must also document that hemolysis has been ruled out along with (near)-normal lactate dehydrogenase and haptoglobin. 18. Estimated creatinine clearance of <30 mL/min, calculated using the formula of Cockcroft and Gault or by direct assessment (i.e., creatinine clearance or EDTA clearance measurement). 19. Breastfeeding or pregnant.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-07-2020
Enrollment:	34
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Acalabrutinib
Generic name:	Acalabrutinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	03-10-2019
Application type:	First submission
Review commission:	METC NedMec

Approved WMO

Date:	14-01-2020
Application type:	First submission
Review commission:	METC NedMec

Approved WMO

Date:	17-03-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-07-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	20-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-11-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-11-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-12-2023
Application type:	Amendment
Review commission:	METC NedMec

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	CTIS2023-507669-24-00
EudraCT	EUCTR2019-001573-89-NL
ClinicalTrials.gov	NCT#notyetpostedonclinicaltrials.gov,butstudycanbefoundusingstudycodeD8220C00008
CCMO	NL70210.041.19