A phase IIIb, multi-center, open-label, randomized study of tolerability and efficacy of oral asciminib versus nilotinib in patients with newly diagnosed Philadelphia Chromosome Positive Chronic Myelogenous Leukemia in Chronic Phase (CABL001J12302)

Published: 31-10-2022
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This study has been transitioned to CTIS with ID 2024-510947-71-00 check the CTIS register for the current data. Primary:To assess the tolerability of asciminib versus nilotinib with respect to the time to discontinuation of study treatment due to...

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

Summary

ID

NL-OMON51567

Source
ToetsingOnline

Brief title
CABL001J12302

Condition

- Leukaemias

Synonym
leukemia; blood cancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: Asciminib, Chronic Myeloid Leukemia, Nilotinib, Philadelphia chromosome positive

Outcome measures

Primary outcome

Time to discontinuation of study treatment due to adverse event.

Secondary outcome

Discontinuation due to lack of efficacy, treatment failure, disease

progression, suboptimal response, death.

Patient-reported disease-related symptoms, functioning, and health-related

quality of life.

Adverse events.

Study description

Background summary

Considerable advancements in treatment of patients with CML-CP have increased the life expectancy of patients making it a chronic disease requiring long term medication. This emphasizes the need for treatments that combine high efficacy with a favorable safety profile as improving over the currently available options. There remains an unmet medical need for newly diagnosed patients with CML-CP requiring chronic treatment and for a specific targeted treatment option that is highly efficacious while minimizing adverse events.
To assess if asciminib may address these needs, the ongoing Phase III study CABL001J12301 sets out to evaluate primarily the efficacy of asciminib in newly

diagnosed Chronic Myelogenous Leukemia (CML) patients.
The primary purpose of this Phase IIIb study is to focus on the patient relevant outcomes and to assess the tolerability of asciminib, as it translates in study treatment discontinuations due to adverse events, in comparison with that of the second generation Tyrosine Kinase Inhibitor nilotinib, in adult patients with newly diagnosed Ph+ CML-CP. The study also aims to assess treatment impact on quality of life. Generating such data is patient relevant as well as deemed important for Health Technology Assessment bodies* decision making.

Study objective

This study has been transitioned to CTIS with ID 2024-510947-71-00 check the CTIS register for the current data.

Primary:
To assess the tolerability of asciminib versus nilotinib with respect to the time to discontinuation of study treatment due to adverse event.
Secondary:
• Efficacy of asciminib versus nilotinib in terms of discontinuation due to lack of efficacy/treatment failure/disease progression/suboptimal response/death.
• Effect of asciminib versus nilotinib on patient-reported disease-related symptoms, functioning, and health-related quality of life.
• Safety and tolerability profile of asciminib versus nilotinib during the course of study.

Study design

This is a phase IIIb, multi-center, open-label, randomized study of oral asciminib 80 mg QD versus nilotinib 300 mg BID in adult patients with newly diagnosed Ph+ CML-CP. It is planned to randomize approximately 541 patients in the study in a 1:1 randomization to asciminib or nilotinib. Randomization will be stratified based on European Treatment Outcome Study (EUTOS) long-term survival (ELTS) score (low versus intermediate versus high) to help achieve a balance between the treatment arms.
The primary purpose of this study is to assess the tolerability of asciminib in comparison with that of nilotinib. Study duration approximately 4.5-5 years. Approximate treatment duration for an individual participant is expected to be between 2 to 4.5 years dependent on when the patient enrolls in the study. Visits are planned every 2 weeks for the first month of treatment and every 12 weeks until end of treatment.

Intervention

Participants will be assigned at Day 1 to one of the following 2 treatment arms

in a ratio of 1:1:
Arm 1: Asciminib tablets 80 mg QD administered under fasting conditions.
Arm 2: Nilotinib capsules 300 mg BID administered under fasting conditions.

Study burden and risks

Risk: Adverse events of the study medication.
Burden:
• Visits: Screening visit. Treatment period: During 1st 12 weeks4 times study visit (on 1st day of treatment period and 2, 4 and 12 weeks after start of treatment). Thereafter every 12 weeks until the end of treatment. End of treatment visit.
• Phone call 4 weeks after end of treatment and every 12 weeks thereafter.
• Physical examination, including blood pressure, pulse, temperature, weight: every visit.
• Blood tests (fasting for glucose and lipids, approx. 15-35 mL): every visit.
• Pregnancy test (if relevant) every month (if necessary at home, result to be communicated to investigator by phone).
• EKG 4 times.
• Bone marrow assessment during screening, if not performed within the last 3 months. If necessary to be repeated during the treatment period.
• Questionnaires:
QLQ-C30, CML24 (every 4-24 weeks during the 1st year, end of 2nd year and end of treatment, 3 times during follow-up).
PRO-CTCAE, FACT GP5 (every week during the 1st 6 months and every 4 weeks thereafter, 3 times during follow-up).
Optional:
• Use of data and remaining body material for other research.
• Trial Feedback Questionnaire about the patient*s feedback on trial experience (3 times).

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. Males or females >= 18 years of age.
2. CML-CP within 3 months of diagnosis.
3. Diagnosis of CML-CP (European Leukemia Network 2020 criteria) with cytogenetic confirmation of the Ph chromosome. Documented CML-CP will meet all the criteria as mentioned in item 4 on page 10 of the protocol.
4. Evidence of typical BCR::ABL1 transcript. See item 5 on protocol page 10 for details.
5. ECOG performance status of 0 or 1.
6. Adequate end organ function as defined in item 7 on protocol page 10.
7. The laboratory values mentioned in item 8 on protocol pages 10/11 must be within normal limits or must have been corrected to within normal limits with supplements prior to randomization

Exclusion criteria

1. Previous treatment of CML with any other anticancer agents or prior stem cell transplant, with the exception of hydroxyurea and/or anagrelide.
2. Known cytopathologically confirmed CNS infiltration.
3. Impaired cardiac function or cardiac repolarization abnormality. See item 3 on protocol page 11 for details.
4. Severe and/or uncontrolled concurrent medical disease that in the opinion of the investigator could cause unacceptable safety risks or compromise compliance with the protocol. See item 5 on protocol page 11 for examples.
5. History of significant bleeding disorder. See item 5 on protocol page 11 for details.

6. Major surgery within 4 weeks prior to study entry or not recovered from prior surgery.
7. History of other active malignancy within 3 years prior to study entry. See item 7 on protocol page 11 for exceptions.
8. History of acute pancreatitis within 1 year prior to randomization or medical history of chronic pancreatitis.
9. History of chronic liver disease leading to severe hepatic impairment, or ongoing acute liver disease.
10. Known history of chronic Hepatitis B (HBV), or chronic Hepatitis C (HCV) infection. See item 10 on protocol page 12 for details.
11. History of HIV unless well-controlled on a stable dose of anti-retroviral therapy at the time of screening.
12. Impairment of GI function or GI disease that may significantly alter the absorption of study treatment. See item 12 on protocol page 12 for details...
13. Participation in a prior investigational study within 30 days prior to randomization or within 5 half-lives of the investigational product, whichever is longer.
14. Pregnant or lactating women
15. Women of child-bearing potential not using highly effective methods of contraception. See item 15 on protocol page 12 for details.

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):	25-07-2023
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Scemblix
Generic name:	Asciminib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tasigna
Generic name:	Nilotinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	31-10-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-01-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-09-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-12-2023
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	CTIS2024-510947-71-00
EudraCT	EUCTR2022-000995-21-NL
ClinicalTrials.gov	NCT05456191
CCMO	NL82770.056.22