A phase III, multi-center, open-label, randomized study of oral asciminib versus Investigator selected TKI in patients with newly diagnosed Philadelphia Chromosome Positive Chronic Myelogenous Leukemia in Chronic Phase

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Primary:To compare the efficacy of asciminib versus Investigator selected TKI with respect to the proportion of patients that are in Major Molecular Response at Week 48. To compare the efficacy of asciminib versus Investigator selected TKI, within...

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

Summary

ID

NL-OMON51998

Source
ToetsingOnline

Brief title
CABL001J12301

Condition

- Leukaemias

Synonym
Leukemia, Philadelphia Chromosome Positive Chronic Myelogenous Leukemia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ABL001, Chronic phase, Ph+CML, Tyrosine Kinase Inhibitor

Outcome measures

Primary outcome

Major Molecular Response.

Secondary outcome

Additional efficacy parameters.

Pharmacokinetic parameters (Cmax, Tmax, AUCtau, AUClast, CL/F).

Safety parameters (type, frequency and severity of AEs, changes in lab values outside the pre-determined ranges, relevant ECG changes, vital signs and physical examination changes).

Exploratory parameters (biomarkers, pharmacogenetics, healthcare resource utilization, questionnaires).

Study description

Background summary

Despite the significant advances in the treatment of chronic myelogenous leukemia (CML) thanks to the introduction of tyrosine-kinase inhibitors (TKIs), many patients treated with two or more TKIs experience intolerance. In addition resistance rates in later treatment lines remain high (see protocol page 21, item 1.1.2).
Asciminib (ABL001) is a novel investigational treatment specifically targeting

the ABL myristoyl pocket (STAMP). As a STAMP inhibitor, asciminib might help address TKI resistance and intolerance. Asciminib is being evaluated for the treatment of patients with CML (see protocol page 22, item 1.2.1).
Results at 24 weeks from a phase III study in patients with Philadelphia chromosome positive CML in chronic phase previously treated with two or more TKIs demonstrate that, asciminib nearly doubled the major molecular response rate compared to bosutinib (25.5% vs. 13.2%). Complete cytogenetic response at 24 weeks was 40.5% for asciminib and 24.2% for bosutinib. Safety and tolerability data (grade >=3 AEs, treatment discontinuation due to AEs, dose reduction or interruption due to AEs) were more favorable in the asciminib arm (see protocol page 24, item 1.2.2.2).
In 2020 EMA has granted asciminib the orphan status. In 2021 FDA has granted asciminib breakthrough therapy designation for adults with Philadelphia chromosome positive CML in the chronic phase.

The purpose of this pivotal study is to compare the efficacy of asciminib with that of BCR-ABL1 TKIs, such as imatinib, nilotinib, dasatinib and bosutinib in adult patients with newly diagnosed Philadelphia chromosome positive CML in the chronic phase.

Study objective

Primary:
To compare the efficacy of asciminib versus Investigator selected TKI with respect to the proportion of patients that are in Major Molecular Response at Week 48.
To compare the efficacy of asciminib versus Investigator selected TKI, within the stratum of patients with imatinib as the pre-randomization selected TKI, with respect to the proportion of patients that are in Major Molecular Response at Week 48

Secondary:
To compare the efficacy of asciminib versus Investigator selected TKI, with respect to the proportion of patients that are in Major Molecular Response at Week 96.
To compare the efficacy of asciminib versus Investigator selected TKI, within the stratum of patients with imatinib as the pre-randomization selected TKI, with respect to the proportion of patients that are in Major Molecular Response at Week 96.

Study design

Phase III multicenter open-label randomized (1:1) study, designed to compare the efficacy of the asciminib tablets 80 mg QD versus Investigator selected TKI for the treatment of newly diagnosed, previously untreated patients with Philadelphia Chromosome positive CML in the chronic phase. The Investigator

selected TKI will be one of the following treatment options for first-line treatment of CML in the chronic phase:
• Imatinib tablets 400 mg QD
• Nilotinib capsules 300 mg BID
• Dasatinib tablets 100 mg QD
• Bosutinib tablets 400 mg QD.
Dose escalation for asciminib or nilotinib is not permitted. Dose escalation for the other investigator selected TKIs is allowed (see protocol page 52).
Study treatment until end of study (5 years after last patient first visit) or treatment failure, disease progression, intolerance or investigator or patient decision.
In case of premature discontinuation: follow up for survival until end of study.

Intervention

Treatment with asciminib versus imatinib, or nilotinib, or dasatinib, or bosutinib.

Study burden and risks

Risk: Adverse events of the study medication.
Burden:
• Visits: screening, week 1, 2, 4, 6, 8, 10, 12 and every 12 weeks thereafter, end of study.
• Physical examination: every visit.
• Blood draws: every visit, fasting, 15-60 mL blood per occasion.
• Pregnancy tests: monthly blood (urine if blood test not feasible).
• ECG: screening, week 1, 2, 4, 10, 12, 48, 96, end of study.
• Bone marrow biopsy: <=once.
• Questionnaires: PRO-CTCAE and FACIT GP5 (at home) weekly first 6 months, monthly thereafter. QLQ-C30, QLQ-CML24 and EQ-5D-5L 8 visits in total.
Optional:
• Blood sample for pharmacogenetics (6 mL).

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. Male or female patients with newly (< 3 monhts) diagnosed CML-CP >= 18 years of age.
2. Diagnosis of CML-CP with cytogenetic confirmation of Philadelphia chromosome
3. ECOG performance status of 0, or 1.
4. Adequate end organ function

Exclusion criteria

1. Previous treatment of CML with any other anticancer agents including chemotherapy and/or biologic agents or prior stem cell transplant
2. Known cytopathologically confirmed CNS infiltration.
3. Impaired cardiac function or cardiac repolarization abnormality
4. History of acute pancreatitis within 1 year of prior to randomization or medical history of chronic
pancreatitis.
5. Pregnancy, lactation, insufficient contraception for females of childbearing potential .

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):	08-11-2022
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Asciminib
Generic name:	Asciminib
Product type:	Medicine
Brand name:	Bosulif
Generic name:	bosutinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	dasatinib
Generic name:	Sprycel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Glivec
Generic name:	imatinib

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tasigna
Generic name:	nilotinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	17-11-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-12-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-01-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-06-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-08-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2021-000678-27-NL
ClinicalTrials.gov	NCT04971226
CCMO	NL78371.029.21