A multi-center, open-label study to determine the dose and safety of oral asciminib in pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP), previously treated with one or more tyrosine kinase inhibitors.

Published: 17-08-2022
Last updated: 27-12-2024

This study has been transitioned to CTIS with ID 2023-508129-28-00 check the CTIS register for the current data. The primary objective of this study is to characterize the pharmacokinetic (PK) profile of asciminib in pediatric patients, with the…

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

Summary

ID

NL-OMON54333

Source
ToetsingOnline

Brief title
CABL001i12201

Condition

- Leukaemias

Synonym
blood cancer, chronic leukemia

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: Chronic Myeloid Leukemia, Chronic Phase, Philadelphia-postive, Therapy Resistant

Outcome measures

Primary outcome

The primary objective of this study is to characterize the pharmacokinetic (PK)

profile of asciminib in pediatric patients, with the goal of identifying the

pediatric formulation dose (fed) leading to asciminib exposure comparable to 40

mg BID in adult patients (fasted).

Secondary outcome

The secondary objectives of this study are:

* To assess the safety and tolerability of asciminib.

* To assess pharmacodynamic markers of asciminib*s anti-leukemic activity.

* To assess acceptability and palatability of the pediatric formulation.

* To assess long-term safety of asciminib.

Study description

Background summary

CML is a form of cancer of the bonemarrow and has 3 phases, the chronic fase is the first fase. In this fase, in this fase there are often few noticable effects. Without sufficient treatment the chronic fase can proceed into the second and third fases.

The form of CML treated in this study is Philadelphia chromosoom-positive. This means that there is an aberrant chromosome in the bonemarrow. This chromosome contains a fusion gene: the BCR-ABL gene. This gene produces a protein that causes CML, the BCR-ABL protein.

Asciminib is a tyrosinekinaseinhibitor (TKI), which is a form of targeted therapy. These types of drugs inhibit the BCR-ABL protein, and thereby kills CML-cells. TKIs work for the majority of patients with CML, however it is possible for resistance to a current treatment with TKIs to form. In which case the effectiveness of treatment might diminish or even stop. This is because the BCR-ABL gene can mutate and no longer be susceptable to a particular TKI. At that time it might be necessary to switch to a different TKI.

Asciminib has not yet been approved by the Dutch health authority, but has been approved for treatment of adults with CML by the FDA. Prior to this the effects of asciminib have been studied in various forms of leukemia in different fases of the disease in 530 adults. For younger childeren an additional formulation consisting of 1mg mini-tablets has been developed. The mini-tablets are kept in a capsule to allow for more precise dosing, capsules varying from 5 to 50 mg of asciminib are available and dosing will be determined based on body weight.

Study objective

This study has been transitioned to CTIS with ID 2023-508129-28-00 check the CTIS register for the current data.

The primary objective of this study is to characterize the pharmacokinetic (PK) profile of asciminib in pediatric patients, with the goal of identifying the pediatric formulation dose (fed) leading to asciminib exposure comparable to 40 mg BID in adult patients (fasted).

Study design

This is a multi-center, open-label, single arm study to determine the appropriate dose of asciminib (pediatric formulation) in pediatric patients aged 1 to < 18 years old with Ph+ CML-CP, who are resistant or intolerant to at least one prior TKI.
There will be two study treatment groups:
* The pediatric formulation group, consisting of Part 1, Part 2 and part 3, in which the participants receive a body weight adjusted dose of pediatric mini-tablets with food, Part 1 and 2 will have BID dosing, part 3 will explore

QD dosing.
* The exploratory adult formulation group, in which the participants receive a flat dose of asciminib 40 mg BID of the adult tablet in the fasted state.

Intervention

Asciminib in 40mg tablet formulation, or mini-tablets in capsule form.

Study burden and risks

Participation in this study exposes the participant to risks associated with using asciminib (the possible side effects) and the possible side-effects of the study assessments. See above sections for more details, or protocol section 8.

Contacts

Public
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL
Scientific
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adolescents (12-15 years)

Adolescents (16-17 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

* Male or female participants:
a. Pediatric formulation group: >= 1 and less than 18 years of age at study entry.
b. Adult formulation group: >= 14 and less than 18 years of age and body weight of >= 40 kg at study entry.
* Participants with Ph+ CML-CP must meet all of the following laboratory values at the screening visit. In the case where bone marrow blast and promyelocyte counts are available, these will be accepted if done within 56 days prior to the screening visit, to avoid unnecessary repetition of this test.
a. 15% blasts in peripheral blood and bone marrow
b. < 30% combined blasts plus promyelocytes in peripheral blood and bone marrow
c. < 20% basophils in the peripheral blood
d. Neutrophils >= 1.5 x 10^9/L (or white blood cell (WBC) >= 3 x 10^9/L if neutrophils are not available) and platelet count >= 100 x 10^9/L
e. No evidence of extramedullary leukemic involvement, with the exception of hepatosplenomegaly
* Prior treatment with a minimum of one TKI.
* Failure or intolerance to the most recent TKI therapy at the time of screening.
* Evidence of typical BCR-ABL fusion gene (BCR-ABL1) transcript [e14a2 and/or e13a2] at the time of screening which are amenable to standardized real time quantitative polymerase chain reaction (RQPCR) quantification.

Exclusion criteria

* Known presence of the T315I mutation prior to study entry.
* Known second chronic phase of CML after previous progression to AP/BC.
* Previous treatment with a hematopoietic stem-cell transplantation.
* Patient planning to undergo allogeneic hematopoietic stem cell transplantation.
* Cardiac or cardiac repolarization abnormality.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2022
Enrollment:	1
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Scemblix
Generic name:	asciminib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	17-08-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	10-02-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	21-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-05-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-06-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-08-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	30-08-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-11-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-12-2023
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	CTIS2023-508129-28-00
EudraCT	EUCTR2021-001286-20-NL
ClinicalTrials.gov	NCT04925479
CCMO	NL79020.041.22