A Study to Investigate Tolerability and Efficacy of Asciminib (Oral) Versus Nilotinib (Oral) in Adult Participants (≥18 Years of Age) With Newly Diagnosed Philadelphia Chromosome Positive Chronic Myelogenous Leukemia in Chronic Phase (Ph+ CML-CP)

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Main Information

Primary registry identifying number
LBCTR2023025267

Protocol number
CABL001J12302

MOH registration number

Study registered at the country of origin
Yes

Study registered at the country of origin: Specify

Type of registration
Prospective

Type of registration: Justify
N/A

Date of registration in national regulatory agency

Primary sponsor
Novartis Pharma AG

Primary sponsor: Country of origin
Novartis Pharma AG

Date of registration in primary registry
13/09/2023

Date of registration in national regulatory agency

Public title
A Study to Investigate Tolerability and Efficacy of Asciminib (Oral) Versus Nilotinib (Oral) in Adult Participants (≥18 Years of Age) With Newly Diagnosed Philadelphia Chromosome Positive Chronic Myelogenous Leukemia in Chronic Phase (Ph+ CML-CP)

Acronym

Scientific title
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

Acronym
ASC4START

Brief summary of the study: English
The study is designed to compare the tolerability of asciminib versus nilotinib for the treatment of newly diagnosed, previously untreated patients with Positive Chronic Myelogenous Leukemia in Chronic Phase (Ph+ CML-CP)

Brief summary of the study: Arabic
ب حول تحمّل وفعالية أسكيمينيب الفموي مقابل نيلوتينيب لدى المرضى3دراسة متعدّدة المراكز ومفتوحة التسمية وعشوائيّة التوزيع في المرحلة الذين تمّ تشخيص إصابتهم حديثًا بسرطان الدم النقوي المزمن الإيجابي لكروموسوم فيلادلفيا في المرحلة المزمنة

Health conditions/problem studied: Specify
Philadelphia Chromosome-Positive Chronic Myeloid Leukemia

Interventions: Specify

Drug: Asciminib
Asciminib 80 mg QD administered under fasting conditions
Other Name: ABL001
Drug: Nilotinib
Nilotinib 300 mg BID administered under fasting conditions

Key inclusion and exclusion criteria: Inclusion criteria

Inclusion Criteria:

1- Patients with CML-CP within 3 months of diagnosis.
2- Diagnosis of CML-CP (ELN 2020 criteria) with cytogenetic confirmation of the Philadelphia chromosome

Documented chronic phase CML will meet all the below criteria Baccarani et al 2013:

< 15% blasts in peripheral blood and bone marrow,
< 30% blasts plus promyelocytes in peripheral blood and bone marrow,
< 20% basophils in the peripheral blood,
PLT count ≥ 100 x 10^9/L (≥ 100,000/mm3), except treatment induced thrombocytopenia
No evidence of extramedullary leukemic involvement, with the exception of hepatosplenomegaly.
3- Evidence of typical BCR::ABL1 transcript [e14a2 and/or e13a2] which is amenable to standardized RQ-PCR quantification by the central laboratory assessment.
4- ECOG performance status of 0 or 1.
5- Adequate end organ function as defined by:

Total bilirubin (TBL) < 3 x ULN; patients with Gilbert's syndrome may only be included if TBL ≤ 3.0 x ULN or direct bilirubin ≤ 1.5 x ULN,
CrCl ≥ 30 mL/min as calculated using Cockcroft-Gault formula, Serum lipase ≤ 1.5 x ULN. For serum lipase > ULN - ≤ 1.5 x ULN, value must be considered not clinically significant and not associated with risk factors for acute pancreatitis.

6- Patients must have the following laboratory values within normal limits or corrected to within normal limits with supplements prior to randomization:

Potassium (potassium increase of up to 6.0 mmol/L is acceptable if associated with CrCl* ≥ 90 mL/min),
Total calcium (corrected for serum albumin); (calcium increase of up to 12.5 mg/dl or 3.1 mmol/L is acceptable if associated with CrCl* ≥ 90 mL/min),
Magnesium (magnesium increase of up to 3.0 mg/dL or 1.23 mmol/L if associated with CrCl* ≥ 90 mL/min),
For patients with mild to moderate renal impairment (CrCl* ≥ 30 mL/min and <90 mL/min) - potassium, total calcium (corrected for serum albumin) and magnesium should be within normal limits or corrected to within normal limits with supplements prior to randomization.

CrCl as calculated using Cockcroft-Gault formula.
Other protocol-defined Inclusion/exclusion criteria will apply

Key inclusion and exclusion criteria: Gender

Both

Key inclusion and exclusion criteria: Specify gender

Key inclusion and exclusion criteria: Age minimum

18

Key inclusion and exclusion criteria: Age maximum

99

Key inclusion and exclusion criteria: Exclusion criteria

Exclusion Criteria:

1- Previous treatment of CML with any other anticancer agents including chemotherapy and/or biologic agents or prior stem cell transplant, with the exception of hydroxyurea and/or anagrelide.
2- Known cytopathologically confirmed CNS infiltration (in absence of suspicion of CNS involvement, lumbar puncture not required).
3- Impaired cardiac function or cardiac repolarization abnormality including but not limited to any one of the following:

History of myocardial infarction (MI), angina pectoris, coronary artery bypass graft (CABG) within 6 months prior to starting study treatment.
Clinically significant cardiac arrhythmias (e.g., ventricular tachycardia), complete left bundle branch block, high-grade AV block (e.g., bifascicular block, Mobitz type II and third degree AV block).
QTcF ≥ 450 ms (male patients), ≥460 ms (female patients) on the average of three serial baseline ECG (using the QTcF formula). If QTcF ≥ 450 ms and electrolytes are not within normal ranges, electrolytes should be corrected and then the patient re-screened for QTcF.
Long QT syndrome, family history of idiopathic sudden death or congenital long QT syndrome, or any of the following:
Risk factors for Torsades de Pointes (TdP) including uncorrected hypokalemia or hypomagnesemia, history of cardiac failure, or history of clinically significant/symptomatic bradycardia.
Concomitant medication(s) with a "Known risk of Torsades de Pointes" per www.crediblemeds.org that cannot be discontinued or replaced 7 days prior to starting study drug by safe alternative medication.
Inability to determine the QTcF interval.
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 (e.g. uncontrolled diabetes, active or uncontrolled infection; uncontrolled arterial or pulmonary hypertension, uncontrolled clinically significant hyperlipidemia).
5- History of significant congenital or acquired bleeding disorder unrelated to cancer.
6- Major surgery within 4 weeks prior to study entry or patients who have not recovered from prior surgery.
7- History of other active malignancy within 3 years prior to study entry with the exception of previous or concomitant basal cell skin cancer and previous carcinoma in situ treated curatively.
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. Testing for Hepatitis B surface antigen (HBs Ag) and Hepatitis B core antibody (HBc Ab/anti HBc) will be performed at screening. If anti-HBc is positive, HBV-DNA evaluation will be carried out at screening. A patient having positive HBV-DNA will not be enrolled in the study. Also, a patient with positive HBsAg will not be enrolled in the study. HCV Ab testing will also be performed at screening. For details on the criteria see Appendix 4.
11- History of Human Immunodeficiency Virus (HIV) unless well-controlled on a stable d dose of anti-retroviral therapy at the time of screening.
Other protocol-defined Inclusion/exclusion criteria will apply

Type of study

Interventional

Type of intervention

Pharmaceutical

Type of intervention: Specify type

N/A

Trial scope

Therapy

Trial scope: Specify scope

N/A

Study design: Allocation

Randomized controlled trial

Study design: Masking

Open (masking not used)

Study design: Control

Active

Study phase

3

Study design: Purpose

Treatment

Study design: Specify purpose

N/A

Study design: Assignment

Parallel

Study design: Specify assignment

N/A

IMP has market authorization

No

IMP has market authorization: Specify

Name of IMP

Asciminib

Year of authorization

Month of authorization

Type of IMP

Immunological

Pharmaceutical class

tyrosine kinase inhibitor (TKI)

Therapeutic indication

Philadelphia Chromosome-Positive Chronic Myeloid Leukemia

Therapeutic benefit

Treatment

Study model
N/A

Study model: Explain model
N/A

Study model: Specify model
N/A

Time perspective
N/A

Time perspective: Explain time perspective
N/A

Time perspective: Specify perspective
N/A

Target follow-up duration

Target follow-up duration: Unit

Number of groups/cohorts

Biospecimen retention
Samples with DNA**

Biospecimen description
Samples will be shipped to ICON Specialty Lab

Target sample size
5

Actual enrollment target size

Date of first enrollment: Type
Anticipated

Date of first enrollment: Date
17/04/2023

Date of study closure: Type
Anticipated

Date of study closure: Date
15/03/2027

Recruitment status
Pending

Recruitment status: Specify

Date of completion

IPD sharing statement plan
Yes

IPD sharing statement description
Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data availability is according to the criteria and process described on www.clinicalstudydatarequest.com

Additional data URL
https://clinicaltrials.gov/ct2/show/record/NCT05456191?term=CABL001J12302&draw=2&rank=1

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinicaltrials.gov	NCT05147220

Sources of Monetary or Material Support

Name
Novartis Pharma AG

Secondary Sponsors

Name
NA

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Public	Ali Bararbachli	Beirut	Lebanon	+961 3 612434	bazarbac@aub.edu.lb	American University of Beirut Medical Center
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Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
American University of Beirut Medical Center	Ali Bazarbachli	Oncology - Hematology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	23/11/2022	Rami Mahfouz	rm11@aub.edu.lb	961 (0) 1 350 000 ext:5445

Countries of Recruitment

Name
France
Czech Republic
Germany
Hungary
Bulgaria
Slovakia
Canada
Greece
Italy
Malaysia
Netherlands
Oman
South Africa
Switzerland
United States of America

Health Conditions or Problems Studied

Condition	Code	Keyword
Philadelphia Chromosome-Positive Chronic Myeloid Leukemia	Chronic myeloid leukaemia (C92.1)	CML

Interventions

Intervention	Description	Keyword
Consenting, IMP administration, Laboratory testing, Imaging	Consenting, IMP administration, Laboratory testing, Imaging	Consenting, IMP administration, Laboratory testing, Imaging

Primary Outcomes

Name	Time Points	Measure
Time to discontinuation of study treatment due to adverse event (TTDAE)	From date of first dose to date of treatment discontinuation due to AE, assessed up to 4.5 years	TTDAE is defined as the time from the date of first dose of study treatment to the date of discontinuation of study treatment due to adverse event (AE)

Key Secondary Outcomes

Name	Time Points	Measure
Percentage of participants with Major Molecular response (MMR) at scheduled data collection time points	Screening, Week 4, Week 12 and thereafter every 12 weeks until End of Treatment (EOT) and EOT, assessed up to approximately 4.5 years	MMR will be assessed using fusion gene of the BCR and ABL genes (BCR-ABL) transcript levels measured by realtime quantitative polymerase chain reaction. The percentage of participants with MMR at each time point will be assessed
Percentage of participants with Major Molecular response (MMR) by scheduled data collection time points	Screening, Week 4, Week 12 and thereafter every 12 weeks until End of Treatment (EOT) and EOT, assessed up to approximately 4.5 years	MMR will be assessed using BCR-ABL transcript levels measured by realtime quantitative polymerase chain reaction. The percentage of participants who meet the criteria for having achieved the endpoint (MMR) at or before the specified visit will be calculated
Percentage of participants with MR4.0 at scheduled data collection time points	Screening, Week 4, Week 12 and thereafter every 12 weeks until End of Treatment (EOT) and EOT, assessed up to approximately 4.5 years	MR4.0 will be assessed using BCR-ABL transcript levels measured by realtime quantitative polymerase chain reaction. The percentage of participants with MR4.0 at each time point will be assessed
Percentage of participants with MR4.0 by scheduled data collection time points	Screening, week 4, week 12 and thereafter every 12 weeks until End of Treatment (EOT) and EOT, assessed up to approximately 4.5 years	MR4.0 will be assessed using BCR-ABL transcript levels measured by realtime quantitative polymerase chain reaction. The percentage of participants who meet the criteria for having achieved the endpoint (MR4.0) at or before the specified visit will be calculated
Percentage of participants with MR4.5 at scheduled data collection time points	Screening, Week 4, Week 12 and thereafter every 12 weeks until End of Treatment (EOT) and EOT, assessed up to approximately 4.5 years	MR4.5 will be assessed using BCR-ABL transcript levels measured by realtime quantitative polymerase chain reaction. The percentage of participants with MR4.5 at each time point will be assessed
Percentage of participants with MR4.5 by scheduled data collection time points	Screening, Week 4, Week 12 and thereafter every 12 weeks until End of Treatment (EOT) and EOT, assessed up to approximately 4.5 years	MR4.5 will be assessed using BCR-ABL transcript levels measured by realtime quantitative polymerase chain reaction. The percentage of participants who meet the criteria for having achieved the endpoint (MR4.5) at or before the specified visit will be calculated
Percentage of participants with Complete Hematological response (CHR) at scheduled data collection time points	Screening, Week 4, Week 12 and thereafter every 12 weeks until End of Treatment (EOT) and EOT, assessed up to approximately 4.5 years	Hematologic response will be assessed by complete blood count and physical examination at each visit. The percentage of participants with CHR at each time point will be assessed

Percentage of participants with Complete Hematological response (CHR) by scheduled data collection time points	Screening, Week 4, Week 12 and thereafter every 12 weeks until End of Treatment (EOT) and EOT, assessed up to approximately 4.5 years	Hematologic response will be assessed by complete blood count and physical examination at each visit. The percentage of participants who meet the criteria for having achieved the endpoint (CHR) at or before the specified visit will be calculated
Percentage of participants with BCR::ABL1 ratio ≤1% by Week 48 and Week 96	Week 48 and Week 96	The percentage of participants who meet the criteria for having achieved BCR::ABL1 ratio ≤1% at or before the specified visit will be calculated
Duration of MMR	From the date of the first documented molecular response at MMR level to the date of first documented loss of MMR or death due to any cause, whichever occurs first, assessed up to approximately 4.5 years	Duration of MMR is defined as the time between the date of the first documented achievement MMR and the earliest date of loss of MMR, treatment failure, progression to AP/BC, or CML-related death
Duration of MR4.0	From the date of the first documented molecular response at MR4 level to the date of first documented loss of the response level or death due to any cause, whichever occurs first, assessed up to approximately 4.5 years	Duration of MR4.0 is defined as the time between the date of the first documented achievement MR4 and the earliest date of loss of MR4, treatment failure, progression to AP/BC, or CML-related death
Duration of MR4.5	From the date of the first documented molecular response at MR4.5 level to the date of first documented loss of the response level or death due to any cause, whichever occurs first, assessed up to approximately 4.5 years	Duration of MR4.5 is defined as the time between the date of the first documented achievement MR4.5 and the earliest date of loss of MR4.5, treatment failure, progression to AP/BC, or CML-related death
Time to first MMR	From the date of randomization to the date of the first MMR, assessed up to approximately 4.5 years	Time to first MMR is defined as the time from the date of randomization to the date of the first documented occurrence of MMR
Time to first MR4.0	From the date of randomization to the date of the first MR4, assessed up to approximately 4.5 years	Time to first MR4.0 is defined as the time from the date of randomization to the date of the first documented occurrence of MR4
Time to first MR4.5	From the date of randomization to the date of the first MR4.5, assessed up to approximately 4.5 years	Time to first MR4.5 is defined as the time from the date of randomization to the date of the first documented occurrence of MR4.5
Time to treatment failure (TTF)	Up to approximately 4.5 years	TTF is defined as the time from date of randomization to the first/earliest documented date of any of the following events: Treatment failure per European leukemia network (ELN) criteria, Confirmed loss of MMR (in 2 consecutive tests) at any time while on study treatment, Discontinuation from study treatment due to any reason
Event free survival (EFS)	Up to approximately 4.5 years	EFS is defined as the time from the date of the first dose of study treatment to the earliest occurrence of treatment failure, confirmed lost of MMR, discontinuation due to AE, progression to AP/BC, and death from any cause
Progression free survival (PFS)	Up to approximately 4.5 years	PFS is defined as the time from the date of randomization to the earliest occurrence of progression to AP/BC or death from any cause
Overall survival (OS)	Up to approximately 4.5 years	OS is defined as the time from the date of randomization to the date of death from any cause
Time to treatment discontinuation (TTD) due to selected reasons	Up to approximately 4.5 years	TTD is the time from the date of first dose of study treatment to the date of discontinuation of study treatment due to lack of efficacy, treatment failure, disease progression, suboptimal response or death

Change from baseline in overall scores and individual scales of the European organization for research and treatment of cancer - quality of life questionnaire (EORTC QLQ-C30)	Baseline, every 4 weeks from Week 4 to Week 12, after Week 24, Week 48, Week 96, EOT and every 4 weeks until 12 weeks after EOT, assessed up to approximately 4.5 years	Change from baseline in Overall Scores and individual domains of the EORTC QLQ-C30. The EORTC QLQ-C30 contains 30 items and is composed of both multi-item scales and single-item measures based on the participant's experience over the past week. These include five functional scales (physical, role, emotional, cognitive and social functioning), three symptom scales (fatigue, nausea/vomiting, and pain), six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea and financial impact) and a global health status/QoL scale
Change from baseline in overall scores and individual scales of the European organization for research and treatment of cancer CML module (EORTC QLQ-CML24)	Baseline, every 4 weeks from Week 4 to Week 12, after Week 24, Week 48, Week 96, EOT and every 4 weeks until 12 weeks after EOT, assessed up to approximately 4,5 years	Change from baseline in Overall Scores and individual domains of the EORTC QLQ-CML24. The EORTC QLQ-CML24 assesses specific concepts relevant to the experience of patients with CML. The QLQ-CML24 has 24 items which assess symptom burden, impact on daily life and on worry/mood, body image problems, and satisfaction with care and with social life based on the participant's experience over the past week

Trial Results

Summary results

Study results globally

Date of posting of results summaries

Date of first journal publication of results

Results URL link

Baseline characteristics

Participant flow

Adverse events

Outcome measures

URL to protocol files