A Phase 3, Multi-center, Open-label, Randomized Study of Oral ABL001 Versus Bosutinib in Patients With Chronic Myelogenous Leukemia in Chronic Phase (CML-CP), Previously Treated With 2 or More Tyrosine Kinase Inhibitors

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Main Information

Primary registry identifying number
LBCTR2019010185

Protocol number
CABL001A2301

MOH registration number
49983/2017

Study registered at the country of origin
Yes

Study registered at the country of origin: Specify

Type of registration
Retrospective

Type of registration: Justify
LCTR was already initiated, original file was previously submitted

Date of registration in national regulatory agency
21/12/2017

Primary sponsor
Novartis Pharma Services Inc.

Primary sponsor: Country of origin
Novartis Pharmaceuticals

Date of registration in primary registry
30/01/2019

Date of registration in national regulatory agency
21/12/2017

Public title
A Phase 3, Multi-center, Open-label, Randomized Study of Oral ABL001 Versus Bosutinib in Patients With Chronic Myelogenous Leukemia in Chronic Phase (CML-CP), Previously Treated With 2 or More Tyrosine Kinase Inhibitors

Acronym
ASCEMBL

Scientific title
A Phase 3, Multi-center, Open-label, Randomized Study of Oral ABL001 Versus Bosutinib in Patients With Chronic Myelogenous Leukemia in Chronic Phase (CML-CP), Previously Treated With 2 or More Tyrosine Kinase Inhibitors

Acronym

Brief summary of the study: English
The purpose of this pivotal study is to compare the efficacy of ABL001 with that of bosutinib in the treatment of patients with CML-CP having previously been treated with a minimum of two prior ATP -binding site TKIs with BCR-ABL ratios ≥ 1% IS at screening.

Brief summary of the study: Arabic
عن طريق الفم مقابل دواء بوسوتينيب لدى المرضى ABL001 مفتوحة اللصاقة، متعددة المراكز حول دواء3دراسة جزافيّة في المرحلة المصابين بسرطان الدم النقوي المزمن في المرحلة المزمنة، المعالجين سابقًا بمثبّطيْن أو أكثر لكيناز التيروزين

Health conditions/problem studied: Specify
Chronic Myelogenous Leukemia

Interventions: Specify
ABL001, Bosutinib

Key inclusion and exclusion criteria: Inclusion criteria

Male or female patients with a diagnosis of CML-CP ≥ 18 years of age

Patients must meet all of the following laboratory values at the screening visit:
•< 15% blasts in peripheral blood and bone marrow
•< 30% blasts plus promyelocytes in peripheral blood and bone marrow
•< 20% basophils in the peripheral blood
•≥ 50 x 109/L (≥ 50,000/mm3) platelets
•Transient prior therapy related thrombocytopenia (< 50,000/mm3 for ≤ 30 days prior to screening) is acceptable
•No evidence of extramedullary leukemic involvement, with the exception of hepatosplenomegaly

BCR-ABL1 ratio ≥ 1% IS according to central laboratory at the screening examination

Prior treatment with a minimum of 2 prior ATP-binding site TKIs (i.e. imatinib, nilotinib, dasatinib, radotinib or ponatinib)

Failure (adapted from the 2013 ELN Guidelines Bacarrani 2013) or intolerance to the most recent TKI therapy at the time of screening
•Failure is defined for CML-CP patients (CP at the time of initiation of last therapy) as follows. Patients must meet at least 1 of the following criteria.
•Three months after the initiation of therapy: No CHR or > 95% Ph+ metaphases
•Six months after the initiation of therapy: BCR-ABL1 ratio > 10% IS and/or > 65% Ph+ metaphases
•Twelve months after initiation of therapy: BCR-ABL1 ratio > 10% IS and/or > 35% Ph+ metaphases
•At any time after the initiation of therapy, loss of CHR, CCyR or PCyR
•At any time after the initiation of therapy, the development of new BCR-ABL1 mutations which potentially cause resistance to study treatment
•At any time after the initiation of therapy, confirmed loss of MMR in 2 consecutive tests, of which one must have a BCR-ABL1 ratio ≥ 1% IS
•At any time after the initiation of therapy, new clonal chromosome abnormalities in Ph+ cells: CCA/Ph+
•Intolerance is defined as:
•Non-hematologic intolerance: Patients with grade 3 or 4 toxicity while on therapy, or with persistent grade 2 toxicity, unresponsive to optimal management, including dose adjustments (unless dose reduction is not considered in the best interest of the patient if response is already suboptimal)
•Hematologic intolerance: Patients with grade 3 or 4 toxicity (absolute neutrophil count [ANC] or platelets) while on therapy that is recurrent after dose reduction to the lowest doses recommended by manufacturer

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

Known presence of the T315I or V299L mutation at any time 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, including any of the following:
• History within 6 months prior to starting study treatment of myocardial infarction (MI), angina pectoris, coronary artery bypass graft (CABG)
• Clinically significant cardiac arrhythmias
• QTcF at screening ≥450 msec (male patients), ≥460 msec (female patients)
• 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)
• Concomitant medication(s) with a known risk of Torsades de Pointes per www.qtdrugs.org that cannot be discontinued or replaced 7 days prior to starting study drug by safe alternative medication.
• Inability to determine the QTcF interval
• Severe and/or uncontrolled concurrent medical disease
• History of acute pancreatitis within 1 year of study entry or past medical history of chronic pancreatitis
• History of acute or chronic liver disease
• Treatment with medications that meet one of the following criteria and that cannot be discontinued at least one week prior to the start of treatment with study treatment
• Moderate or strong inducers of CYP3A
• Moderate or strong inhibitors of CYP3A and/or P-gp
• Women of child-bearing potential, unless they are using highly effective methods of contraception during dosing and for 3 days after last dose of ABL001.
• Sexually active males unless they use a condom during intercourse while taking the drug during treatment and for 3 days after stopping treatment and should not father a child in this period. A condom is required to be used also by vasectomized men as well as during intercourse with a male partner in order to prevent delivery of the drug via semen.

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
Other

Study design: Specify assignment
2:1

IMP has market authorization
No

IMP has market authorization: Specify

Name of IMP
ABL001

Year of authorization

Month of authorization

Type of IMP
Cell therapy

Pharmaceutical class
orally bioavailable specific BCR-ABL inhibitor with a novel mechanism of action.

Therapeutic indication
patients with Chronic Myelogenous Leukemia-CP who had prior treatment with two or more ATP binding site TKIs

Therapeutic benefit
increase OS & PFS

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

Biospecimen description

Samples without DNA

Bone marrow aspirate samples, Hematology , chemistry , coagulation, hepatitis , Liver function tests , are sent to Covance central laboratory, Navigate biopharma, molecular MD and Histogene X .

Target sample size

5

Actual enrollment target size

1

Date of first enrollment: Type

Actual

Date of first enrollment: Date

05/09/2018

Date of study closure: Type

Actual

Date of study closure: Date

21/12/2022

Recruitment status

Recruiting

Recruitment status: Specify

Date of completion

29/02/2020

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.

Additional data URL

https://clinicaltrials.gov/ct2/show/record/NCT03106779?id=cabl001a2301&rank=1

Admin comments

Trial status

Approved

Secondary Identifying Numbers

Full name of issuing authority	Secondary identifying number
Clinical Trials.Gov	NCT03106779

Sources of Monetary or Material Support

Name
Novartis Pharma Services Inc.

Secondary Sponsors

Name
NA

Contact for Public/Scientific Queries

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Centers/Hospitals Involved in the Study

Center/Hospital name	Name of principles investigator	Principles investigator speciality	Ethical approval
Bellevue Medical Center	Dr Dany Abi Gerges	Hematology Oncology	Approved
American University of Beirut Medical Center	Dr. Ali Bazarbachi	Hematology Oncology	Approved
Hotel Dieu De France	Dr Joseph Kattan	Hematology Oncology	Approved

Ethics Review

Ethics approval obtained	Approval date	Contact name	Contact email	Contact phone
American University of Beirut Medical Center	05/06/2018	Fuad Ziyadeh	fz05@aub.edu.lb	+961 (0) 1 350 000 ext:5445
Hotel Dieu de France	02/10/2017	Nancy Alam	nancy.alam@usj.edu.lb	+961 1421000 ext 2335
Bellevue Medical Center	23/11/2017	Ghassan Maalouf	gmaalouf@bmc.com.lb	+961 1 682666 ext 7600

Countries of Recruitment

Name
Lebanon
Argentina
Australia
Belgium
Bulgaria
Canada
Czech Republic
France
Germany
Hungary
Italy
Japan
Republic of Korea
Netherlands
Turkey
United States of America
Saudi Arabia
United Kingdom

Health Conditions or Problems Studied

Condition	Code	Keyword
Chronic Myelogenous Leukemia	Leukaemia, unspecified (C95.9)	CML

Interventions

Intervention	Description	Keyword
Physical examination, Vital Sign, Height and weight, ECOG performance status, Laboratory chemistry and hematology, Serology, Electrocardiogram (ECG), Echocardiogram, Pulmonary function tests, PK sampling (full/sparse), Bone Marrow Biopsy, Patient Report Outcomes (MDASI-CML, PGIC, WPAI, EQ--5D-5L, resource	ICF, Lab tests, physical examination, ECG	Lab, ECG, ICF, BMA

Primary Outcomes

Name	Time Points	Measure
Major Molecular Response (MMR) rate	24 weeks	24 wks

Key Secondary Outcomes

Name	Time Points	Measure
Major Molecular Response (MMR) rate	96 weeks after the last patient received the first study dose	96 weeks after first dose
Complete Cytogenetic response rate	24,48,96 weeks	24,48,96 weeks

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