An Open-label, Phase 2 Study of ACP-196 in Subjects with Mantle Cell Lymphoma

Published: 13-04-2015
Last updated: 18-07-2024

The purpose of this study is to evaluate the efficacy, activity, safety, pharmacodynamics and pharmacokinetics of ACP-196 in treating subjects with Mantle Cell Lymphoma (MCL)

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas non-Hodgkin's B-cell
Study type	Interventional

Summary

ID

NL-OMON53032

Source
ToetsingOnline

Brief title
ACE-LY-004

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
Mantle Cell Lymphoma, MCL

Research involving
Human

Sponsors and support

Primary sponsor: ACERTA PHARMA B.V.
Source(s) of monetary or material Support: Acerta Pharma BV

Intervention

Keyword: acalabrutinib, ACP-196, Mantle Cell Lymphoma

Outcome measures

Primary outcome

To determine the activity of acalabrutinib in subjects with relapsed/reractory (R/R) MCL as measured primarily by response rate. In addition, activity of acalabrutinib will be assessed by duration of response, progression-free survival and overall survival.

Secondary outcome

* To characterize the safety profile of acalabrutinib

* To characterize the pharmacokinetic (PK) profile of acalabrutinib

* To evaluate the PD effects of acalabrutinib

Study description

Background summary

Bruton tyrosine kinase (Brk) is an enzyme that is expressed among cells of hematopoietic origin, including B-cells. Btk regulates multiple cellular processes. Investigation from first generation Btk inhibitors in subjects with Waldenströms disease showed rapid reduction in IgM and improved hematocrit. Acerta Pharma, has optimized novel Btk inhibitors and in nonclinical studies ACP-196 showed good results in activity and safety.

Study objective

The purpose of this study is to evaluate the efficacy, activity, safety, pharmacodynamics and pharmacokinetics of ACP-196 in treating subjects with Mantle Cell Lymphoma (MCL)

Study design

This study is a phase 2, multicenter, open-label clinical trial evaluating the safety and efficacy of ACP-196 in subjects (n=117) with previously treated MCL. Subjects will be enrolled into 2 cohorts based on prior Bortezomib exposure.

Intervention

Protocol treatment: 100mg ACP-196 twice daily

Study burden and risks

not applicable

Contacts

Public
ACERTA PHARMA B.V.

Kloosterstraat 9
Oss 5349 AB
NL
Scientific
ACERTA PHARMA B.V.

Kloosterstraat 9
Oss 5349 AB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Men and women >= 18 years of age.
• Pathologically confirmed MCL, with documentation of monoclonal B cells that have a chromosome translocation

t(11;14)(q13;q32) and/or overexpress cyclin D1.
• Disease has relapsed after or been refractory to >= 1 prior therapy for MCL and now requires further treatment.
• Documented failure to achieve at least partial response (PR) with, or documented disease progression after, the most recent treatment regimen.
• Presence of radiographically measurable lymphadenopathy or extranodal lymphoid malignancy (defined as the presence of >= 1 lesion that measures >= 2.0 cm in the longest dimension and >= 1.0 cm in the longest perpendicular dimension as assessed by computed tomography [CT] scan).
• At least 1, but no more than 5, prior treatment regimens for MCL (Note: Subjects having received >= 2 cycles of prior treatment with bortezomib or any other commercially available proteasome inhibitor, either as a single agent or as part of a combination therapy regimen, will be considered to be proteasome inhibotor-exposed.)
• Eastern Cooperative Oncology Group (ECOG) performance status of <= 2.
• Agreement to use acceptable forms of contraception during the study and for 30 days after the last dose of study drug if sexually active and able to bear or beget children.
• Agreement to refrain from sperm donation during the study and for 30 days after the last dose of study drug.
• Willing and able to participate in all required evaluations and procedures in this study protocol including swallowing capsules without difficulty.
• Ability to understand the purpose and risks of the study and provide signed and dated informed consent and authorization to use protected health information (in accordance with national and local subject privacy regulations).

Exclusion criteria

• Prior malignancy, except for adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, or other cancer from which the subject has been disease free for >= 2 years or which will not limit survival to < 2 years. Note: these cases must be discussed with the Acerta Pharma medical monitor.
• A life-threatening illness, medical condition or organ system dysfunction which, in the investigator*s opinion, could compromise the subject*s safety, interfere with the absorption or metabolism of ACP-196, or put the study outcomes at undue risk.

• Significant cardiovascular disease such as uncontrolled or symptomatic arrhythmias, congestive heart failure, or myocardial infarction within 6 months of screening, or any Class 3 or 4 cardiac disease as defined by the New York Heart Association Functional Classification.
• Malabsorption syndrome, disease significantly affecting gastrointestinal function, or resection of the stomach or small bowel, gastric bypass, symptomatic inflammatory bowel disease, or partial or complete bowel obstruction.
• Any immunotherapy within 4 weeks of first dose of study drug.
• The time from the last dose of the most recent chemotherapy or experimental therapy to the first dose of study drug is < 5 times the half-life of the previously administered agent(s).
• Prior exposure to a BCR inhibitor (eg, Btk inhibitors or phosphoinositide-3 kinase [PI3K] inhibitors).
• Ongoing immunosuppressive therapy, including systemic or enteric corticosteroids for treatment of MCL or other conditions. Note: Subjects may use topical or inhaled corticosteroids or low-dose steroids (<= 10 mg of prednisone or equivalent per day) as therapy for comorbid conditions. During study participation, subjects may also receive systemic or enteric corticosteroids as needed for treatment-emergent comorbid conditions.
• Grade >= 2 toxicity (other than alopecia) continuing from prior anticancer therapy including radiation.
• Known history of human immunodeficiency virus (HIV) or active infection with hepatitis C virus (HCV) or hepatitis B virus (HBV) or any uncontrolled active systemic infection.
• Major surgery within 4 weeks before first dose of ACP-196.
• Uncontrolled autoimmune hemolytic anemia or idiopathic thrombocytopenia purpura.
• History of stroke or intracranial hemorrhage within 6 months before the first dose of ACP-196.
• Requires anticoagulation with warfarin or a vitamin K antagonist.
• Absolute neutrophil count (ANC) < 0.5 x 109/L or platelet count < 25 x 109/L unless due to disease involvement in the bone marrow.
• Creatinine > 2.5 x institutional upper limit of normal (ULN); total bilirubin > 2.5 x ULN (unless due to Gilbert*s disease); and aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 2.5 x ULN unless disease related.
• Significant screening electrocardiogram (ECG) abnormalities including atrial fibrillation, 2nd-degree AV block type II, 3rddegree AV block, Grade >= 2 bradycardia, or QTc > 480 msec.
• Breastfeeding or pregnant.

• Concurrent participation in another therapeutic clinical trial.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-04-2015
Enrollment:	17
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ACP-196
Generic name:	ACP-196

Ethics review

Approved WMO Date:	13-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	08-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-06-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	29-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-05-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-06-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	12-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	19-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-12-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	07-02-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	EUCTR2014-002117-28-NL
CCMO	NL52044.018.15