A Randomized, Double-blind, Placebo-controlled Phase 3 Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor, PCI-32765 (Ibrutinib), in Combination with Bendamustine and Rituximab (BR) in Subjects With Newly Diagnosed Mantle Cell Lymphoma

Published: 19-03-2013
Last updated: 23-04-2024

Primary ObjectiveThe primary objective of this study is to evaluate whether the addition of ibrutinib to bendamustine and rituximab will result in prolongation of PFS in subjects with newly diagnosed MCL who are 65 years of age or older.Secondary...

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

Summary

ID

NL-OMON52974

Source
ToetsingOnline

Brief title
PCI-32765MCL3002 or SHINE study.

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
Mantel cell lymphome or Non-Hodgekin lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Farmaceutisch bedrijf: Janssen-Cilag International NV

Intervention

Keyword: Front Line MCL treatment, Ibrutinib, Mantel Cell Lymphoma

Outcome measures

Primary outcome

Primary Objective

The primary objective of this study is to evaluate whether the addition of

ibrutinib to bendamustine and rituximab will result in prolongation of PFS in

subjects with newly diagnosed MCL who are 65 years of age or older.

Secondary outcome

The secondary objectives are:

• To evaluate overall survival

• To evaluate the CR rate and overall response rate (CR+PR)

• To evaluate patient-reported lymphoma symptoms and concerns as measured by

the Lym subscale of the Functional Assessment of Cancer Therapy-Lymphoma

(FACT-Lym)

• To evaluate the minimal residual disease (MRD) negative rate

• To evaluate duration of response

• To evaluate time-to-next treatment (TTNT)

• To evaluate the safety of ibrutinib when combined with BR

• To characterize the pharmacokinetics of ibrutinib and explore the potential

relationships between ibrutinib metrics of exposure with relevant clinical,

pharmacodynamic, or biomarker information

Study description

Background summary

Hypothesis
The primary hypothesis of the study is that ibrutinib in combination with BR compared with BR alone will prolong PFS in subjects with newly diagnosed MCL who are 65 years of age or older.

Study objective

Primary Objective
The primary objective of this study is to evaluate whether the addition of ibrutinib to bendamustine and rituximab will result in prolongation of PFS in subjects with newly diagnosed MCL who are 65 years of age or older.
Secondary Objectives
The secondary objectives are:
• To evaluate overall survival
• To evaluate the CR rate and overall response rate (CR+PR)
• To evaluate patient-reported lymphoma symptoms and concerns as measured by the Lym subscale of the Functional Assessment of Cancer Therapy-Lymphoma (FACT-Lym)
• To evaluate the minimal residual disease (MRD) negative rate
• To evaluate duration of response
• To evaluate time-to-next treatment (TTNT)
• To evaluate the safety of ibrutinib when combined with BR
• To characterize the pharmacokinetics of ibrutinib and explore the potential relationships between ibrutinib metrics of exposure with relevant clinical, pharmacodynamic, or biomarker information
Exploratory Objectives
The exploratory objectives are:
• To evaluate patient-reported outcomes (PRO) related to well-being and general health status utilizing the FACT-Lym and EuroQol (EQ-5D-5L)
• To explore biomarkers identified from other studies of ibrutinib in samples collected for MRD assessments

Study design

A Randomized, Double-blind, Placebo-controlled Phase 3 Study

Intervention

One group of patients will receive daily capsules of Ibrutinib, while the other group of patients will receive daily placebo capsules.

Study burden and risks

It is possible that treatment with ibrutinib may increase the risk of bruising or bleeding, particularly in subjects receiving antiplatelet agents or anticoagulants. Subjects receiving antiplatelet agents in conjunction with ibrutinib should be observed closely for any signs of bleeding and ibrutinib should be held in the event of major bleeding events defined as adverse event of special interest. For complete overview: see patienmt information leaflet.

Contacts

Public
Janssen-Cilag

Graaf Engelbertlaan 75
Breda 4837 DS
NL
Scientific
Janssen-Cilag

Graaf Engelbertlaan 75
Breda 4837 DS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Elderly (65 years and older)

Inclusion criteria

- Diagnosis of mantle cell lymphoma (MCL) reviewed and approved by central laboratory: diagnosis must include morphology and expression of either cyclin D1 in association with other relevant markers (eg, CD19, CD20, PAX5) and CD5 or evidence of t(11;14) as assessed by cytogenetics, fluorescent in situ hybridization (FISH), or polymerase chain reaction (PCR), - Clinical Stage II, III, or IV by Ann Arbor Classification, - At least 1 measurable site of disease according to Revised Response Criteria for Malignant Lymphoma, - No prior therapies for MCL, - Eastern Cooperative Oncology Group (ECOG) performance status grade 0 or 1, - Hematology and biochemical laboratory values within protocol-defined limits, - Agrees to protocol-defined use of effective contraception, - Negative blood or urine pregnancy test at screening

Exclusion criteria

- Major surgery within 4 weeks of random assignment, - Known central nervous system lymphoma, - Diagnosed or treated for malignancy other than MCL, except: malignancy treated with curative intent and with no known active disease present for >=3 years before random assignment; adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease; adequately treated cervical carcinoma in situ without evidence of disease, - Patients for whom the goal of therapy is tumor debulking prior to stem cell transplant, - History of stroke or intracranial hemorrhage within 6 months prior to random assignment, - Requires anticoagulation with warfarin or equivalent vitamin K antagonists, - Requires treatment with strong CYP3A inhibitors, - Clinically significant cardiovascular disease such as uncontrolled or symptomatic arrhythmias, congestive heart failure, or myocardial infarction within 6 months of Screening, or any Class 3 (moderate) or Class 4 (severe) cardiac disease as defined by the New York Heart Association Functional Classification, - Vaccinated with live, attenuated vaccines within 4 weeks of random assignment, - Known history of human immunodeficiency virus (HIV) or active hepatitis C virus or active hepatitis B virus infection or any uncontrolled active systemic infection requiring intravenous antibiotics, - Any life-threatening illness, medical condition, or organ system dysfunction which, in the investigator*s opinion, could compromise the patient*s safety, interfere with the absorption or metabolism of ibrutinib capsules, or put the study outcomes at undue risk

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-10-2013
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ibrutinib
Generic name:	Ibrutinib
Product type:	Medicine
Brand name:	Levact
Generic name:	bendamustin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	MabThera
Generic name:	rituximab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	19-03-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	02-08-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	17-10-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	30-10-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	08-11-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	17-12-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	13-03-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	17-03-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	24-03-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	14-04-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	14-11-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	20-01-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO
Date: 06-02-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 11-03-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 22-04-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 07-05-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 10-07-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 11-08-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO

Date:	19-10-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	24-11-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	03-12-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	17-12-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	06-06-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	28-06-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO
Date: 12-04-2017

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 16-06-2017

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 04-08-2017

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 01-12-2017

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 11-04-2018

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO
Date: 18-06-2018

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO

Date:	12-07-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	23-08-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	21-12-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	21-03-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	08-05-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	20-06-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	18-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	11-11-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	24-02-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	04-03-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	26-05-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	02-06-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	07-09-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	03-11-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	31-12-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	12-02-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	09-04-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	02-06-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	17-03-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	11-04-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	02-09-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	24-11-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	11-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	03-03-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.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	EUCTR2012-004056-11-NL
CCMO	NL43318.058.13