A Randomized, Double-blind, Placebo-controlled Phase 3 Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor, PCI-32765 (Ibrutinib), in Combination with Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP) in Subjects With Newly Diagnosed Non-Germinal Center B-Cell Subtype of Diffuse Large B-Cell Lymphoma

Published: 27-09-2013
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OBJECTIVES of the Study:Primary ObjectiveTo evaluate if the addition of ibrutinib to R-CHOP prolongs event-free survival (EFS) compared withR-CHOP alone in subjects with newly diagnosed non-GCB DLBCL.Secondary ObjectivesTo compare ibrutinib in...

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

Summary

ID

NL-OMON47458

Source
ToetsingOnline

Brief title
PCI-32765DBL3001 or PHOENIX study

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
Non-GCB subtype of Diffuse Large B-Cell Lymphoma or Non-Hodgkin's lymphoma (NHL)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Diffuse Large B-Cell Lymphoma, Ibrutinib, Newly Diagnosed Non-Germinal Center B-Cell

Outcome measures

Primary outcome

Primary Objective

To evaluate if the addition of ibrutinib to R-CHOP prolongs event-free survival

(EFS) compared with

R-CHOP alone in subjects with newly diagnosed non-GCB DLBCL.

Secondary outcome

Secondary Objectives

To compare ibrutinib in combination with R-CHOP versus R-CHOP alone with regard

to progression-free

survival (PFS), overall survival, complete response [CR] rate, patient-reported

lymphoma symptoms and

concerns, treatment benefit of ibrutinib in subjects with the ABC subtype based

on gene expression

profiling (GEP), and safety. Additional secondary objectives are to

characterize the pharmacokinetics of

ibrutinib and explore the potential relationships between ibrutinib metrics of

exposure with relevant

clinical or biomarker information.

Study description

Background summary

Hypothesis:
Ibrutinib in combination with R-CHOP will prolong EFS in subjects with newly diagnosed
non-GCB DLBCL compared with R-CHOP alone.

Study objective

OBJECTIVES of the Study:

Primary Objective
To evaluate if the addition of ibrutinib to R-CHOP prolongs event-free survival (EFS) compared with
R-CHOP alone in subjects with newly diagnosed non-GCB DLBCL.

Secondary Objectives
To compare ibrutinib in combination with R-CHOP versus R-CHOP alone with regard to progression-free
survival (PFS), overall survival, complete response [CR] rate, patient-reported lymphoma symptoms and
concerns, treatment benefit of ibrutinib in subjects with the ABC subtype based on gene expression
profiling (GEP), and safety. Additional secondary objectives are to characterize the pharmacokinetics of
ibrutinib and explore the potential relationships between ibrutinib metrics of exposure with relevant
clinical or biomarker information.

Study design

A Randomized, Double-blind, Placebo-controlled Phase 3 Study of the Bruton's

Tyrosine Kinase (BTK)
Inhibitor, PCI-32765 (Ibrutinib), in Combination with Rituximab, Cyclophosphamide, Doxorubicin,
Vincristine, and Prednisone (R-CHOP) in Subjects With Newly Diagnosed Non-Germinal Center B-Cell
Subtype of Diffuse Large B-Cell Lymphoma

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

Hemorrhagic Adverse Events:
Ibrutinib is known to affect platelet function in vitro; the clinical significance of this effect is
unknown. There have been reports of subjects having hemorrhagic events, including subdural
hematomas, while on treatment with study drug. It is difficult to comprehensively evaluate these
subjects as to whether or not the clinical presentation is attributable to ibrutinib. Other risk
factors for subdural hematoma may include age, history of fall, and concomitant use of warfarin.

Contacts

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Janssen-Cilag

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- No prior treatment for diffuse B-cell lymphoma (DLBCL) ;- Histologically-confirmed nongerminal center B-cell subtype DLBCL ;- Stage II (not candidates for local x-ray therapy), III, or IV disease by the Ann Arbor Classification ;- At least 1 measurable site of disease according to Revised Response Criteria for Malignant Lymphoma ;- Revised International Prognostic Index score of ><=1 ;- Eastern Cooperative Oncology Group performance status grade of 0, 1, or 2 ;- Hematology and biochemical laboratory values within protocol- efined parameters prior to random assignment and at baseline ;- Left ventricular ejection fraction within institutional normal limits, as determined by echocardiography or multiple uptake gated acquisition (MUGA) scan ;- Agrees to protocol-defined use of effective contraception (for women, these restrictions apply for 12 months after the last dose of rituximab or 1 month after the last dose of study drug, whichever is later; for men, these restrictions apply for 12 months;after the last dose of rituximab or 3 months after the last dose of study drug, whichever is later) ;- Men must agree to not donate sperm during and after the study for 12 months after the last dose of rituximab or 3 months after the last dose of study drug, whichever is later ;- Women of childbearing potential must have a negative serum or urine pregnancy test at screening

Exclusion criteria

- Major surgery within 4 weeks of random assignment ;- Known central nervous system or primary mediastinal lymphoma ;- Prior history of indolent lymphoma ;- Diagnosed or treated for malignancy other than DLBCL, 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 carcinoma in situ without evidence of disease ;- 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 ;- Prior anthracycline use >=150 mg/m2 ;- 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 ;- Known history of human immunodeficiency virus or active hepatitis C virus or active hepatitis B virus infection or any uncontrolled active systemic infection requiring intravenous antibiotics ;- Women who are pregnant or breastfeeding ;- 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):	05-06-2014
Enrollment:	22
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ibrutinib
Generic name:	N/A

Ethics review

Approved WMO Date:	27-09-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-12-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-12-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-06-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-12-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-02-2015

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-11-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-02-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-11-2017

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-05-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2013-000959-40-NL
ClinicalTrials.gov	NCT01855750
CCMO	NL45535.018.13