A Multicenter, Randomized, Double-blind, Placebo-controlled Phase 3 Study of the Bruton*s Tyrosine Kinase (BTK) Inhibitor, Ibrutinib, in Combination with Rituximab versus Placebo in Combination with Rituximab in Treatment Naïve Subjects with Follicular Lymphoma

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This study has been transitioned to CTIS with ID 2023-507271-21-00 check the CTIS register for the current data. Analysis Study:To evaluate whether the addition of ibrutinib to rituximab will result in prolongation of progression-free survival (PFS...

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

Summary

ID

NL-OMON54492

Source
ToetsingOnline

Brief title
PCYC-1141-CA PERSPECTIVE

Condition

- Lymphomas non-Hodgkin's B-cell

Synonym
Follicular lymphoma, lymphoma

Research involving
Human

Sponsors and support

Primary sponsor: Pharmacyclics
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Follicular lymphoma, Ibrutinib, Progression free survival

Outcome measures

Primary outcome

Progression-free survival (PFS)

Secondary outcome

• Overall response rate (ORR)

• Overall Survival (OS)

• Infusion-related reaction rate (Arm A vs. Arm B)

• Frequency, severity, seriousness, and relatedness of adverse events (AEs)

• Duration of response (DOR) as assessed by investigator

Study description

Background summary

Pharmacyclics LLC (Sponsor) is studying ibrutinib in combination with rituximab in participants with follicular lymphoma. Ibrutinib (IMBRUVICA®) has been approved in many regions, including the United States (US) for indications of cancer other than follicular lymphoma (FL), which is your type of cancer. Rituximab (Rituxan®) is approved by the US FDA for the treatment of follicular lymphoma and other diagnoses. However, the two study medications ibrutinib and rituximab have not been approved for use in combination to treat follicular lymphoma. Please read carefully the sections on risks and benefits of the study later in this consent form.
Ibrutinib is a type of drug called a *kinase inhibitor*. *Kinases* are proteins

inside cells that help cells live and grow. The specific kinase inhibited or *blocked* by ibrutinib is believed to help blood cancer cells live and grow. By inhibiting the activity of this specific kinase, it is possible that the ibrutinib may kill the cancer cells or stop them from growing.
Rituximab is a type of drug called a *monoclonal antibody*. It is believed that rituximab works by using the body*s immune system to attack the cancer. Rituximab may work by attaching to the cancer cells (lymphocytes) and causing the cells to die or by signaling your immune system to destroy the cancer cells.

Study objective

This study has been transitioned to CTIS with ID 2023-507271-21-00 check the CTIS register for the current data.

Analysis Study:
To evaluate whether the addition of ibrutinib to rituximab will result in prolongation of progression-free survival (PFS) when compared with rituximab alone in treatment naïve subjects with follicular lymphoma.

Study design

This is a randomized, double-blind, placebo-controlled Phase 3 study designed to assess the efficacy and safety of ibrutinib in combination with rituximab compared to placebo in combination with rituximab in treatment naïve subjects with follicular lymphoma.

Intervention

Subjects randomized to the investigational arm (Arm A) will receive ibrutinib 560 mg PO daily continuously in combination with rituximab 375 mg/m2 IV once weekly for the first 4 weeks of study treatment (Cycle 1: Days 1, 8, 15, and 22) and as maintenance therapy beginning Cycle 3, Day 1 given as a single dose of 375 mg/m2 IV every 8 weeks for up to 12 additional doses (approximately 2 years). In the control arm (Arm B) subjects will receive placebo PO daily continuously in combination with rituximab 375 mg/m2 IV once weekly for the first 4 weeks of study treatment (Cycle 1: Days 1, 8, 15, and 22), and as maintenance therapy beginning with Cycle 3, Day 1 given as a single dose of 375 mg/m2 IV every 8 weeks up to 12 additional doses (approximately 2 years).

Administration of study treatment will continue until disease progression or unacceptable toxicity. Subjects who discontinue study treatment in the absence of disease progression will continue to be followed for response. Subjects who discontinue study treatment due to any reason and have not withdrawn consent for follow up, will be followed for overall survival. Subsequent anticancer therapies, best response to therapy, and information about other malignancies

will be collected.

Study burden and risks

Given the toxicity seen with standard combination treatment regimens in patients who are elderly or infirm, an initial chemotherapy- free regimen such as rituximab and ibrutinib may be an attractive treatment option if found to be well tolerated and to have significant anti-tumor activity. Data from clinical trials in high-risk
CLL and MCL have shown that the combination of ibrutinib and rituximab has a favorable
safety profile with enhanced efficacy.

Contacts

Public
Pharmacyclics

Gateway Boulevard 1000
South San Francisco CA 94080
US
Scientific
Pharmacyclics

Gateway Boulevard 1000
South San Francisco CA 94080
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Histologically confirmed diagnosis of follicular lymphoma CD20+ (Grade 1, 2 or 3a) Ann Arbor Stage II, III or IV disease.
* Measurable disease
* Subjects 70 years of age or older; OR subjects 60-69 years of age who have one or more comorbidities.
* Meets one or more Groupe d'Etude des Lymphomes Folliculaire (GELF) criteria.
* Adequate hematologic function within protocol-defined parameters.
* Adequate hepatic and renal function within protocol-defined parameters.
* ECOG performance status score of 0-2.

Exclusion criteria

* Transformed lymphoma
* Prior treatment for follicular lymphoma
* Central nervous system lymphoma or leptomeningeal disease
* Currently active, clinically significant cardiovascular disease

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):	07-08-2018
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Imbruvica
Generic name:	ibrutinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-06-2017
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-08-2017
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-02-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	18-05-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-05-2018
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	05-03-2019
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-03-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-04-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-05-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	29-10-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	31-10-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-04-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-07-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-11-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-12-2020
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-06-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-06-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-04-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-04-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-12-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-05-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-05-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-09-2023
Application type:	Amendment

Review commission: METC Brabant (Tilburg)

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
EU-CTR	CTIS2023-507271-21-00
EudraCT	EUCTR2016-003202-14-NL
ClinicalTrials.gov	NCT02947347
CCMO	NL61775.028.17