A Prospective, Open-Label, Single-Arm, Phase 2, Multicenter Study Evaluating the Efficacy of Venetoclax Plus Ibrutinib in Subjects with T-Cell Prolymphocytic Leukemia

Published: 10-09-2019
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The primary objective is to demonstrate the efficacy in subjects with R/R T-PLL treated with venetoclax plus ibrutinib.

Ethical review	Approved WMO
Status	Completed
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON50080

Source
ToetsingOnline

Brief title
M18-803

Condition

- Leukaemias

Synonym
Rare & aggressive T-lymphoid malignancy, T-Cell Prolymphocytic Leukemia

Research involving
Human

Sponsors and support

Primary sponsor: AbbVie Deutschland GmbH & Co. KG
Source(s) of monetary or material Support: AbbVie

Intervention

Keyword: efficacy, T-PLL

Outcome measures

Primary outcome

The primary endpoint is the ORR which is defined as the proportion of subjects

achieving CR, CRi, or PR as their best response (per investigator assessment)

in R/R subjects.

Secondary outcome

Key secondary endpoints are as follows:

• PFS

• Duration of response

• Time-to-progression

• Overall survival

• Number of eligible subjects reaching autologous or allogeneic transplant

• Event-free survival

• Disease Control rate

Study description

Background summary

T-cell prolymphocytic leukemia (T-PLL) is a rare and aggressive T-lymphoid malignancy characterized by proliferation of post-thymic prolymphocytes, usually refractory to current treatment strategies or complicated by relapse

and associated with short overall survival. Thus far, alemtuzumab remains the most effective treatment option in patients with T-PLL; however, despite relatively high response rates (50% to 90%), all patients eventually relapse with a median progression-free survival (PFS) of less than 12 months. Allogeneic stem cell transplantation is considered a treatment goal for eligible patients since long survival durations have been observed.

In 2 recent ex vivo drug screening studies, consistent activities of B-cell lymphoma (BCL)-2 inhibition in T-PLL were observed. Venetoclax is a potent, selective, and orally bioavailable small molecule inhibitor of BCL-2. However, potential mechanisms of resistance may develop through BCL-2 and BCL-XL induction. Ex vivo drug combination studies in primary T-PLL subject samples demonstrated that T-PLL cell-specific synergism of venetoclax was highest with ibrutinib.

Study objective

The primary objective is to demonstrate the efficacy in subjects with R/R T-PLL treated with venetoclax plus ibrutinib.

Study design

This study is an open-label, single-arm, Phase 2, multicenter study evaluating the efficacy of venetoclax plus ibrutinib.

Intervention

All subjects will receive venetoclax orally once daily (QD) plus Ibrutinib dosed orally QD.

Study burden and risks

Effective treatment options remain dismal for patients with R/R T-PLL as well as for treatment-naïve patients who have no access or are ineligible to treatment with alemtuzumab. The recently reported ex vivo data and very limited subject data provide rationale for a clinical study with the combination of venetoclax and ibrutinib. Clinical data from this same combination target dose regimen has also recently been presented for a different indication (i.e., CLL [CAPTIVATE study]). Early data from 163 subjects show a spectrum of adverse events (AEs) consistent with the historic safety profile of single-agent ibrutinib and single-agent venetoclax with no new safety signals and promising activity (77% undetectable minimal residual disease in peripheral blood after 6 months of therapy).

Subjects will be visiting the hospital more frequently and a 7-day hospitalization is required during ramp-up of venetoclax. There will be more

frequent blood draws. Subjects will undergo CT-scans and a bone marrow biopsy if a CT-scan indicates a CR/CRi. Subjects will be tested for hepatitis B, C, HIV, pregnancy, and TLS and are asked to complete a dosing diary.

Contacts

Public
AbbVie Deutschland GmbH & Co. KG

Knollstrasse -
Ludwigshafen 67061
DE
Scientific
AbbVie Deutschland GmbH & Co. KG

Knollstrasse -
Ludwigshafen 67061
DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male or female subjects, at least 18 years old, with a diagnosis of R/R T-PLL that requires treatment and suitable for oral administration of study drugs.
- Subjects should meet the following disease activity criteria: an Eastern Cooperative Oncology Group performance status <= 2.
- Subjects should have laboratory values meeting the following criteria:
• Alanine aminotransferase/aspartate aminotransferase <= 3 × the upper limit of normal (ULN);

• Adequate liver function as indicated by a total bilirubin <= 1.5 x ULN
(subjects with documented Gilbert's syndrome may have bilirubin > 1.5 × ULN)
• Absolute neutrophil count > 1000/µL;
• Platelet count > 50,000/µL;
• Creatinine clearance >= 50 mL/minute; and
• Hemoglobin > 8 g/dL.

Exclusion criteria

-

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	26-07-2020
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ABT-199
Generic name:	Venetoclax
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Imbruvica

Generic name:	ibrutinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	10-09-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-01-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-02-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-03-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-11-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-01-2021
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	27-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-02-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-02-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2018-002179-17-NL
ClinicalTrials.gov	NCT03873493
CCMO	NL70384.042.19

Study results

Date completed: 22-06-2021

Results posted: 31-10-2022

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File