A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Study of Navitoclax in Combination with Ruxolitinib Versus Ruxolitinib in Subjects with Myelofibrosis

Published: 05-08-2020
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Primary objective: To evaluate the effect of navitoclax in combination with ruxolitinib on splenomegaly response when compared to ruxolitinib in subjects with myelofibrosis.Secondary objectives:• To evaluate the effect of navitoclax in combination...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON54363

Source
ToetsingOnline

Brief title
TRANSFORM-1 or M16-191

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
cancer in the bonemarrow, Myelfibrosis

Research involving
Human

Sponsors and support

Primary sponsor: AbbVie B.V.

Source(s) of monetary or material Support: AbbVie

Intervention

Keyword: Myelfibrosis

Outcome measures

Primary outcome

Reduction in spleen volume is measured by Magnetic Resonance Imaging (MRI) or Computed Tomography (CT), per International Working Group (IWG) criteria at week 24

Secondary outcome

Secondary Efficacy Endpoints:

• Reduction in total symptom score (TSS) at Week 24 from baseline as measured by Myelofibrosis Symptom Assessment Form (MFSAF) v4.0

• Duration of SVR35

• Change in fatigue at Week 24 from baseline as measured by the PROMIS Fatigue SF 7a

• Change in physical functioning, as measured by the physical functioning domain of the EORTC QLQ-C30, or death

• Anemia response per IWG criteria

• At least 35% reduction in spleen volume from baseline (SVR35) as measured by MRI or CT scan, per IWG criteria

• Reduction in grade of bone marrow fibrosis from baseline as measured by the European consensus grading system

• Overall survival

• Leukemia-free survival

• Overall response of clinical improvement per IWG criteria.

Study description

Background summary

Myelofibrosis is a type of bone marrow cancer that usually develops slowly and disrupts body's normal production of blood cells. It causes bone marrow scarring, leading to severe anemia that can cause weakness and fatigue. It can also cause a low number of blood-clotting cells called platelets, which increases risk of bleeding. Myelofibrosis often causes an enlarged spleen. The purpose of this study is to see if a combination of navitoclax and ruxolitinib is more effective and safe in assessment of change in spleen volume when compared to ruxolitinib in participants with myelofibrosis.

Study objective

Primary objective:
To evaluate the effect of navitoclax in combination with ruxolitinib on splenomegaly response when compared to ruxolitinib in subjects with myelofibrosis.

Secondary objectives:
• To evaluate the effect of navitoclax in combination with ruxolitinib on the onset, magnitude, and duration of disease response, including Total Symptom Score (TSS), effects on spleen, bone marrow fibrosis, and anemia.
• To evaluate the effect of navitoclax in combination with ruxolitinib on measures of health-related quality of life (HRQoL), including fatigue, and physical functioning.
• To evaluate the effect of navitoclax in combination with ruxolitinib on overall survival (OS) and leukemia-free survival.

Study design

Randomized, double-blind, placebo controlled

Intervention

Participants will receive oral navitoclax tablet with oral ruxolitinib tablet or oral ruxolitinib tablet with oral placebo (no active drug) tablet and treatment may continue till the participant cannot tolerate the study drug, or benefit is not achieved, or other reasons which qualify for discontinuation of

the study drug

Study burden and risks

There may be a higher treatment burden for participants in this trial compared to their standard of care. Participants will attend regular visits during the course of the study at a hospital or clinic. The effect of the treatment will be checked by medical assessments, blood tests, Magnetic Resonance Imaging (MRI), bone marrow tests, checking for side effects, and completing questionnaires

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Subject >= 18 years of age.
• Subject with a documented diagnosis of primary myelofibrosis (MF) or secondary MF (post polycythemia vera [PPV] -MF or post essential thrombocythemia [PET] - MF) as defined by the World Health Organization classification.
• Subject must be able to complete the Myelofibrosis Symptom Assessment Form (MFSAF) on at least 4 out of the 7 days immediately preceding the date of randomisation
- Subject classified as intermediate-2 or high-risk MF as defined by the Dynamic International Prognostic Scoring System Plus (DIPSS+).
• Subject has splenomegaly defined as spleen palpation measurement >= 5 cm below costal margin or spleen volume >= 450 cm^3 as assessed centrally by MRI or CT scan.
• Subject has at least 2 symptoms measurable (score >= 3) or a total score of >= 12, as measured by the MFSAF v4.0.
• Subject with an Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2.

Exclusion criteria

• Subject must not have received prior treatment with a JAK-2 inhibitor.
• Subject must not have received prior treatment with a BH3-mimetic compound or bromodomain and extra-terminal motif (BET) inhibitor.
• Subject must not be eligible for stem cell transplantation at time of study entry due to age, comorbidities, or unfit for unrelated or unmatched donor transplant and other criteria per National Comprehensive Cancer Network guidelines.
• Subject must not receive medication that interferes with coagulation or platelet function within 3 days prior to the first dose of study drug or during the study treatment period.

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):	06-05-2021
Enrollment:	7
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Navitoclax
Generic name:	Navitoclax
Product type:	Medicine
Brand name:	Ruxolitinib
Generic name:	Jakavi
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	05-08-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-10-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	29-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-12-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-03-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-06-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-08-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-10-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-12-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-12-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	28-12-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-02-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-05-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-08-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-11-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-12-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-02-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-06-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	23-10-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-01-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-08-2024
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	EUCTR2020-000097-15-NL
ClinicalTrials.gov	NCT04472598
CCMO	NL73951.042.20