A phase 3 randomized, double-blind study of ianalumab (VAY736) versus placebo in addition to eltrombopag in patients with primary immune thrombocytopenia (ITP) who had an insufficient response or relapsed after first line steroid treatment (VAYHIT2)

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This study has been transitioned to CTIS with ID 2024-512890-28-00 check the CTIS register for the current data. The purpose of this study is to assess the efficacy and safety of ianalumab (VAY736) compared to placebo in addition to second-line…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Platelet disorders
Study type	Interventional

Summary

ID

NL-OMON56456

Source
ToetsingOnline

Brief title
CVAY736Q12301

Condition

- Platelet disorders

Synonym
low platelet count, Primary immune thrombocytopenia

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: B-cell Activating Factor Receptor (BAFF-R) blockade, B-cell depletion, ianalumab (VAY736), Primary immune thrombocytopenia (ITP)

Outcome measures

Primary outcome

Time from randomization to treatment failure defined as the time from

randomization until :

- platelet counts below 30 G/L), later than 8 weeks from randomization,

- start of a new ITP treatment due to any reasons, need for a

- rescue treatment (e.g.corticosteroids, IVIG, or platelet transfusion) later

than 8 weeks from randomization,

- ineligibility to taper or inability to discontinue eltrombopag

- death (whatever the cause)

Time to treatment failure (TTF) will be assessed in each treatment group and

each of the two doses of ianalumab (ianalumab+eltrombopag) will be compared to

the control arm (placebo+eltrombopag).

Secondary outcome

• Complete Response (CR) rate at each time point defined as the proportion of

participants with any platelet count of at least 100 G/L in the

absence of rescue treatment or new ITP treatment

• Response rate at each timepoint defined as the proportion of participants with any platelet count of at least 50 G/L in the absence of rescue treatment or new ITP treatment

• Complete Response (CR) rate at each time point defined as the proportion of participants with any platelet count of at least 100 G/L in the absence of rescue treatment or new ITP treatment

• Response rate at each time point defined as the proportion of participants with any platelet count of at least 50 G/L in the absence of rescue treatment or new ITP treatment

• Best response rate over all timepoints defined as proportion of participants with a best response of either response or complete response

• Time from randomization to date of first response and time from randomization to date of first complete response

• Duration of response is defined as the time from achievement of response to treatment failure

• Duration of complete response(CR) is defined as the time from achievement of CR to loss of CR

• Probability to be in treatment failure-free (as defined for the primary efficacy endpoint) at the end of the planned treatment period (end of Week 24)

• Frequency of adverse events and other safety parameters

• Number of severe infections and proportion of participants with severe infection

• Proportion of participants with bleeding events according to WHO Bleeding Scale

• Number and proportion of participants receiving rescue treatment

• Change from baseline on total score of the PROMIS SF v1.0 Fatigue 13a

• Change from baseline in ITP PAQ domain scores of Symptoms, Fatigue, Bother, Activity

• B-cell levels:

- Change from baseline in the frequency (% within the CD45) and absolute number of CD19+ B-cell counts

- Time to first occurrence of B-cell recovery, defined as >=80% of baseline or >=50 cells/µL

• Immunoglobulins:

- Change from baseline in immunoglobulin levels

• Ianalumab concentration in serum and PK parameters after the first and last dose in a subset of participants

• Incidence and titer of anti-ianalumab antibodies in serum (Anti-Drug-Antibody (ADA) assay) over time

Study description

Background summary

Immune Thrombocytopenia (ITP) is a rare, acquired, immune-mediated disease of adults and children, characterized by transient or persistent decrease of the platelet count and, depending upon the degree of thrombocytopenia, increased risk of bleeding. Primary ITP is defined by the absence of other causes or disorders that may be associated with thrombocytopenia. Secondary forms include thrombocytopenias that are due to an underlying disease or to drug exposure

Currently approved and available second-line therapies, such as TPO-RAs, are able to induce a high rate of response, but they are required to be taken life-long in order to maintain response.

Chronic treatment with additional lines of therapy may further lead to a more treatment-refractory, difficult-to-treat disease over time, with very low platelet counts and increased bleeding risk. It is therefore important that the most effective treatment is established in the early phase of the disease (first- or second-line).

Consequently, there remains a significant unmet medical need for new, potentially disease-modifying therapies in the early stages of ITP that are well tolerated, require shorter course of treatment that is more convenient for patients, and induce a high rate of response, which is also maintained after end of the treatment period.

Study objective

This study has been transitioned to CTIS with ID 2024-512890-28-00 check the CTIS register for the current data.

The purpose of this study is to assess the efficacy and safety of ianalumab (VAY736) compared to placebo in addition to second-line eltrombopag in adults with primary immune thrombocytopenia

Study design

This is a multicenter, randomized, double-blinded phase 3 study to assess the efficacy and safety of two different doses of ianalumab (3 and 9 milligram (mg)/ kilogram (kg)) compared to placebo in adults with primary ITP (platelets count < 30 G/L) treated with eltrombopag. After completion of screening period, participants will enter 16-week randomized combination treatment period in one of the following three arms: Arm A (eltrombopag once daily + 4 cycles of ianalumab 3 mg/kg intravenously every 4 weeks), Arm B (eltrombopag once daily + 4 cycles of ianalumab 9 mg/kg intravenously every 4 weeks), Arm C (eltrombopag once daily + 4 cycles of placebo intravenously every 4 weeks). After the 16-week of combination treatment period of eltrombopag + ianalumab/placebo, eltrombopag will be tapered until discontinuation for a maximum of 8-weeks. After the treatment period, all participants will enter a follow-up period to be monitored for efficacy and safety or safety only, depending on how the participant responded to the study treatment. Efficacy and safety follow-up will last until loss of TFR or up to 39 months after randomization of the last participant, whichever occurs first. Safety follow-up will be performed for at least 20 weeks (Short Term Safety Follow-Up (STSFU)) and up to 2 years after the last ianalumab/placebo dose (Long Term Safety Follow-Up (LTSFU)).

Intervention

VAY736 (ianalumab) 3 or 9 mg/kg or placebo in addition to eltrombopag

Study burden and risks

Potential burden and risk to participants includes potential side effects of study medications and inconveniences of procedures:

Possible side effects of eltrombopag (as described in the package leaflet).
Possible side effects of ianalumab
- Upper respiratory tract infections
- Urinary tract infections
- Drip-related reactions
- Infection of the lower respiratory tract
- Herpes infection of the mouth or inflammation of the conjunctiva of the eye

Blood tests can hurt or cause bleeding. Sometimes a person gets dizzy or faints.
ECG patches can cause skin irritation

Also the time investment of tests and investigations:
Physical examination, blood pressure/pulse measurement. eye examination, blood test, urinalysis, EKG, completing questionnaires and pregnancy test (if participant can become pregnant)

See protocol and investigator's brochure for additional information on risks and benefits.

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

1. Male or female patients aged 18 years and older on the day of signing the informed consent. 2. A signed informed consent must be obtained prior to participation in the study. 3. A diagnosis of primary ITP, with insufficient response to, or relapse after a first-line corticosteroid therapy. 4. Patients with Platelet count below 30 G/L for whom eltrombopag is clinically indicated as per physician*s discretion and with no contraindication to receive eltrombopag.

Exclusion criteria

1. ITP patients who received second-line ITP treatments (other than corticosteroid therapy ± IVIG) including splenectomy. However, patients exposed to thrombopoietin receptor agonists (TPO-RAs) for a limited time (max one week) before screening are eligible.
2. Patients with key lab abnormalities and patients with Evans syndrome or any other cytopenia (patients with low grade anemia related to bleeding or iron deficiency are eligible).
3. Patients with history of clinically significant hematological disorders, or with marked altered hematologic parameters
4. Patients with current or history of life-threatening bleeding
5. Patient that are Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV), HBsAg positive are excluded. Participants who are hepatitis core antibody (HBcAb) positive are also executed unless all of the following criteria are met: HbsAg and HBV DNA are negative, participant has no pre existing liver fibrosis, hepatitis B monitoring is implemented , including regular ALT testing and HBV DNA testing. Antiviral prophylaxis with entecavir must be initiated prior randomization and must continue during the treatment

period and at least 12 months after the last dose of ianalumab /placebo. If antiviral prophylaxis with entecavir is not allowed as per local guidelines or local clinical practice, clinically contraindicated or not accepted by the patient, participants who are HBsAg negative and HBcAb positive are not eligible.
6. Patients with known active or uncontrolled infection requiring systemic treatment during screening period.
7. Patients with hepatic impairment
8. Patients with concurrent coagulation disorders and/or receiving anti-platelet or anticoagulant medication with an exemption of low dose of acetylsalicylic acid (<=150 mg daily).
9. Female patients who are pregnant or nursing

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:	Recruiting
Start date (anticipated):	23-10-2023
Enrollment:	4
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	nvt
Generic name:	Ianalumab

Product type:	Medicine
Brand name:	Revolade
Generic name:	eltrombopag
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	31-10-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-12-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-09-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	14-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-03-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	CTIS2024-512890-28-00
EudraCT	EUCTR2022-001627-32-NL
ClinicalTrials.gov	NCT05653219
CCMO	NL82422.056.22