A Phase 3 Study of the Hepcidin Mimetic Rusfertide (PTG-300) in Patients with Polycythemia Vera

Published: 23-07-2022
Last updated: 14-09-2024

This study has been transitioned to CTIS with ID 2023-509750-58-00 check the CTIS register for the current data. In this study, we look at how safe the new medicinal product rusfertide is for the treatment of Polycythemia vera. And how well it works...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haematopoietic neoplasms (excl leukaemias and lymphomas)
Study type	Interventional

Summary

ID

NL-OMON53847

Source
ToetsingOnline

Brief title
PTG-300-11

Condition

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
Osler-Vaquez disease, Polycythemia vera

Research involving
Human

Sponsors and support

Primary sponsor: Protagonist Therapeutics, Inc.
Source(s) of monetary or material Support: Protagonist Therapeutics;Inc.

Intervention

Keyword: Polycythemia Vera, PTG-300, PV, Rusfertide

Outcome measures

Primary outcome

Proportion of subjects achieving a response starting at Week 20 through Week 32 (inclusive) who receive rusfertide compared to placebo. A response is defined as absence of phlebotomy eligibility.

Phlebotomy eligibility is defined as either:

• a confirmed hematocrit >=45% and that is at least 3% higher than the baseline hematocrit (value immediately prior to randomization at Week 0); confirmation required within 1 to 7 days,

or

• a hematocrit >=48%.

Hematocrit values from each clinical site*s local laboratory will be used for the primary endpoint.

Secondary outcome

1. Mean number of phlebotomies between Weeks 0 through 32 (inclusive).

2. Proportion of subjects with all hematocrit values <45% between Week 0 through Week 32 (inclusive). A single transient hematocrit value >=45% is allowed. Hematocrit values from each clinical site*s local laboratory will be used for this endpoint.

3. Mean change from baseline in total fatigue score based on Patient Reported Outcome Measurement Information System (PROMIS) Short Form 8a at Week 32.

4. Mean change from baseline in total score based on Myelofibrosis Symptom Assessment Form (MFSAF) v4.0 at Week 32. The weekly total symptom score at Week 32 will be calculated by averaging daily total symptom scores over a 7-day interval during the week immediately prior to Week 32 (inclusive).

Other secondary endpoints:

Part 1a - Week 0 through Week 32 (inclusive):

Comparison of rusfertide to placebo during randomized, double-blind, placebo-controlled, addon parallel phase

• Median time to first hematocrit >=45% after randomization.

• Proportion of subjects with at least one hematocrit >=48%.

• Proportion of subjects who maintain absence of phlebotomy eligibility.

• Mean change from baseline at each scheduled assessment in individual questions and the total fatigue score based on PROMIS Short Form 8a.

• Mean change from baseline at each scheduled assessment in individual symptom score and the total score based on MFSAF v4.0.

• Proportion of subjects with a baseline score >=2 who have at least a 2-point change in worst fatigue at each scheduled assessment based on MFSAF v4.0.

• Proportion of subjects with a baseline score >=2 who have at least a 2-point change in worst itching at each scheduled assessment based on MFSAF v4.0.

• Mean change from baseline at each scheduled assessment in individual symptom score and the total score based on MPN-SAF TSS 10.

• Mean change from baseline in Patient Global Impression of Severity (PGI-S) at

each scheduled assessment.

• Proportion of subjects with at least one unit improvement in the PGI-S from baseline, i.e., a >= 1 point decrease in the PGI-S, e.g., a change from *Moderate (2)* to *Mild (1)* or *Mild (1)* to *None (0)* at each scheduled visit.

• Proportion of subjects with a rating on the Patient Global Impression of change (PGI-C) of either *much better* or *a little better* at each scheduled assessment.

• Mean PGI-C at each scheduled assessment.

• Mean change from baseline in the individual domain scores and the total EORTC QLQ-C30 score at Week 32.

Parts 1a + 1b: Week 0 through Week 52

• Proportion of subjects originally randomized to rusfertide achieving absence of phlebotomy eligibility (durable response) for 52 weeks.

• Median time to first confirmed hematocrit >=45% during Part 1b excluding Part 1a.

• Median time to first phlebotomy during Part 1b excluding Part 1a.

Safety:

Part 1a + Part 1b + Part 2: Week 0 through Week 156

• Frequency distribution will be presented for treatment emergent adverse events (TEAEs), serious TEAEs and AEs of special interest (AESI).

• Clinical safety laboratory tests, physical examination, vital signs (heart

rate, systolic and diastolic blood pressure, respiratory rate) and 12-lead

electrocardiogram (ECG) findings will be summarized.

Study description

Background summary

Polycythemia Vera is a blood disease in which patients make too many red blood cells. Patients are at increased risk of blood clots, strokes and heart attacks because they have too many red blood cells. Treatment is designed to maintain red blood cells at a safe level. Hematocrit is the routine blood test used to monitor the number of red blood cells and control of Polycythemia Vera.

The purpose of this study is to determine whether the study medicine, rusfertide is safe and effective for treating Polycythemia Vera. Rusfertide (also known as PTG-300) is an experimental study medicine that lowers the level of iron in the blood. Iron is required for production of red blood cells.

Study objective

This study has been transitioned to CTIS with ID 2023-509750-58-00 check the CTIS register for the current data.

In this study, we look at how safe the new medicinal product rusfertide is for the treatment of Polycythemia vera. And how well it works.

Study design

This is a Phase 3 study in subjects with polycythemia vera, which consists of 5 phases: screening, treatment (part 1a, 1b and 2) and safety follow-up.

Treatment Part 1a:
During Part 1a, we will treat the subject for 32 weeks with study drug or placebo once a week.
For Part 1a, we will have 2 groups:
• Group 1. The people in this group will get the study drug. The starting dose of the study drug is 20 mg per week and the dose may be adjusted by the research centre staff, if necessary, to control the subject's hematocrit.
• Group 2. The people in this group will get placebo (a 'fake medicinal product').
A draw will decide which treatment (study drug or placebo) the subject is given. The subject will have a 50% (1 in 2 chance) of receiving the study drug and a 50% (1 in 2 chance) of receiving placebo. The subject and the

investigator do not know which group he/she is in. But if it is important for the health of the subject, this can be looked up.

Treatment Part 1b: If the subject completes part 1a, the subject will continue in part 1b, in which he/she will be treated with the study drug once per week for 20 weeks. Part 1b is open label, which means that both the subject and the investigator do know that the subject will be given the study drug and which dose the subject was given.

•Part 2: long term extension for 2 years weeks during which all subjects who complete Part 1b will continue to receive the study drug once a week, twice a week, or once every two weeks.

Post-Treatment Safety follow-up
Subjects who complete the study or who terminate early from the study will undergo a follow-up evaluation of safety approximately 4 weeks after the last dose of study drug.
Additionally, approximately 6 months and 12 months after the last dose of study drug administration subjects will be contacted (e.g., phone) to determine if there has been a development of new cancers.

Intervention

Rusfertide (also known as PTG-300) is an experimental study drug that lowers the level of iron in the blood. Iron is required for production of red blood cells.

Study burden and risks

Burden: during the study, the patient has to visit the study site. Subjects will receive the study drug (or placebo only phase 1a) by a subcutaneous injection. A physical examination will be performed, vital signs, spleen size (MRI or ultrasound), cardiac activity and rhythm will be assessed and blood and urine will be collected. Furthermore, the patient has to fill in questionnaires that can be confrontable.

risks: the study drug may cause side effects

benefit: The study drug may improve control of Polycythemia Vera but that is not certain. Polycythemia Vera may come back or get worse at any time during this study.

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

Inclusion Criteria: Subjects must meet ALL of the following inclusion criteria:

1. Male and female subjects aged 18 (or the minimum country specific age of consent if >18) years or older.
2. Subject understands the study procedures, is willing and able to adhere to study requirements and agrees to participate in the study by giving written informed consent.
3. Meet revised 2016 World Health Organization (WHO) criteria for the diagnosis of polycythemia vera.
4. Phlebotomy requiring defined as ALL of the following:
a. At least 3 phlebotomies due to inadequate hematocrit control in 28 weeks before randomization or at least 5 phlebotomies due to inadequate hematocrit control in 1 year before randomization, and
b. Last phlebotomy due to inadequate hematocrit control within 3 months before randomization, and

c. No phlebotomy within 6 days prior to randomization.
Note: Phlebotomies performed within an 8-day period will be counted as a single phlebotomy.
5. CBC values immediately prior to randomization:
a. Hematocrit <45%,
b. WBC 4000/µL to 20,000/µL (inclusive) and
c. Platelets 100,000/µL to 1,000,000/µL (inclusive).
6. Eastern Cooperative Oncology Group (ECOG) performance status 0, 1 or 2.
7. Women of childbearing potential (WOCBP) agree to use medically acceptable contraception (<1% annual failure rate) during the study and for 30 days after the last dose of study drug.
8. A female subject must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction during the study and for a period of 30 days after receiving the last dose of study medication.
9. Men with partners of childbearing potential agree to use medically acceptable contraception (<1% annual failure rate) during the study and for 90 days after the last dose of study drug. In addition, men must use a condom during the study and for 90 days after the last dose of study drug regardless of the partner*s childbearing potential.
10. A male subject must agree not to donate sperm for the purpose of reproduction during the study and for a minimum of 90 days after receiving the last dose.
11. Subjects receiving cytoreductive therapy at randomization must be on a stable PV therapy regimen as follows:
a. Hydroxyurea - at least 2 months
b. JAK inhibitor - at least 2 months
c. Interferon - at least 6 months
Note: A *stable dose regimen* of cytoreductive therapy does not mean an unchanged dose regimen. Temporary adjustments in dose regimen or temporary suspension of dosing are allowed. However, the total weekly dose of hydroxyurea and JAK inhibitor or total monthly dose of interferon may not be higher at randomization than the dose at the beginning of the pre-randomization observation period. The pre-randomization observation period is
2 months for hydroxyurea and JAK inhibitor and 6 months for interferon
12. Subjects treated with phlebotomy alone at randomization must have stopped:
a. Hydroxyurea at least 2 months before screening
b. JAK inhibitor at least 2 months before screening
c. Interferon at least 6 months before screening

Exclusion criteria

Exclusion Criteria: Subjects must not meet ANY of the following exclusion criteria to be enrolled:

1. Clinically meaningful laboratory abnormalities at Screening including, but

not limited to:
a. Estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m2
b. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >=2.5 × upper limit of normal (ULN)
c. Total bilirubin >1.5 × ULN.
Note: Screening laboratory tests with abnormal results (if considered by the investigator to be transient and inconsistent with the subject*s clinical condition) may be repeated within the screening window to confirm abnormal results. If results return to protocol acceptable limits within the screening period, the subject may enter the study. Use local labs for CBC and use central labs for all other eligibility lab tests.
2. Subjects who require phlebotomy at hematocrit levels lower than 45%.
3. Pregnant or lactating females.
4. Clinically significant thrombosis (e.g., deep vein thrombosis or splenic vein thrombosis) within 2 months prior to randomization.
5. Active or chronic bleeding within 2 months prior to randomization.
6. Meets the criteria for post-polycythemia vera myelofibrosis as defined by the International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT).
7. Any infection requiring systemic therapy within 1 month of dosing except controlled HIV, hepatitis B and hepatitis C. Prophylactic therapies are allowed.
8. Any serious or unstable medical condition (e.g., poorly controlled HIV infection) or uncontrolled psychiatric condition as judged by the Investigator that would impair the subject*s ability to participate in the study.
9. Major surgical procedure within 2 months prior to randomization unless the subject has fully recovered from surgery or planned major elective surgery during the study.
10. History of invasive malignancies within the last 5 years, except
a. localized cured cancer (e.g., prostate cancer and cervical cancer)
b. localized cured in situ or stage 1 squamous cell carcinoma of the skin, basal cell carcinoma of the skin, or in situ melanoma of the skin.
11. Subjects with in situ or stage 1 squamous cell carcinoma of the skin, in situ or stage 1 basal cell carcinoma of the skin, or in situ melanoma of the skin identified during the required dermatology examination at screening unless the cancer is adequately treated (i.e., treatment that is expected to be curative, such as Mohs surgery) before randomization. Note: Suspicious lesions should be biopsied and results available before randomization.
12. Subjects with active alcohol or drug addiction that would interfere with their ability to comply with study requirements.
13. Subjects who do not complete at least 4 days of Myelofibrosis Symptom Assessment Form version 4.0 (MFSAF v4.0) assessments within 1 week prior to randomization.
14. Receipt of an investigational agent within 2 months or 5 half-lives, whichever is longer, prior to randomization.
15. Received busulfan, pipobroman or Phosphorus within 7 months prior to screening.

16. Subjects with hypersensitivity to rusfertide or to any of the excipients or placebo.
17. Subjects with any lesion or mass detected by physical examination or imaging during screening that is suspicious for malignancy unless evaluated and assessed to be not malignant

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):	01-08-2023
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Rusfertide
Generic name:	Rusfertide

Ethics review

Approved WMO

Date:	23-07-2022
Application type:	First submission

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-10-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-01-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-08-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	CTIS2023-509750-58-00
EudraCT	EUCTR2021-004732-29-NL
ClinicalTrials.gov	NCT05210790
CCMO	NL80653.100.22