A Phase III, multicenter, randomized, double-blind study to assess efficacy and safety of two doses of crizanlizumab versus placebo, with or without hydroxyureal/hydroxycarbamide therapy, in adolescent and adult sickle cell disease patients with vaso-occlusive crises (STAND)

Published: 23-04-2019
Last updated: 07-09-2024

This study has been transitioned to CTIS with ID 2023-508689-14-00 check the CTIS register for the current data. To compare the efficacy of 7.5 mg/kg of crizanlizumab versus placebo on the annualized rate of VOC leading to healthcare visit, in…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Red blood cell disorders
Study type	Interventional

Summary

ID

NL-OMON52956

Source
ToetsingOnline

Brief title
CSEG101A2301 - STAND

Condition

- Red blood cell disorders

Synonym
Sickle cell disease

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: crizanlizumab, Fase III, sicklecell disease, vaso-occlusive crises

Outcome measures

Primary outcome

Annualized rate of VOC events leading to healthcare visit in each treatment

group over the first year post-randomization

Secondary outcome

Annualized rate of all VOCs leading to healthcare visit and treated at home

over the first year post randomization

Duration of VOC leading to healthcare visit over the first year post

randomization

Number and percentage of subjects free from VOCs leading to healthcare visit in

each group over the first year post randomization

The time to first and second VOC calculated

Annualized rate of visits to clinic, Emergency room (ER) and hospitalizations,

•Annualized rate of VOCs managed at home over the first year post randomization

Study description

Background summary

Sickle cell disease is a genetic blood disorder, which early on progresses into a systemic disease. Vaso-occlusion is the hallmark of SCD and can lead to serious acute and chronic complications. Vascular dysfunction, inflammation, and P-selectin mediated cell-to-cell and cell-to-endothelium adhesion play an important role in the pathophysiology of SCD. Vaso-occlusive crisis (VOC) is the most common clinical manifestation of SCD. Every VOC increases morbidity and can result in organ damage/failure and/or death .
Preventive treatments to reduce the number of VOCs are limited. HU/HC is approved to reduce the frequency of painful crises and the need for transfusions

Crizanlizumab binds to P-selectin with high affinity, blocking its interaction with its ligands. Extensive pre-clinical data have established P-selectin as a key mediator of VOC in SCD and suggest that its blockade could eliminate or reduce VOC.

Study objective

This study has been transitioned to CTIS with ID 2023-508689-14-00 check the CTIS register for the current data.

To compare the efficacy of 7.5 mg/kg of crizanlizumab versus placebo on the annualized rate of VOC leading to healthcare visit, in addition to standard of care

To compare the efficacy of 5.0 mg/kg of crizanlizumab versus placebo on the annualized rate of VOC leading to healthcare visit, in addition to standard of care

Study design

multicenter, randomized, double-blinded, parallel-group Phase 3 study randomized 1:1:1

Intervention

crizanlizumab /placebo infusion over 30 minutes, every 4 weeks.

Study burden and risks

RISK : adverse events due to treatment with crizanlizumab of placebo
burden: cycles of 4 weeks during 5 years of study participation

during monthly visits : physical examinations, blooddraws, administration of study medication
during the first year daily questionnaire (19 questions) and weekly questionaires

every year a ECHO

Contacts

Public
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL
Scientific
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Written informed consent must be obtained prior to any screening procedures
2. Male or female patients aged 12 years and older on the day of signing informed consent.
3. Confirmed diagnosis of SCD by Hb electrophoresis or HPLC (performed locally). All SCD genotypes are eligible, genotyping is not required for study entry,
4. Experienced at least 2 VOCs leading to healthcare visit within the 12 months prior to screening visit as determined by medical history. Prior VOC leading to healthcare visit must resolve at least 7 days prior to Week 1 Day 1 and must include:
a. Pain crisis defined as an acute onset of pain for which there is no other medically determined explanation other than vaso- occlusion
b. a visit to a medical facility and/or healthcare professional,
c. and receipt of oral/parenteral opioids or parenteral nonsteroidal antiinflammatory drug (NSAID) analgesia,
Acute chest syndrome (ACS), priapism and hepatic or splenic sequestration will be considered VOC in this study.

5. If receiving HU/HC or erythropoietin stimulating agent or L-glutamine, must have been receiving the drug for at least 6 months prior to screening visit and plan to continue taking at the same dose and schedule until the subject has reached one year of study treatment,
6. Patients must meet the following central laboratory values at the screening visit:
* Absolute Neutrophil Count >=1.0 x 109/L
* Platelet count >=75 x 109/L
* Hemoglobin: for adults (Hb) >=4.0 g/dL and for adolescents (Hb) >=5.5 g/dL
* Glomerular filtration rate >= 45 mL/min/1.73 m2 using CKD-EPI formula in adults, and Schwartz formula in adolescents
* Direct (conjugated) bilirubin < 2.0 x ULN
* Alanine transaminase (ALT) < 3.0 x ULN, 7. ECOG performance status <=2.0 for adults and Karnofsky >= 50% for adolescents

Exclusion criteria

1. History of stem cell transplant.
2. Participating in a chronic transfusion program (pre-planned series of transfusions for prophylactic purposes) and/or planning on undergoing an exchange

transfusion during the duration of the study; episodic transfusion in response to worsened anemia or VOC is permitted., 3. Contraindication or hypersensitivity to any drug or metabolites from similar class as study drug or to any excipients of the study drug formulation.
4. Received active treatment on another investigational trial within 30 days (or 5 half-lives of that agent, whichever is greater) prior to Screening visit or plans to
participate in another investigational drug trial., 5. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant unless they are using highly effective methods of
contraception during dosing and for 15 weeks after stopping treatment.
6. Concurrent severe and/or uncontrolled medical conditions which, in the opinion of the Investigator, could cause unacceptable safety risks or compromise participation in the study.
7. History or current diagnosis of ECG abnormalities indicating significant risk of safety
8. Not able to understand and to comply with study instructions and requirements.

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):	03-10-2019
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	crizanlizumab
Generic name:	crizanlizumab

Ethics review

Approved WMO Date:	23-04-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-06-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	27-02-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-02-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	29-06-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	16-07-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	10-09-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	21-10-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	22-02-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl
Approved WMO Date:	16-06-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	28-07-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	22-02-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	09-03-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	08-06-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-08-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	15-09-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	28-11-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	08-12-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	11-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	14-03-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	11-06-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	14-07-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	04-09-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	20-11-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	CTIS2023-508689-14-00
EudraCT	EUCTR2017-001746-10-NL
ClinicalTrials.gov	NCT03814746
CCMO	NL69556.098.19