SOAR Trial Interventional phase II single-arm study to assess efficacy and safety of Eltrombopag combined with cyclosporine as first line therapy in adult patients with severe acquired aplastic anemia.

Published: 29-03-2017
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Primary: To evaluate the efficacy of eltrombopag + cyclosporine as first-line therapy on overall hematologic response (neutrophil, platelet, hemoglobin) by 6 months.Secondary: Overall hematologic response (neutrophil, platelet, hemoglobin) by 3 and...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Anaemias nonhaemolytic and marrow depression
Study type	Interventional

Summary

ID

NL-OMON50032

Source
ToetsingOnline

Brief title
CETB115E2403, SOAR trial

Condition

- Anaemias nonhaemolytic and marrow depression

Synonym
acquired severe aplastic anemia

Research involving

Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis

Intervention

Keyword: anemia, aplastic, cyclosporine, eltrombopag

Outcome measures

Primary outcome

Overall hematologic response (neutrophil, platelet, hemoglobin) by 6 months.

Secondary outcome

Overall hematologic response (neutrophil, platelet, hemoglobin) by 3 and 12 months, duration of hematologic response, disease relapse rate, clonal evolution, number of transfusions, time without transfusions, overall survival, symptoms and result of quality of life questionnaires, adverse events, pharmacokinetic parameters.

Study description

Background summary

The standard of care for the treatment of aplastic anemia patients who are not candidate for HSCT was immunosuppressive treatment (IST) for a long time. There are several limitations of IST in severe aplastic anemia (SAA), e.g. the majority of the responses observed following initial IST are partial with only a few patients achieving normal blood counts, 1/3 of patients are refractory to initial IST, hematologic relapses occur in 35% of responders following initial response to IST, among relapsed patients chronic use of cyclosporine A is not infrequent which often leads to toxicities and clonal evolution is still observed in 10-15% of patients.
In order to address these limitations, efforts to improve initial IST in treatment-naïve patients with the addition of mycophenolate mofetil and

sirolimus to standard horse anti-thymocyte globulin/cyclosporine A (h-ATG/CsA) or use of lymphocytotoxic agents have not yielded the expected better outcomes when compared to standard (h-ATG/CsA).
The most important advance in SAA in the recent years has been the seminal observation that a thrombopoietin receptor agonist, eltrombopag, has activity in SAA.
The lack of availability of anti-thymocyte globulin (ATG) in several countries has left a large proportion of patients with SAA with limited treatment options and poor outcome. In this context, the combination of cyclosporine and eltrombopag, 2 therapies with different modes of action, is an attractive therapeutic option to address this unmet medical need.
The main objective of this study is to assess the safety and efficacy of eltrombopag and cyclosporine in outpatient setting for the treatment-naïve SAA patients mainly in countries where h-ATG is not available.

Study objective

Primary:
To evaluate the efficacy of eltrombopag + cyclosporine as first-line therapy on overall hematologic response (neutrophil, platelet, hemoglobin) by 6 months.
Secondary:
Overall hematologic response (neutrophil, platelet, hemoglobin) by 3 and 12 months, duration of hematologic response, disease relapse rate, clonal evolution, need for and independence of blood and platelet transfusion, overall survival, symptoms and quality of life, safety and tolerability, pharmacokinetics.

Study design

interventional phase II, single-arm, multicenter, open-label, study to investigate the efficacy and safety of the combination of eltrombopag and cyclosporine in treatment-naive patients with SAA as first line therapy administered for 6-months
a follow-up for up to 24 -months of all patients who responded and not responded at month 6
Responders will receive cyclosporine only, up to 24 months with a taper regimen. After which EOS will take place for safety reasons.
Non-responders will stop eltrombopag and cyclosporine after 6 months, cyclosporine will be stopped for non-responders in 2nd part from 6-24 months
Approx. 50 patients.

Intervention

Treatment with eltrombopag and cyclosporine.

Study burden and risks

Risk: Adverse effects of eltrombopag in combination with cyclosporine and cyclosporine alone.
Burden: Screening 2 weeks, treatment with eltrombopag and cyclosporine 6 months, treatment with alone cyclosporine 18 months. safety visits 30days after last treatmen
40 visits in 2 years. Duration mostly 1-2 hours.
Physical examination: 6 times.
Blood tests (20 ml/occasion): every visit; 1 day with 8 h PK measurements with 5 blood draws.
Pregnancy test (if relevant): every 3-4 weeks, to be conducted partly at home.
Bone marrow sample:4 times.
ECG: max5 times.
Questionnaires: FACIT-Fatigue, FACT-TH18, EQ-5D-5L: 12 times.
Eye examination : 5 times.
Neurological examination : 5 times.
Optional storage and use of the remaining blood and tissue for future research.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Male and female >= 18 years of age.
• Severe aplastic anemia characterized by a. Bone marrow cellularity <30% (excluding lymphocytes) and b. At least two of the following (peripheral blood):
- Absolute neutrophil count <500/ µL
- Platelet count <20000/ µL
- Absolute reticulocyte count <60000/ µL
• Normal ECG (see protocol page 40 for details).

Exclusion criteria

• Fanconi anemia.
• Evidence of a clonal hematologic bone marrow disorder. See protocol page 40 for details.
• Prior immunosuppressive therapy with cyclosporine, alemtuzumab, r- or h-ATG and TPO-R agonists.
• Liver cirrhosis.
• Infection not adequately controlled with appropriate therapy.
• Moribund or concurrent hepatic, renal, cardiac, neurologic, pulmonary, infectious, cancer or metabolic disease of such severity that it would interfere with a proper completion of study visits or treatment.
• Pregnant or nursing (lactating) women.
• Females and males not using adequate contraception. See protocol page 45 for more details.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Neoral
Generic name:	Cyclosporine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Revolade
Generic name:	Eltrombopag
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	29-03-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	21-07-2017
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	27-09-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	16-10-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	06-05-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	10-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	18-11-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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	EUCTR2016-002814-29-NL
ClinicalTrials.gov	NCT02998645
CCMO	NL60184.058.17