# Effectiveness of Somatostatin Analogues in patients with Gastric antral vascular ectasia and symptomatic gastrointestinal bleeding: SAGAVE-trial

Published: 19-01-2021
Last updated: 21-12-2024

Primary Objective: To investigate the efficacy and safety of octreotide treatment (a somatostatin analogue) in decreasing the transfusion requirements (IV iron infusions and / or red blood cell transfusions) in patients with GI bleeding caused by…

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Gastrointestinal haemorrhages NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON49336

**Source**
ToetsingOnline

**Brief title**
SAGAVE-trial

### Condition

- Gastrointestinal haemorrhages NEC

**Synonym**
1) Gastric Antral Vascular Ectasia. 2) Watermelon stomach.

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Radboud Universitair Medisch Centrum

**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Gastric Antral Vascular Ectasia, Iron deficiency anemia, Octreotide, Somatostatin analogue

## Outcome measures

### Primary outcome

The absolute and percentage difference in the mean / median number of intravenous (IV) iron infusions and the mean / median number of red blood cell (RBC) transfusions that was given between the baseline period (26 weeks prior to study inclusion) and the treatment study period (of 26 weeks) and the percentage of patients with a "succesful response", defined as a decrease of >= 50% in the number of IV iron infusions and / or number of RBC transfusions.

### Secondary outcome

The absolute mean / median difference and the percentage mean and median difference between the baseline period (26 weeks prior to study inclusion) and the treatment study period (26 weeks) in:

- Number of endoscopic treatments

- Patient reported outcome measures (PROMS): which include quality of life (measured by the SF-36) and level of fatigue (measured by the multidimensional fatigue inventory (MFI)-20)

The absolute mean / median difference and the percentage mean / median difference at baseline (< 7 days before inclusion) between and after 4 weeks, 12 weeks, and 26 weeks of the study period in the value of:

- Hemoglobin and ferritin levels

The absolute number of (S)AE's reported during the treatment study period (of 26 weeks) and the absolute number of patients and percentage of patients that reported at least one (S)AE.

# Study description

### Background summary

Gastric Antral Vascular Ectasia (GAVE) is an important cause of difficult to manage bleeding, especially in older patients. There is a lack of effective, long-term treatment in patients with GAVE. Many patients are therefore transfusion dependent due to rebleeding despite endoscopic intervention. In other vascular disorders of the gastrointestinal tract (angiodysplasia and hereditary hemorrhagic telangiectasia) octreotide appears to decrease bleeding episodes.

### Study objective

Primary Objective: To investigate the efficacy and safety of octreotide treatment (a somatostatin analogue) in decreasing the transfusion requirements (IV iron infusions and / or red blood cell transfusions) in patients with GI bleeding caused by GAVE, who are refractory to endoscopic therapy.

Secondary Objective(s): To investigate the efficacy of octreotide in: decreasing the endoscopic treatment frequency, increasing the health-related quality of life and decreasing the level of fatigue.

### Study design

Multicenter prospective cohort pilot study (addition of octreotide to the standard of care) in 12 endoscopic treatment refractory patients, with iron infusion and / or red blood cell transfusion dependency. The broad inclusion criteria are applicable to a wide range of GAVE patients with GI bleeding and the trial is set up to conform clinical practice as much as possible. Three centers (Radboudumc, Amsterdam UMC, LUMC) will recruit patients for inclusion. Patients who give informed consent will be treated for 26 weeks with octreotide + standard of care. Endoscopic treatments are, on the discretion of the treating physician, allowed during the trial as part of standard of care.

Follow-up will be at 30 weeks (4 weeks after the last injection).

### Intervention

Octreotide LAR 20mg (Sandostatine) every 4 weeks given during 26 weeks (treatment period).

### Study burden and risks

The burden consists of extra visits (4 times), physical examinations (2 times), blood samples (4 times), and questionnaires (2 times). Patients will also be exposed to the somatostatin analogue Sandostatin LAR and thereby are at risk for known side-effects. The potential benefit for participating patients is that Sandostatin may reduce the need for iron infusions and/or red blood cell blood transfusions by decreasing the number of rebleeds in these patients.

## 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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Patients older than 18 years with written informed consent.
- Endoscopic diagnosis of GAVE, confirmed within the last 12 months
- Endoscopic refractory: at least 1 endoscopic APC, RFA, or other treatment modality performed within 12 months OR unable to receive endoscopic treatment (e.g. Pacemaker, ICD) OR patient has repeatedly indicated that they do not want endoscopic treatment OR treating physician had deemed further endoscopic treatment not relevant
- Substantial transfusion dependency: at least 4 blood units and / or intravenous iron (per 500mg) in the 6 months prior to study inclusion with:
* At least one serum ferritin below < 30 ug/l within the last 6 months requiring iron infusion above or equal to 1 g and/or
* Haemoglobin below 5.6 mmol/l (9.0 g/dl) or are in need of transfusions due to anaemia related symptoms within the last 6 months requiring red blood cell transfusion above.

## Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Insulinoma
- Uncontrolled diabetes mellitus as defined by HbA1c >64 mmol/ml, despite adequate therapy,
- Symptomatic cholecystolithiasis (possible side effect octreotide),
- Pregnancy or nursing women or women have a pregnancy wish during the study period.
- Liver cirrhosis Child-Pugh C
- Chronic or acute pancreatitis
- Patients with other plausible causes of gastrointestinal bleeding (e.g. severe portal hypertensive gastropathy and oesophageal varices which have recently bled)
- Bradycardia (heart rate below 50)*
- Hypersensitivity to the active ingredient (octreotide) or to auxiliary materials of the study medication
- Severe diseases / comorbidities with a life expectancy < 1 year
- Use of other anti-angiogenic drug treatment (thalidomide and / or bevacizumab)
*If a patient has a heart rate below 60 and uses cardiovascular medication that affect the heart rate (e.g. beta blockers and calcium channel blockers) the prescribing specialist (or another competent specialist) will be consulted

about the possibility to adjust the dose of these medicines. Patients with a heartrate below 50 (despite dose adjustments) will be excluded from participation.

# Study design

## Design

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

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 06-04-2021 |
| Enrollment: | 14 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Octreotide |
| Generic name: | Sandostatin |
| Registration: | Yes - NL outside intended use |

# Ethics review

Approved WMO

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|---|---|
| Date: | 19-01-2021 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

Approved WMO

| | |
|---|---|
| Date: | 04-02-2021 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

# 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 | EUCTR2020-004075-41-NL |
| CCMO | NL75077.091.20 |
| Other | NL8824 |