Guselkumab for hidradenitis suppurativa, a mode of action study.

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Primary objective: To investigate changes in inflammatory pathways induced by IL-23p19 blockade with guselkumab, in HS lesional skin at week 16 compared to baseline (t=0).Secondary objectives:- To determine the efficacy of 4 doses of guselkumab of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin and subcutaneous tissue disorders
Study type	Interventional

Summary

ID

NL-OMON48592

Source
ToetsingOnline

Brief title
HiGUS trial

Condition

- Skin and subcutaneous tissue disorders

Synonym
ectopic acne, Hidradenitis suppurativa

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: farmaceutische industrie,Janssen-Cilag

Intervention

Keyword: Biologics, Guselkumab, Hidradenitis suppurativa

Outcome measures

Primary outcome

A. Expression levels of inflammatory cytokine protein and mRNA in HS lesional skin, compared to perilesional skin and unaffected skin.

B. Alterations in serum protein profile (using SOMAscan, Luminex or Olink)

Secondary outcome

C. Clinical efficacy:

* Reduction in total AN count

* Hidradenitis Suppurativa Clinical Response (HiSCR)

* International Hidradenitis Suppurativa Severity Score System (IHS4)

* Photographic evaluation

D. Patient reported outcomes measures:

* Patient global assessment,

* Pain Numeric Rating Scale (pain NRS) to assess pain

* Itch Numeric Rating Scale (itch NRS) to assess itch

* Dermatology Life Quality Index (DLQI)

* Hidradenitis Suppurativa Quality of Life (HS-QoL)

E. Safety and tolerability:

* Vital signs, adverse events, safety laboratories

Study description

Background summary

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease impairing quality of life to a great extent. The pathogenesis of HS has not been clarified yet, however, it is generally accepted that both, the innate and the adaptive immune system have a central role in inducing an aberrant inflammatory response. Systemic treatment of HS is therefore often aimed at suppression of the immune response. Several studies have investigated the cytokine profile of HS and showed that IL-23/Th17 and IL-12/Th1 pathways are overexpressed in HS lesional skin. We demonstrated a 9-fold differential expression of IL-23 p19 in HS lesions compared to healthy control skin (unpublished). In a recent open label study, the IL-12/IL-23 inhibitor ustekinumab was shown to be clinically effective in the majority of HS patients.
Guselkumab is a human monoclonal antibody directed against the IL-23 p19 subunit, recently registered for psoriasis, another auto-inflammatory skin disease. It has been shown that IL-23 has an key role in the inflammatory response in HS, maybe of greater significance in HS than IL-12, as this cytokine is involved in Th17 cell regulation, which are important in a variety of other auto-inflammatory diseases, and which is a potent inducer of keratinocyte proliferation.

As the IL-23/Th17 pathway is central in the pathogenesis of HS, we hypothesize that guselkumab will probably show disease modifying effect on gene expression and cytokine levels in HS skin.

Study objective

Primary objective:
To investigate changes in inflammatory pathways induced by IL-23p19 blockade with guselkumab, in HS lesional skin at week 16 compared to baseline (t=0).
Secondary objectives:
- To determine the efficacy of 4 doses of guselkumab of 200 mg at week 0, 4, 8 and 12 in moderate to severe chronic hidradenitis suppurativa patients, by clinical response rate at week 16
- To assess the short-term the safety and tolerability of guselkumab 200 mg in moderate to severe chronic hidradenitis suppurativa patients at week 16.
- To assess the effect of guselkumab on patient reported outcomes measures.
- To assess effect of guselkumab on changes in levels of inflammatory cytokines and other biomarkers in the peripheral blood.

Study design

A multicenter open-label mode of action study.

Intervention

Twenty patients with moderate to severe hidradenitis suppurativa will be treated with guselkumab 200 mg at week 0, 4, 8 and 12. The total duration of the treatment period per subject is 16 weeks.

Study burden and risks

Eligible patients will be recruited during routine clinical consultations in the department of Dermatology of the UMCG and Erasmus MC. There is a total of 6 site visits. The screening comprises a short medical exam, disease severity assessment, serum test and for women also a pregnancy test. Twenty subjects will be receiving treatment with guselkumab 200 mg. Per subject a total number of five blood samples and seven small skin biopsies will be obtained. Participants will be asked to fill in the following questionnaires: PGA, DLQI, HS-QoL HSIA and NRS scores five times. Clinical photographs (optional) will be taken at defined intervals, the vital signs (blood pressure and heart rate) measured five times. At every visit a short medical exam will be performed and patients will be asked about possible side effects.

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

Adult (* 18 years of age) male or female patients with moderate to severe HS (i.e. a PGA of 3 or more) with a treatment history of at least one systemic anti-in*ammatory / immunosuppressive agent; HS diagnosis of at least 1 year; minimum of two anatomical locations with HS lesions and a minimum of 4 active abscesses and/or inflammatory nodules (AN).

Exclusion criteria

Contra-indication for guselkumab; previous use of guselkumab; use of treatment with biologics or any immunosuppressives for HS in the last 3 months prior to randomization; presence of other uncontrolled major disease; pregnant or lactating women.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2019
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Guselkumab
Generic name:	Guselkumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	24-05-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-07-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-02-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2018-002978-52-NL
CCMO	NL67147.042.18