A Phase 4, Double-Blind, Randomized, Placebo-Controlled Multicenter Study to Assess the Safety and Efficacy of Adalimumab Used in Conjunction with Surgery in Subjects with Moderate to Severe Hidradenitis Suppurativa

Published: 18-05-2016
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Primary objective:Assess the safety and efficacy of adalimumab prior to surgery in subjects with moderate to severe HS who are surgical candidates.Secondary objectives:Assess the impact of adalimumab on the planned HS surgical site before surgery,...

Ethical review	Approved WMO
Status	Completed
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON47251

Source
ToetsingOnline

Brief title
SHARPS

Condition

- Autoimmune disorders
- Skin and subcutaneous tissue disorders NEC
- Skin and subcutaneous tissue therapeutic procedures

Synonym
Hidradenitis Suppurativa; acne ectopica; acne inversa

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Adalimumab, Hidradenitis Suppurativa, Placebo controlled, Surgery

Outcome measures

Primary outcome

The primary efficacy variable is the proportion of subjects achieving HiSCR (Hidradenitis Supprative Clinial Response) at Week 12. HiSCR is defined as at least a 50% reduction in the HS abscess plus inflammatory nodule [AN] count with no increase in abscess count and no increase in draining fistula count relative to Baseline.

Secondary outcome

The secondary endpoints include the proportion of subjects achieving HiSCR-es (defined as the HiSCR excluding the HS surgical site) at Weeks 12 and 24, the change in surface area of the HS surgical site at Week 12, and the proportion of subjects at Week 12 that require less extensive surgical than the surgical plan (determined at Baseline) or no surgery.

Study description

Background summary

Hidradenitis suppurativa (HS), also known as acne inversa is a chronic systemic relapsing inflammatory disease primarily affecting the skin in intertriginous

areas, i.e., axillae, groin, and inframammary region. Hidradenitis suppurativa is characterized by recurrent inflamed deep-seated acneiform nodules that result in abscesses and chronic draining sinus tract formation leading to scarring, disfigurement, and life-altering disability. Its negative impact on quality of life is extreme, mainly due to the lack of early recognition, accurate diagnosis, and appropriate management. HS has a profoundly negative impact on patients* physical, social, and economic lives, with a higher morbidity index than urticaria, neurofibromatosis, psoriasis, atopic dermatitis, or alopecia. HS patients, mainly women, lose an average of 2-7 days of work per year. HS creates a substantial burden of disease, particularly in those subjects with more severe manifestations.

Prior to the Adalimumab Clinical Trial program, the only placebo-controlled trial of HS demonstrated modest efficacy with the use of topical clindamycin. Other treatments for HS include: medical treatment (e.g., systemic combination therapy with clindamycin and rifampicin, intra-lesional triamcinolone), surgical treatment (radical excision, marsupialization, and de-roofing), and laser treatment (carbon dioxide [CO2] laser and neodymium-doped yttrium aluminum garnet [Nd:YAG] laser). It is difficult to evaluate the efficacy for these interventions because their use is described in open-label, frequently retrospective, case series and case reports, with variable, but typically short term follow-up.

Case series and case reports have shown that inhibitors of TNF-α are effective in treating HS. Thus AbbVie conducted Phase 2 and Phase 3 clinical trials, demonstrating the clinical efficacy and safety of adalimumab in subjects with moderate to severe HS.

Adalimumab is a recombinant human immunoglobulin G1 (IgG1) monoclonal antibody containing only human peptide sequences. Adalimumab binds with high affinity and specificity to soluble TNF-α but not to lymphotoxin-α (TNF-β). TNF-α is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Elevated levels of TNF-α are thought to play an important role in pathologic inflammation. Adalimumab binds specifically to TNF-α and neutralizes the biological function of TNF-α by blocking its interaction with the p55 and p75 cell surface TNF-α receptors. Adalimumab received approval in the EU for treatment of active moderate to severe HS in 2015. Additional updates regarding approved indications can be found in the current edition of the Humira Summary of Product Characteristics (SmPC).

Patients undergoing surgery for HS lesions were not studied in the registration trials; therefore there are no placebo-controlled data that inform the physician regarding the impact of adalimumab on HS lesions in the patient who is undergoing surgery as part of therapy to manage the disease. Based on the medical need, AbbVie considers use of adalimumab in conjunction with surgery as part of the treatment for moderate to severe HS, and further investigation is

warranted into the safety and efficacy of combined treatment.

Study objective

Primary objective:
Assess the safety and efficacy of adalimumab prior to surgery in subjects with moderate to severe HS who are surgical candidates.

Secondary objectives:
Assess the impact of adalimumab on the planned HS surgical site before surgery, evaluate the safety and efficacy of adalimumab when used after surgery, evaluate Patient Reported Outcomes (PRO) related to health status, HS-related symptoms (e.g., drainage, swollen skin), physical functioning, treatment satisfaction, and work/activity impairment. The pharmacokinetics (PK) and immunogenicity of adalimumab following subcutaneous (SC) injection in this HS surgical population will also be assessed.

The purpose of the photos and digital imaging sub-study is to determine whether the use of digital imaging proves to be a more efficient and precise measurement of skin wound healing compared to tracing on acetate paper.

Study design

This is a Phase 4, Interventional, Double-Blind, Randomised, Placebo-Controlled, Multicenter study.

Intervention

Subjects receive subcutaneous injections of adalimumab for the duration of 23 weeks in addition to the standard of care for HS. In this case, patients undergo surgery (excision of HS site) as part of their standard of care. Where needed additional examinations are applicable, e.g. physicial examination, blood draws and questionnnaires. When subjects have given approval for imaging, photographs will be taken of their HS lesions.

For patients who are participating in the optional exploratory (extra) study: extra blood draws (total 164,5 ml; fasting), 5 skin-swabs, obtaining skin-biopsies (total of 6) and maintaining and analysis of leftover surgical tissue. The patient can choose which materials are collected for this optional study.

Study burden and risks

Adalimumab therapy has a well-established and well described safety profile based on extensive post-marketing experience and continued clinical trial patient exposure since the first approved indication in 2002 for rheumatoid

arthritis. The safety and efficacy of adalimumab in HS has been explored in the Phase 2 trial and in two Phase 3 trials. To date, 733 subjects with HS have been studied in adalimumab clinical studies in the HS clinical program, for a total of 836.3 patient-years of adalimumab exposure. Treatment-emergent adverse events (TEAEs) were reported in 595 subjects (81.2%) for a rate of 417.6 events/100 patient-years. Worsening hidradenitis, nasopharyngitis, headache, and upper respiratory tract infection were the most frequently reported TEAEs.

Efficacy data from the adalimumab HS clinical program demonstrate that the recommended adalimumab dosing regimen is an effective treatment for inflammatory lesions and skin pain of HS among moderate to severe HS subjects who had an inadequate response or were intolerant to oral antibiotic therapy.

Subjects enrolled in this study will be eligible patients who will have surgical intervention as part of their routine care. Standard practices regarding perioperative and operative care will be under the direction of the dermatologist and/or surgeon and will not be directed per this protocol. It is expected the routine risks of surgery will be essentially unchanged by participation in this study. The subject will be closely followed for any adverse events and the relationship to study drug as assessed by the Study Investigator will be recorded and analysed. As described above for active HS lesions, there is the possibility that adalimumab may positively affect the active HS lesions in the planned surgical site, which might then allow for a less extensive surgical intervention. Adalimumab is predicted to have neither a positive or negative impact on fibrotic lesions within the HS surgical site.

Contacts

Public
AbbVie

Wegalaan 9
Hoofddorp 2132 JD
NL
Scientific
AbbVie

Wegalaan 9
Hoofddorp 2132 JD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male and female subjects between the ages of 18 and 65, inclusive;;- Subject must have skin lesions that are diagnostic of HS for at least 1 year (365 days) prior to the Baseline visit;- Subject must have at least 3 distinct anatomical regions involved with inflammatory (also termed *active*) HS lesions; including;(a) either an axilla or unilateral inguinal region (limited to the inguinal-crural fold and adjacent areas) that requires excisional surgery (hereinafter designated the *HS surgical site*), and ;(b) with at least one of the other affected HS regions (e.g., contralateral inguinal region, buttocks, inframammary region; hereinafter designated the 'HS non-surgical sites) rated as Hurley Stage II or III;- Subject must have a total abscess and inflammatory nodule (AN) count of greater than or equal to 3 at the Baseline visit within the HS non-surgical sites;- The HS surgical site must contain at least one active HS lesion;- The HS surgical site must require excisional surgery and is large enough to require healing by secondary intention as assessed by the designated surgeon

Exclusion criteria

- Subject has a draining fistula count of greater than 20 at the Baseline visit;- Subject requires surgery at any anatomical site other than an unilateral axilla or inguinal region site ;- Subject requires surgical management prior to Week 13, based on the designated surgeon's assessment;- Subject requires, based on designated surgeon's assessment, excisional surgery with primary closure, partial surgical reduction of the excised area with surgical suture, or reconstruction techniques as the method of closure being most beneficial for the subject

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	11-01-2017
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Humira
Generic name:	Adalimumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	18-05-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	22-07-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	30-01-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-04-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-04-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-08-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-08-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-10-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-01-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	08-02-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-04-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2015-005161-23-NL
CCMO	NL56623.078.16

Study results

Date completed: 17-10-2019

Results posted: 07-05-2020

First publication
06-05-2020

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File