Protocol I1F-MC-RHBS;A 52-Week Multicenter, Randomized, Blinded, Parallel Group Study Comparing the Efficacy and Safety of Ixekizumab to Ustekinumab in Patients with Moderate to Severe Plaque Psoriasis

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

Summary

ID

NL-OMON42355

Source
ToetsingOnline

Brief title
IXORA - S

Condition

- Autoimmune disorders
- Epidermal and dermal conditions

Synonym
plaque psoriasis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: ixekizumab, plaque psoriasis, ustekinumab

Outcome measures

Primary outcome

Efficacy: The primary efficacy endpoint is PASI 90 response at Week 12.

Safety: The following safety measures will be assessed in this study: serious adverse events, adverse events (AEs), AEs of special interest, physical evaluations, chest x-ray and tuberculosis testing, vital signs, laboratory evaluations (including safety-related immune markers such as neutrophil counts).

Health Outcomes: The following health outcome measures will be administered in this study: Itch NRS, DLQI, Skin Pain VAS, HADS, Short Form (36-item) Health Survey, patient*s global assessment of disease severity, Work Productivity Activity Impairment questionnaire - psoriasis and European Quality of Life - 5 Dimensions 5Level + Bolt On.

Secondary outcome

Efficacy: Secondary endpoints will be PASI 100, PASI 90, PASI 75, sPGA, Nail Psoriasis Severity Index, Psoriasis Scalp Severity Index, Palmoplantar Psoriasis Severity Index, and body surface area percentage involvement of psoriasis.

Study description

Background summary

Psoriasis is a relatively common chronic inflammatory skin disease, characterized by the formation of red, thick, scaly plaques on the skin, which is often accompanied by itching. Overall, patients' quality of life, work productivity and sleep can be severely impacted by this condition. The currently available treatments are topical therapy, phototherapy and systemic therapy. The first two are not sufficiently effective in patients with moderate to severe psoriasis. Systemic therapy seems to be more promising, but most conventional drugs have limited applicability due to toxicity and side effects. Biological agents show higher rates of improvement, but still the rate of improvement is limited and treatment is often discontinued due to side effects, such loss of efficacy. Increasing levels of clearance result in greater improvements in quality of life. The greatest benefit is expected with at least 90% response and complete clearance of plaques. IL-17A was recently identified as an important factor in the formation of psoriasis. Ixekizumab (LY2439821) is a humanized immunoglobulin G subclass (IgG4) monoclonal antibody (MAb) designed and engineered to selectively inhibit IL-17A (IL-17A).

Previous phase 3 studies with ixekizumab have demonstrated positive benefit/risk profiles. 80 mg ixekixumab every two weeks yielded better outcomes than every 4 weeks in the initial treatment period.

Ustekinumab is currently considered one of the most effective drugs for the treatment of moderate-to-severe psoriasis.
The purpose of Study I1F-MC-RHBS (RHBS) is to compare the efficacy and safety of ixekizumab 80 mg Q2W (12-week induction regimen) followed by Q4W (maintenance regimen) to ustekinumab in patients with moderate-to-severe psoriasis over 52 weeks of treatment.

Study objective

The primary objectives of this study are to assess whether 80 mg ixekizumab every 2 weeks (Q2W) is:
• noninferior to ustekinumab at Week 12 in the treatment of patients with moderate-to-severe plaque psoriasis as measured by proportion of patients achieving 90% improvement in Psoriasis Area and Severity Index (PASI; PASI 90), and then
• superior to ustekinumab at Week 12 in the treatment of patients with moderate-to-severe plaque psoriasis as measured by proportion of patients achieving PASI 90
The key secondary objectives of this study are to compare the following efficacy and health outcomes measures between ixekizumab Q2W and ustekinumab at

the 12-week study time point:
• proportion of patients achieving a >=75% improvement in PASI from baseline (PASI 75)
• proportion of patients achieving a 100% improvement in PASI from baseline (PASI 100)
• binary proportion of patients achieving an sPGA of 0 [remission]
• proportion of patients with a static Physician Global Assessment (sPGA) (0,1) with at least a 2-point improvement from baseline
• proportion of patients achieving dermatology-specific quality of life index (DLQI) (0,1)
• proportion of patients reaching Itch Numeric Rating Scale (NRS) responder definition (decrease of
4 points in the Itch NRS in patients with baseline score >=4 points)
• change from baseline in Itch NRS
• change from baseline in Skin Pain visual analog scale (VAS)

Study design

Study I1F-MC-RHBS is a Phase 3b, multicenter, randomized, blinded, double-dummy, active-comparator, and parallel-group study examining the effect on PASI 90 measured at 12 weeks for ixekizumab versus ustekinumab and subsequent time points for up to 52 weeks in patients with moderate-to-severe psoriasis.
The following treatment groups will be assessed in this study:
• Ixekizumab 80 mg, subcutaneous (SC) injection. After a starting dose of 160 mg (two 80-mg SC injections) at randomization (Week 0), 80 mg will be self-injected SC Q2W, starting at Week 2 until Week 12, and then Q4W thereafter.
• Ustekinumab: 45 mg SC injection for patients <100 kg AND 90 mg SC injection for patients >100 kg.
Injection at randomization (Week 0), at Week 4, and then Q12W thereafter (Weeks 16, 28, and 48). The study will consist of 4 periods:
• Period 1: Screening Period lasting up to 35 days before Period 2
• Period 2: Induction Period from Week 0 (baseline) up to Week 12
• Period 3: Maintenance Period from Week 12 up to Week 52
• Period 4: Post-Treatment Follow-Up Period occurring from last treatment period visit or EarlyTermination Visit (ETV) for a minimum of 12 weeks following that visit

Intervention

Investigational Product, Dosage, and Mode of Administration or Intervention:
80 mg ixekizumab: A starting dose of 160 mg (Week 0) will be given as a 2 SC injections, followed by 80 mg given as 1 SC injection Q2W (Weeks 2, 4, 6, 8, 10, and 12), and then 80 mg given as 1 SC injection Q4W (Weeks 16, 20, 24, 28, 32, 36, 40, 44, and 48).

Reference Therapy, Dose, and Mode of Administration or Comparative Intervention:
45 mg ustekinumab (for patients <=100 kg): A 45-mg dose of ustekinumab (Week 0 and Week 4) will be given as 1 SC injection, and then Q12W (Weeks 16, 28, and 40) thereafter.
Or 90 mg ustekinumab (for patients >100 kg): A 90-mg dose of ustekinumab (Week 0 and Week 4) will be given as 1 SC injection, and then Q12W (Weeks 16, 28, and 40) thereafter.
Planned Duration of Treatment:
Up to 52 weeks for ixekizumab over 4 Periods (Screening Period: up to 35 days before Period 2; Induction Period:
12 weeks; Maintenance Period: 40 weeks; and Post-Treatment Follow-Up Period: 12 weeks after the date of the patient*s ETV or last regularly scheduled visit).

Study burden and risks

There are several risks involved with the study drug. The most common side effects associated with ixekizumab are: Runny nose and sore throat; cold symptoms; Upper respiratory tract infection; Injection site reaction;Headache; Worsening of rheumatoid arthritis; Urinary tract infection; Sinus irritation; Injection site pain; Injection site redness; Diarrhea; Back pain; Bronchitis; High blood pressure; Dizziness; Joint pain; Cough; Nausea; Vertigo.
The comparator, Ustekinumab can have side effect. The subject undergo a number of study procedures, such as filling out questionnaires, blood draws, subcutaneous injections, x rays and genetic testing. These procedures may also be accompanied by certain risks. The combination of treatments and the procedures may also have other unknown risks. These risks are desribed in the informed consent form.

Subjects taking part in this study suffer from moderate to severe psoriasis. Most established therapies show limited improvements and/or have side effects. By inhibiting IL-17A a larger and long-lasting effect may be obtained. Previous studies with ixekizumab showed positive benefit/risks. In addition, this study has no placebo-only group, so patient will always receive a treatment. The comparator is currently considered one of the most effective drugs for this condition.

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

-Are at least 18 years of age;-Have had moderate to severe plaque psoriasis for at least 6 months;-Have had a failure, contraindication, or intolerability to at least 1 systemic;therapy (including cyclosporine, methotrexate, or phototherapy)

Exclusion criteria

-Have forms of psoriasis other than plaque psoriasis. ;-Have recently received certain treatments for their psoriasis (in particular within the last 4 weeks but the restriction can go up to 12 months for some treatments). ;-Have received ustekinumab. ;-Have already been treated with ixekizumab or another drug with a similar mode of action.;-Have received excessive sun exposure or have used tanning booths within 4 weeks prior to receiving treatment in this study or expect to do so during the study.;-Have recently received a live vaccine (within 12 weeks prior to receiving treatment in this study) or plan to do so during the study. ;-Have had a vaccination with Bacillus Calmette-Guerin (BCG) within the past year.;-Have an active or recent infection. ;-Have active or dormant tuberculosis.;-Have a compromised immune system.;-Have another disease which is not currently under control, including heart disease, uncontrolled arterial hypertension, mental illness, and other diseases.;Have either a current diagnosis or a recent history of malignant disease.;-Have allergies to certain treatments or latex.;-Are pregnant or breastfeeding.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-10-2015
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ixekizumab
Generic name:	Ixekizumab
Product type:	Medicine
Brand name:	Stelara
Generic name:	Ustekinumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	22-06-2015
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

Approved WMO Date:	05-08-2015
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-05-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-05-2016
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-02-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-02-2017
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2015-000892-28-NL

Register	ID
CCMO	NL53793.028.15