A Multicenter, Randomized, Double-Blind Study Comparing the Efficacy and Safety of Ixekizumab Versus Placebo in Patients with Moderate-to-Severe Genital Psoriasis

Published: 08-06-2016
Last updated: 15-02-2024

Primary objective: To assess whether ixekizumab is superior to placebo at Week 12 in the treatment of patients with moderate-to-severe genital psoriasisMajor Secondary Objective:To assess whether ixekizumab is superior to placebo at Week 12 in the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Epidermal and dermal conditions
Study type	Interventional

Summary

ID

NL-OMON53160

Source
ToetsingOnline

Brief title
I1F-MC-RHBQ IXORA-Q

Condition

- Epidermal and dermal conditions

Synonym
genital psoriasis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Genital Psoriasis, Ixekizumab (LY2439821)

Outcome measures

Primary outcome

The proportion of patients achieving sPGA of Genitalia (0,1) at Week 12

Secondary outcome

Mean change from baseline in the genital psoriasis itch NRS item within the

GPSS at Week 12

Study description

Background summary

Chronic plaque psoriasis is a common, lifelong, and life-shortening chronic inflammatory skin disease with an estimated prevalence in populations of approximately 3% which manifests as prototypic red, thick, and scaly plaques (Greaves and Weinstein 1995). Psoriasis has been shown to have a significant impact on the overall health of patients with considerable effects on social functioning and quality of life.

Approximately 29% to 63% of patients with chronic plaque psoriasis are impacted by psoriatic lesions in the genital area at some point during the course of the disease (Fouéré et al. 2005; Meeuwis et al. 2010, 2011a; Ryan et al. 2015). Due to moisture and maceration, genital psoriasis
can sometimes lack the characteristic scale present at other body sites (Buechner 2002; Weichert 2004). Both penile and vulvar psoriatic lesions generally appear as symmetrical, bright red thin plaques with a well-defined edge (Buechner 2002; Welsh et al. 2003; ISSVD 2014 [WWW]; Meeuwis et al. 2015). Painful fissures and erosions can also be a problematic clinical feature of genital psoriasis (Barchino-Ortiz et al. 2012; Guglielmetti et al. 2012; Meeuwis et al. 2015), and severe pruritus may lead to scratching with significant excoriations and lichenification (Weichert

2004; Guglielmetti et al. 2012).

When compared to psoriasis patients without genital involvement, quality of life was found to be significantly worse in patients with genital lesions (Meeuwis et al. 2011b, Ryan et al. 2015). Overall Dermatology Life Quality Index (DLQI) score, all domain scores, and DLQI Question 9 (skin caused sexual difficulties) were significantly worse for those psoriasis patients with current genital involvement compared to those without genital lesions. Itch and sexual impairment have been reported as key bothersome issues for patients with genital psoriasis (Meeuwis et al. 2015; Ryan et al. 2015).

Despite the significant impact on quality of life and sexual health, genital psoriasis is often not discussed by patients (AAD Work Group et al. 2011; Meeuwis et al. 2012; Andreassi and Bilenchi 2014), and health care professionals do not routinely question or examine patients for its presence in clinical practice (Farber and Nall 1992; AAD Work Group et al. 2011). While patients with genital psoriasis often do not discuss their symptoms with health care providers, many patients report actively treating their genital lesions (Meeuwis et al. 2012). Therefore, this may indicate a risk of self-treatment in the genital area using medications that were originally prescribed for treatment of other body locations. Inappropriate self-treatment has the potential to result in less than optimal or over-treatment (for example, with potent corticosteroids) and significant adverse reactions. Although genital psoriasis appears to be pathophysiologically identical to plaque psoriasis in other skin regions, the skin in this area is highly sensitive and at increased risk of adverse reactions to topical treatments (CDA 2009 [WWW]; Meeuwis et al. 2011a; Guglielmetti et al. 2012). Moreover, currently available topical agents may not offer an optimal or even appropriate level of clinical improvement or tolerability, especially for patients with moderate-to-severe genital psoriasis. Weaker potency corticosteroids often have limited efficacy for use in maintenance treatment (Welsh et al. 2003), and the use of higher potency corticosteroids is limited due to the development of skin atrophy and striae (Linden and Weinstein 1999). Irritation is commonly reported with vitamin D analogs (Scott et al. 2001; Mason et al. 2013), and they may not be tolerated in the genital region (CDA 2009 [WWW]). Topical calcineurin inhibitors such as pimecrolimus and tacrolimus may improve genital psoriasis but can cause irritancy or a burning sensation, are not helpful in many patients (Menter et al. 2009; Meeuwis et al. 2011[a]), and are not indicated for the treatment of psoriasis. Beyond such topical therapies, there is rather limited evidence for viable therapeutic options to adequately manage genital psoriasis. For instance, psoralen and ultraviolet A (PUVA) and narrowband ultraviolet B (UVB) are not advised for use in the genital region due to potential carcinogenic adverse effects (Stern et al. 1990; Stern et al. 1994; Stern et al. 2002).

Currently, there are limited data from clinical trials, particularly

well-controlled therapeutic interventional studies, which measure the efficacy of treatments for genital psoriasis. To date, the only published treatment studies of genital psoriasis include open-label studies of topical treatments (Jemec and Baadsgaard 1993; Rallis et al. 2005; Martín Ezquerra et al. 2006; Bissonnette et al. 2008), a recent open-label study of a stepwise treatment algorithm (Meeuwis et al. 2015), and scattered case reports.

Study objective

Primary objective:

To assess whether ixekizumab is superior to placebo at Week 12 in the treatment of patients with moderate-to-severe genital psoriasis

Major Secondary Objective:

To assess whether ixekizumab is superior to placebo at Week 12 in the treatment of patients with moderate-to-severe genital psoriasis as measured by change in itch

Study design

Study I1F-MC-RHBQ (RHBQ) is a Phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group, outpatient study examining the efficacy and safety of ixekizumab as compared to placebo in patients with moderate-to-severe genital psoriasis. The study consists of 4 periods: Screening Period, Blinded Treatment Period, Period 3: Open-Label Treatment Period and Post-Treatment Follow-Up

Intervention

The Blinded Treatment Period (Period 2) involves a comparison of ixekizumab 80 mg Q2W (starting dose of 160 mg) and placebo Q2W. All doses are administered via SC injection.

All patients assigned to ixekizumab 80 mg Q2W regimen will receive a starting dose of 160 mg ixekizumab as 2 SC injections. The placebo group will receive 2 SC injections of placebo at this visit as well, to maintain the blind. Afterwards, the dose of investigational product will consist of 1 SC injection of ixekizumab or placebo.

At Week 12, during the Open-Label Treatment Period (Period 3), all patients will be reassigned to ixekizumab 80 mg Q4W. Patients originally assigned to placebo will receive a blinded ixekizumab starting dose of 160 mg as 2 SC injections. To maintain blinding, patients originally assigned to ixekizumab 80 mg Q2W will receive a blinded ixekizumab 80-mg dose

and a placebo dose at Week 12. Dosing may be increased in the Open-Label Treatment Period (Period 3) to ixekizumab 80 mg Q2W, starting at Week 24 through Week 40 (at Visit 9 [Week 24], Visit 10 [Week 28], or Visit 11 [Week 40]), if the patient is eligible to receive additional investigational product.

Study burden and risks

There are several risks involved with the study drug. The most common side effects associated with lxekizumab 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 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 procedures may also have other unknown risks.

Subjects taking part In this study suffer from moderate to severe genital psoriasis. While patients with genital psoriasis often do not discuss their symptoms with health care providers, many patients report actively treating their genital lesions (Meeuwis et al. 2012). Therefore, this may indicate a risk of self-treatment in the genital area using medications that were originally prescribed for treatment of other body locations. Inappropriate self-treatment has the potential to result in less than optimal or over-treatment (for example, with potent corticosteroids) and significant adverse reactions. Although genital psoriasis appears to be pathophysiologically identical to plaque psoriasis in other skin regions, the skin in this area is highly sensitive and at increased risk of adverse reactions to topical treatments (CDA 2009 [WWW]; Meeuwis et al. 2011a; Guglielmetti et al. 2012). Moreover, currently available topical agents may not offer an optimal or even appropriate level of clinical improvement or tolerability, especially for patients with moderate-to-severe genital psoriasis. Weaker potency corticosteroids often have limited efficacy for use in maintenance treatment (Welsh et al. 2003), and the use of higher potency. By Inhibiting IL-17A a larger and long-lasting effect may be obtained. Previous studies with ixekizumab showed positive benefit/risks.Based on the Phase 3 psoriasis clinical trial outcomes, ixekizumab therapy in patients with moderate-to-severe genital psoriasis could address an unmet patient need and a clinical research gap identified by the dermatology community and the American Academy of Dermatology Psoriasis Guidelines of Care Working Group (Ryan et al. 2014).

Contacts

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Trial sites

Listed location countries

Australia, Austria, Belgium, Canada, Netherlands , Turkey, United States of America

Eligibility criteria

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

Inclusion criteria

Are male or female patients of 18 years or older
Present with chronic plaque psoriasis based on a diagnosis of chronic plaque psoriasis for at least 6 months before baseline
Have moderate-to-severe psoriasis in the genital area
Have failed to respond to, or are intolerant of, at least 1 topical therapy (corticosteroids, calcineurin inhibitors and/or vitamin D analogs) used for treatment of psoriasis affecting the genital area
Must agree to use reliable method of birth control

Exclusion criteria

Pustular, erythrodermic, and/or guttate forms of psoriasis
Have a history of drug-induced psoriasis
Have recently received certain treatments with ixekizumab, secukinumab, or brodalumab, or another drug with similar mode of action
Cannot avoid excessive sun exposure or use of tanning booths for at least 4 weeks prior to baseline and during the study
Are currently enrolled in any other clinical trial involving an investigational product
Serious disorder or illness other than plaque psoriasis
Had a live vaccination within 12 weeks prior to baseline (Week 0, Visit 2), intend to have a live vaccination during the course of the study or within 12 weeks of completing treatment in this study
Had a vaccination with Bacillus Calmette-Guérin (BCG) within 12 months prior to baseline
Are women who are lactating or breast feeding

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-07-2016
Enrollment:	9
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ixekizumab
Generic name:	Ixekizumab

Ethics review

Approved WMO Date:	08-06-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Not approved Date:	15-11-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-02-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-04-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-07-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-12-2017
Application type:	Amendment
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	2015-002628-14
CCMO	NL55635.091.16