A Randomized, Double-Blind, Multicenter, Equivalence Study of ONS-3010 and Humira® for the Treatment of Patients with Moderate to Severe Plaque Psoriasis

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Primary:• To demonstrate the therapeutic equivalence of ONS-3010 (adalimumab biosimilar) compared toHumira® (adalimumab) in patients with plaque psoriasis Secondary:• To assess the safety, tolerability, and immunogenicity of ONS-3010 compared to...

Ethical review	Approved WMO
Status	Pending
Health condition type	Skin and subcutaneous tissue disorders NEC
Study type	Interventional

Summary

ID

NL-OMON42923

Source
ToetsingOnline

Brief title
ONS-3010-002 study in patients with moderate to severe plaque psoriasis

Condition

- Skin and subcutaneous tissue disorders NEC

Synonym
plaque psoriasis, recurrent skin disease with chapped and dry skin

Research involving
Human

Sponsors and support

Primary sponsor: Oncobiologics Limited
Source(s) of monetary or material Support: Oncobiologics Inc

Intervention

Keyword: humira, ONS-3010, phase 3, plaque psoriasis

Outcome measures

Primary outcome

Primary efficacy endpoint:

• PASI 75 response rate at Week 17

Secondary outcome

Secondary efficacy endpoints:

• PASI 75 and PASI 90 response rate over time

• PASI value and change in PASI from baseline at each visit

• Change from baseline in sPGA at each visit

• Percentage of patients with sPGA of 0 (clear) or 1 (almost clear) at each

visit

• Change from baseline in Dermatology Life Quality Index (DLQI) at each visit

Safety endpoints:

• Incidence of treatment-emergent AEs (TEAEs) and serious AEs (SAEs)

• Incidence and risk difference between treatment groups of AEs of special

interest:

- Serious infections, including tuberculosis and other opportunistic

infections

- Malignancies

- Injection site reactions

-Hypersensitivity reactions including anaphylaxis

- Liver enzyme elevations

- Demyelinating diseases

- Lupus-like syndromes

- Heart failure

- Hematologic reactions

• Incidence of circulating anti-drug antibodies (ADAs)

• Incidence of neutralizing antibodies

• Clinically significant changes in laboratory values

Please refer to the sub study protocol for additional pharmacodynamic endpoints

Study description

Background summary

The prevalence of psoriasis, a chronic, immunomediated, inflammatory skin disorder, is estimated to be 1 to 6% in industrialized nations. Plaque psoriasis is the most common type of psoriasis, occurring in >80% of affected patients, and is characterized by sharply demarcated, erythematous, silvery white scales typically observed on the elbows, knees, scalp,umbilicus, and lumbar area. Moderate to severe disease is associated with a substantial impairment of the physical and psychological quality of life.
Newer biologic therapies have been designed to modify or regulate specific mechanisms involved in the overproduction of skin cells and inflammation causing psoriasis.One category of biologics selectively inhibits proinflammatory cytokines, such as tumor
necrosis factor alpha (TNF-α), that play a key role in psoriasis

Humira® (adalimumab), one of the TNF-α antagonists used to treat psoriasis, is

a recombinant
human immunoglobulin monoclonal antibody containing only human peptide sequences. Humira is approved for use in the United States (US) and the European Union (EU) for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.

Oncobiologics is developing ONS-3010, a biosimilar of Humira containing the active substance adalimumab. The indications for ONS-3010 are proposed to be the same as currently approved for Humira, and the dosage forms, route of administration, and dosing regimens for
ONS-3010 are to be the same as for Humira for each indication.

The bioequivalence and safety results of the Phase 1 PK study support the next step to the current Phase 3 study of ONS-3010 and Humira in treating patients with moderate to severe plaque psoriasis.

Study objective

Primary:
• To demonstrate the therapeutic equivalence of ONS-3010 (adalimumab biosimilar) compared to
Humira® (adalimumab) in patients with plaque psoriasis

Secondary:
• To assess the safety, tolerability, and immunogenicity of ONS-3010 compared to Humira in patients with
plaque psoriasis

Objective of the sub study:
* To explore the pharmacodynamic effects of ONS-3010 compared to Humira (adalimumab)

Study design

This study is a randomized, double-blind, multicenter,
equivalence study of ONS-3010 and Humira for the treatment of patients with moderate to severe plaque psoriasis.
Approximately 452 patients will be randomized in a 1:1 ratio
to receive subcutaneous injections of ONS-3010 or Humira. There are 3 periods: the screening period, the primary treatment period, and the switching period. The screening period, approximately 4 weeks long for each patient, will be used to assess eligibility. At baseline (Week 0), patients who are eligible will be randomized to 1 of the 2 treatment groups (Humira or ONS-3010). During the primary treatment period (Weeks 0-16), patients will receive their randomized treatment for 17 weeks (80 mg initial dose, followed by 40 mg every 2 weeks

starting 1 week after the initial dose). Primary efficacy assessments will be performed at Week 17.
At Week 17, half of the Humira patients will be randomly assigned to a Switch group. During the switching period
(Weeks 17-23), the Switch group will receive ONS-3010, the other half of the Humira group will continue on Humira, and
the ONS-3010 group will continue on ONS-3010. Safety and efficacy assessments will be performed at Week 25 after the
switching period.
At Week 25, patients may choose to participate in a long-term extension study (Study ONS-3010-003) to continue study treatment through Week 47. Patients who choose not to participate in the extension study will return to the clinic at Week 27 for follow-up assessments.

Sub study:
This is a randomized, double-blind, single-center, sub-study to explore the pharmacodynamics of ONS-3010 and Humira for the treatment of patients with moderate to severe plaque psoriasis, with an optional extension to compare the long-term therapeutic and biologic effects.

Intervention

Investigational therapy:
ONS-3010 (adalimumab biosimilar), administered as a subcutaneous injection with a prefilled syringe. The initial dose is 80 mg (Week 0), and subsequent doses are 40 mg every 2 weeks, starting 1 week after the initial dose (Week 1). Starting with the Week 1 dose, patients will self-administer the doses at home (except at Weeks 3, 9 en 13, when patients may administer the dose in the clinic or at home after the clinic visit, and at Week 17, when the dose will be administered in the clinic).

Reference therapy:
Humira® (adalimumab), administered as a subcutaneous injection with a prefilled syringe. The initial dose is 80 mg (Week 0), and subsequent doses are 40 mg every 2 weeks, starting 1 week after the initial dose (Week 1). Starting with the Week 1 dose, patients will self-administer the doses at home (except at Weeks 3,9 en 13, when patients may administer the dose in the clinic or at home after the clinic visit, and at Week 17, when the dose will be administered in the clinic).

Study burden and risks

Participation in this research takes about 29-31 weeks and will involve 7 visits to the research centre. At the end of the study there is a possibility to participate in an addition 27 week extension study.
Visits to the research center for the main study take approx 1.5- 2 hours. The

following test/procedures will take place: 1x check medical history, 8x vital signs, 6x completion DLQI, 1x complete physical exam, 4x limited physical exam, 2x pregnancy test (women of childbearing potential(repeat only in case menstrual cycle is delayed with ore than 1 month), 2x TB test, 1x chest X ray (only in case of positive TB test and if not done within 12 weeks prior to screening), 1x ECG, 7x blood draw, 8x examination psoriasis, during all visits concomitant medications will be discussed and any adverse events, 6x diary check.

Patients who participate in the sub study will have an additional visit for blood draw and two additional tubes of blood draw during the planned visits. There will be 2D, 3D, 360 degree photo's performed (7x), psoriasis score will be done (6x) as well as skin analysis plaster (6x).

Most common side effects:

The most commonly (occur in 1 in 10 people or more) reported side effects in research studies of Humira were injection site reactions (see bullet above), infections (for example, colds, influenza-like illness, sinusitis), headache, rash, increased lipid levels, decreased red blood cell and white blood cell levels, elevated liver enzyme levels, nausea (feeling sick to your stomach), vomiting, abdominal pain, and musculoskeletal pain. In the study of ONS 3010 in healthy volunteers, the most common side effects were injection site reactions, infections, fatigue, and headache.
• Uncommon , but serious, side effects of Humira have included cancers and serious infections leading to hospitalization or death, including tuberculosis, bacterial sepsis (blood infection), and invasive fungal infections.
• Since ONS-3010 is investigational, there may be risks and side effects that are unknown. All drugs have a possible risk of an allergic reaction.
• During the washout period where prior psoriasis medications will be stopped, there may be seen an increase in psoriasis symptoms.

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

• Men or women at least 18 years of age at the time of screening
• Chronic plaque-type psoriasis diagnosed for at least 6 months before randomization and stable for at least 2 months before screening.Patients will be considered to have stable disease if there have been no new lesions while other lesions remain significantly the same, even if the affected surface area is extensive.
• Moderate to severe psoriasis as defined at screening and baseline by meeting all of the following criteria:
o Psoriasis area severity index (PASI) score of 12 or greater
o Static physician global assessment (sPGA) score of 3 or greater (based on a scale of 0 to 5)
o Body surface area affected by plaque-type psoriasis of 10% or greater
• Chronic plaque-type psoriasis patients who have previously received phototherapy or systemic psoriasis therapy at least once or who are candidates for such therapies in the opinion of the Investigator
• Women of childbearing potential and all males must use an acceptable form of birth control throughout the study. Women of childbearing potential must agree to continue using birth control for 5 months after the last dose. Acceptable methods of birth control include surgery (bilateral tubal ligation, vasectomized partner), hormonal contraceptive (oral, patch, injectable, implantable, intravaginal), intrauterine device, or double physical barrier such as condom plus diaphragm. Postmenopausal status for >1 year will also satisfy this requirement. Also, males are not to donate sperm during the study or for 16 weeks after the last dose.
• Ability and willingness to self-administer study drug
• Ability to read and understand the informed consent form and provide written consent

Exclusion criteria

• Forms of psoriasis other than chronic plaque-type
• Drug-induced psoriasis
• Ongoing use of prohibited psoriasis treatments. Washout periods prior to baseline (first dose of study drug) for prior psoriasis treatments are as follows:
o >=2 weeks for topical medications and ultraviolet B phototherapy
o >=4 weeks for psoralen plus ultraviolet A phototherapy
o >=4 weeks for nonbiologic systemic therapies
o >=12 weeks for other biologic therapies
o >=12 months for alkylating agents
• Exposure to live or live-attenuated vaccines within 8 weeks prior to the screening visit
• Previous exposure to adalimumab
• Treatment with an investigational agent within 12 weeks or 5 half-lives of the drug prior to screening, whichever is longer
• Prior treatment with tumor necrosis factor inhibitors with lack of efficacy as per clinical judgment (primary failure)
• Major surgery within 8 weeks prior to screening or planned to take place during the study period
• Active ongoing inflammatory diseases other than psoriasis that might confound the evaluation of the benefit of study treatment
• History of cancer or lymphoproliferative disease (other than successfully treated non-melanoma skin cancer or localized carcinoma in situ of the cervix)
• History of neurological symptoms suggestive of central nervous system demyelinating disease
• Acute infection requiring treatment with parenteral antibiotics within 4 weeks prior to baseline (first dose of study drug) or oral/topical antibiotics within 2 weeks prior to baseline
• History of human immunodeficiency virus 1 or 2, hepatitis B, or hepatitis C
• Presence of chronic or acute infection at screening, including positive result for active tuberculosis (TB) or untreated latent TB (eg, positive QuantiFERON® test result without any prior history of active or latent TB, and without evidence of active infection), where the patient is not willing to undergo prophylactic treatment
• History of chronic infection or infections within the past 2 years requiring hospitalization or administration of intravenous antibiotics (without evidence of a cure)
• Known hypersensitivity or history of anaphylactoid reaction(s) to adalimumab or its excipients
• Presence of New York Heart Association Class III/IV heart failure
• History of congestive heart failure, recent cerebrovascular accident, or any other condition that, in the opinion of the Investigator, would put the patient at risk by participation in the study
• History of clinically significant cardiac, respiratory (except for mild asthma), renal, hepatic, hematologic, gastrointestinal, neurologic, or psychiatric disease ordisorder, or any other uncontrolled medical illness
• Pregnant, a positive pregnancy test, or intending to become pregnant during or within 5 months after completion of the study, or breastfeeding.
• Impaired bone marrow or hepatic or renal function, including the following:

o Hemoglobin <7.14 mmol/L (11.5 g/dL) for males or <6.21 mmol/L (10.0 g/dL) for females, absolute neutrophil count <1.5 x 109/L (1500 cells/µL), platelets <100 x 109/L (100,000/µL)
o Total bilirubin >=1.5 x the upper limit of normal (ULN), excluding cases where elevated bilirubin can be attributed to Gilbert*s syndrome
o Alanine aminotransferase and aspartate aminotransferase >=1.5 x ULN
o Creatinine >=1.5 x ULN

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	29-09-2016
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Humira
Generic name:	Adalimumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	ONS-3010
Generic name:	adalimumab biosimilar

Ethics review

Approved WMO Date:	13-07-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-08-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2015-004614-26-NL
CCMO	NL56764.056.16