A Multicentre, Randomised, Double-Dummy, Double-Blind Study Evaluating Two Doses of Adalimumab versus Methotrexate (MTX) in Paediatric Subjects with Chronic Plaque Psoriasis (Ps)

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

Summary

ID

NL-OMON37563

Source
ToetsingOnline

Brief title
M04-717 study

Condition

- Epidermal and dermal conditions

Synonym
Not applicable

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Adalimumab, methotrexate, Paediatric, Psoriasis

Outcome measures

Primary outcome

-The proportion of the subjects achieving a >= PASI 75 response at Week 16a standard dose versus MTX.

-The proportion of subjects achieving a PGA 0, 1 at Week 16a, standard dose versus MTX

Secondary outcome

-The proportion of subjects achieving a PASI 90 at Week 16a, standard dose versus MTX

-The proportion of subjects achieving a PASI 100 at Week 16a, standard dose versus MTX

-Change from baseline in the Children*s Dermatology Life Quality Index (CDLQI) scores at Week 16a, standard dose versus MTX

-Change from baseline in the Paediatric Quality of life Inventory (PedsQL) scores at Week 16a, standard dose versus MTX

-The proportion of subjects achieving PGA 0, 1 upon completion of retreatment (Period C) according to the original randomised group assignment in Period A (standard dose adalimumab versus low dose of adalimumab)

-Time to loss of disease control (Period B) according to the original

randomised group assignment in Period A (standard dose adalimumab versus low

dose adalimumab and MTX)

Study description

Background summary

Psoriasis is a chronic immunologic disease characterized by marked inflammation and thickening of the epidermis, resulting in thick, scaly plaques involving the skin. It affects 1-3% of the general population with North America and Europe having the highest disease prevalence. There are different forms of psoriasis which are classified by de cutaneous presentation.
Psoriasis in childhood and adolescents most commonly manifests as plaque and guttate psoriasis. The most common type of Psoriasis seen among very young children is napkin psoriasis/psoriatic diaper rash. There is controversy, however, whether or not this is true psoriasis or whether it represents other dermatologic conditions.
The most commonly used topical therapies in children include corticosteroids, calcipotriol and tazarotene, salicylic acid, tar and anthralin.
Systemic treatments include among others cyclosporin A and methotrexate (MTX). In addition there are the TNF-alpha inhibitor. Data have indicated that inhibitors of TNF-alpha are efficacious in treating psoriasis in adults.
Adalimumab is a recombinant human immunoglobin (IgG1) monoclonal antibody containing only human peptide sequences. Adalimumab binds with high affinity and specificity to soluble TNF-alpha, but not to TNF-beta. Less side effects and an extended response to treatment are expected because adalimumab is completely human. This study will be performed with pediatric patients.

Study objective

The objectives of this study are to determine the safety and efficacy of two doses of adalimumab versus MTX in paediatric subjects with chronic plaque psoriasis, to determine the time to loss of disease control and the ability to regain response upon retreatment, and to examine the pharmacokinetics and immunogenicity of adalimumab following SC administration in this subject population.

Study design

A multi-centre study

Intervention

The study consists of four periods, period A, B,C, and the
-In Period A the subjects will be randomized into three groups in a 1:1:1 ratio. These subjects receive a standard dose of adalimumab (0,4 mg/kg up to a maximum of 40 mg) every other week and weekly MTX placebo , a low dose of adalimumab (0.2 mg/kg up to a maximum of 20mg) every other week and weekly MTX placebo or weekly MTX (0,1 mg/kg at baseline and 0,4 mg/kg after obtaining acceptable lab results up to 25mg/wk) and adalimumab placebo every other week. Period A has a duration of 16 weeks and up to week 8 there is the option of an early escape to Period D.
-Subjects with a good response in Period A (PASI 75 and PGA 0, 1) will enter Period B and will be withdrawn form active therapy. The subjects without a good response in Period A will enter Period D. Period B has a duration of up to 36 weeks. Subjects who experience loss of disease control will enter Period C. Subjects who do not experience loss of disease control during Period B will enter Period D without medication.
-Subjects who experience loss of disease control in Period B will enter Period C. Subjects who received the standard dose of adalimumab at the beginning of the study will also receive this during Period C, the subjects who received the low dose of adalimumab at the beginning of the study will also receive this during Period C and subjects who received MTX at the beginning of the study will receive the standard dos of adalimumab. Period C has a duration of 16 weeks. After this Period all subjects will enter Period D.
-Period D has a duration of 52 weeks and is the Follow up period.
Subjects who transfer from Period A directly to Period D receive the open label standard dose of adalimumab. Subjects who transfer from Period B to Period D will not receive medication unless they experience loss of disease control in Period D. In this case, they will receive the blinded standard dose of adalimumab if they received the standard dose of adalimumab or MTX in Period A. If they received the low dose of adalimumab in Period A, they will also receive the blinded low dose of adalimumab in Period D.
Subjects who transfer from Period C to Period D will continue with the (blinded) dose they received in Period C. Subjects who experience loss of disease control in Period D will have the option to receive open label standard dose of adalimumab.

Study burden and risks

The subjects will take part in the study for a minimum of 56 weeks (based on a minimum of 4 weeks in Period A and a maximum of 52 weeks in Period D). The maximum time in the study will be 120 weeks (based upon a subject losing control of disease at Week 36b and completing all other study periods).

During the screening visit a PPD (Mantoux) or QuantiFERON - TB test will be done. If the test result is positive, chest x-rays will also be done. The

subject will be exposed to a small amount of radiation during the x-rays of the chest. This radiation is not considered to be a significant risk.
Blood samples will be taken during the study in Period A (Week 0a, 1a, 4a, 8 16a), Period B (Week 4b, 12b, 16b), Period C (Week 0c 4c, 11c) and Period D (Week 0d, 4d, 16d, 52d).
Urine samples will also be taken during screening, Period A (Week 0a, 16a), Period C (Week 0c), Period D (Week 0d, 4d, 16d, 52d). Furthermore, If a subjects decides to stop participating in the study, blood will be drawn and urine will be collected during the last visit (early termination visit).
Blood will be drawn from subjects who can become pregnant during screening for the pregnancy test. During all other visits, urine will be taken for the pregnancy test.
The subjects will also be asked to complete the CDLQI, PedsQL and CDI:S questionnaires during Period A (Week 0a, 4a,8a, 16a), all visits during Period B, Period C (Week 0c, 1c, 4c 8c, 11c), Period D (0d, 1d, 4d, 8d, 11d) and during the early termination visit if the subject decides to stop participating in the study.

The subject may experience adverse events when the study drug is used. The most common adverse events of adalimumab were reactions at the injection site. Subjects suffered from redness, itching, bruising, pain and/or swelling of the injection site. Most injection site reactions were described as mild and most of them disappeared without having to stop the administration of study medication.
Other frequently reported side effects (rate of >= 5 %) of adalimumab in subjects participating in the clinical studies in order of decreasing frequency are: nasopharyngitis, upper respiratory infection, headache, nausea, bronchitis, diarrhea, cough, sinusitis, influenza (flu), hypertension (increase in blood pressure), urinary tract infection, back pain, and rash.

Men and women who are sexually active should use a reliable contraceptive method as described in the protocol. The use of certain medications is not permitted if the subject is participating in the study, these medications are listed in the protocol.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

1. Subject is >= 4 years and < 18 years of age;;2. Subject weighs >= 13 kg;;3. Subject must have failed to respond to topical therapy;;4. Subject must need systemic treatment to control his/her disease and meet one of the following:;• PGA >= 4;• Body surface area (BSA) involved > 20%;• Very thick lesions with BSA > 10%;• PASI > 20;• PASI > 10 and at least one of the following:;• Active psoriatic arthritis unresponsive to non-steroid anti-inflammatory drugs (NSAIDs);• Clinically relevant facial involvement;• Clinically relevant genital involvement;• Clinically relevant hand and/or foot involvement;• CDLQI > 10;5. If subject is < 12 years of age and resides in a geographic region where heliotherapy is practical, subject must have failed to respond, be intolerant, or have a contraindication to heliotherapy, or is not a suitable candidate for heliotherapy;;6. If >=12 years of age, subject must have failed to respond, be intolerant, or have a contraindication to phototherapy, or is not a suitable candidate for phototherapy;;7. Subject must have a clinical diagnosis of psoriasis for at least 6 months as determined by the subject's medical history and confirmation of diagnosis through physical examination by the Investigator;;8. Subject must have stable plaque psoriasis for at least 2 months prior to Baseline;

Exclusion criteria

1. Prior biologic use other than prior treatment with etanercept;;2. Treatment with etanercept therapy within 4 weeks prior to the Baseline visit;;3. MTX use within the past year or prior

MTX use at any time where the subject did not respond, or did not tolerate MTX;;4. Contraindication for treatment with MTX during the study;;5. Erythrodermic Ps, generalized or localized pustular Ps, medication-induced or medication exacerbated Ps or new onset guttate Ps;;6. Infection(s) requiring treatment with intravenous (IV) anti-infectives within 30 days prior to the Baseline Visit or oral anti-infectives within 14 days prior to the Baseline Visit;;7. Treatment of Ps with topical therapies such as corticosteroids, vitamin D analogs, or retinoids within 7 days prior to the Baseline visit;;8. Treatment of Ps with UVB phototherapy, excessive sun exposure, or the use of tanning beds within 7 days prior to the Baseline visit;;9. Treatment of Ps with PUVA phototherapy, non-biologic systemic therapies for the treatment of Ps, or systemic therapies known to improve Ps within 14 days prior to the Baseline visit;

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):	04-09-2012
Enrollment:	10
Type:	Actual

Medical products/devices used

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

Brand name:	methotrexate
Generic name:	methotrexate
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-05-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-08-2012
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-11-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-03-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-07-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-10-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-06-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-09-2014

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	EUCTR2009-013072-52-NL
ClinicalTrials.gov	NCT01251614
CCMO	NL39898.091.12