A randomized, double blind, placebo-controlled, double-dummy study to assess microneedle delivery in comparison to subcutaneous injection of adalimumab in healthy volunteers

Published: 16-05-2018
Last updated: 11-04-2024

1) To evaluate the pain, acceptability and local tolerability of intradermal microneedle injection compared to subcutaneous injection in healthy volunteers.2) To evaluate the safety, pharmacokinetics, pharmacodynamics, and immunogenicity of...

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

Summary

ID

NL-OMON46242

Source
ToetsingOnline

Brief title
Adalimumab microneedles in healthy volunteers

Condition

- Other condition
- Immune disorders NEC

Synonym
Route of administration for immunosuppressive drug

Health condition

Route of administration

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: the department of paediatric rheumatology of the Leiden University Medical Center by a grant to dr. Rebecca ten Cate

Intervention

Keyword: Adalimumab, Healthy volunteers, Microneedle, Pharmacokinetics

Outcome measures

Primary outcome

Safety endpoints

- (Serious) adverse events ((S)AE)

- Vital signs and clinical laboratory assessment

- ECG

- Locale tolerance:

1) VAS for pain, separate for injection and insertion pain, using (1) the Faces

Pain Scales Revised (official Dutch translation); (2) 100 points VAS;

2) Irritation; itching; spontaneous reporting;

3) Clinical evaluation in a standardized manner by physician (appendix 1).

- Clinical imaging of the skin: these data might provide insight into the

mechanisms of intradermal drug delivery and might serve as future comparison

for other studies examining intradermal administration of biologicals. The

following assessments will be performed:

* Clinical photography

* Thermal imaging

* Optical coherence tomography

* Laser speckle contrast imaging

Immunogenicity endpoint

- Formation of anti-adalimumab antibodies (AAA)

Acceptability endpoints

- Questionnaire on perception, convenience, and fear for injection

Pharmacokinetic endpoints

- Area under the concentration-time curve (AUC);

- Maximal concentration (Cmax);

- Time to maximal concentration (Tmax);

- Half-life (T1/2);

- Clearance (Cl);

- Bioavailability (F).

Pharmacodynamic endpoints

- Ex vivo cytokine levels

Secondary outcome

N.A.

Study description

Background summary

Adalimumab (Humira, AbbVie) is a highly effective treatment for a variety of auto-immune/auto-inflammatory diseases including juvenile idiopathic arthritis (JIA). Adalimumab works by binding to tumor necrosis factor alpha (TNF), hereby preventing its interaction with the TNF receptor. In the presence of complement, adalimumab can also lyse TNF-expressing cells.

Adalimumab is administered via subcutaneous injection, which has the major drawback of being perceived as unpleasant and painful, especially during long term use for both adults and children. As subcutaneous administration may therefore eventually jeopardize treatment adherence, there is a clear need for less invasive alternatives to administer highly effective biological drugs such as adalimumab.

Study objective

1) To evaluate the pain, acceptability and local tolerability of intradermal microneedle injection compared to subcutaneous injection in healthy volunteers.
2) To evaluate the safety, pharmacokinetics, pharmacodynamics, and immunogenicity of adalimumab after administration using microneedles versus subcutaneous injection in healthy volunteers.
3) To explore the usability of optical coherence tomography, clinical photography, and thermal imaging in the evaluation of intradermal injections

Study design

This is a double blind, placebo controlled, double-dummy study. The study physician will administer the injection and is thus unblinded to the type of injection. All injection site assessments will be performed by (a) study independent member of the clinical staff.
Sterile saline injection will be used as a negative control. Subjects will receive an injection with both sterile saline (SC or ID) and adalimumab (SC or ID). Subjects will be randomized to one of the four arms:

1A) adalimumab SC and saline ID
1B) saline ID and adalimumab SC
2A) saline SC and adalimumab ID
2B) adalimumab ID and saline SC

The maximum duration between treatments will be 5 minutes.

After a single dose of adalimumab, pharmacokinetic, pharmacodynamics, tolerability and immunogenicity data will be collected and monitored for a total of 70 days post dose, as the half-life of adalimumab after subcutaneous

injection in adults is approximately two weeks

Intervention

Adalimumab

Study burden and risks

Burden: measurements, SC and ID injections, local irritability, blood sampling, lifestyle restrictions and time investment.
Risks: potential adverse events

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Eligible subjects must meet all of the following inclusion criteria at screening:
1) Healthy male / female subjects, 18 to 45 years of age, inclusive at screening;
2) Good health, based upon the results of medical history, physical examination, vital signs, ECG, and laboratory profiles of both blood and urine;
3) Body mass index (BMI) between 18 and 30 kg/m2, inclusive at screening, and with a minimum weight of 50 kg;
4) Willing to practice an approved method of birth control and not breastfeeding throughout the study and for five months after study drug administration, as advised in the drug formulary (2). If the trial subject is female, surgical sterilization or postmenopausal status for >1 year will satisfy this requirement. All female subjects are required to have a negative pregnancy test at screening and at baseline (pre-dose);
5) Fitzpatrick skin type I-II (Caucasian type);
6) Suitable site for intradermal injection on the legs, as assessed by the investigator;
7) Able and willing to provide written informed consent.

Exclusion criteria

Eligible subjects must meet none of the following exclusion criteria at screening:
1) Immune-compromised (known or expected immune deficiency, disease, or use of medication that may affect the immune system);
2) Diagnosed with tuberculosis (TB, as per positive skin test [Mantoux] or interferon gamma release assay), or history of TB, or latent TB, or recent contact with TB (patient); having travelled to countries where TB is endemic within eight weeks of planned drug administration or planning to travel to countries where TB is endemic from the moment of drug administration until three months after the end of the study;
3) Any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug (including adalimumab);
4) History of chronic infection, or infections within the past two years requiring hospitalization or administration of intravenous antibiotics;
5) Receipt of any live vaccination within three months prior to study drug administration, or intention to undergo live vaccinations from the moment of drug administration until four months after the end of study;
6) Positive hepatitis B surface antigen (HBsAg), hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening;
7) Evidence of any active or chronic disease (hematologic, renal, hepatic, cardiovascular, neurologic, endocrinal, gastrointestinal, oncologic, pulmonary, immunologic, or psychiatric disorder) or condition that could interfere with, or for which the treatment of might interfere with the conduct of the study, or that would pose an unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, and body temperature) and ECG). Minor deviations from the normal range may be accepted, if judged by the investigator to have no clinical relevance;

8) History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 21 units alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent;
9) Consumption of alcohol within the 48-hour period prior to study drug administration;
10) Smoke more than 10 cigarettes per day prior to screening or use tobacco products equivalent to more than 10 cigarettes per day and/or unable to abstain from smoking whilst in the unit;
11) Positive screen for recreational drugs or alcohol;
12) Is demonstrating excess in xanthine consumption (more than eight cups of coffee or equivalent per day);
13) Unlikely to comply with the study protocol and/or to complete the study or required study procedures, including being unlikely or unable to return for follow-up visits;
14) Use of any medication (prescription or over-the-counter (OTC) within 14 days of study drug administration, or use of herbal supplements, dietary supplements or multivitamins within 7 days of study drug administration or less than five half-lives (whichever is longer), or receipt of any drug by injection within 30 days of study drug administration, with the exception of contraceptives, hormonal replacement therapies, and paracetamol (up to 4g/day). Other exceptions will only be made if the rationale is clearly documented by the investigator;
15) Donation of over 500 mL of blood within three months prior to screening or donation of plasma within 14 days prior to screening;
16) Previous exposure to any biological;
17) Participation in an investigational drug or device study within 3 months prior to screening or more than 4 times in the past year;
18) 18) Excessive sun exposure of the injection site area within 3 weeks of enrollment;
19) Consideration by the investigator, for any reason, that the subject is an unsuitable candidate to receive adalimumab or otherwise participate in the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-05-2018
Enrollment:	24
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	16-05-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-05-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-07-2018
Application type:	Amendment

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	EUCTR2018-001533-41-NL
CCMO	NL65800.056.18