Final Study Report

Study Title: A non-inferiority study on dose reduction of adalimumab in psoriasis patients who are overtreated (SUPRA-A)

EU reference number: 2019-001918-42

Clinical Investigation identification number (CIV ID): not applicable

Study protocol/CIP code: TDM-ADA2019 (SUPRA-A)

Investigational device / medicinal product: Adalimumab

ClinicalTrials.gov identifier: NCT04028713

Sponsor: Ghent University Hospital

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Date of report: *21/03/2023*

By signing this final study report, I acknowledge that the information is accurate and complete.

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Date signature Coordinating Investigator: 21/03/2023

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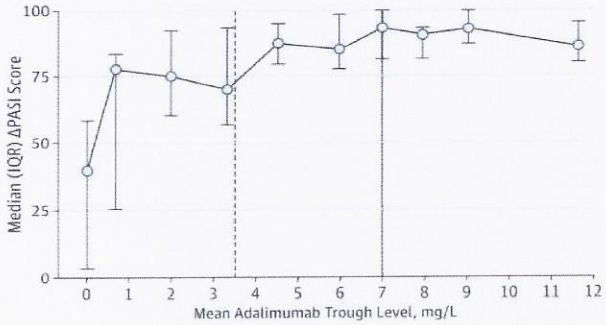
1. Introduction

Psoriasis is a chronic inflammatory disease that primarily affects the skin through red, scaly lesions that cause uncomfortable itch and pain. Biologics, like adalimumab, are used for the treatment of moderate-to-severe psoriasis.

Adalimumab was approved by the EMA (European Medicines Agency) in 2003 for the treatment of psoriasis. It is a fully human monoclonal antibody, which binds to free circulating TNFα, preventing it from activating TNF receptors. In the clinic, adalimumab is currently prescribed according to an 'one dose fits all' dosing regimen despite interindividual variability in pharmacokinetic and immunological response towards adalimumab. So nowadays, all psoriasis patients are treated according to an identical dosing regimen, namely one subcutaneous injection (80 mg) at week 0, followed by subcutaneous injections once every other week (40 mg).

This principle leads to potential over- or undertreatment in some patients. In 2015, our group defined the therapeutic window of adalimumab in a psoriatic cohort (Figure 1). Here, adalimumab concentrations exceeding 7 µg/ml (full vertical line*) had no additional value to therapeutic response.[1] Patients with these supratherapeutic Ctrough levels may achieve similar therapeutic effects with a lower concentration (through longer dosing intervals), which will reduce costs as well.

This study consists of two parts. **In the main study we investigate whether dose reduction of adalimumab in patients with supratherapeutic adalimumab Ctrough levels is non-inferior to standard dosing of adalimumab.** The results of this main study could guide physicians and patients and would prevent trial-and-error treatment modifications.



**In this study we take into account a higher threshold level of 8 µg/mL as upper limit of the therapeutic window of adalimumab. This in order to compensate for potential variation in the analytic method which is used (lateral flow vs. ELISA)*

In addition, we will perform a substudy in order to validate the use of a home micro-sampling technique (Mitra®) for the monitoring of adalimumab concentrations. Patients can themselves collect Mitra samples at home and send the samples by regular mail to the laboratory for subsequent evaluation of adalimumab trough concentrations, without first coming to the hospital. The use of home sampling would facilitate the implementation of therapeutic drug monitoring in a real world clinical setting.

2. Objectives of the study

2.1 Primary objectives

Main study: The proportion of patients in each group in clinical remission (absolute PASI < 2) at year 1 after optimization (non-inferiority of intervention).

Substudy (*UZ Gent patients only*): Optimization of extraction protocol for adalimumab serum trough levels and anti-drug antibodies (ADA) derived from micro-sampling technique (Mitra).

2.2 Secondary objectives

- The proportion of patients in each group who relapses [defined as the need for dose escalation (not in the standard based dosing arm)]
- The proportion of patients in each group with serum trough levels (Ctrough) of adalimumab within the optimal interval
- The proportion of patients in each group with anti-drug antibodies (ADA) against adalimumab (ADA positivity)
- Evaluation of the cost-effectiveness of the intervention
- Recording of demographic parameters during disease course monitored at baseline and at every visit (reflected by incidence, prevalence, mortality, standardized comorbidity incidence ratios and associations/risk factors)
- Quality adjusted life years (QALY)
- Determine inter- and intrapatient variability (IPV)
- HRQoL EQ-5D-5L

3. Investigational Medicinal Product

3.1 Composition and dosing

The active substance 'adalimumab' is a fully human monoclonal antibody, which binds to free circulating TNFα, preventing it from activating TNF receptors. Adalimumab is available as a solution for subcutaneous injection in pre-filled syringes or pre-filled pens. Each 0.8 ml single dose pre-filled syringe or pre-filled pen contains 40 mg of adalimumab. The recommended dose is 80 mg as a single dose (loading dose), followed by 40 mg every other week.
Patients in the dose tapering group of the main study will follow an off-label dosing regimen, either 40 mg every 3 weeks or 40 mg every 4 weeks.

3.2 Producer

Example given: Humira
AbbVie Biotechnology GmbH
Knollstrasse
67061 Ludwigshafen
Germany

However, any other producer of an approved drug with the active substance 'adalimumab' is accepted in this clinical trial.

3.3 Distributor

For the main study, the distribution of adalimumab is established in collaboration with the pharmacy of the university hospital Ghent. Adalimumab was ordered by the pharmacy on prescription and delivered to the dermatology department where the adalimumab was labelled on site with an annex 13 label (see 3.6) At each study visit in UZ Ghent (week 0 and week 12 or 13), the patients received a batch of adalimumab pens/syringes on site in order to self-administer adalimumab at home at the appropriate time points (depending on the study group in which the patients is randomized).

If patients still have adalimumab supply at home, the patients will be asked to bring the adalimumab to the clinic where it will be labelled on site. Afterwards, the patients can self-administer adalimumab at home at the appropriate time points (depending on the study group in which the patient is randomized).

3.4 Packaging

The active substance 'adalimumab' is packed as a pre-filled syringe or prefilled pen.

3.5 Administration way

The active substance 'adalimumab' is administered by subcutaneous injection by the patient or by medical staff members.

3.6 Labelling

The active substance 'adalimumab' will be was delivered at the department of dermatology at UZ Ghent by the hospital pharmacy on prescription. All packages of adalimumab were labelled on site with an annex 13 label in accordance with the appropriate laws. An example of the label is provided below.

EudraCT N°: 2019-001918-42
Patiënt ID nr°/ Identifiant du sujet/ ID des Probanden:

_____
Initialen/ Initales/Initialen:___
Datum visite/ Date de visite/Datum des Besuchs:

_____
ENKEL VOOR STUDIEGEBRUIK
SEULEMENT POUR USAGE D'ETUDE
NUR FÜR STUDIENZWECKE
PROF.DR. JO LAMBERT Tel: +32 9 33 22287

3.7 Storage conditions

The prefilled syringes/pens with the active substance 'adalimumab' will be stored on site in temperature-controlled fridges ranging from 2-8 °C., not frozen, and protected from light. Vigorous shaking of the product should be avoided. The sterile product does not contain preservatives and is designed for single use only. Prior to administration, the product should be inspected visually for particulate matter and discoloration. If discoloration (other than a slight yellow color), visible opaque particles, or other foreign particles are observed in the solution, the product should not be used. At each study visit in UZ Ghent (week 0 and week 12 or 13), the patients will receive a batch of adalimumab pens/syringes on site in order to self-administer adalimumab at home at the appropriate time points (depending on the study

group in which the patients is randomized). Patients need to store the adalimumab pre-filled pens/syringes at 2-8 °C until 30 minutes before administration (standard of care).

4. Investigational Medical Device

Not applicable.

5. Study Protocol Summary

5.1 Study design

Main study: A prospective, single blinded, randomized (1:1), non-inferiority study evaluating dose reduction of the active substance 'adalimumab' in psoriasis patients who are overtreated.

Substudy: A prospective, clinical validation study evaluating the use of Mitra® as home sampling device for evaluation of adalimumab trough concentrations in a real world setting.

5.2 Inclusion criteria

Each potential participant must satisfy all the following criteria to be enrolled in the main study (A) or substudy (B) respectively:

1. Participants must be >18 years of age.[A-B]
2. Participants must have a diagnosis of chronic plaque-type psoriasis[B] for at least 6 months (with or without PsA), prior to inclusion. [A]
3. Participants must be treated with adalimumab according to the standard dosing regimen during maintenance [A-B]
4. Participant must remain on a highly effective method of birth control during the study or during the entire treatment with adalimumab (whichever is longer). [A-B]
5. Participants must agree not to receive a live virus or live bacterial vaccination at least 3 months (or longer as indicated in the package insert of the relevant vaccine) prior to the first administration of study intervention (except for varicella and MMR vaccines), during the study, or within 3 months after the last administration of study intervention. [A-B]
6. Participants must avoid prolonged sun exposure and use of tanning booths or other ultraviolet light sources during study and are not allowed to use topical steroids from 7 days before randomization until the end of the study [A-B]
7. Participants must sign an ICF indicating that he or she understands the purpose of, and procedures required for, the study and is willing to participate in the study. [A-B]

5.3 Exclusion criteria

Any potential participant who meets any of the following criteria will be excluded from participating in the main study(A) or substudy (B):

1. Participants who have currently a predominant nonplaque forms of psoriasis (e.g. Erythrodermic, guttate, pustular). [A-B]
2. Participants who are pregnant, nursing or planning a pregnancy or fathering a child while enrolled in the study or within 12 weeks after receiving the last administration of study intervention. [A-B]
3. Participants who have received, or are expected to receive, any live virus or bacterial

vaccination (with the exception of varicella or MMR vaccines) within 3 months (or longer as indicated in the package insert of the relevant vaccine) prior to the first administration of study intervention, during the study, or within 12 weeks after the last administration of study intervention. [A-B]

4. Participants who have known allergies, hypersensitivity or intolerance to adalimumab or its excipients. [A-B]
5. Participants who are unable or unwilling to undergo multiple venipunctures. [A-B]

5.4 Primary endpoint

Main study: The proportion of patients in each group in clinical remission (absolute PASI < 2) at year 1 after optimization (non-inferiority of intervention).

Substudy (UZ Gent patients only): Optimization of extraction protocol for adalimumab serum trough levels and anti-drug antibodies (ADA) derived from micro-sampling technique (Mitra).

5.5 Secondary endpoints

The proportion of patients in each group who relapses [defined as the need for dose escalation (not in the standard based dosing arm)]
- The proportion of patients in each group with serum trough levels (Ctrough) of adalimumab within the optimal interval
- The proportion of patients in each group with anti-drug antibodies (ADA) against adalimumab (ADA positivity)
- Evaluation of the cost-effectiveness of the intervention
- Recording of demographic parameters during disease course monitored at baseline and at every visit (reflected by incidence, prevalence, mortality, standardized comorbidity incidence ratios and associations/risk factors)
- Quality adjusted life years (QALY)
- Determine inter- and intrapatient variability (IPV)
- HRQoL EQ-5D-5L

5.6 Procedures

5.6.1 Adalimumab administration

In the main study: Adalimumab will be self-administered subcutaneously at home according to the dosing regimen which will be defined at week 0 (randomization).

Patient in group A will continue the standard dosing regimen of adalimumab, meaning subcutaneously injection of 40 mg every other week. Patients in group B will subcutaneously administrate 40 mg adalimumab once every 3 weeks. If patients of group B still have 3x supratherapeutic serum trough levels of adalimumab (week 0, week 7 and week 10), these patients will be continuing adalimumab self-administration every 4 weeks. Injection sites include the front of thighs, the lower abdomen or the back of the upper arms. Different sites

should be used for consecutive injections.

5.6.2 Blood sampling

Main study: At every study visit (screenings (3x), week 0, week 7, week 10*, week 12, week 24, week 36 and week 48) blood samples will be collected by the study site personnel in order to determine the Ctrough and ADAs of adalimumab.

* only applicable for patients in the dose tapering group

5.6.3 Determine serum drug concentrations of adalimumab

Lateral flow (LF) and ELISA

All adalimumab Croughs will be determined using ELISA (RIDASCREEN® ADM monitoring) and lateral flow assay (RIDA®QUICK ADM Monitoring) at week 0 and week 13. If drug concentrations below the detection limit are measured, the concentration of anti-drug antibodies will also be determined via ELISA (RIDASCREEN® Anti-ADM Antibodies). The analysis will take place in the laboratory of KU Leuven. The transportation of the samples to KU Leuven will be coordinated by UZ Gent.

Micro-sampling

To be able to build a PK(PD) model for adalimumab, Croughs will also be measured in weekly sampled micro-samples (Mitra) in a maximum of 40 patients. Micro-samples (Mitra) are chosen as they minimally increase the burden of patients and can be performed at home. Protocol for extraction needs to be optimized and a conversion rate (in comparison with serum) needs to be calculated.

After enrollment of the patient for micro-sampling, kits for finger pricks will be provided. During their first visit after inclusion for this part, the study nurse will teach each patient how to collect blood on the card. Patients will be asked to sample micro-samples (Mitra) on days 0, 3, 5, 7, 14, 21, 28, 35, 42 and 49 (±1 day) after the first drug injection post-inclusion. Venous puncture for serum preparation will be collected on days 0, 14 & 28 (standard dosing regimen) or 0, 21 & 42 (tapering regimen). The micro-samples will be collected during those hospital visits and stored at room temperature. After extraction, analysis of micro-samples extracts will be performed through ELISA. To calculate the serum/micro-samples conversion rate, a direct comparison of micro-samples and serum will be done. The analysis will be performed in UZ Ghent.

5.6.4 Determine anti-drug antibodies of adalimumab

The adalimumab anti-drug antibody concentrations will be determined using a validated ELISA (RIDASCREEN® anti-ADM Antibodies). The analysis will take place in the laboratory of KU Leuven.

5.6.5 Efficacy evaluations

Psoriasis Area and Severity Index (PASI)

The disease severity will be assessed using the Psoriasis Area and Severity Index (PASI). See appendix 1 for more detailed information.

Investigator's Global Assessment (IGA)

The disease severity will be assessed using the Investigator's Global Assessment (IGA). See appendix 2 for more detailed information.

Dermatology Life Quality Index (DLQI)

The impact of the disease on the patient will be assessed using the dermatology life quality index (DLQI). See appendix 3 for more detailed information.

HRQoL EQ-5D-5L questionnaire

EQ-5D-5L is a standardized instrument developed by the EuroQol Group as a measure of health-related quality of life that can be used in a wide range of health conditions and treatments. The EQ-5D-5L consists of a descriptive system and the EQ VAS. (EQ-5D © 2018 EuroQol Research Foundation). See appendix 4 for more detailed information.

Flowchart main study

	Screening 1 Site	Screening 2 Site	Screening 3* UZ Gent	Week 0 (Randomization) UZ Gent	Week 6 (± 2d) Site	Week 9** (± 2d) Site	Week 12 (± 2d) UZ Gent	Week 24 (± 2d) Site	Week 36 (± 2d) Site	Week 48 (stud termination vis Site
Study Procedures										
Inclusion- & exclusion criteria	x	x	x							
Randomization				x						
Informed consent	x									
Demographics	x									
Medical history	x									
Height	x									
Weight	x			x	x	x	x	x	x	x
Concomitant therapy	x	x	x	x	x	x	x	x	x	x
Adverse events	x	x	x	x	x	x	x	x	x	x
PASI	x	x	x	x	x	x	x	x	x	x
IGA	x	x	x	x	x	x	x	x	x	x
BSA	x	x	x	x	x	x	x	x	x	x
DLQI				x	x	x	x	x	x	x
EQ-5D-5L				x	x	x	x	x	x	x
Hematology				x				x		x
Determination of serum adalimumab concentration	x	x	x	x	x	x	x	x	x	x
Determination of anti-adalimumab antibodies (only if subtherapeutic Ctrough levels are measured)	x	x	x	x	x	x	x	x	x	x

*Screening 3: only applicable for patients who had only 1 out of 2 supratherapeutic serum trough concentration at screening 1 and 2
**Week 9: only applicable for patients in the dose tapering group who have had supratherapeutic serum drugconcentrations at week 0 and week 6
BSA= body surface area; DLQI = Dermatology Life Quality Index; IGA= Investigator's Global Assessment; PASI= Psoriasis Area and Severity Index

UZ GENT UNIVERSITEIT GENT

Flowchart substudy (only applicable for UZ Gent patients)

	Day 0 (Randomization) UZ Gent	Day 3 Home	Day 5 HOME	Day 7 HOME	Day 14 HOME or UZ Gent	Day 21 HOME or UZ Gent	Day 28 HOME or UZ Gent	Day 35 HOME	Day 42 HOME or UZ Gent
Inclusion- & exclusion criteria	x								
Informed consent	x								
Demographics	x								
Medical history	x								
Height	x								
Weight	x								
Concomitant therapy	x				X (if UZG)	X (if UZG)	X (if UZG)		X (if UZG)
Adverse events	x				X (if UZG)	X (if UZG)	X (if UZG)		X (if UZG)
PASI	x				X (if UZG)	X (if UZG)	X (if UZG)		X (if UZG)
IGA	x				X (if UZG)	X (if UZG)	X (if UZG)		X (if UZG)
BSA	x				X (if UZG)	X (if UZG)	X (if UZG)		X (if UZG)
DLQI	x				X (if UZG)	X (if UZG)	X (if UZG)		X (if UZG)
EQ-5D-5L	x				X (if UZG)	X (if UZG)	X (if UZG)		X (if UZG)
Mitra sampling at home									
Standard dose regimen	x	x	x	x	x	x	x	x	x
Tapering regimen (1x/3w)	x	x	x	x	x	x	x	x	x
Mitra sampling in the lab	x								
Standard dose regimen	x				x		x		
Tapering regimen (1x/3w)	x					x			x
Blood sampling (EDTA + serum)									
Standard dose regimen	x				x		x		
Tapering regimen (1x/3w)	x					x			x

5.7 Randomisation and blinding

After enrollment, each consecutive patient is assigned a randomization number according to a 1:1 computer generated randomization to ensure that selection bias is minimal. The allocation table will be uploaded in the randomization module of REDCap by the project manager.

In the main study, the outcome parameters (PASI and IGA score) will be assessed by an independent and blinded physician to avoid bias. There will be no direct patient-physician relationship between the study patient(s) and the blinded physician as clinical follow-up of these patients will not be performed by the blinded physician. Therefore, these clinical follow-ups will be scheduled by the study coordinators or nurses on the agendas of fellow dermatologists (not the blinded physician). Every site should have a blinded physician to make the assessments. If the blinded physician is available, he/she will preferably perform the evaluations in person with the patient. If the blinded physician is not available at that time, photographs may be taken, which the blinded physician will then evaluate afterwards. In addition, the blinded physician will sign an agreement in which he/she declares to not access the electronic patients file of the study patients voluntarily. This agreement will be kept in the trial master file. In order to prevent (in)voluntarily deblinding of the physician, the physician will have no access to the study documents, neither the source data (apart from the PASI and IGA) or the eCRF (REDCap) as these PASI and IGA will be kept separately from the other study documents. Furthermore, the trial master file(s) will be kept by the study coordinator(s) in a locked closet. Patients, (principal) investigator, study nurse(s) and study coordinator(s) will know which treatment is assigned. Therefore, the following outcomes will not be blinded because they are scored by the patient and interpreted by the investigator: DLQI and EQ-5D-5L.

5.8 Monitoring and quality measures

The Clinical Trial Unit of Health, innovation and research institute (HIRUZ) Clinical of the Ghent University Hospital was responsible for the monitoring by assigning qualified monitors for on-site and remote monitoring following the ICH-GCP guidelines.

HIRUZ is a leading knowledge and expertise centre of UZ Gent in collaboration with Ghent University (UGent) for translational biomedical research and innovation with a multidisciplinary management and a broad local, national and international network. The main objective of HIRUZ is to advise and guide (academic) researchers so clinical research is conducted in accordance with the current International Conference of Harmonisation Good Clinical Practice (ICH-GCP) guideline and the applicable (inter)national regulatory requirements. The tasks performed by HIRUZ aim to increasing protection of rights, safety and well-being of study subjects, their data and/or human body materials and increase data integrity of data / material collected during clinical studies. HIRUZ has ample experience in ICH-GCP-compliant advice & preparation of EC/FAGG dossiers, monitoring, project management, safety reporting and data management of multicentre investigator driven clinical trials, including KCE Trials. In addition, HIRUZ has a Quality Management System in place for investigator-initiated studies (IIS) for which U(Z) Gent is acting as sponsor, or has adopted sponsor responsibilities and/or is participating site.

6. Study analysis

Power calculation according to a non-inferiority design with limit set at 20 % and success percentage at 66 % leads us to randomization of 70 patients per study arm (power of 80 % and significance level 0.05 %; MedCalc). Taking dropouts into account, this totals to 78 patients per arm.

6.1 Analysis of the samples

Serum samples were analyzed on site by experienced lab technicians or PhD students and in collaboration with the laboratory for therapeutic and diagnostic antibodies at the KU Leuven by use of validated ELISAs (RIDASCREEN® ADM Monitoring and RIDASCREEN® anti-ADM Antibodies) or by use of lateral flow assay (RIDA®QUICK ADM Monitoring) at the University Hospital of Ghent.

According to protocol, anti-adalimumab antibodies will be evaluated in serum samples collected from all participants according to the schedule of activities, only if the measured adalimumab serum drug concentrations were below the limit of detection. The analysis will take place in the laboratory for therapeutic and diagnostic antibodies at the KU Leuven. As during the trial, no measured adalimumab serum drug concentration was below the limit of detection, no anti-drug antibodies were measured.

During the study, all blood samples were be stored in the biobank of the UZ Ghent dermatology department (BIODIP) under the supervision of prof. dr. Jo Lambert according to the applicable biobank regulatory and/or other requirement(s).

6.2 Statistical analysis

Descriptive statistics included counts and proportions for categorical data, and median, mean, interquartile range, and range for continuous data. Graphical data displays have been used to summarize the data.

All statistical testing have been performed 2-sided at a significance level of 0.05.

7. Independent Ethics Committee and Competent Authority

OVERVIEW APPROVED DOCUMENTS		
Initial submission Central EC: - Protocol v4.0 dd. 22-Nov-2019 - Protocol summary v3.0 dd. 11-Oct-2019 - ICF dose tapering v4.0 dd. 30-Mar-2020 - ICF dose tapering v5.0 dd. 23-Apr-2020 - ICF biobank v3.0 dd. 18-Feb-2020 - SmPC Humira® - DLQI questionnaire (NL) - EQ-5D-5L questionnaire (NL) - Patient diary group A, Patient diary group B and Patient diary group C v2.0 dd. 11-Oct-2019 - PASI template v2.0 dd. 11-Oct-2019 - IGA template v2.0 dd. 11-Oct-2019 - Subject card v2.0 dd. 22-Nov-2019 - Agreement note with UZ Gent Pharmacy	**Approval Central EC:** 2020-04-22 (ICF dose tapering v5.0 was submitted to the central EC right after approval of the initial submission package, but EC allowed the version to be included into the initial package anyway.)	***Approval date FAMPH: NA***
Initial submission FAHMP : - Protocol v3.0 dd 14-May-2019 - Protocol summary v2.0 dd. 14-May-2019 - Label - SmPC Humira®	**Approval Central EC:** NA	**Approval FAHMP:** 2019-07-30
Amendment 1 FAHMP : - Protocol v4.0 dd. 22-Nov-2019 - Protocol summary v3.0 dd. 11-Oct-2019	**Approval Central EC:** NA	**Approval FAHMP:** 2020-01-09

8. Results

8.1 Subject enrollment and demographics

Site	Not active yet?	Active?	Closed?	Number of Subjects included?	Date of first inclusion?	date of site closure (LPLV)
AZ Sint-Jan, Bruges	X		12/09/2022	0		NA
AZ Sint-Rembert, Torhout	X	X	29/09/2022	1	07/07/2021	25/01/2022
Dermatologie Maldegem	X		19/09/2022	0		NA

AZ Sint-Lucas, Ghent	X		27/10/2022	0		NA
AZ Maria Middelares, Ghent	X		29/09/2022	0		NA
UZ Ghent		X	28/09/2022	18	16/02/2021	22/03/2022

During a recruitment period of more than 1 year, 19 patients were included. Of these 19 patients, 10 patients were eligible for randomization.

From these 10 patients, 6 were randomized (1:1) in the intervention arm. With the exception of one patient, all patients were male. The cohort had a mean age of 54.2 years, with a mean disease duration of 30.5 years. Treatment duration with ADM ranged from 3.9 years to 12.8 years, with a mean psoriasis area and severity index (PASI) at start of therapy of 8.2. Before randomization, all patients were screened with ELISA for supratherapeutic ADM serum trough concentrations (>8 µg/mL). Patients were randomized if on two out of three time points, supratherapeutic trough levels were measured. Overall, patients had a mean ADM concentration of 9.6 µg/mL during screening, ranging from 7.6 to 13.1 µg/mL.

Seven participants agreed to be included in the substudy for microsampling. All patients were highly educated Caucasian men with an average age of 50.3 years. The range of ADM serum trough concentrations obtained in the screening of this subcohort was the same as the one mentioned above, with a mean of 9.7 µg/mL; five participants were randomized to the intervention group.

As the inclusion rate did not resemble the planned inclusion rate and we were unable to improve the inclusion rate any further, we decided to end the study prematurely. **A notification of end of study was submitted to the ethic committee as well as to the competent authorities on June 15th 2022.**

8.2 Study specific results

As the study was prematurely ended due to too low number of inclusions, **we were unable to analyze the primary and secondary outcomes of the trial.** Below, we give an overview of the preliminary analysis which was performed on the limited data obtained in the main and substudy. These results were published in the Journal of Clinical Medicine by Soenen et al. [2]

1. Demographics of the study cohort

The SUPRA-A trial recruited a total of 19 patients, of whom 10 were randomized (1:1) in the intervention arm (n=6) or the standard dosing arm (n=4). With the exception of one patient, all patients were male. The cohort had a mean age of 54.2 years, with a mean disease duration of 30.5 years. Treatment duration with ADM ranged from 3.9 years to 12.8 years, with a mean psoriasis area and severity index (PASI) at start of therapy of 8.2. Before randomization, all patients were screened with ELISA for supratherapeutic ADM serum trough concentrations (>8 µg/mL). Patients were randomized if on two out of three time points, supratherapeutic

trough levels were measured. Overall, patients had a mean ADM concentration of 9.6 µg/mL during screening, ranging from 7.6 to 13.1 µg/mL.

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2. Rapid Testing of Adalimumab Is Feasible and Valuable in Clinical Setting

A total of 15 samples were collected from 10 patients on week 0 and from 5 patients on week 13. One patient in the control arm had dropped out before the sampling of week 13, hence the missing time point. ADM serum levels were measured using RIDA®QUICK ADM Monitoring lateral flow assay (R-Biopharm AG, Darmstadt, Germany), according to the manufacturer's instructions. In short, after a 5 min pre-incubation of 1:500 diluted sample with "Solution A" and "Solution B" and 15 min developing time on the lateral flow strip, the lateral flow strips were read using a portable reader (RIDA®- QUICK SCAN II, R-Biopharm AG, Darmstadt, Germany). The RIDA®QUICK ADM Monitoring allows quantification of ADM in the 0.5–25.0 µg/mL range.[3]

Lateral flow testing was performed independently by two researchers and showed a mean coefficient of variation (CV) of 7.6% (median: 6.4%; range: 0.0–25.1%), which is slightly lower than the interassay precision reported by the manufacturer.[3] The ADM concentrations in these serum samples ranged from 2.9 to 16.2 µg/mL. Based on simple linear regression, a significant concentration-dependent variation of the LFT measurements was observed.

Next, LFT-obtained ADM concentrations (the mean of replicate measurements for both assessments was used) were compared to ELISA-based quantification. The results showed a good agreement with the reference assay, as indicated by a correlation coefficient R^2 of 0.89, which is somewhat lower than the correlation coefficient (R^2 = 0.95) previously reported by the manufacturer.[3] The Bland–Altman analysis yielded a mean bias of −0.03 µg/mL, indicating the absence of a significant systematic bias between LFT and ELISA. Noteworthy, the span covered by the upper and lower limits of agreement (LoA) (−1.98–1.93 µg/mL) is rather big, given the relative narrow therapeutic window of ADM, i.e., 3.51–7.0 µg/mL.[1,4] This may influence clinical decision-making as categorization of patients as sub- or supratherapeutic may differ, depending on the method of analysis used. However, relatively limited number of samples were included at the timepoint of analysis and ideally, more patients would have helped to further substantiate this finding.

3. VAMS Is Suitable for Extraction of Adalimumab

For validation of the VAMS extraction protocol, the extraction efficiency of ADM from VAMS tips was evaluated by spiking the blood of healthy volunteers with known ADM concentrations, ranging from 0 to 20 µg/mL. Extracts were measured 5 times on different days with an in-house ADM ELISA and a mean extraction efficiency was obtained of 114.4% (SD 13.9%, CV 12.2%).

4. Feasibility of Home Sampling by Non-Experienced Patients Using VAMS

Until present, seven patients were included, resulting in 136 capillary VAMS samples (68 replicates; 4 missing), 40 venous VAMS samples (20 replicates; 2 missing) and 19 serum samples (2 missing) which were eligible for ADM quantification. Ten capillary VAMS samples were excluded from analysis after visual inspection due to undersampling (7.4%).

First, the quality of the patient sampling technique was assessed by comparing biological replicates of capillary VAMS. The difference between the replicates was determined (n = 65) and the CV was calculated. The CV obtained for capillary VAMS samples was 13.5%, which was slightly, though significantly higher than the CV of 7.5% observed for venous VAMS samples (Chi2-test, $\alpha = 0.05$). The latter were prepared by a trained nurse, dipping the VAMS tips in EDTA-anticoagulated venous whole blood. Overall, **a very good correlation was observed between biological replicates of the capillary VAMS samples, with no concentration- or time-dependent variation in the imprecision of home sampling.**

Next, we evaluated how quantification of ADM obtained with VAMS would compare to simultaneously collected serum (gold standard). Hereto, we first compared ADM concentrations obtained from venous VAMS samples with those obtained from the corresponding serum samples. **A good correlation between ADM concentrations in venous VAMS samples [7.32 ± 2.78; 6.92 (5.24–8.63)] and in serum [8.56 ± 2.7; 8.4 (7.3–10.5)] was observed, with a Pearson correlation of 0.87 [mean ± SD; median (IQR), µg/mL].**

Then, we examined the concordance of the results obtained from capillary VAMS samples (obtained by patient self-sampling) and simultaneously collected venous VAMS samples. Figure 5c depicts a Pearson correlation of r = 0.91. From the Bland–Altman analysis, a mean significant bias of 1.30 µg/mL was apparent, with 95% CI 0.72–1.87 (p = 0.0002). This implies that ADM concentrations in venous VAMS samples are overall slightly higher than in capillary VAMS samples, collected at the same time point. This capillary venous difference illustrates the need for the application of a capillary-venous correction factor. **Based on our cohort, a capillary-venous correction factor of 1.28 was found.**

Finally, we compared ADM concentrations obtained from capillary VAMS samples with those obtained from the corresponding serum samples. A good correlation between ADM concentrations in capillary VAMS samples [5.67 ± 2.47; 5.48 (3.52–7.61)] and in serum [8.56 ± 2.7; 8.4 (7.3–10.5)] was observed, with a Pearson correlation of 0.87 [mean ± SD; median (IQR), µg/mL]. A significant mean bias of 2.7 µg/mL (95% CI: 1.96, 3.35) was found by Bland–Altman analysis ($p < 0.0001$), implying that lower concentrations are obtained from VAMS samples, compared to the corresponding serum samples, which can be expected, as ADM resides in the serum/plasma fraction of blood. By multiplying the ADM concentration from capillary VAMS samples with the capillary-venous and blood-serum correction factors of, respectively, 1.28 and 1.22, the calculated ADM serum concentration was determined. To note, this may be an overcorrection due to the small sample size of this cohort.

5. Patient Experience with VAMS

All participants completed the substudy according to the protocol, which by itself was already considered to be a success regarding acceptance of VAMS as a collection technique. All samples, shipped by regular mail, were received within an acceptable time frame (on average 5 days, range [3,4,5,6,7,8]).

Next, we used a questionnaire to evaluate the patients' perception on self-sampling at home based on Van Uytfanghe et al. and Mbughuni et al., with minor adaptations.[5,6] The questionnaire consisted of 10 main questions and gauged about the clarity of instructions, experience, performance, user-friendliness, acceptability/pain and preference.

All patients (n = 7) completed the survey. Five out of seven participants (71.4%) had a higher degree (bachelor or master). Except one, none of the respondents had experience with performing VAMS before. All patients judged the **clarity of the instructions to be clear or very clear and evaluated the performance as very or rather user-friendly and feasible**. None of the patients felt the need to consult for additional information. All patients self-sampled, except for one participant, who stated their partner was a nurse who performed the finger prick . **On a scale of 1 (not painful at all) to 10 (very painful), participants scored 3 or less, with 60% rating it a zero.** Moreover, with the exception of one patient, all patients scored finger prick sampling as less painful compared to a conventional blood draw. With a higher degree of flexibility/autonomy and no transportation to the clinic, this translates to **the vast majority (85.7%) preferring this type of sampling over a conventional blood draw.**

For VAMS to be adopted by patients in the context of TDM in psoriasis, we inquired into patients' acceptance. All participants scored the technique as user-friendly for use at home. In addition, all patients agreed that it would be feasible to perform this regularly. When asked about an acceptable frequency to use VAMS, a monthly basis had the most votes. Although patients were positive about this sampling technique, more than half of the patients was uncertain about the reliability of the sampling technique, reflecting the gap of knowledge.

9. Safety

No AEs were reported during the trial. There have been no SAEs during the trial.

10. Device deficiencies

Not applicable.

11. Protocol deviations

We kindly refer to the list of protocol deviations, exported from the e-CRF of the trial on 20th of March 2023.

12. Discussion and overall conclusions

Although we were unable to assess the primary and secondary outcomes of the main trial, we have been reporting on the preliminary analysis performed on the limited dataset of the main- and substudy.

In the substudy, we investigated the home-based use of VAMS by psoriasis patients treated with ADM for drug quantification. We focused on both the technical performance and the patient's user experience. From a technical perspective, our extraction protocol showed a satisfactory extraction efficiency, with adequate reproducibility. As TDM is based on narrow therapeutic windows, a robust extraction is essential to ensure appropriate interpretation and treatment management plan. Patients' performance assessed by replicates was deemed acceptable, with a CV of 13.5%. As no long-term data were collected, at this point no conclusions can be drawn related to 'performance fatigue'. Performance compared to a trained nurse also showed satisfactory results with a slightly, though significantly higher CV than the CV derived under controlled circumstances for sampling, 7.5%. Based on this, it could be estimated that home sampling accounted for 11.2% of the total imprecision of the method.

In addition, a good correlation between the three matrices, capillary VAMS samples, venous VAMS samples and serum was obtained. At this point it is too early to make definitive statements on whether capillary samples can yield data that can reliably steer dose adaptations (this will become clear in the ongoing trial and was beyond the scope of the current pilot study). However, the data so far indicate that 2 kinds of corrections are required to predict serum concentrations based on capillary blood concentrations: a capillary-venous correction of 1.28, and a blood-serum correction of 1.22. The latter is obvious, as ADM resides in the serum fraction of blood, and 20 µL of (dried) blood only contains ~12 µL of serum (in the case of ~40% haematocrit blood). However, more data are needed to validate these correction factors and verify these on independent sample sets. In future, these data will provide further insight into the suitability of VAMS as an adequate substitute for conventional sampling for ADM TDM.

Besides the technical suitability of microsampling for TDM of ADM in psoriasis patients, it is also important to acknowledge the patients' perception, as they are the end users. Based on our questionnaire, it can be concluded that the patients were overall positive about home-based microsampling. Even more, participants in this pilot study preferred this type of sampling over a conventional blood draw, but this needs to be confirmed in a larger cohort. This is in agreement with results obtained by Morgan et al., who showed that 81% of the participants preferred VAMS collection, and is in line with the preference for VAMS in the cohort studied by Verougstraete et al. [7] Essential to implementation, we also investigated the time it took for a sample to reach our laboratory. Based on our limited data, the time window was deemed acceptable for psoriasis management with ADM. Most biologics are administered from twice a month to every 3 months—rendering an average of 5 transport days (range: 3–8 days) acceptable for the physician to adapt the management plan.

In this paper, we did not address the impact of storage conditions on extraction efficiency. However, we refer to Bloem et al. where a similar technique has been investigated for several storage conditions.[8] In addition, Li et al. obtained very encouraging drug recovery data after short and long term storage for biotherapeutics daclizumab and trastuzumab.[9] Ideally, when patients require a change in management plan, results should become available relatively fast, making long-term storage impact irrelevant. The impact of parameters such as temperature and humidity should be investigated in real world settings for conclusive evidence. To lower the threshold of using VAMS within the patient community and empower patients to monitor their drug concentrations, in the future, microsampling kits could become available at the pharmacy, or could be provided by the treating physician upon treatment with biologics.

After sampling, trough drug concentrations are traditionally measured by ELISA, requiring laboratory equipment (e.g., a shaker and dedicated reader) and are time-consuming. An additional disadvantage of ELISA is the ratio of performance time to sample size. As ELISA is standard-dependent, a single sample run is considered wasteful. To this end, the (complementary) use of immunochromatographic lateral flow testing allows for a more satisfactory ratio of performance time to sample size. The LFT assay investigated here was demonstrated to be applicable in clinical practice, with a turnover time of less than 30 min after serum preparation. Although it was compared to only one ELISA kit for ADM quantification, our data show acceptable results for clinical applicability. As the therapeutic window of ADM is relatively narrow[1,4], interpretation of results should be done taking into account the type of assay. In the limited dataset from this study, a good agreement was found between LFT and ELISA, suggesting that no adaptation of the therapeutic window would be required when implementing this LFT assay—obviously, more samples are required to further substantiate this finding. The current LFT assay was performed on serum samples, and its compatibility with VAMS remains to be elucidated. Ultimately, a combination of both tools would truly enable rapid and easy monitoring.

Limitations of this pilot study inherently include the small sample size for both microsampling and rapid testing. In addition, we did not address various conditions to assess the impact on both tools. For instance, we currently lack data on storage conditions and how ADM concentrations in VAMS samples are affected. All LFT measurements were executed by trained lab personnel. As all measurements were performed in an academic hospital setting, extrapolation to private practices is limited. It should also be noted that the used LFT cassettes are not compatible with all LFT-readers.

Strengths of this study reside in the affinity with real world evidence as SUPRA-A is considered a pragmatic trial, in addition to the use of public postal services for sample transport. Furthermore, participants had access to adequate educational material to execute microsampling. Lastly, in addition to laboratory evaluations, we also considered and investigated the study participants as end users—rendering this study comprehensive.

Overall conclusion

Microsampling for ADM TDM in the context of psoriasis treatment is a valuable alternative to traditional blood sampling, enabling patient-centric TDM. VAMS, as applied here, can be performed by non-experienced patients at home, potentially allowing to reach a greater patient community. In addition, rapid testing by LFT of ADM allows the dermatologist to rapidly obtain results that may impact a patient's treatment plan.

The results presented here provide preliminary evidence, revealing that LFT and microsampling are promising tools to facilitate TDM of ADM in clinical practice. Though the data is from a limited sample size, both tools pose interesting fields of further investigation for TDM in psoriasis.

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Appendix 1: Summary of results for lay persons (English)

1. Clinical trial identification

Study Title: A non-inferiority study on dose reduction of adalimumab in psoriasis patients who are overtreated (SUPRA-A)

EU reference number: 2019-001918-42

Clinical Investigation identification number (CIV ID): not applicable

Study protocol/CIP code: TDM-ADA2019 (SUPRA-A)

Investigational device / medicinal product: Adalimumab

ClinicalTrials.gov identifier: NCT04028713

National Coordinator/ Coordinating Investigator:

Prof. dr. Jo Lambert

Department of Dermatology

Ghent University Hospital

Funder: This research was funded by the Research Foundation—Flanders (FWO), Belgium (T003218N).

2. Name and contact details of the sponsor

Sponsor: Ghent University Hospital

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Funder: This research was funded by the Research Foundation—Flanders (FWO), Belgium (T003218N).

3. General information

In clinical practice, the treatment of psoriasis with adalimumab is currently still based on a 'one size fits all'* principle, despite the possible patient-specific differences in uptake and response to

adalimumab. Thus, all patients are treated according to the same dosing schedule. For adalimumab, this means one subcutaneous injection (80mg) at week 0, followed by one subcutaneous injection (40mg) at week 1, and then one subcutaneous injection (40mg) every two weeks. However, this principle leads to some patients being dosed too much or too little on adalimumab than is actually clinically necessary. In a previous study, we showed that even 1 in 3 psoriasis patients receive a higher dose than probably clinically necessary.

In clinical practice, the aim is always to obtain a maximum clinical effect with the lowest possible therapeutic dose. Now that the individual concentration determination of biologicals (i.e. biological medicines), as well as adalimumab is easily possible, therapeutic drug monitoring can be applied. In other words, based on the measured drug concentrations* in the blood, the dose of adalimumab can be individually adjusted to a personalized and cost-effective treatment schedule.

In this study, we aim to taper the dose of adalimumab in patients with a good clinical response and supratherapeutic (i.e. higher than therapeutically necessary) drug concentrations of adalimumab. In other words, we investigate whether, by measuring serum drug concentrations or therapeutic drug monitoring, it is possible to reduce the dosing frequency of adalimumab in patients who may be overtreated, while maintaining the clinical response. The results obtained here will provide more insight into which minimal concentration* of adalimumab leads to a good clinical response for the individual patient. The measured drug concentrations in the blood will help to individually adjust the dose of adalimumab to a personalized and cost-effective treatment regimen.

**Non-inferiority research: studies with the aim of demonstrating that a new technique/treatment is no less effective than a standard treatment, i.e. non-inferior*
**One size fits all: the same for everyone; in this context it means 'the same dose for everyone'*
**Drug concentration: the amount of a drug/drug in the blood expressed by volume. Minimum concentration: what minimum amounts of adalimumab are required in the blood to produce a good clinical response*

4. Population of subjects

4.1 Inclusion criteria

Each potential participant must satisfy all the following criteria to be enrolled in the main study (A) or substudy (B) respectively:

1. Participants must be >18 years of age.[A-B]
2. Participants must have a diagnosis of chronic plaque-type psoriasis[B] for at least 6 months (with or without PsA), prior to inclusion. [A]
3. Participants must be treated with adalimumab according to the standard dosing regimen during maintenance [A-B]
4. Participant must remain on a highly effective method of birth control during the study or during the entire treatment with adalimumab (whichever is longer). [A-B]
5. Participants must agree not to receive a live virus or live bacterial vaccination at least 3 months (or longer as indicated in the package insert of the relevant vaccine) prior to the first administration of study intervention (except for varicella and MMR vaccines), during the study, or within 3 months after the last administration of study intervention. [A-B]
6. Participants must avoid prolonged sun exposure and use of tanning booths or other ultraviolet light sources during study and are not allowed to use topical steroids from 7 days before randomization until the end of the study [A-B]

7. Participants must sign an informed consent indicating that he or she understands the purpose of, and procedures required for, the study and is willing to participate in the study. [A-B]

4.2 Exclusion criteria

Any potential participant who meets any of the following criteria will be excluded from participating in the main study(A) or substudy (B):

1. Participants who have currently a predominant nonplaque forms of psoriasis (e.g. Erythrodermic, guttate, pustular). [A-B]
2. Participants who are pregnant, nursing or planning a pregnancy or fathering a child while enrolled in the study or within 12 weeks after receiving the last administration of study intervention. [A-B]
3. Participants who have received, or are expected to receive, any live virus or bacterial vaccination (with the exception of varicella or MMR vaccines) within 3 months (or longer as indicated in the package insert of the relevant vaccine) prior to the first administration of study intervention, during the study, or within 12 weeks after the last administration of study intervention. [A-B]
4. Participants who have known allergies, hypersensitivity or intolerance to adalimumab or its excipients. [A-B]
5. Participants who are unable or unwilling to undergo multiple venipunctures. [A-B]

Overall, the SUPRA-A trial recruited a total of 19 patients, of whom 10 were randomized (1:1) in the intervention arm (n=6) or the standard dosing arm (n=4). With the exception of one patient, all patients were male. The cohort had a mean age of 54.2 years.

5. Investigational medicinal products used

Drug	Description	Route of administration	Normal dose	First step dose reduction	Second step dose reduction
Adalimumab (Humira®)	Adalimumab is a recombinant human monoclonal antibody targeted against tumour necrosis factor-α	Subcutaneous	40 mg / 2 weeks	40 mg / 3 weeks	40 mg / 4 weeks

6. Description and frequency of adverse reactions

No AEs were reported during the trial and there have been no SAEs during the trial.

7. Overall results and comments on the outcome of the clinical trial

Microsampling (i.e. fingerprick) for quantification of adalimumab concentration in blood the context of psoriasis treatment is a valuable alternative to traditional blood sampling, enabling patient-centric therapeutische drug monitoring. The fingerprick method, as applied here, can be performed by non-experienced patients at home, potentially allowing to reach a greater patient community. In addition, rapid testing by lateral flow test to quantify adalimumab allows the dermatologist to rapidly obtain results that may impact a patient's treatment plan.

In short, the results presented here provide preliminary evidence, revealing that lateral flow testing and microsampling are promising tools to facilitate therapeutic drug monitoring of adalimumab in clinical practice. Though the data is from a limited sample size, both tools pose interesting fields of further investigation for TDM in psoriasis.

Appendix : Samenvatting van de resultaten voor het brede publiek (Dutch)

1. Identificatie van de klinische studie

Titel: Een niet-inferioriteitsonderzoek* naar dosisreductie van adalimumab in psoriasis patiënten die overbehandeld worden.

EU referentienummer: 2019-001918-42

Studie protocol: TDM-ADA2019 (SUPRA-A)

Investigational medicinal product: Adalimumab

ClinicalTrials.gov identifier: NCT04028713

Nationale onderzoekscoördinator:

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Universitair Ziekenhuis Gent

2. Naam en contactgegevens van de sponsor

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Financieerder: Dit Onderzoek werd gefinancierd door Fonds Wetenschappelijk Onderzoek (FWO), België (T003218N).

3. Algemene informatie

In de klinische praktijk, is de behandeling van psoriasis met adalimumab voorlopig nog steeds op een 'one size fits all'* principe gebaseerd, desondanks de mogelijke patiënt specifieke verschillen in opname en respons op adalimumab. Alle patiënten worden dus volgens hetzelfde doseringsschema behandeld. Voor adalimumab betekent dit één onderhuidse injectie (80mg) op week 0, gevolgd door één onderhuidse injectie (40mg) op week 1 en vervolgens één onderhuidse injectie (40mg) om de twee weken. Dit principe leidt er echter toe dat sommige patiënten op adalimumab te veel of te weinig gedoseerd

worden dan eigenlijk klinisch noodzakelijk is. In een vorige studie, toonden we aan dat zelfs 1 op de 3 psoriasispatiënten een hoger dosis krijgt dan waarschijnlijk klinisch noodzakelijk is.

In de klinische praktijk wordt steeds het bekomen van een maximaal klinisch effect met de laagst mogelijke therapeutische dosis nagestreefd. Nu de individuele concentratiebepaling van biologicals (i.e. biologische geneesmiddelen), alsook adalimumab vlot mogelijk is, kan men therapeutische drug monitoring toepassen. Met andere woorden kan op basis van de gemeten geneesmiddelconcentraties* in het bloed, de dosis adalimumab individueel aangepast worden tot een gepersonaliseerd en kosteneffectief behandelingsschema.

In deze studie beogen we de dosis adalimumab af te bouwen bij patiënten met een goede klinische respons en supratherapeutische (i.e. hoger dan therapeutisch noodzakelijk) geneesmiddelconcentraties van adalimumab. Of met andere woorden, we gaan na of, door het meten van serum geneesmiddelconcentraties ofwel therapeutische drug monitoring, het mogelijk is om bij patiënten die mogelijks overbehandeld worden, de doseringsfrequentie van adalimumab te verlagen, mits behoud van de klinische respons. De hier behaalde resultaten zullen meer inzicht verschaffen welke minimale concentratie* van adalimumab een goede klinische respons met zich meebrengt voor de individuele patiënt. De gemeten geneesmiddelconcentraties in het bloed zullen bijdragen om de dosis adalimumab individueel aan te passen tot een gepersonaliseerd en kosteneffectief behandelingsschema.

Niet-inferioriteitsonderzoek: studies met als doel het aantonen dat een nieuwe techniek/behandeling niet minder effectief is dan een standaardbehandeling, ofwel niet-inferieur
One size fits all: voor iedereen hetzelfde; in deze context betekent dit 'voor iedereen dezelfde dosis'
Geneesmiddelconcentratie: de hoeveelheid van een geneesmiddel/drug in het bloed uitgedrukt per volume.
Minimale concentratie: welke minimale hoeveelheden van adalimumab in het bloed nodig is om een goede klinische respons voort te brengen

4. Studiepopulatie

De SUPRA-A-studie rekruteerde in totaal 19 patiënten, van wie er 10 werden gerandomiseerd (1:1) in de interventiearm (n=6) of de standaarddoseringsarm (n=4). Met uitzondering van één patiënt waren alle patiënten mannelijk. De cohorte had een gemiddelde leeftijd van 54,2 jaar.

5. Geneesmiddel gebruikt in deze studie

Geneesmiddel	Beschrijving	Toedieningweg	Standaard dosering	Eerste stap dosis reductie	Tweede stap dosis reductie

Adalimumab (referentie: Humira®)	Humaan monoklonaal antilichaam gericht tegen tumor-necrosis factor- α	Subcutaan (spuit of pen)	40 mg / 2 w	40 mg / 3 w	40 mg / 4 w

6. Beschrijving en frequentie van neveneffecten

Gedurende de studie werden er geen neveneffecten gerapporteerd die mogelijks gerelateerd werden aan het gebruik van het onderzoeksproduct.

7. Resultaten en besluit van de klinische studie

De vingerprikanalyse voor bepaling van de concentratie adalimumab in bloed in de context van psoriasisbehandeling is een waardevol alternatief voor traditionele bloedafname, waardoor patiëntgerichte therapeutische drug monitoring mogelijk wordt. De vingerprikmethode, zoals hier toegepast, kan door niet-ervaren patiënten thuis worden uitgevoerd, waardoor mogelijk een grotere patiëntengemeenschap kan worden bereikt. Bovendien stellen sneltesten voor bepaling van adalimumab de dermatoloog in staat om snel resultaten te verkrijgen die van invloed kunnen zijn op het behandelplan van een patiënt.

Kortom, de hier gepresenteerde resultaten leveren voorlopig bewijs, waaruit blijkt dat sneltesten en de vingeprikanalyse veelbelovende hulpmiddelen zijn om TDM van ADM in de klinische praktijk te vergemakkelijken. Hoewel de gegevens afkomstig zijn van een beperkte steekproefomvang, vormen beide tools interessante onderzoeksgebieden voor TDM bij psoriasis.