An open-label, randomised, Phase IV study, to assess the efficacy and safety of tildrakizumab in patients with moderate-to-severe chronic plaque psoriasis who are non-responders to dimethyl fumarate therapy.

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Primary objectiveTo assess the efficacy of tildrakizumab treatment (as assessed by PASI 75) in moderate-to-severe plaque psoriasis patients who are non-responders to DMF. Secondary objectivesTildrakizumab- To assess the efficacy of tildrakizumab...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Epidermal and dermal conditions
Study type	Interventional

Summary

ID

NL-OMON48282

Source
ToetsingOnline

Brief title
TRANSITION (M-14745-41)

Condition

- Epidermal and dermal conditions

Synonym
plaque psoriasis, Psoriasis vulgaris

Research involving

Human

Sponsors and support

Primary sponsor: TFS Trial Form Support BV
Source(s) of monetary or material Support: Industry

Intervention

Keyword: moderate-to-severe chronic plaque psoriasis, non-responders to dimethyl fumarate, Phase IV study, tildrakizumab

Outcome measures

Primary outcome

Primary Endpoint (Part 2)

Proportion of patients who were non-responders to DMF at Week 16 that were

treated with Tildrakizumab and achieved a PASI 75 at week 40.

Secondary outcome

Secondary endpoints (Part 1 and Part 2):

Efficacy endpoints (Part 1)

- Proportion of patients achieving PASI 50, PASI 75 and PASI 90 responses at

Week 8 and Week 16 Visits of the Part 1

- Proportion of patients achieving absolute PASI scores of <=5, <=3 and <=1 at

Week 8 and Week 16 Visits of the Part 1

- Absolute PASI score and change in the absolute PASI score at Week 8 and Week

16 Visits of the Part 1

- Absolute BSA score and change from baseline in the absolute BSA score at Week

8 and Week 16 Visits of the Part 1

- Proportion of patients achieving PGA, ScPGA* and PPPGA* scores of 0 or 1 at

Week 8 and Week 16 Visits of the Part 1

- Absolute PGA, ScPGA* and PPPGA* scores and change in the absolute PGA, ScPGA* and PPPGA* scores at Week 8 and Week 16 Visits of the Part 1

- Proportion of patients achieving DLQI scores of 0 or 1 at Week 8 and Week 16 Visits of the Part 1

- Absolute DLQI score and change from baseline in the absolute DLQI score at Week 8 and Week 16 Visits of the Part 1

- Absolute Skindex-16 score and change from baseline in the absolute Skindex-16 score at Week 8 and Week 16 Visits of the Part 1

- Absolute pruritus-VAS score and change from baseline in the absolute pruritus-VAS score at Week 8 and Week 16 Visits of the Part 1

- Absolute MOS score and change from baseline in the absolute MOS score at Week 16 Visit of the Part 1

Efficacy endpoints (Part 2)

- Proportion of patients achieving PASI 50, PASI 75, PASI 90, and PASI 100 responses at each visit of the Part 2.

- Proportion of patients achieving absolute PASI scores of <=5, <=3 and <=1 at each visit of the Part 2

- Absolute PASI score and absolute and percentage change from baseline in the absolute PASI score at each visit of the Part 2

- Absolute BSA score and change from baseline in the absolute BSA score at each visit of the Part 2

- Proportion of patients achieving PGA, ScPGA* and PPPGA* scores of 0 or 1 at each visit of the Part 2

- Absolute PGA, ScPGA* and PPPGA* scores and absolute and percentage change from baseline in the absolute PGA, ScPGA* and PPPGA* scores at each visit of the Part 2Proportion of patients achieving DLQI score of 0 or 1 at Week 32 and Week 40 Visits of the Part 2

- Absolute DLQI score and absolute and percentage change from baseline in the absolute DLQI score at Week 32 and Week 40 Visits of the Part 2

- Absolute Skindex-16 score and absolute and percentage change from baseline in the absolute Skindex-16 score at Week 32 and Week 40 Visits of the Part 2

- Absolute pruritus-VAS score and absolute and percentage change from baseline in the absolute pruritus-VAS score at each visit of the Part 2

- Absolute MOS score and absolute and percentage change from baseline in the absolute MOS score at Week 40 Visit of the Part 2

* Only in patients with scalp involvement

* Only in patients with palmar or plantar involvement

Safety endpoints

- Safety and tolerability as assessed by vital signs, physical examination, safety laboratory and Treatment-Emergent Adverse Events (TEAEs)

Other Endpoints

- Proportion of patients withdrawing from the trial at each visit and overall, as well as time to withdrawal

- Treatment compliance

- Proportion of patients using TCS at each visit and overall, as well as

duration of TCS treatment

Study description

Background summary

Dimethyl fumarate (DMF) and Tildrakizumab have both been approved in the European Union as systemic treatments for adult patients with moderate-to-severe plaque psoriasis in need of systemic therapy. There is no data available on the efficacy, safety and tolerability of tildrakizumab in patients who are non-responders to DMF.

Study objective

Primary objective
To assess the efficacy of tildrakizumab treatment (as assessed by PASI 75) in moderate-to-severe plaque psoriasis patients who are non-responders to DMF.

Secondary objectives
Tildrakizumab
- To assess the efficacy of tildrakizumab treatment (as assessed by PASI, BSA, PGA, scalp PGA and palmoplantar PGA) in moderate-to-severe plaque psoriasis patients who are non-responders to DMF.
- To assess the efficacy of tildrakizumab treatment according to Patient Reported Outcome (PRO) results (DLQI, Skindex-16, pruritus-VAS and MOSS) in moderate-to-severe plaque psoriasis patients who are non-responders to DMF.
- To assess the safety and tolerability of tildrakizumab treatment in moderate-to-severe plaque psoriasis patients who are non-responders to DMF.

Dimethyl Fumarate
- To assess the efficacy of DMF treatment (as assessed by PASI, BSA, PGA, scalp PGA and palmoplantar PGA) in moderate-to-severe plaque psoriasis patients.
- To assess the efficacy of DMF treatment according to PRO results (DLQI, Skindex-16, pruritus-VAS and MOSS) in moderate-to-severe plaque psoriasis patients.
- To explore patient*s adherence rate to DMF treatment in moderate-to-severe plaque psoriasis patients
- To assess the safety and tolerability of DMF treatment in moderate-to-severe plaque psoriasis patients

Study design

This is a multicentre, randomized, parallel group, open label phase IV clinical study in patients with moderate-to-severe chronic plaque psoriasis.

The study consists of two parts. Part 1 will include one Screening Period Visit and the first 16 weeks of the Treatment Period (seven visits: two virtual visits and five on-site visits). Virtual visit are visits in which patients do not assist to the centre, but still Investigators should enter data in the electronic Case Report Form (eCRF) based on the medical record or the information that patients have entered in the Study App. During Part 1 of the study all participants receive DMF.
Non-responders continue in Part 2 of the study and will recieve tildrakizumab. Part 2 will include the last 24 weeks of the Treatment Period (three additional visits) and a virtual Safety Follow-up Visit,. For patients who have received only DMF the Safety Follow-up Visit will take place 4 weeks after the last DMF dose, while for patients who have received tildrakizumab this visit will take place 17 weeks after the last tildrakizumab dose (i.e. 5 half-lives).

Intervention

Eligible patients will receive DMF standard scheme from Baseline to Week 16 (Part 1 of the study). The DMF standard scheme will follow the guidance of the SmPC posology. As such, in the first week, patients should take DMF 30 mg once daily (one tablet in the evening). In the second week, patients should take DMF 30 mg twice daily (one tablet in the morning and one in the evening). In the third week, patients should take DMF 30 mg three times daily (one tablet in the morning, one at midday, and one in the evening). In the fourth week, treatment should be switched to only one tablet of DMF 120 mg in the evening. Patients should then increase the dose of DMF by one 120 mg tablet per week at different times of day for the subsequent 5 weeks. The maximum daily dose taken by a patient should be 720 mg (3 x 2 tablets of DMF 120 mg).
Non-responders will continue in Part 2 of the study and receive tildrakinumab.. The dose of tildrakizumab will be 100 mg (as per the SmPC), and will be administered as subcutaneously (SC) injection at Weeks 16, 20 and 32. In patients with certain characteristics (e.g. high disease burden, body weight >= 90 kg) 200 mg may provide greater efficacy. Investigators will be allowed to prescribe either of the two doses depending on the individual patient*s characteristics at the beginning of the Part 2. Once a dose is chosen and treatment with tildrakizumab is initiated, dose changes (e.g. from 100mg to 200mg or vice versa) will not be allowed

Study burden and risks

The amount and number of blood samples: 7 times, total amount for the entire study is 50ml.
The number of site visits can either be 8 (incl. 2 virtual visits) for Part 1 of the study or 12, for Parts 1 and 2
Physical examinations incl vital signs:2 (Part 1) or 3 times (Parts 1 and 2)
Blood and urine tests, Questionnaires on health and skin, Pregnancy test (urine, except one blood test at screening): 6 (Part 1) or 9 times (Parts 1 and

2).
Photographs of skin lesions (for 50 subjects total, and only if separate consent is given): 2 (Part 1) or 3 times (Parts 1 and 2)
Risks associated with the investigational products are described under E9.

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

1. Ability to understand and comply with the requirements of the study and communicate with the Investigator, and written, signed and dated informed consent given before any study related activity is performed.
2. Male or female, aged 18 years at the time of the Screening Visit.
3. Diagnosed with chronic plaque psoriasis of at least 6 months prior to the Screening Visit, and has stable active plaque-type psoriasis (stable is defined

as without clinically significant flares during the 12 weeks before the Baseline Visit).
4. Moderate-to-severe plaque psoriasis at the Screening and Baseline visits as defined by PASI score of >= 10
5. Complete record of at least the last 12 months prior to the Screening Visit of anti-psoriatic previous topical, phototherapy and non-biologic systemic treatments, if any.
6. Candidate for systemic treatment for plaque psoriasis at the Screening Visit
7. General good health, or a stable medical condition not considered likely to interfere with the conduct of the clinical study, as determined by the Investigator based upon results of medical history, laboratory results (within normal or clinically acceptable range limits) and physical examination (no clinical significant abnormal findings). Investigators are encouraged to consult with the Sponsor if there are questions regarding the significance of any out of range values.
8. Unlikely to conceive, as indicated by at least one *yes* answer to the following questions:
a. Patient is a male.
b. Patient is a surgically sterilized female by hysterectomy or bilateral tubal ligation.
c. Patient is a postmenopausal female >=45 years of age with >1 year since last menses. If a patient is <45 years of age, or cessation of menses is more than 3 months and less than 1 year, follicle stimulating hormone must be documented as elevated into the postmenopausal range (>60 mIU/mL) at the Screening visit.
d. Patient is a non-sterilized and pre-menopausal female using a highly effective medically accepted method of contraception, during the study period and for 4 or 17 weeks after the last dose of DMF or tildrakizumab respectively. Explanatory note: Highly effective methods of birth control are defined as a method with less than 1% failure rate (e.g. hormone implants, hormone injections, some intrauterine devices, vasectomized partner or sexual abstinence) or the use of two methods of contraception (e.g. one barrier method [condom, diaphragm or cervical/vault caps] with spermicide and one hormonal contraceptive [e.g. combined oral contraceptives, patch, vaginal ring, injectables and implants])
9. For female patients of child-bearing potential, a negative serum pregnancy test at the Screening Visit and a negative urine pregnancy test at the Baseline Visit. Additionally, they must agree to have urine pregnancy tests while on study medication.

Exclusion criteria

1. Female patients who are currently pregnant, who intend to become pregnant during the course of the study, or who are breastfeeding. Also if there is unwillingness/inability for the patients (women or men) to use appropriate measures of contraception (if necessary).

2. Current forms of psoriasis other than chronic plaque-type (e.g. erythrodermic, guttate, or pustular psoriasis)
3. Drug-induced psoriasis (i.e., a new onset or current exacerbation of psoriasis from beta-blockers, calcium channel blockers, or lithium) at the Screening Visit
4. History or evidence of skin disease (atopic dermatitis, eczema) or conditions (scarring, open wounds) other than chronic plaque-type psoriasis that might interfere with the study conduct or evaluations, or which exposes the patient to unacceptable risk by study participation
5. History of hypersensitivity or allergy to the study drugs or its excipients,which includes lactose*.
*People with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or
glucose-galactose malabsorption should not be included in the study.
6. History of or concurrent malignancy (excluding successfully treated basal cell carcinoma, squamous cell carcinoma of the skin in situ, squamous cell carcinoma with no evidence of recurrence within 5 years or carcinoma in situ of the cervix that has been adequately treated).
7. History of or current relevant autoimmune diseases (e.g. lupus-like syndromes) other than psoriasis.
8. Active significant gastrointestinal problems (ulcers, diarrhoea, etc.) at the Screening Visit
9. Severe renal impairment (creatinine clearance <30 mL/min, estimated glomerular filtration rate [eGFR] using CKD-EPI Creatinine Equation) or significant proteinuria (3+ or higher measured by dipstick) at the Screening Visit.
10. Any of the following haematological abnormality at the Screening Visit:
a. Platelet count < 100,000/mm3
b. White blood cell count < 3,000 cells/mm3,
c. Lymphocyte count <1.000/µl,
d. Haemoglobin, haematocrit, or red blood cell count outside 30 % of the upper or lower limits of normal for the laboratory
11. Abnormal liver enzymes at the Screening Visit:
a. If an enzyme was >3x the upper limit of the normal range (ULN): aspartate amino transferase (AST; serum glutamic oxaloacetic transaminase [SGOT]), alanine amino transferase (ALT; serum glutamic pyruvic transaminase [SGPT]), gamma-glutamyl-transferase (GGT), alkaline phosphatase (ALP)
b. If bilirubin was >2x ULN, for the other liver enzymes >2x ULN was exclusionary
12. Active infectious disease at the Screening Visit
13. Known positive test for human immunodeficiency virus or any other immunosuppressive disease
14. Known latent or active tuberculosis (TB) at the Screening visit
15. History (within 2 years prior to the Screening Visit) or evidence/indication of current drug and/or alcohol abuse or dependence, according to the judgment of the Investigator
16. Previous exposure to fumarate-based drug or a biologic systemic treatment

(e.g. tumour necrosis factor-alpha inhibitors, IL-17 inhibitors, IL-17R inhibitors, IL-12/23 p40 inhibitors, IL-23p19 inhibitors or experimental biological product)
17 Have had a live vaccination within 4 weeks prior to the Baseline Visit, or intend to have a live vaccination during the course of the study, or have participated in a vaccine clinical study within 12 weeks of the Baseline Visit
18 Patient who intend to use any concomitant medication not permitted by this study or who have not undergone the required washout period, prior to the Baseline Visit, for a particular prohibited medication:
a. Topical psoriasis treatment (e.g. topical corticosteroids, vitamin A analogues, vitamin D analogues, coal tar, anthracene derivatives, salicylic acid preparations): 2 weeks
b. Phototherapy (e.g. UV-B light phototherapy, Psoralen-UVA therapy, tanning salon or home-administered UVB): 4 weeks
c. Conventional systemic anti-psoriatic drugs (e.g. cyclosporine, methotrexate, apremilast or acitretin) excluding fumarate-based drugs: 4 weeks
d. Any other immunosuppressive medication (e.g. cytostatics, etc.): 6 months
19. Concomitant treatment with immunomodulating or systemic corticosteroid.
20. Participating in a drug investigational trial within the 30 days (or five half-lives, whichever is longer) prior to enrolment.
21. Concurrent systemic therapy with drugs that may interfere with the study drugs taken within the defined washout period
22. Previously included in the current study
23. Patient who is employee at the research site or Almirall
24. Patient with any other serious or uncontrolled physical or mental dysfunction that, as judged by the Investigator, could place the patient at higher risk derived from his/her participation in the study, could confound the results of the study or is likely to prevent the patient from complying with the requirements of the study or completing the study.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Ilumetri
Generic name:	tildrakizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Skilarence
Generic name:	dimethyl fumarate
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-08-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-11-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	24-12-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-08-2020
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	EUCTR2019-000817-35-NL
CCMO	NL69610.091.19

Study results

Results posted: 18-10-2022

Summary results
Trial never started

First publication
29-09-2022

URL result
URL
Type
int
Naam

M2.2 Samenvatting voor de leek
URL

Internal documents
File