1. TITLE PAGE

CONFIDENTIAL

ABBREVIATED CLINICAL STUDY REPORT

Clinical Study Report Code: M-14745-44

Name of the investigational medicinal product: Not applicable
Indication studied: Moderate-to-severe chronic plaque psoriasis
Phase of the study: IV

"A PHASE IV INTERVENTIONAL STUDY TO ASSESS THE DISEASE-MODIFYING EFFECT OF LONG-TERM TREATMENT WITH TILDRAKIZUMAB IN ADULT PATIENTS WITH MODERATE-TO-SEVERE PLAQUE PSORIASIS"
(Protocol No. M-14745-44; Eudract No. 2019-003218-15)

Statistical Report No. (if applicable): Not applicable
Pharmacokinetics Report No. (if applicable): Not applicable
Date of initiation of the study: 29 January 2020
Date of early study termination (if applicable): 31 July 2020
Date of completion of the study: Not applicable
Date of completion of the Report: 15 January 2021

Company / Sponsor:
Almirall S.A.
[redacted]

Co-ordinating Investigator:
[redacted]

Director Global Clinical Operations
[redacted]

The study was performed in accordance with Good Clinical Practices (GCP) including the archiving of essential documents

2. SYNOPSIS

Name of Sponsor / Company: Almirall, S.A. **Name of Finished Product:** N.A. **Name of Active Ingredients:** N.A.	**Individual Study Table Referring to Part of the Dossier** **Volume:** **Page:**	**(For National Authority Use only)**

Title of Study: A PHASE IV INTERVENTIONAL STUDY TO ASSESS THE DISEASE-MODIFYING EFFECT OF LONG-TERM TREATMENT WITH TILDRAKIZUMAB IN ADULT PATIENTS WITH MODERATE-TO-SEVERE PLAQUE PSORIASIS

Investigators:
This study was conducted by 3 investigators in Poland (see Appendix 16.1.4).

[redacted]

Study centres:
This study was conducted in a total of 2 sites (see Appendix 16.1.4).

[redacted]

Publication (reference):
None

Studied period (years): Date study initiated (first screening): 29 January 2020 Date study finalised (last subject last visit): 28 August 2020	**Phase of development:** IV

Objectives:

Primary objective

To describe blood and skin inflammatory biomarkers and its correlation with psoriasis disease severity over time after having discontinued long-term treatment with tildrakizumab.

Secondary objectives

- To assess time to disease relapse in the overall and in the different tildrakizumab responder populations
- To assess changes in disease status (Psoriasis Area and Severity Index [PASI], Body surface area [BSA], Physician´s Global Assessment [PGA], nail PGA [nPGA], and scalp PGA [scPGA]) from baseline and until the End of Study (EoS)
- To assess changes in Patient Reported Outcomes (PROs) from baseline and until the EoS.

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Methodology:

This was a multicentre, interventional, prospective, phase IV clinical study. The main aim was to evaluate the psoriasis disease control over time in patients who have received tildrakizumab for at least the last 5 years and have discontinued it and to describe blood and skin inflammatory biomarkers and its correlation with disease relapse. Overall, approximately 47 subjects from 3 centres in Poland were expected to be included. After a 6-month inclusion period, up to 9 visits every 12 weeks were scheduled. Subjects were to remain in the study for up to 96 weeks or until they initiate any systemic therapy for psoriasis (including phototherapy), whichever occured first.

The study was prematurely terminated by the Sponsor on 31 July 2020 due to the inability to recruit enough patients within the time frame established . A total of 9 of the initially planned 47 subjects were included in the study. As per the study design, only adult subjects who have completed the long-term extension of the reSURFACE 2 study in Poland were potentially eligible to be included in the present study. Thus, the subjects' pool was limited and irreplaceable.

All participating sites were promptly notified to discontinue ongoing subjects.

Number of subjects (planned and analysed):

	Total
Planned:	47
Screened:	9
Completed the study:	0
Full Analysis Set	9
Per-Protocol Set	5

Diagnosis and main criteria for inclusion:

Please see Section 9.3.

Test product, dose and mode of administration, batch number, expiry date:

Not applicable. Subjects did not receive any study medication during the study.

Duration of treatment:

Not applicable.

Reference therapy, dose and mode of administration, batch number, expiry date:

Not applicable.

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Criteria for evaluation:

Primary Variables:

- Blood and skin inflammatory biomarkers (YES [presence of inflammatory biomarkers]/NO [no presence of inflammatory biomarkers]) at each applicable visit

Skin biopsies were optional. None of the included patients granted permission for skin biopsies.

- Proportion of patients with psoriasis relapse during the 96-week follow-up period (YES [relapse]/ NO [disease control]), where relapse is defined using the following thresholds:

  - PASI >3* (in patients who had a PASI ≤3 at baseline)
  - PASI >5* (in patients who had a PASI ≤5 at baseline)
  - Dermatology Quality of Life Index (DLQI) >5* (in patients who had a DLQI ≤5 at baseline)
  - Initiation of any topical drug/medication for psoriasis†^
  - Initiation of any systemic therapy for psoriasis (biologic or non-biologic)†

*Only to be considered at first occurrence

†To be considered at every occurrence

^Only apply to topical drugs/medications (not soaps, shampoos, emollients, keratolytics, etc. will be included in this group)

Secondary Variables:

- Time to relapse during the 96-week follow-up period, defining relapse as the above mentioned categories
- Absolute PASI score and change from baseline in the absolute PASI score over time, and at EoS visit
- Absolute BSA score and change from baseline in the absolute BSA score over time, from baseline to EoS visit
- Absolute DLQI and DLQI-R scores and change from baseline in the absolute DLQI and DLQI-R scores over time, from baseline to EoS visit
- Absolute PGA, nPGA and scPGA scores and change in the absolute PGA, nail PGA and scalp PGA scores over time, from baseline to EoS visit
- Absolute pain- and pruritus-Numeric Rating Scale (NRS) scores and change from baseline in the absolute pain- and pruritus-NRS scores over time, from baseline to EoS visit
- Safety outcomes will include adverse events, physical examination, vital signs, and clinical laboratory assessments (haematology and biochemistry)

Statistical methods:

Analysis Populations

Due to the early termination of the study, there was only one statistical analysis population:

The Full Analysis Set (FAS) was defined as all patients who attended baseline visit and received a patient number.

A Per Protocol population (PP) was also defined in the protocol, although due to the limited number of subjects included none of the statistical evaluations were repeated for a PP.

Statistical Methods

The statistical approach for the analysis of primary and secondary variables is described below. Further specification of the analyses can be found in Appendix 16.1.9.

Due to the early termination of the study, the analyses defined in the Statistical Analysis Plan (SAP) have been changed and adapted from the clinical study protocol (CSP):

- Primary and some secondary objectives (relapse during the 96-week follow-up period and time to relapse) were impossible to asses because there were no data collected.
- Other objectives as changes from baseline or shift tables for laboratory values, vital signs or physical examination were removed from the analysis because there were not enough data collected in the study.

SUMMARY – CONCLUSIONS

Efficacy Results:

Due to the early study termination, only 9 subjects were included, and none of them finalized the 96 weeks of follow up. Therefore, the evolution of psoriasis over time once tildrakizumab is stopped could not be analysed. As a result, there are no efficacy conclusions.

Safety Results:

A total of 7 AEs were reported in 4 (44.4%) subjects, of which one was of moderate severity (exacerbation of psoriasis) and 6 were of mild severity (radiculitis [n=1], hair loss [n=1], uterine dilation and curettage [n=1], dyslipidemia [n=1] and exacerbation of psoriasis [n=2]). None of the AEs was serious, fatal or led to discontinuation of the study.

CONCLUSIONS:

This was a phase IV study that aimed to evaluate the disease-modifying effect of long-term treatment with tildrakizumab in adult patients with moderate-to-severe plaque psoriasis. The study was terminated prematurely with 9 subjects included at that time. The reason for study termination was due to the inability to recruit enough patients within the time frame established.

Due to the early study termination and limited data, the evolution of psoriasis disease severity over time after having discontinued long-term treatment with tildrakizumab could not be analysed; therefore, this study could not report any conclusion.

DATE OF REPORT:
15 January 2021