Clinical Study Report Synopsis

Cromoglicate in Psoriasis

An exploratory study evaluating the efficacy of cromoglicate cream compared to cream vehicle in the treatment of itch in psoriasis

A phase 2 exploratory, prospective, randomised, double-blind, vehicle-controlled, left/right comparison study with twice daily topical administration for 14 days

LEO Pharma A/S
Clinical Development and Safety

LP0075-34
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Clinical Study Report Synopsis Statement

Approval Statement, Sponsor

The following persons have approved this Clinical Study Report Synopsis on behalf of LEO Pharma A/S using electronic signatures:

[redacted]
[redacted] Biostatistics and Data Management

[redacted]
[redacted] Medical Department

Approval Statement, Investigator

The international co-ordinating investigator approves the Clinical Study Report Synopsis by manually signing the International Co-ordinating Investigator Clinical Study Report Approval Form, which is a separate document adjoined to this report.

The following person has approved this Clinical Study Report Synopsis:

Prof. Dr. med. [redacted]
International Co-ordinating Investigator

SYNOPSIS

Name of Sponsor/Company: LEO Pharma A/S
Name of Finished Product: Cromoglicate cream, 40 mg/g
Name of Active Ingredient: Sodium Cromoglicate
Title of Trial: Cromoglicate in Psoriasis
Investigators: [redacted], Prof. Dr. med., [redacted], Germany was coordinating investigator.
Trial Centre(s): One site in Germany
Publication(s) based on the trial: None at the time of this clinical study report
Trial Period: Date of first enrolment (informed consent signed and CRF started): 29-Nov-2012 Date of last completed: 11-Apr-2013 — Phase of Development:2
Objectives: The primary objective of this trial was to investigate the clinical efficacy on itch of treatment with cromoglicate cream in subjects with itchy psoriasis. The secondary objectives of this trial were to investigate the safety of treatment with cromoglicate cream in subjects with itchy psoriasis, and to investigate pharmacodynamic parameters related to itch and the mode of action of cromoglicate.
Methodology: This was an exploratory, prospective, randomised, double-blind, vehicle-controlled, left-right comparison trial in subjects with itchy psoriasis. Each subject was treated twice daily for 14 days with cromoglicate cream or cream vehicle on an estimated 2-3% body surface area treatment area on each bilateral side of the body. Visits were conducted on Days 0 and 14 and a telephone interview was conducted on Day 3. Safety evaluation was based on adverse event reporting and vital signs. Efficacy assessments included subject's assessment of itch using a visual analogue scale, a 4-point scale, and a 7-point itch scale.
Number of Subjects (Planned and Analysed): A total of 30 subjects were planned and 30 subjects were randomised in the trial. All subjects completed the trial.
Diagnosis and Main Criteria for Inclusion: Diagnosis: Psoriasis Main inclusion criteria: The trial included adult subjects of either sex with a diagnosis of stable plaque psoriasis with a symmetric distribution on the body. Further, each subject needed to have two symmetrically placed treatment areas of 2 to 3% body surface area, each including at least one itchy psoriasis plaque. Both these intended treatment areas had to have a baseline itch of at least 40 mm on a visual analogue scale with a maximum difference of 10 mm between the two areas. The disease severity at baseline as assessed with the Physician's Global Assessment could be mild, moderate, or severe, but needed to be the same for both treatment areas.
Investigational Product, Dose and Mode of Administration, Batch Number: Cromoglicate cream (40 mg/g), twice daily, topical Batch number: 122647101
Duration of Treatment: Fourteen days
Reference Therapy, Dose and Mode of Administration, Batch Number: Vehicle cream, twice daily, topical Batch number: 122627101:

Name of Sponsor/Company: LEO Pharma A/S

Name of Finished Product: Cromoglicate cream, 40 mg/g

Name of Active Ingredient: Sodium Cromoglicate

Criteria for Evaluation:

Primary Endpoint – Efficacy

The primary endpoint was change from baseline to end of treatment in subject's assessment of maximal and average intensity of itch within last 12 hours.

Secondary Endpoints – Efficacy:

The secondary endpoints were:

- Change in 4-point itch scale from baseline to end of treatment
- Change in 7-point itch scale from baseline to end of treatment
- Change in duration of itch from baseline to end of treatment
- Physician´s Global Assessment of treatment areas

Safety:

Safety evaluation included any adverse events reported, any adverse drug reaction reported and reasons for withdrawal from trial.

Statistical Methods:

The primary efficacy endpoints, change from baseline to end of treatment in subject's assessment of maximum and average itch within last 12 hours, were compared between cromoglicate cream and vehicle cream using a paired Wilcoxon test.

If data for Day 14 was missing a last observation carried forward approach was used.

The secondary endpoints, change in 4-point itch scale from baseline to end of treatment, and change in 7-point itch scale from baseline to end of treatment were analysed using a paired Wilcoxon text.

Summary – Conclusions

Study Population:

A total of 30 subjects (mean age 50.5 years) were randomised in the trial. The majority of subjects were white (93.3%), non-Hispanic/Latino (100%) and had Fitzpatrick skin types II or III (90%). The majority of subjects had psoriasis of moderate intensity and the mean duration of psoriasis was 20.8 years. Except for one, all subjects were treated according to the protocol. All 30 subjects completed the trial.

Efficacy Summary:

Both cromoglicate cream and vehicle cream reduced average and maximum itch within last 12 hours. Average itch reduced from approximately 55 to 25 mm on the visual analogue scale and maximum itch from approximately 60 to 30 mm.

According to subject's assessment of present itch on a 4-point scale, both treatments reduced the severity of itch from baseline to end of treatment. According to subject's assessment of change in itch on a 7-point itch scale, the majority of subjects experienced a similar improvement of their itch in both treatment areas from baseline to end of treatment.

The duration of itch was reduced by approximately 2 hours during night-time and 2.5 hours during day-time.

Safety Summary:

Administration of cromoglicate cream was well tolerated in this population. There were no SAEs, few AEs (all mild) and two adverse drug reactions. There were no clinically relevant changes in vital signs recorded during the trial.

Conclusion:

- Cromoglicate did not have an effect on itch in this trial. No clinical or statistical difference between cromoglicate and vehicle cream was observed in any of the efficacy endpoints used in the trial.
- The effect on itch by the cream vehicle was large - approximately 50% reduction in average itch for both night-time and day-time itch.
- Administration of cromoglicate cream was safe and well tolerated in this relatively small population of subjects with itchy psoriasis.

LP0075-34 Clinical Study Report Synopsis Clinical Study Report Synopsis - English

ELECTRONIC SIGNATURES

Electronic signature made within eDoc LEO by LEO Pharma A/S employees or employees of any LEO Pharma A/S affiliate located anywhere in the world, are to be considered to be legally binding equivalent of traditional handwritten signatures.

Signed by	Meaning of Signature	Server Date (dd-MMM-yyyy HH:mm 'GMT'Z)
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[redacted]	[redacted], Medical Approval	20-Dec-2013 07:54 GMT+01