Clinical Trial Report Synopsis

Patient insights following use of LEO 90100 aerosol foam and Daivobet® gel in subjects with psoriasis vulgaris

Design of trial:

An international, multi-centre, prospective, open-label, randomised, 2-arm, cross-over study with 2 weeks once daily treatment in subjects with psoriasis vulgaris

The clinical trial, including the archival of essential documents, was conducted in compliance with the clinical trial protocol, GCP, and the applicable regulatory requirement(s).

LEO Pharma A/S

Trial ID: LP0053-1030
Date: 29-Jul-2016
Version: Final
Clinical Trial Report Synopsis Statement

Approval Statement, LEO Pharma A/S

The following persons have approved this clinical trial report synopsis using electronic signatures as presented on the last page of this document:

, MSc Stat
, Global Clinical Operations

, MD, PhD
, Medical Science and Safety

Approval Statement, International Coordinating Investigator

The international coordinating investigator approves the clinical trial report synopsis by manually signing the International Coordinating Investigator Clinical Study Report Approval Form, which is a separate document adjoined to the clinical trial report.

The following person has approved this clinical trial report synopsis:

, MD, PhD
International coordinating investigator
Trial Registration Number  
NCT02310646

EudraCT number  
2014-003072-24

Title of Trial  
Patient insights following use of LEO 90100 aerosol foam and Daivobet® gel in subjects with psoriasis vulgaris

Investigators  
Dr. [Redacted], Canada, was appointed as signatory investigator

Trial Centres  
This trial was conducted at 15 centres in 2 countries (Canada, Germany) and coordinated at [Redacted], Canada.

Publications  
None at the time of the final clinical trial report.

Clinical Trial Period  
Date of First Subject First Visit: 10-Feb-2015
Date of Last Subject Last Visit: 03-Aug-2015

Development Phase  
Phase 3b

Objectives  
The objective of the trial was to gather insight on how product attributes affect usability by investigating the factors that are thought to influence patient preference to topical anti-psoriatic treatments

Methodology  
This was an international, multi-centre, prospective, open-label, randomised, 2-arm, 2-week cross-over trial in subjects with psoriasis vulgaris. Subjects were randomised to once daily treatment with LEO 90100 aerosol foam for 1 week followed by Daivobet® gel for 1 week, or vice-versa. The products were applied to psoriasis plaques on the trunk and/or limbs. Prior to randomisation, a washout period of up to 4 weeks was included if needed. Subjects had 3 study visits, i.e. Baseline (Day 1), Week 1 (Day 8) and Week 2 (Day 15). A safety follow-up visit was scheduled 14 (±2) days after the last on-treatment visit, if required.

At each visit, subjects completed some of the following questionnaires (tools): Subject’s Assessment of Behaviour and Attitudes (SABA), Dermatology Life Quality Index (DLQI), Topical Product Usability Questionnaire (TPUQ), Comparison to Latest Topical Treatment (CLTT), Vehicle Preference Measure (VPM), and Subject’s Preference Assessment (SPA). All tools were developed in-house with the exception of the DLQI and VPM.

The SABA and DLQI tools were completed at Baseline only and served to collect data on the subject’s attitude to psoriasis as well as their quality of life. The 4 other tools assessed the 2 products and/or the subject’s latest topical anti-psoriatic treatment (only if used within 3 months prior to study start [CLTT analysis set]). The TPUQ and CLTT tools each consisted of 26 items grouped under 4 domains (application, formulation, container, satisfaction). The SPA tool assessed the items under the application, formulation, and container domains (22 items), in addition to an item on overall preference. The CLTT tool was completed at Weeks 1 and 2. The same subgroup (CLTT analysis set) also completed the TPUQ at Baseline when this tool assessed their latest topical treatment. All subjects completed the TPUQ and VPM at Weeks 1 and 2. The SPA tool was completed at Week 2 only.

The trial also included investigator-assessed measures of disease severity, including the extent and severity of redness, thickness, and scaliness used to calculate the modified Psoriasis Area and Severity Index (m-PASI).

Number of Subjects Planned and Analysed  
200 subjects were planned and 213 subjects were allocated to treatment.

Diagnosis and Main Criteria for Inclusion  
- Age 18 years or above.
- Psoriasis vulgaris on the trunk and/or limbs (excluding psoriasis on the genitals and skin folds) involving 2–30% of the body surface area at Day 1 (Visit 1).
- A Physician’s Global Assessment of disease severity (PGA) of at least mild on trunk and/or limbs at Day 1 (Visit 1).
- A modified PASI (m-PASI) score of at least 2 on the trunk and/or limbs at Day 1 (Visit 1).
**Test Product, Dose and Mode of Administration, Batch Number**
LEO 90100 (calcipotriol 50 mcg/g and betamethasone [as dipropionate] 0.5 mg/g) applied once daily for 1 week; batch number: P14035

**Duration of Treatment**
Washout up to 4 weeks, treatment up to 2 weeks (treatment for 1 week with each product), follow-up 2 weeks after last visit, if required.

**Reference Product, Dose and Mode of Administration, Batch Number**
Daivobet® gel (calcipotriol 50 mcg/g and betamethasone [as dipropionate] 0.5 mg/g) applied once daily for 1 week; batch number: 133007101

**Criteria for Evaluation**
- Within subject difference in response to TPUQ items between trial treatments.
- Within subject difference in response to TPUQ between the latest topical anti-psoriatic treatment and each of the 2 trial treatments.
- Responses to CLTT for each of the 2 trial treatments.
- Within subject difference in response to VPM items between trial treatments.
- Overall treatment preference (SPA, Week 2) and association with baseline characteristics.
- Reasons for overall preference as assessed by SPA at Week 2.

**Statistical Methods**

**Within subject difference in response to TPUQ items between trial treatments**
Each response category was assigned a numeric score (-2 [strongly disagree or very dissatisfied] to 2 [strongly agree or very satisfied]). The period differences for the 2 groups of subjects defined by treatment sequence were compared using the Wilcoxon Rank Sum Test.

Summary scores were calculated by summing numeric scores for items under each domain, i.e., application (items 1-9), formulation (items 10-18), container (items 19-22), and satisfaction (items 23-25). In addition, a total TPUQ summary score (questions 1-25) was calculated. The summary scores were analysed in the same way as the individual questions.

For the 5 summary scores and item 26 (overall satisfaction), within subject differences between treatments were analysed in exploratory analyses of variance using stepwise forward selection (entry significance level 5%) with most baseline characteristics, country, treatment sequence, and treatment effect (numeric difference in percentage change in m-PASI) as potential explanatory factors.

**Within subject difference in response to TPUQ between the latest topical anti-psoriatic treatment and each of the 2 trial treatments**
Within subject differences to latest topical treatment were tested with Wilcoxon Signed Rank Tests.

**Responses to CLTT for each of the 2 trial treatments**
Only descriptive statistics were used.

**Within subject difference in response to VPM items between trial treatments**
Each response category was assigned a numeric score (-3 [extremely unappealing] to 3 [extremely appealing]). A summary score was defined as the sum of all questions. The period differences for the 2 groups of subjects defined by treatment sequence were compared using the Wilcoxon Rank Sum Test.

**Overall treatment preference (SPA, Week 2) and association with baseline characteristics**
The statistical significance of each of 7 baseline characteristics (age class, gender, PGA, psoriasis phenotype [localised or widespread; thin or thick plaques; small or large plaques; Type I or type II onset age]) was tested in a 2 factor logistic regression model including treatment sequence and each baseline characteristic as factors. Overall preference was also analysed in an exploratory logistic regression model using stepwise forward selection (entry significance level 5%) with most baseline characteristics, country, treatment sequence and treatment effect as potential explanatory factors.

Reasons for overall preference as assessed by SPA at Week 2
Only descriptive statistics were used.
Summary of Results

Trial Population
213 subjects were treated [109 subjects in the foam-gel treatment group; 104 subjects in the gel-foam treatment group] with at least one application/dose of investigational medicinal product (safety analysis set), and 211 subjects completed the trial. Two subjects discontinued the trial (voluntary withdrawal, lost to follow-up). 212 subjects were included in the full analysis set (FAS). No major protocol deviations were observed during the trial. 118 subjects in the FAS had used topical treatment within 3 months prior to Baseline and were included in the CLTT analysis set. The trial population comprised 133 (62.7%) men and 79 (37.3%) women. The mean age was 51.9 years (range 19 to 84 years); the mean duration of psoriasis was 19.9 years. The mean m-PASI score was 6.8 (median 5.8; range 2 to 30).

Questionnaire Results

Within subject difference in response to TPUQ items between trial treatments

Application Domain
- Significantly higher scores were observed for the gel than for the foam for the following items: ‘Ease of application’ (mean score 1.5 versus 1.1; p=0.001), ‘ease of application on psoriasis lesions only’ (mean score 1.4 versus 0.9; p<0.001), ‘ease of spreading’ (mean score 1.7 versus 1.5; p=0.004), and ‘good for use on small areas’ (mean score 1.4 versus 1.0 ; p<0.001) as well as the application summary score (mean score 12.8 versus 11.1; p=0.002).

Formulation Domain
- The foam was rated significantly higher than the gel for 2 items, i.e., ‘gave an immediate feeling of relief’ (mean score 1.0 versus 0.7; p=0.004) and ‘felt soothing to my skin’ (mean score 1.2 versus 1.0; p=0.001).
- The gel was rated significantly higher than for foam for 2 items, i.e., ‘not greasy’ (mean score 0.3 versus 0.0; p=0.04) and ‘odourless’ (mean score 1.6 versus 1.3; p<0.001).

Container Domain
- The gel was rated significantly higher than the foam for 3 items, i.e., ‘easy to use container’ (mean score 1.4 versus 1.1; p<0.001), ‘easy to keep container clean’ (mean score 1.4 versus 1.2; p=0.046) and ‘accurately dispense wanted amount’ (mean score 1.5 versus 0.9; p<0.001). The summary score was also significantly higher in favour of the gel (mean score 5.6 versus 4.3; p<0.001).

Satisfaction Domain
- No significant differences between the treatments were observed (mean scores for foam ranging from 1.2 to 1.3; mean scores for gel ranging from 1.1 to 1.3).

Total TPUQ Score and Overall Satisfaction
- The total TPUQ score was significantly higher for the gel than the foam (mean score 29.9 versus 26.8; p=0.007).
- No significant difference in overall satisfaction (item 26) was observed between the treatments (mean score of 1.1 [foam] versus 1.2 [gel]; p=0.43)

Within subject difference in response to TPUQ between the latest topical anti-psoriatic treatment and each of the 2 trial treatments

Application Domain
- The foam was rated significantly higher than the latest topical treatment for 4 items (‘good for use on larger areas’ [mean score 1.4 versus 0.9; p<0.001], ‘quick to apply’ [mean score 1.5 versus 1.2; p=0.01], ‘total time spent acceptable’ [mean score 1.6 versus 1.1; p<0.001] and ‘easily incorporated into daily routine’ [mean score 1.5 versus 1.0; p<0.001]). The foam was rated significantly lower than the latest topical treatment for 1 item (‘ease of application on psoriasis lesions only’ [mean score 0.9 versus 1.3; p=0.020]).
- The gel was rated significantly higher than the latest topical treatment for all items but 3 (‘ease of application’, ‘ease of application on psoriasis lesions only’, and ‘quick to apply’).

Formulation Domain
- The foam was rated significantly higher than the latest topical treatment for all items but 1 (‘odourless’).
- The gel was rated significantly higher than the latest topical treatment for all items.

Container Domain
- The scores for the foam were similar to the scores for latest topical treatment.
- The gel was rated significantly higher than the latest topical treatment for the item ‘I could accurately dispense the amount of medication I wanted to use’ (mean score 1.5 versus 1.0; p<0.001). The total container score was also higher for the gel than the latest topical treatment (mean score 5.5 versus 4.6; p=0.042).

Satisfaction Domain
- Both the foam and the gel had significantly higher scores than the latest topical treatment for all items.
**Total TPUQ Score and Overall Satisfaction**

- Both the foam and the gel achieved a significantly higher TPUQ sum score than the latest topical treatment (mean total TPUQ scores of 28.4 [foam; p<0.001] and 29.0 [gel; p<0.001] versus 19.4 [latest topical treatment]).
- For the overall satisfaction item (#26), both the foam and the gel were rated significantly higher than the latest topical treatment (mean overall satisfaction scores of 1.2 [foam; p<0.001] and 1.1 [gel; p<0.001] versus 0.3 [latest topical treatment]).

**Responses to CLTT for each of the 2 trial treatments**

**Application, Formulation, Container and Satisfaction Domains**

- For the foam, the highest rated item was ‘likelihood to recommend this product’, with 72.2% of the subjects preferring foam over latest topical treatment for this item.
- For the gel, the highest rated item was ‘likelihood to use the product regularly’, with 67.5% of the subjects preferring gel over latest topical treatment for this item.

**Overall Satisfaction**

- Overall, 76.5% of the subjects preferred the foam over the latest topical treatment. The proportion preferring foam was similar among subjects who used ointments (77.1%) and creams (80.9%) within the last 3 months prior to Baseline.
- Overall, 70.2% of the subjects preferred the gel over the latest topical treatment. The proportion preferring gel was higher if latest topical treatment was an ointment (80.6%) than if it was a cream (67.6%).

**Within subject difference in response to VPM items between trial treatments**

- None of the differences but 1 were significant: A significantly higher score was observed for the gel than for the foam for the item ‘how it smells’ (mean scores of 1.9 versus 1.6; p=0.003). The other differences were not significantly different.

**Overall treatment preference (SPA, Week 2) and association with baseline characteristics**

- The overall preference was equally shared between the 2 treatments, with 105 subjects (50.5%) of subjects preferring the gel and 103 (49.5%) of subjects preferring the foam. Associations with baseline characteristics are described below under ‘Multiple Regression Analyses’.

**Reasons for overall preference as assessed by SPA at Week 2**

**Application Domain**

- The largest proportion of subjects who indicated an item was very important for their overall preference of foam was observed for the item ‘ease of spreading’ (65% of subjects).
- The largest proportion of subjects who indicated an item was very important for their overall preference of gel was observed for the item ‘ease of application on psoriasis lesions only’ (61% of subjects).

**Formulation Domain**

- The largest proportion of subjects who indicated an item was very important for their overall preference was observed for the item ‘lack of staining of clothes/bed linen’ for both products (53% of subjects preferring foam; 54% of subjects preferring gel).

**Container Domain**

- The largest proportion of subjects who indicated an item was very important for their overall preference of foam was observed for the item ‘easy to use container’ (55% of subjects).
- The largest proportion of subjects who indicated an item was very important for their overall preference of gel was observed for the item ‘accurately dispense wanted amount’ (59% of subjects).

**Multiple Regression Analyses**

Multiple regression analyses of TPUQ sum scores and overall preference (SPA) showed several statistically significant factors, of which age group and psoriasis distribution seem to be robust:

- **Age group:** Subjects aged 18 to 39 years seemed to prefer foam while subjects aged 40 to 59 years and ≥60 years seemed to prefer gel.
- **Psoriasis distribution phenotype:** Subjects with a localised distribution seemed to favour foam while subjects with a widespread distribution of psoriasis seemed to favour gel.

**Safety Results**

A total of 21 subjects (9.9%) experienced a total of 21 treatment-emergent adverse events (AEs). No SAEs, severe AEs or AEs leading to withdrawal were observed. Two subjects had AEs which were assessed to be related to the investigational product by the investigator. The most frequent AE was nasopharyngitis, reported by 4 subjects (1.9%); 2 subjects (1.8%) in the foam-gel group and 2 subjects (1.9%) in the gel-foam group. All other treatment-emergent AEs were each reported by 1 subject. The treatments were well tolerated in this population.
Conclusion

- Overall, both products achieved high scores of usability and high satisfaction scores.
- Preference appeared to be influenced by several intrinsic and extrinsic subject characteristics, e.g., age, psoriasis distribution phenotype, and latest topical treatment.
- Overall preference was equally divided between the 2 products, with 50.5% of subjects preferring Daivobet® gel and 49.5% of subjects preferring LEO 90100. Younger subjects seemed to prefer LEO 90100; older subjects seemed to prefer Daivobet® gel.
- Subjects with a localised distribution seemed to favour LEO 90100 while subjects with a widespread distribution of psoriasis seemed to favour Daivobet® gel.
- Both products were generally preferred over the subjects’ previous topical treatments which were mostly ointments or creams; however, limitations of the trial design should be acknowledged for this evaluation.
- LEO 90100 was rated higher than Daivobet® gel for the items ‘gave an immediate feeling of relief’ and ‘felt soothing to my skin’ while Daivobet® gel was rated higher than LEO 90100 for items related to ease of application, precision of application, and user friendliness of the container (‘easy to use container’ and ‘accurately dispense wanted amount’). Daivobet® gel was also scored significantly higher than the foam for the formulation items ‘not greasy’ and ‘odourless’.
- LEO 90100 and Daivobet gel®, each applied for 1 week, were both well tolerated in this population.
**ELECTRONIC SIGNATURES**

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