Ergebnisbericht nach § 42b AMG

Name of sponsor/comany:	InfectoPharm GmbH, Heppenheim, Von-Humboldt-Str. 1, 64646 Heppenheim
Name of finished product:	Permethrin cream 2.5% and 5%
Name of active ingredient:	Permethrin

Titel of study:

Multicentre, randomised, double-blind, controlled phase III study on treatment of papulopustular rosacea with permethrin cream 5% (InfectoScab®) versus permethrin cream 2.5% versus metronidazole cream 0.75% (Rozex®)

Study code:

PAROP

Principal investigator:

PD Dr. med. Maurizio Podda
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Dermatologie
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64297 Darmstadt

Study centres:

6 investigators (dermatologists) in 6 study centres in Germany;
a list of investigators and study centres is attached at the end of this report.

Studied period:

First patient first visit: March 06, 2012

Last patient last visit: November 26, 2012

Publication:

Not applicable

Objectives:

The primary objective of the study is to prove that permethrin cream is non-inferior to metronidazole cream with respect to efficacy, as assessed by the changes of the Inflammatory Lesion Count (ILC) between baseline and the final visit after 84 days.

Secondary objectives comprise the investigation of the effects of the study medications on secondary efficacy criteria (e.g. number of papules, number of pustules, severity of the disease) and the assessment of safety (e.g. adverse drug reactions).

Methodology:

- Randomised, double-blind, multicentre, parallel group study with two dosages of the test medication and active comparator

- Adaptive study design with planned interim analysis after 90 patients have finalised the pilot phase of the study

- Discontinuation of one permethrin arm after the interim analysis

- Study duration and treatment duration for each patient: 84 days

- Evaluation of the Inflammatory Lesion Count (ILC), defined as the sum of the number of papules and the number of pustules on the face

- Evaluation of the severity of the rosacea by means of a 4-point erythema score

- Evaluation of the severity of the disease by the patient by means of a visual analogue scale

- Documentation of all adverse events during the study

Number of patients:

Planned: 90 (pilot study) (planned for main phase: about 300)

Analysed: 90 (main phase not started)

Diagnosis and main criteria for inclusion:

- Age between 30 and 75 years

- Clinically diagnosed acute papulopustular rosacea

- Presence of symptoms of papulopustular rosacea for at least 3 months

- Inflammatory Lesion Count (ILC) on the face between 6 and 24. The ILC is defined as the sum of the number of papules (with diameter > 0.5 mm) and the number of pustules

Test product, dose and mode of administration:

Test products:
Permethrin Cream 5% (InfectoScab®, active ingredient: permethrin 5 %)
Permethrin Cream 2.5% (active ingredient: permethrin 2.5 %)

Dose: twice daily

Mode of administration: topical administration in thin layers on the affected parts of the skin

Duration of treatment:

84 consecutive days

Reference therapy, dose and mode of administration:

Reference product:
Metronidazole cream 0.75% (Rozex®)

Dose: twice daily

Mode of administration: Topical administration in thin layers on the affected parts of the skin

Criteria for evaluation:

Efficacy:

Primary efficacy variable:

Change of the ILC between baseline (Day 0) and final visit (Day 84), calculated as "value at Day 84 minus value at Day 0"

Secondary efficacy variables:

- Change of the ILC between baseline (Day 0) and visits Day 14, Day 28 and Day 56

- Value of ILC at visits Day 14, Day 28, Day 56 and Day 84

- Number of papules at visits Day 14, Day 28, Day 56 and Day 84

- Change of the number of papules between baseline (Day 0) and visits Day 14, Day 28, Day 56 and Day 84

- Number of pustules at visits Day 14, Day 28, Day 56 and Day 84

- Change of the number of pustules between baseline (Day 0) and visits Day 14, Day 28, Day 56 and Day 84

- Erythema score at visits Day 14, Day 28, Day 56 and Day 84

- Change of the erythema score between baseline (Day 0) and visits Day 14, Day 28, Day 56 and Day 84

- Evaluation of severity of the disease by the patient at visit Day 84 and change between baseline (Day 0) and visit Day 84

- Premature discontinuation because of insufficient efficacy of the study medication and/or application of an additional effective rosacea therapy (yes/no)

Safety:

- Number and classification of adverse events and adverse drug reactions

- Premature discontinuations and related reasons

- Evaluation of tolerability of the study medication by the patient at visit Day 84

Statistical methods:

Originally planned analysis for the main phase of the study: Non-inferiority of the permethrin cream chosen for the main phase vs. metronidazole cream.

Since the study was terminated after the pilot phase, the analysis was based solely on the data from the pilot phase. Hence, no confirmatory testing could be performed.

Efficacy results:

The study was terminated after the pilot phase had been finalised. Therefore, no confirmatory results regarding the efficacy could be obtained.

Safety results:

For a total of 14 patients adverse drug reactions (ADR) were reported, i.e. adverse events with an at least possible or not assessable causal relationship with the study medication. None of the ADRs were rated as serious. No relevant differences between the treatment groups could be observed.

Conclusion:

Because the study was terminated after the pilot phase had been finalised, no confirmatory results could be generated with regard to efficacy. The safety of all three treatments, permethrin cream 2.5 %, 5 %, and metronidazole cream 0.75 %, appeared to be safe in the treatment of papulopustular rosacea.

Date of report:

18.11.2013

Recruitment stop:

According to the study protocol, the PAROP trial was planned to be subdivided into a pilot phase (with 90 patients - 3 arms) and a main phase (about 300 patients envisaged - 2 arms). Between both phases, a recruitment stop and an interim analysis of the results of the pilot phase were planned, which had been initially predefined in the study protocol before the start of the pilot phase. The recruitment stop of the pilot phase was on 4th September 2012. The clinical part of the pilot phase was finalised on 26th November 2012 (last visit last patient). Due to unexpected high standard deviations obtained from the interim analysis, it was decided not to start the confirmatory main phase of the PAROP trial.

Amendments:

No amendments