Clinical Study Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Bayer HealthCare

Clinical Trial Results Synopsis

Study Design Description		
Study Sponsor:	Bayer HealthCare AG	
Study Number:	1401201	NCT00408330
Study Phase:	II	
Official Study Title:	A double-blind, randomized, vehicle-controlled, 6-week exploratory multicenter pilot study of the efficacy and safety of azelaic acid (AzA) 15% gel in the topical treatment of mild to moderate seborrheic dermatitis of the face	
Therapeutic Area:	Dermatology	
Test Product		
Name of Test Product:	Other AzA 15% gel (SH H 655 BA; gel containing 15% azelaic acid; Finacea)	
Name of Active Ingredient:	Azelaic acid	
Dose and Mode of Administration:	Twice daily administration; 0.5 g gel per application; topical application to facial area	
Reference Therapy/Placebo		
Reference Therapy:	Vehicle (non-medicated gel base of AzA 15% gel; SH H 655PBA)	
Dose and Mode of Administration:	Twice daily administration; 0.5 g gel per application; topical application to facial area	
Duration of Treatment:	6 weeks	
Studied period:	Date of first subjects' first visit:	19 DEC 2006
	Date of last subjects' last visit:	29 MAR 2007
Premature Study Suspension / Termination:	No	
Substantial Study Protocol Amendments:	Amendment no. 1 (dated 10 JAN 2007) was followed from the very beginning of the study although it was dated after start of enrollment of the first subject. It specified the following modifications: • Addition of pregnancy at baseline (positive urine pregnancy test, and women of childbearing potential not using reliable contraception methods) as exclusion criteria. • Removal of subjects from treatment or assessment if they became pregnant during the study. • Urine pregnancy test for women of childbearing potential to confirm absence of pregnancy as additional baseline evaluation as well as Week 6/End of study medication activity. • If a subject probably became pregnant (menstruation more than 4 days overdue) a urine pregnancy test had to be performed as additional Week 1, 2, and 4 activities.	
Study Centre(s):	This study was conducted at 4 sites in Germany.	
Methodology:	It was an exploratory, parallel-group study. Subjects were examined by the investigator at baseline (screening and baseline visits could be merged to one visit), on Week 1 (Day 7), Week 2 (Day 14), Week 4 (Day 28), and Week 6 (Day 42). At each of these 5 visits, the single	

	merged to one visit), on Week 1 (Day 7), Week 2 (Day 14), Week 4 (Day 28), and Week 6 (Day 42). At each of these 5 visits, the single clinical symptoms for all affected areas, the investigator's global assessment, and adverse events (AEs) were assessed and recorded in the case record form (CRF). An investigator's and subject's rating of overall improvement was performed at the end of study treatment. Likewise, the subject's overall assessment of local tolerability was performed at the end of study treatment.
Indication/ Main Inclusion Criteria:	Indication: Clinical diagnosis of mild to moderate seborrheic dermatitis of the facial area Inclusion criteria: • Written informed consent • Male or female subjects with a minimum age of 18 years • Stable or exacerbating seborrhoic dermatits of the face area • Investigator's Global Assessment (IGA) score at baseline of 2 to 4 (on a scale from 0 to 5) • Willingness and capability to follow all study procedures
Study Objectives:	Overall: The objective was to explore the efficacy and safety of AzA 15% gel (SH H 655 BA) applied twice daily for 6 weeks in the treatment of seborrheic dermatitis of the face using its vehicle (VEH, non-medicated gel base of AzA 15% gel, SH H 655PBA) as comparator. Primary: Not applicable Secondary: Not applicable
Evaluation Criteria:	Efficacy (Primary): • Total facial sum score (TFSS) [defined as the sum of individual severity scores (from 0 to 5) for scaling, erythema (inflammation), and itching across all target areas (5 target areas: Eyebrows and bridge of the nose, Scalp hairline / forehead, Nasolabial folds, Chin / perioral area), Posterior aspect of the ear] • IGA of acute disease status (from 0 to 5) • Dichotomized IGA ("Success" was defined as the scores "none (clear)" or "minimal"; "Failure" was defined as "mild", "moderate", "pronounced" or "severe") Efficacy (Secondary): • Single symptom sum score (SSSS) [sum across all target areas for the single symptom (scaling, erythema (inflammation), itching) with a range from 0 (individual symptom was "clear" for all 5 areas) to 25 (individual symptom was "severe" for all 5 areas)] • Investigator's and patient's global assessment on overall improvement (score with 6 categories, from "excellent improvement" =1, to "deterioration" = 6)

	Safety: • AEs • Patient's global assessment on local tolerability (score with 6 categories, from "excellent" = 1, to "non-acceptable" =5; "no opinion" = 6)
Statistical Methods:	Efficacy (Primary): • Calculation of statistics, exploratory Wilcoxon rank-sum test • Calculation of frequencies and statistics, exploratory Wilcoxon rank-sum test • Calculation of frequencies, exploratory exact Fisher test Efficacy (Secondary): • Calculation of statistics, exploratory Wilcoxon rank-sum test • Calculation of frequencies, exploratory Wilcoxon rank-sum test Safety: • Calculation of incidences Calculation of frequencies
Number of Subjects:	Planned: AzA: 32 subjects, vehicle (VEH): 16 subjects Analyzed: SAF (safety): AzA: 32 subjects, VEH: 15 subjects FAS (full-analysis set): AzA: 32 subjects, VEH: 15 subjects • PPS (per-protocol set): AzA: 30 subjects, VEH: 10 subjects

Study Results

Results Summary — Subject Disposition and Baseline

A total of 47 subjects were randomized, 32 of them were exposed to AzA and 15 to VEH. These subjects comprised the safety set and the FAS set as well. Thirty subjects of the AzA group and 10 subjects of the VEH group were considered evaluable per-protocol.

Five subjects (2 on AzA, 3 on VEH) discontinued the study treatment prematurely.

Most subjects randomized were male (84% for AzA, 87% for VEH). The mean age was 48.3 years (range: 20.0 - 77.0) and 49.1 years (range: 27.0 - 65.0) in the AzA and VEH groups, respectively. The mean weight was 81.3 kg (range: 56.0 - 105.0) and 84.8 kg (range: 62.0 - 110.0) in the AzA and VEH groups, respectively, and the mean height was 177.3 cm (range: 156.0 - 192.0) and 179.7 cm (162.0 - 192.0) in the AzA and VEH groups, respectively. There was no inhomogeneity between the treatment groups, neither in the demographics nor in the main baseline variables. All of the randomized subjects were Caucasians.

The compliance with study treatment was at least 90% in all subjects receiving AzA and in 87% of those receiving VEH.

Results Summary — Efficacy

At baseline, the mean total facial sum score in the AzA group was slightly lower than in the VEH group (not statistically significant). After the first and the second weeks of treatment, the mean total facial sum score decreased significantly in the AzA group compared to the VEH group for FAS ($p = 0.0009$ and $p = 0.0011$ for Week 1 and Week 2, respectively). After the second week of treatment, the total facial sum score showed no more relevant decrease in the AzA group, however, continued to decrease in the VEH group.

Owing to this time course of changes of the total facial sum score, significant treatment differences were not observed at any other time point including last observation carried forward (LOCF) approaches. Similar results, including significant differences at Week 1 and Week 2, were observed for the PPS population.

The other primary variable, the IGA, showed the same pattern. Fruthermore, the IGA was dichotomized into "success" (clear and minimal) and "failure" (mild, moderate, pronounced and severe). In the AzA group 25 out of 32 subjects (78.1%) and in the VEH group 9 out of 15 subjects (60.0%) were rated as "success" at the last visit (not statistically significant).

The analysis of the single symptoms indicated that treatment response was achieved at Week 1 and Week 2 concerning erythema and scaling, but not for itching.

The global assessment of overall improvement by the investigator was rated "excellent" or "marked improvement" for 71% of the subjects in the AzA group and for 40% in the VEH group. The respective estimates for the subjects' assessments were 65% and 40%. Deteriorations were seen only in the VEH group. They occurred in the opinion of 2 investigators and 3 subjects. The two-sided Wilcoxon rank-sum test indicated differences between treatment groups for investigator's overall assessment favoring AzA. The subjects' opinion showed trend-like treatment differences (not statistically significant).

Results Summary — Safety

Two subjects from the VEH group were withdrawn due to adverse events (application site erythema/irritation). Overall, the incidence of application site irritations was higher in the AzA group (17 subjects, 53%) compared to the VEH group (5 subjects, 33%). In two subjects from each group, such occurrences were classified as severe; the remaining cases were classified as mild to moderate. One subject in each group experienced pruritus. All other AEs were isolated occurrences.

There was no serious AE (SAE), or any other notable finding or evidence for adverse reactions not yet listed in the current SPC (summary of product characteristics).

The tolerability of the study medication was rated as "excellent" or "good" by 12 out of 31 patients (38.7%) in the AzA group and by 8 out of 15 patients (53.3%) in the VEH group and as "acceptable" by 17 patients (54.8%) in the AzA group and by 4 patients (26.7%) in the VEH group.

Conclusion(s)

In this study, AzA showed beneficial effects in the treatment of seborrheic dermatitis of the face during the first 2 weeks of treatment. Later on, the symptoms diminished anyhow, presumably reflecting the natural fluctuations of the disease.

Publication(s): none

Date Created or Date Last Updated:	04 APR 2012	Date of Clinical Study Report:	20 MAY 2008

Investigational Site List

Marketing Authorization Holder in Germany	
Name	Bayer HealthCare AG
Postal Address	D-51368 Leverkusen, Germany
Sponsor in Germany	
Legal Entity Name	Intendis GmbH
Postal Address	Max-Dohrn-Strasse 10, D-10589 Berlin, Germany

List of Investigational Sites

No	Facility Name	Street	ZIP Code	City	Country
1	SCIderm Scientific Research	Stephansplatz 5	20354	Hamburg	Germany
2	Private Practice	Neue Strasse 9	21244	Buchholz	Germany
3	Private Practice	Bahnhofstrasse 1	15831	Blankenfelde-Mahlow	Germany
4	Private Practice	Lesserstrasse 199	22049	Hamburg	Germany

Product Identification Information

Product Type	Drug
US Brand/Trade Name(s)	Finacea
Brand/Trade Name(s) ex-US	Azelan, Finacea 15% gel, Skinoren, Skinoren gel, Zelaika,
Generic Name	Azelaic Acid
Main Product Company Code	BAY39-6251
Other Company Code(s)	n. a.
Chemical Description	Nonanedioic acid
Other Product Aliases	SH H 655 BA

Date of last Update/Change: 30 May 2012