Science For A Better Life

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.

Date of study report:	23 JUN 2008
Study title:	A randomized, double-blind, single center, intra-individual comparison study with repeated application to assess the wound-healing efficacy of a 5% Dexpanthenol ointment compared with placebo in patients with superficial, abrasive wounds
Sponsor's study number:	12631
NCT number:	Not applicable
EudraCT number:	2006-005508-14
Sponsor:	Bayer HealthCare
Clinical phase:	Phase IV
Study objectives:	The objective of the study was to investigate the efficacy of Bepanthen® wound healing ointment compared to placebo in a superficial abrasive wound model. The primary objective was the re-epithelization at Day 5. The secondary objectives were: • Re-epithelization at days 2, 3, 4, 6, 7, 8, 9, 10, and 15 • Assessment of cosmetic outcome/acceptance at Day 15 (investigator only) and at Day 36 (investigator and subject) • Documentation and analysis of safety parameters
Test drug:	Dexpanthenol (Bepanthen® Wund- und Heilsalbe, BAY 81-2996)
Name of active ingredient(s):	Dexpanthenol 5%
Dose:	A squeeze of ointment, approximately 0.5 cm in length corresponding to an amount of about 0.3 g of ointment, which is equal to 15 mg dexpanthenol, twice daily (once in the morning and once in the evening)
Route of administration:	Topical application under occlusion
Duration of treatment:	14 days per subject
Reference drug:	Placebo to Bepanthen® wound healing ointment without active ingredient
Name of active ingredient(s):	Not applicable
Dose	A squeeze of ointment, approximately 0.5 cm in length corresponding to an amount of about 0.3 g of ointment twice daily (once in the morning and once in the evening)
Route of administration:	Topical application under occlusion

Duration of treatment:	14 days per subject
Indication:	Wound-healing
Diagnosis and main criteria for inclusion:	Healthy Caucasian subjects of both genders, 18-45 years of age, Fitzpatrick skin type I to IV
Study design:	The study was conducted in a randomized, single-center, intra-individual comparison, double–blind design
Methodology:	The study consisted of screening, treatment phase, and follow-up. Screening was performed about 8 days prior to the start of the treatment. Treatment phase was from Day 1 to Day 14. The follow-up was performed between Day 15 and Day 36. On Day 1, subjects were enrolled and two superficial abrasive wounds were induced at the forearms of each subject with a surgical brush on two different test areas (one at each forearm, below the fossa cubitalis) with a diameter of approximately 1.2 cm. A baseline photo of both wounds was taken for documentation. For each subject, the wounded skin area on one arm was treated with verum, the other with placebo according to the randomization list. After treatment the wounds were covered with a standard bandage at Day 1 to Day 15. The cosmetic outcome/acceptance was assessed at Day 15 (only by the investigator) and Day 36 by the investigator and the subject using a visual analog scale (VAS) ranging from 0 being poor, 5 being moderate to 10 being excellent. Photo documentation was done at Visit 1 (directly after induction of the abrasive wounds) and at all other visits at the test center for support of the visual assessments (study Days 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, and 36). Wound healing was evaluated on a 6-point scale ranging from 0 (=0 % re-epithelization) to 5 (=100 % re-epithelization). All female subjects of childbearing potential were tested for pregnancy on the screening visit using a urine test for human chorionic gonadotropin (hCG). The study duration was approximately 5 weeks per subject. Safety and tolerability of study treatments were monitored throughout the study.
Study center(s):	The study was conducted at a single center in Germany.
Publication(s) based on the study (references):	None at the time of report creation
Study period:	**Study Start Date:** 12 MAR 2007 **Study Completion Date:** 23 APR 2007
Early termination:	Not applicable

Number of subjects:	**Planned:** 28 subjects **Analyzed:** 28 subjects
Criteria for evaluation ***Efficacy:*** Primary parameter: • Wound healing effect (=re-epithelization) at Day 5 of the test product and the placebo Secondary parameters: • Wound healing at Days 2, 3, 4, 6, 7, 8, 9, 10, and 15 after wound induction • Subjective assessment of cosmetic outcome 15 and 36 days after wound induction (VAS) ***Safety:*** Secondary parameters: • Physical examination focused on the skin • Documentation and analysis of adverse events (AEs) • Assessment of infections of wounds • Assessment of irritant and allergic reactions • Pregnancy test (for women of childbearing potential)	
Statistical methods:	Primary analysis was based on the wound healing Measured on a 6-point scale 5 days after wound induction. For statistical comparison of treatments, a Wilcoxon Signed Rank Test was used. Secondary parameters were presented descriptively (frequency distributions, computation of adequate statistical measures) and additionally the Wilcoxon Signed Rank Test was computed to compare wound healing and a paired t-Test to compare the cosmetic outcome between treatments.
Substantial protocol changes:	The study was conducted according to final study protocol from 14 NOV 2006 and included no substantial amendments.

Subject disposition and baseline

Thirty eight subjects were screened for this study. Twenty eight subjects (64.3% females, 35.7% males) with an average age of 35.4 years (ranging from 21-45 years of age), with a mean height of 171.2 cm and a mean weight of 75.9 kg were enrolled in this study and were valid for safety analysis.

In 2 subjects, protocol violations were regarded as major and the subject was therefore excluded from the per protocol (PP) population and were therefore analyzed as intention-to-treat (ITT) population. All other subjects were treated and evaluated according to the protocol (or with minor protocol deviations) and were analyzed as PP population (n=26).

Out of 28 subjects, 4 (14.3%) had Fitzpatrick skin type I, 2 (7.1%) had skin type II, 13 (46.4%) had skin type III, and 9 (32.1%) had skin type IV.

Efficacy evaluation

Primary objective evaluation:

In the following Table 1, mean assessments of re-epithelization at study Day 5 are presented.

The statistical comparison of treatments revealed a p-value of 0.302, indicating no significant difference between Bepanthen® and its placebo at that respective day.

Table 1: Mean re-epithelization scores

PP=26	mean	sd	min	q25	med	q75	max	Diff.
Bepanthen®	2.15	0.54	1	2.0	2	2.0	3	-0.19
Placebo	2.35	0.63	1	2.0	2	3.0	3	

Secondary objectives evaluation:

In the following Table 2, mean assessments of re-epithelization are illustrated over time, including exact p-values from separate Wilcoxon Signed Rank Test per study day.

Table 2: Mean re-epithelization scores over time

PP, n=26	Bepanthen					Placebo					p-value
	mean	sd	min	med	max	mean	sd	min	med	max	
day 2	0.65	0.56	0	1	1.0	0.65	0.49	0	1	1	1.0
day 3	1.08	0.27	1	1	1.0	1.04	0.34	0	1	2	1.0
day 4	1.73	0.45	1	2	2.0	1.73	0.53	0	2	2	1.0
day 6	2.58	0.50	2	3	3.0	2.81	0.49	2	3	4	0.146
day 7	2.77	0.51	2	3	3.0	3.15	0.37	3	3	4	0.006
day 8	3.15	0.37	3	3	3.0	3.50	0.51	3	4	4	0.035
day 9	3.54	0.51	3	4	4.0	3.65	0.49	3	4	4	0.648
day 10	3.81	0.40	3	4	4.0	3.81	0.40	3	4	4	1.0
day 15	5.00	0.00	5	5	5.0	5.00	0.00	5	5	5	1.0

At the first days (Days 2-6), after induction of the wounds and at Days 9, 10, and 15 hardly any differences were seen in the wound-healing efficacy between the test product Bepanthen® wound healing ointment and the placebo. At study Days 7 and 8, significant differences in wound healing were seen with better results for the placebo.

The results for the assessment of the cosmetic outcome/acceptance at Day 15 (only investigator) are summarized in Table 3:

Table 3: Cosmetic outcome/acceptance at Day 15 (investigator)

PP=26		n	mean	sd	min	median	max	p-value
day 15 (PP)	Bepanthen	26	7.1	1.36	4.3	7.1	8.9	0.366
	Placebo	26	6.9	1.47	3.1	7.2	9.1	

The cosmetic outcome as assessed by the investigator revealed no statistically significant differences between Bepanthen® wound healing ointment and the placebo.

In the following Table 4, the cosmetic outcome/acceptance at Day 36 is illustrated, judged by the subjects and the investigator:

Table 4: Cosmetic outcome/acceptance at Day 36 (investigator and subject)

PP=26		n	mean	sd	min	median	max	p-value
day 36 Investigator	Bepanthen	26	6.6	1.58	3.4	6.8	9.5	0.508
	Placebo	26	6.7	1.45	3.8	6.6	9.8	
day 36 Subject	Bepanthen	26	6.5	2.38	0.9	6.8	9.9	0.829
	Placebo	26	6.6	2.30	0.5	6.5	9.9	

No statistically significant differences regarding the cosmetic outcome/acceptance was seen at Day 36 neither after assessment of the investigator nor after assessment of the subjects.

Safety evaluation

Twenty non-serious AEs (none of the AEs were study related) occurred in this study in 15 subjects. Sixteen of these AEs were graded as mild, while 4 were judged as moderate. The most common AEs in this study were: common cold, headache, and tooth pain. No relation to the study procedure was seen in any of the AEs. Fourteen subjects recovered without sequelae. One subject recovered with sequelae (wound of a cut injury healed but a scar was left over; however, this cut occurred already during screening period).

One subject complained about itching at study Day 5 after application of Bepanthen® wound healing ointment. Although application of Bepanthen® was not discontinued, no further itching was reported. No other signs of infections or allergic or unusual strong irritant reactions were seen at the superficial wounds during the conduct of the study, neither after application of Bepanthen® wound healing ointment nor after application of the placebo.

There were no pathological findings during the physical examination at screening and at the final visit.

No single skin reaction at the wounded test area, which might be indicative of an infection, was seen during the conduct of the study.

Eighteen subjects (64.3%) had a negative pregnancy test at screening. For all other subjects, a pregnancy test was not applicable since they were not of childbearing potential. All subjects of childbearing potential had used contraception for at least 3 months before study start.

Overall conclusions

- It was the primary objective of this study to investigate the wound-healing efficacy of Bepanthen® wound healing ointment at study Day 5 in comparison to the respective placebo. There were no statistically significant differences between treatments of the superficial wounds with Bepanthen® or with the placebo at study Day 5. For the secondary parameters, no statistically significant differences in favor of Bepanthen® wound healing ointment were observed.

- The relatively low number of AEs, the severity, and the kind of observed AEs indicated no negative aspects regarding safety in this study.

Investigational Site List

Marketing Authorization Holder in Germany	
Name	Bayer Vital GmbH
Postal Address	D-51368 Leverkusen Germany
Sponsor in Germany (if applicable)	
Legal Entity Name	Bayer AG
Postal Address	D-51368 Leverkusen Germany

List of Investigational Sites

No	Investigator Name	Facility Name	Street	ZIP Code	City	Country
1	Klaus-Peter Wilhelm	proDERM GmbH	Kiebitzweg 2	D-22869	Schenefeld	Germany