1 Title Page

Tolerability Study of Posterisan® corte Placebozäpfchen on healthy volunteers

Date of the Report:	20 March 2009
Name of the Investigational Product:	Posterisan® corte Placebozäpfchen
Study purpose:	Demonstration of local tolerance of Posterisan® corte Placebozäpfchen (placebo suppositories)
Study Design:	Prospective, monocentric, open-label
Development Phase of Study:	Phase III
EudraCT-No.:	2007-006165-32
Sponsor Study-No.:	KAD 133
Name of the Sponsor:	Dr. Kade Pharmazeutische Fabrik GmbH
Name of Sponsor Signatory:	Annett Schubert
Name of Sponsor Contact Person:	Dr. Marija Süßkind Rigistraße 2, D-12277 Berlin Tel: +49-30-720820 137 Fax: +49-30-72082 250 e-mail: MarijaSuesskind@kade.de
First Subject Enrolled:	09/2008
Last Subject Completed:	11/2008
Principal Investigator:	Dr. med. Günter Gruhlke Bundesallee 54 10715 Berlin

Confidentiality Statement

This study was conducted in compliance with good clinical practice (GCP). The information provided in this document is strictly confidential. No disclosure should take place without the written authorisation from Dr. Kade Pharmazeutische Fabrik GmbH.

2 Synopsis

Name of Sponsor/Company Dr. Kade Pharmazeutische Fabrik GmbH		
Name of Investigational Product Posterisan® corte Placebozäpfchen		
Name of Active Ingredient no active ingredient		

Title of Study: Tolerability Study of Posterisan® corte Placebozäpfchen on Healthy Volunteers

EudraCT-No.: 2007-006165-32

Sponsor Study-No.: KAD 133

Principle Investigator: Dr. med. Günter Gruhlke

Study Centre: Praxis für Dermatologie, Bundesallee 54, 10715 Berlin

Publication (reference): Not available.

Duration of study (months): 3 (date of first enrolment): 09/2008 (date of last completed): 11/2008	**Phase of development:** III

Objectives:

Primary Objective:

Efficacy: Not applicable.

Tolerance: Incidence of all intolerances.

Secondary Objectives:

Assessment of tolerance by physician

Assessment of tolerance by the volunteers

Safety:

Incidence of all adverse drug reactions.

Methodology: Prospective, monocentric, open-label in accordance with German Drug Law (AMG) and Good Clinical Practice (CPMP/ICH/135/95)

Number of subjects (planned and analysed):

	Total
Planned	20
Enrolled	21
Analysed	21

Diagnosis and main criteria for inclusion:

healthy male und female volunteers, adults ≥18 years, signed informed consent

Exclusion Criteria:

diseases and/or irritations in the anal region, especially of the anal canal and the rectum, pregnancy or lactation, known hypersensitivity against any ingredient of the investigational product, known or suspected drug or alcohol abuse, subject committed to an institution

Investigational product, dose and mode of administration, batch number:

Posterisan® corte Placebozäpfchen: 1 suppository containing 1820.00 mg hard fat and 180.00 mg medium-chain triglycerides.

Administration: 2 suppositories per day rectally applied, preferably after dejection.

Batch number: 110751

Duration of treatment:

10 days

Reference therapy, dose and mode of administration, batch number: not applicable

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Criteria for evaluation:

Tolerability:

Primary objective: Incidence of all intolerances (e.g. itching, burning, pain, redness or bleeding)

Secondary objectives:

Assessment of tolerance by physician on the 5 point ordinal scale*

Assessment of tolerance by the volunteers on the 5 point ordinal scale*

(*5-point ordinal scale: 1 = very good, 2 = good, 3 = satisfactory, 4 = moderate, 5 = poor)

Statistical methods:

Descriptive statistics (mean, maximum, minimum, standard deviation, frequency)

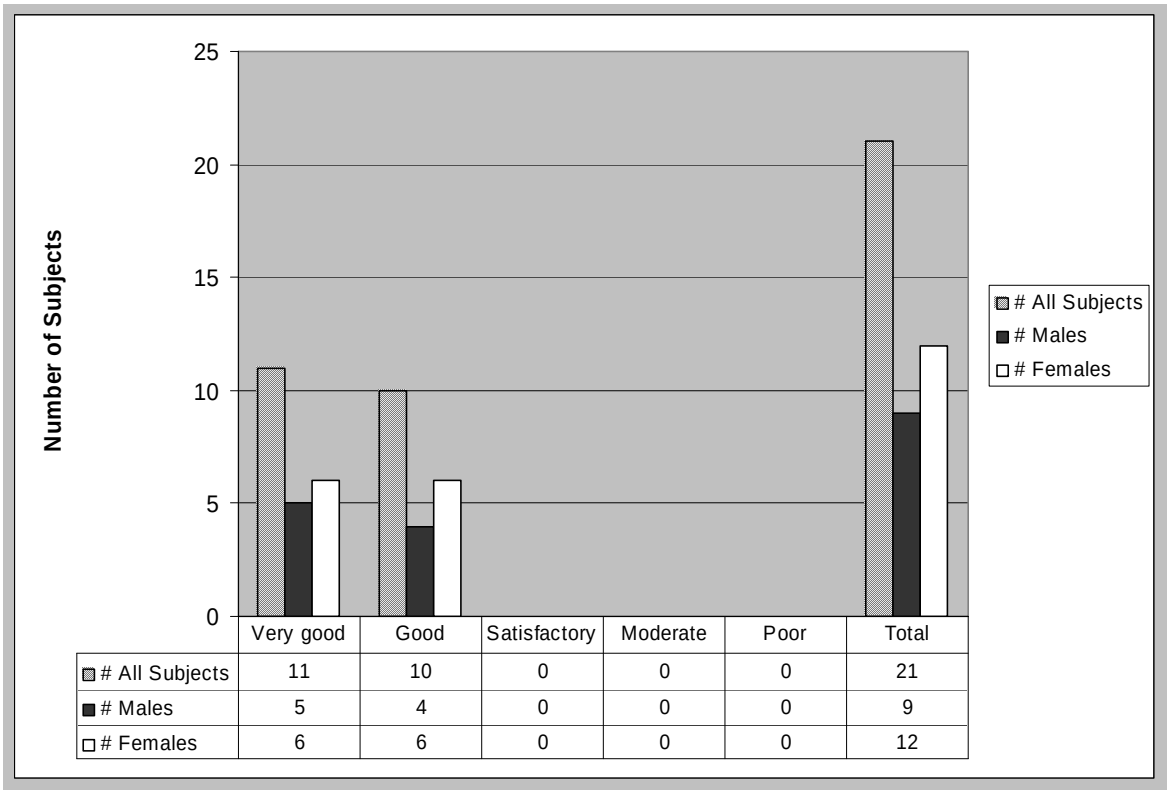
Summary – Conclusions

Results:

Tolerability

The primary objective of this study was to document all gross intolerances such as itching, burning, pain, redness or bleeding having been caused potentially by Posterisan® corte Placebozäpfchen. No such intolerances were observed. Examination of the perianal region as well as proctoscopy did not showe any intolerances in any of the subjects. Therefore, neither at the beginning nor at the end of the study were any abnormalities of the anal region detectable in any of the subjects.

The investigator rated the tolerance of Posterisan® corte Placebozäpfchen as “very good” in 11 subjects (52.38 %) or “good” in 10 subjects (47.62 %). The results are shown below.



	Very good	Good	Satisfactory	Moderate	Poor	Total
# All Subjects	11	10	0	0	0	21
# Males	5	4	0	0	0	9
# Females	6	6	0	0	0	12

Assessment of local tolerance of Posterisan® corte Placebozäpfchen by the investigator

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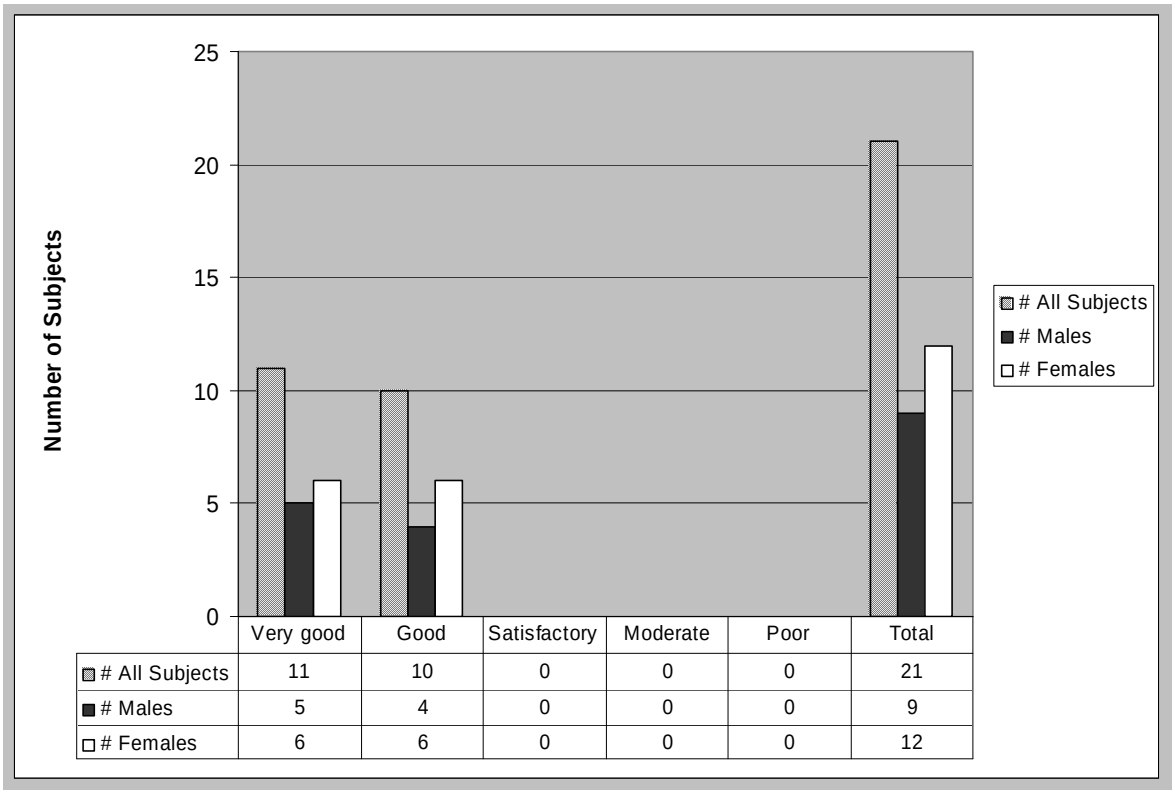
The subjects clasified the tolerance of Posterisan® corte Placebozäpfchen as follows: 11 subjects rated the tolerance as "very good" (52.38 %) and 10 subjects as "good" (47.62 %). The results are shown below.



	Very good	Good	Satisfactory	Moderate	Poor	Total
# All Subjects	11	10	0	0	0	21
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# Females	6	6	0	0	0	12

Assessment of local tolerance of Posterisan® corte Placebozäpfchen by the subjects

Safety:

Only one out of 21 subjects treated with Posterisan® corte Placebozäpfchen experienced an adverse event (i.e. softer faeces), which was mild and suspected to be associated with the suppository application. No medical intervention was required. No systemic side effects and no other serious or non serious adverse events were observed. Therefore, it can be concluded that Posterisan® corte Placebozäpfchen have a good safety profile.

Conclusion:

The clinical study provided clear evidence for the very good tolerance and safety profile of Posterisan® corte Placebozäpfchen. The primary endpoint of this study was to document all gross intolerances (e.g. itching, burning, pain, redness or bleeding) potentially having been caused by Posterisan® corte Placebozäpfchen. However, no such intolerances were observed. The assessment of tolerance was performed by the investigator and the subjects. The overall tolerance was judged as very good and good.

The purpose of this study was to provide evidence for good tolerance of Posterisan® corte Placebozäpfchen. This intention was achieved.

Date of report: 8th April, 2009