GCP Study Synopsis

White spot lesion development in post-orthodontic patients following weekly application of a 1.25% fluoride gel compared to placebo over 6 months

Study Number: GASAS-1002X

EudraCT Number: 2010-020538-24

Collaboration Center:

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Sponsor:

Colgate-Palmolive Europe Sàrl (Colgate)
(merger of GABA International AG with Colgate in January 2014)
Grabetsmattweg
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SYNOPSIS

Name of Sponsor / Company: Colgate-Palmolive Europe Sàrl (Colgate)	Individual Study Table Referring to Part of the Dossier Volume: Page	(For National Authority Use Only)
Name of Product: elmex® gel		
Name of Active Ingredients: Olaflur: 0.231% fluoride Dectaflur: 0.019% fluoride Sodium fluoride: 1% fluoride		

Title of Study: White spot lesion development in post-orthodontic patients following weekly application of a 1.25% fluoride gel compared to placebo over 6 months	
Investigators: Prof. Dr. S. Ruf, Dr. N. Bock, L. Seibold, Dr. E. Gnandt	
Study Centre(s): Justus-Liebig University Giessen University Clinic for Orthodontics Schlangenzahl 14 D-35392 Giessen Germany	
Publication (Reference): Not yet published.	
Study Period: Date of first enrolment:15.04.2011 Date of last completed: 30.09.2013	**Phase of Development**: Phase: IV
Objectives: To monitor the development of white spot lesions (WSLs) and dental status in response to 1.25% fluoride gel applied weekly, compared to placebo, in patients after orthodontic treatment with multibracket appliances	

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Methodology:
This was a randomized, single-center, double-blind, parallel-group, placebo-controlled study conducted in compliance with Good Clinical Practice (GCP) and the Declaration of Helsinki. Patients with at least one WSL with a modified score 1 or 2 (Gorelick et al., 1982) on at least one of the four upper front teeth (UFT) after debonding of multibracket appliances were randomly assigned to the test or placebo group. At the first two visits, subjects received professional tooth cleaning followed by elmex gel application (T0 and T2). Thereafter, the subjects continued tooth brushing with gel at home for 22 weeks. Participants attended six appointments (T0 to T5). At every visit, general health status and concomitant treatments were assessed. Saliva buffer capacity (at T0, T1, T4, and T5) and stimulated salivary flow rate (at T0, T4, and T5) were measured before assessing plaque index, gingival bleeding index, WSL index, and caries activity index. At T0 and T5, oral soft tissue status and DMFT index were also recorded.
At each appointment, photographs of the UFT were taken using a standardized image technique.
Efficacy analysis: The primary efficacy variable (i.e., change in DWL% from baseline to 12 weeks) was analyzed using Mann-Whitney U-test (intent-to-treat population). Secondary variables were analyzed descriptively. The difference in secondary variables (except gingival bleeding index and caries activity index) between the two treatment groups were analyzed using Mann-Whitney U-test (significance level α=0.05). Gingival bleeding index and caries activity index were analyzed using Fisher's exact test (significance level α=0.05).
Safety analysis: The total number of adverse events (AEs), total number of AEs at least possibly related to the study treatment, and total number of subjects affected by at least one AE were calculated per treatment group. AEs were classified by organ system (according to MedDRA terminology). Serious and/or unexpected AEs and AEs resulting in discontinuation or reduction/withdrawal of the study treatment were presented separately.

Number of Subjects (Planned and Analyzed):
46 planned, 39 analyzed for efficacy and safety analysis (placebo: n = 18; elmex® gel: n = 21).

Diagnosis and Main Criteria for Inclusion:
- healthy volunteers (≥11 years) scheduled for bracket removal
- multibracket appliance therapy in the upper jaw for at least one year
- ≥ 1 WSL with a modified score 1 or 2 (Gorelick et al., 1982) on UFT at debonding

Test Product, Dose, and Mode of Administration, Batch Number:
elmex® gel (1.25% fluoride including 1% fluoride from NaF and 0.25% fluoride from Olaflur/Dectaflur), approx. 0.5 g gel or 6.25 mg fluoride, intra-oral, topical.

Duration of Treatment:
24 weeks
- professional gel brushing, 2 weeks (T0 and T2)
- home gel brushing, 22 weeks (T2 to T5)

Reference Therapy, Dose, and Mode of Administration, Batch Number:
Placebo of elmex® gel, approx. 0.5 g gel, intra-oral, topical.

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Criteria for Evaluation:
Efficacy:

Primary variable:
- changes in size of white spot lesions (WSL) at 12 weeks (lesion size to total labial tooth area, DWL%)

Secondary variables:
- changes in size of WSL over study time
- changes in mean pixel brightness value of WSL (%)
- modified WSL index (Gorelick et al., 1982)
- caries activity index (LAA) according to ICDAS II (Ekstrand et al., 2007)
- plaque index (Silness & Löe, 1964)
- gingival bleeding index (Ainamo & Bay, 1975)
- DMFT (Klein et al., 1938)

Additional variables (Protocol Deviation Nº1):
- mean, standard deviation, and central value of RGB of total area of UFT
- mean luminance value (L*) of total area of UFT
- luminance of WSL (brightest spot)
- luminance of sound enamel (mean of two areas)

Safety:
- AEs

Others:
- stimulated salivary flow rate
- saliva buffer capacity
- questionnaire

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Summary – Conclusions

Efficacy Results:

Primary variable:

Treatment with elmex® gel did not lead to a statistically significant difference in the change of DWL% from baseline to 12 weeks compared to the group treated with a placebo gel.

Secondary variables:

Changes in size of WSL over study time: Treatment with elmex® gel did not lead to a statistically significant difference in the change of DWL% from baseline to T1, T2, or T5 compared to the group treated with a placebo gel.

Mean pixel brightness: No statistically significant differences were found at any visit (T0, T1, T2, T3, T4, T5) with respect to the following parameters: modified WSL index, caries activity index, plaque index, gingival bleeding index, and DMFT.

Additional variables (Protocol Deviation Nº1):

No statistically significant differences were found at any visit (T0, T1, T2, T3, T4, T5) for the raw luminance parameters. As described in the protocol deviation, an additional parameter was calculated as the difference in luminance of the WSL and the luminance of normal enamel (two measurements each). From T0 to T4 (12 weeks), no statistically significant differences were detected for the teeth 11, 12, and 22. For tooth 21, a statistically significant difference was found ($p<0.05$), indicating a larger decrease in luminance difference in the group treated with elmex® gel.

Safety Results:

In total, 81 AEs were observed, but none of them was classified as possibly related to the study product. The cause of one AE was classified as unknown. This AE involved redness and swelling of the gingiva at the upper jaw and led to the exclusion of the subject from the study.

Overall, 31 subjects (17 in the elmex® gel group and 14 in the placebo group) were affected by at least one AE. One SAE (no causality) occurred (Morbus Crohn).

Others:

Statistically significant differences were found at visit (T4, T5) with respect to stimulated salivary flow rate. No statistically significant differences were found for saliva buffer capacity at any of the visits.

Conclusion

From a statistical point of view, the effect of elmex gel on the remineralisation of post-orthodontic white spot lesions over 6 months could be shown on a single tooth level, however not on the other upper front teeth investigated.

Date of Report: November 11, 2014