Title:

A randomized, prospective, international, multi-center clinical study to evaluate the peri-implant tissue outcome of abutment-supported XiVE® CAD/CAM supra-structures and directly implant-supported XiVE® CAD/CAM supra-structures (split-mouth) in partly edentulous human subjects.

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A randomized, prospective, international, multi-center clinical study to evaluate the peri-implant tissue outcome of abutment-supported XiVE® CAD/CAM supra-structures and directly implant-supported XiVE® CAD/CAM supra-structures (split-mouth) in partly edentulous human subjects.

Study code
DF0909-1-272-1x-1

Sponsor
Dentsply IH AB (d.b.a Dentsply Sirona Implants)
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Number of subjects/implants
In total:
Enrolled: 20 subjects, 82 implants
Completed: 18 subjects, 72 implants

Study period

First Subject In (FSI)	Oct-2010
Last Subject In (LSI)	Sep-2014
First Subject Out (FSO)	May-2011
Last Subject Out (LSO)	Aug-2017
Database Closure (DBC)	Apr-2021

Background

Knowledge regarding endosseous dental implants and the possibility of successful prosthetic restoration has rapidly expanded over the last years. Computer-aided design (CAD) and computer-aided manufacturing (CAM) technology found its way into dental medicine in the 1980's in terms of chair side ceramic inlay production. Further development of dental CAD/CAM systems enabled prosthetic restoration in various indications and the use of different materials. Meanwhile several CAD/CAM systems with the ability to design and manufacture implant based prosthetic restorations are on the market. The most obvious advantages are high-end precision, material homogeneity, ease of fabrication and customized individual design. Stainless or low-strain fit can only be achieved by an accurate transfer from the intra-oral situation to the cast. However, CAD/CAM fabricated supra-structures can minimize inadequate precision of fit.

With regards to the implant system XiVE® no scientific data describing the influence of the anchorage system (implant/prosthesis or abutment/prosthesis) on the peri-implant hard and soft tissue situation were available at the time of study start. Within the scope of the study these two different supra-structure connection types were assessed.

Rationale

This study was designed to collect data with regards to the peri-implant outcome of abutment-supported restoration and direct implant-fixed restoration. Therefore, a small group of subjects with partly edentulous maxilla was selected to show that both techniques are efficient and safe and to show comparable peri-implant tissue outcome for both methods. At the time of impression forming for each center, treatment method A (= abutment-supported XiVE® CAD/CAM supra-structure) and treatment method B (= direct implant-fixed XiVE® CAD/CAM supra-structure) was randomly assigned to the left or right side of the maxilla i.e. randomization of method A to right or left side and method B to the opposite side.

Study objectives

Primary objective

- To evaluate the hard tissue outcome

Secondary objectives

Key secondary objective

- To evaluate the soft tissue outcome

Other secondary objective(s)

Efficacy

- To evaluate prosthetic success
- To evaluate implant success
- To evaluate the fit of the supra-structure

Safety

- To evaluate the incidence of peri-implant mucositis
- To evaluate the incidence of peri-implantitis
- To evaluate the incidence of other adverse device effects

Study Design

This post-market study was designed as a randomized, prospective, multi-center, split-mouth, study with a 2-year follow-up after placement of the permanent prosthetic restoration.

The study was performed according to the European Directive 93/42 EEC, German Medical Device Law (MPG) and the Medical Devices Regulations 2002 (SI No 618), as amended by the Medical Devices (Amendment) Regulations 2008 No 2936.

At time of study start there was a need for more data regarding the influence of the implant-abutment interface localization on the peri-implant hard and soft tissues, this since there were controversy and discussions in the scientific community.

With this study, data regarding the different restoration concepts (XiVE® CAD/CAM bridges directly fixed on the XiVE® implant, and abutment-supported XiVE® CAD/CAM bridges) were to be collected in order to extend the information about the behavior of the peri-implant tissue when using the XiVE® implant system with or without platform-switching.

The study population was selected to represent the normal non-risk subject population. Only healthy, full aged (enclosed growth) partially edentulous (free-end maxilla) subjects with severely resorbed jaws were asked to participate in the study.

With the posterior maxillary area, the regions from the first premolar to the second molar on both sides were considered. Due to mobile gingiva the third molar region was not included. CAD/CAM bridge was to be evaluated, which required that at least two (2) implants were inserted. The subject had to be in a stable physical and psychological condition to ensure the availability for the 2-year follow-up period.

Each subject was to receive both an abutment-supported XiVE® CAD/CAM supra-structure (treatment method A) and a direct implant-fixed XiVE® CAD/CAM supra-structure (treatment method B) by using the split-mouth model for this study.

It should be noted that the surgical treatment was not part of the study Nevertheless, the surgical and prosthetic parts of the treatment was still followed-up in the study.

Study Population

The study population was selected to represent the normal non-risk subject population. Healthy, full aged (enclosed growth) partially edentulous (free-end maxilla) subjects with severely resorbed jaws were asked to participate in the study. The subjects had to be in a stable physical and psychological condition to ensure the availability for the planned 2-year follow-up period.

Enrollment was to be competitive. If the subject recruitment rate was lower than expected at one site and higher than expected at another, planned allocation numbers were to be transferred from the site

with low subject recruitment to the site with high recruitment rate. This was done to ensure that subject enrollment was completed according to the time plan. Each site had to keep records (Pre-screening log and Enrolment log) of subjects who were considered for enrollment, specifying whether they were enrolled or not, and if not enrolled the reason why. This information was necessary to establish that the subject population was selected without bias.

Subject-selection criteria

Inclusion criteria

1. Subject > 18 years.
2. Female subject of child-bearing potential must use reliable methods of contraception.
3. Subject has partly edentulous maxilla (free-end or large gap in posterior area on both sides).
4. For all implants immobility and clear percussion sound is applicable.
5. The subject is healthy and compliant with good oral hygiene.
6. Favorable and stable occlusal relationship between the remaining teeth.
7. Subject must be reliable, cooperative, and in the opinion of the Investigator, likely to be compliant with study procedures.
8. Subject provides written informed consent signed and dated prior to entering the study.
9. Implantation of XiVE® implants at least 3 months ago.
10. XiVE® implants have been placed primary stable by considering sufficient horizontal and vertical bone dimension.

Exclusion criteria

1. Subject has a history of drug abuse, addiction to medication or alcohol abuse within the previous year.
2. Subject with planned or performed head and neck radiation.
3. Known unavailability of subject for FU Visit(s).
4. Subject has – in the opinion of the investigator - any systemic metabolic disorder or bone disorder or is taking medication that compromises or might have compromised post-operative tissue regeneration or osseointegration.
5. Subject has major bone defects in the implantation area.
6. Subject is taking medication that compromises or might have compromised post-operative healing and/or osseointegration (e. g. bisphosphonates).
7. Subject exhibits an oral infection.
8. Subject has received any investigational drug within 30 days prior to screening.
9. Severe bruxing.
10. Subject has a clinically significant or unstable medical or physiological condition.
11. Female subject is pregnant or lactating or intends to become pregnant during the course of the study.
12. Subject is not willing to participate in the study or not able to understand the content of the study.

Study Products

The final product is a screw retainable metallic supra-structure on implants and the software for the relevant applications. The product in this case is a metallic structure to be veneered with compatible dental ceramic or a combination.

The investigational medical devices (IPs) in this study were CAD/CAM screw retainable supra-structures, such as bridges. The design was generated by using the Isussoft, design software. The final product is a supporting structure for a metallic structure to be veneered with compatible dental ceramic or a combination. The dental lab was the direct customer, and they processed the product into the final shape. The investigator was responsible for the final placement in the mouth of the study subject.

The IPs are the custom made XiVE® CAD/CAM Supra-Structures.

All medical devices used in this study were already available on the market, and they were all used within their approved indication for use. For details see *Table 1. Medical devices used in the study.*

Table 1. Medical devices used in the study.

IPs	Type of medical device	Further description, if applicable *(specifics)*	Manufacturer
Supra-Structure	Treatment method A: CAD/CAM full-arch frameworks Treatment method B: CAD/CAM full-arch frameworks	Treatment method A: abutment-supported restoration Treatment method B: directly implant-fixed restoration	E.S. Healthcare, N. V. – Research Campus 10 – B-3500 Hasselt, Belgium

Statistical Methods

All eligible subjects in the study were included in the statistical evaluation (Intention-To-Treat population, ITT).

Statistical tests were conducted with SPSS (IBM Corp., Armonk, NY) and Excel (Microsoft, Redmond, WA, USA) software.

Descriptive statistics were used to analyze participant and implant characteristics, i.e., mean, Standard deviation (Sd), median, minimum (min), maximum (max) and frequency tables.

A non-parametric statistical approach was applied because of the nature of the data but parametric confidence intervals are also presented. For continuous data e.g. MBL the Wilcoxon Signed Rank test (exact) was used to compare treatment groups (A - B) and for comparisons within each treatment Group A and Group B respectively.

All reported p-values are two-sided. No formal adjustment for multiplicity has been applied. Nominal p-values are presented but not called statistically significant.