

A Prospective, Multicenter Study of the Integration Success of the Eztetic™ Dental Implant System in Immediate Loading Cases

Statistical Plan “ROSE QUARTZ “

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Study Sponsor:



ZIMMER BIOMET

STATISTICAL CONSIDERATIONS AND EVALUATION

The Study Objectives

The objective of the study is to evaluate the safety and efficacy of the Eztetic implants at postoperative 2 years. The safety will be evaluated by the implant related adverse events and the efficacy will be evaluated by implant survival rate and related clinical function parameters including implant mobility, gingival and plaque indices, score of gingival inflammation, peri-implant probing depths (PPD), bleeding on probing (BOP), and marginal bone level changes. The implant survival rate at postoperative 2 years will be the primary endpoint and all of the other function parameters will be the secondary endpoints.

The Study Hypothesis

The primary effectiveness analysis will be performed on per protocol population. The objective of the primary effectiveness analysis is to demonstrate that the Eztetic implants survival rate at postoperative 2 years is non-inferior to the historical 3.7mm TSV implant survival rate of 100% [by Khayat] by non-inferiority margin of 5%:

$$H_0: E_1 - E_0 \leq -\delta_E$$

$$H_a: E_1 - E_0 > -\delta_E$$

Where:

E_0 = 100% survival rate of the 3.7mm TSV implant

E_1 = the survival rate of the Eztetic implants

δ_E = non-inferiority margin for effectiveness, here $\delta_E = 0.05$.

The Statistical Analysis

As primary analysis for the efficacy evaluation, the number and proportion of implants surviving at 2 years will be calculated. The lower bound of the one-sided 95% exact confidence limit of survival proportion will be constructed to compare with the historical performance of 3.7mm TSV survival rate of 100% [by Khayat] minus 5% non-inferiority margin (95%). If the constructed CI lower bound is above the 95%, the inferiority null hypothesis will be rejected. In addition, the survivorship will be estimated by KM methods based on the time unit of follow-up month up to 24 months. The secondary efficacy endpoints will be descriptively summarized and compared with baseline level as applicable based on the data scale at each post-surgery follow-up interval. The appropriate statistical comparison tests will be selected based on the data scale and distribution. Both intraoperative and postoperative adverse event data will be descriptively summarized. In general, the descriptive summaries for continuous data will include mean, standard deviation, minimum, maximum, median and 95% confidence interval. Categorical data will be described as frequencies, percentages, and 95% confidence intervals.

The Sample Size Justification

The sample size for this study is determined by the primary endpoint (survival rate) analysis. Khayat et al reported a survival rate of 100% at 2 years for the 3.7mm TSV implant. With a 5% non-inferiority margin, the Eztetic implant survival rate at 2 years is expected to compare with 95% for non-inferiority inference. Based on the internal evaluation, it is expected that the Eztetic implant will have a 98% survival rate at 2 years. A sample size of 160 produces a one-sided 95% lower-limit exact confidence interval with the precision no larger than 0.03 at the probability of 0.984. When adjusted for 20% attrition rate, sample size 192 is required. This determination procedure was conducted at implant level. The sample size was calculated by SAS9.4 for Windows.