CLINICAL INVESTIGATION PLAN

CIP ID: CSE2017-01K

Establish implant accuracy with X-PSI Knee System

A multi-center, prospective, non-controlled post market study

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STUDY SPONSOR

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1 Synopsis

Title:	Establish implant accuracy with X-PSI Knee System– A multi-center, prospective, non-controlled post market study
Sponsor: **Manufacturer:**	Zimmer GmbH Zimmer CAS
Objectives:	The main purpose of this study is to evaluate the accuracy of the new X-PSI Knee System. This will be achieved by analyzing early postoperative imaging data with regards to the mechanical alignment and compare them with preoperative planning imaging data (reviewed and approved by the surgeon).
Hypothesis:	The use of the new X-PSI Knee System achieves the same accuracy with respect to mechanical alignment as with conventional instrumentation.
Endpoints:	Primary endpoint: Achievement of mechanical leg alignment in HKA frontal plane (± 3 degrees) with X-PSI Knee System is as accurate as with standard instrumentation at 4-6 weeks post operation. The X-PSI Knee System cohort will be compared with current literature (70% of cases within ± 3 degrees). No control group will be studied. Secondary endpoint: Cost-effectiveness as assessed by OR set-up time, surgery time and post-processing time.
Indication/ Target Population:	Patients which are treated either with Persona, Vanguard or NexGen total knee system
Inclusion Criteria:	• Patient is 18 years of age or older. • Patient can follow the X-PSI Knee System imaging protocol as part of standard of care procedures. • Patient gets TKA treatment which follows the criteria of the appropriate Instruction for Use. • Patient is willing and able to cooperate in the required post-operative standard of care. • Patient is willing and able to complete scheduled follow-up evaluations as described in the Informed Consent. • Patient has participated in the study-related Informed

	Consent process and has signed the Ethics Committee approved 'Informed Consent'.
Exclusion Criteria	• Patient is unwilling or unable to give consent or to comply with the follow-up program. • Patient meets exclusion criteria of the appropriate Instruction for Use • Patients who have any condition which would in the judgement of the Investigator place the patient at undue risk or interfere with the study. Any patient who is institutionalized, or is a known drug abuser, a known alcoholic or anyone who cannot understand what is required from them • Patient is known to be pregnant
Study Design:	Multi-centre, prospective, non-controlled
Clinical Phase:	Post market
Number of Subjects:	Data will be collected from 70 TKA cases implanted by use of the X-PSI Knee System in up to 5 study centers
Length of Study:	1.5 years (0.5 year enrolment plus 1 year follow-up): follow-up visits at 4-6 weeks and 1 year post-operatively.
Study Device:	X-PSI Knee System
Scores:	VAS (pain), EQ-5D, Oxford Knee Score
Documentation:	Electronic Data Capture, Oracle

2 Statistical Considerations/ Evaluation

2.1 Handling of Missing and Incomplete Data

Data will be considered "missing" for the primary endpoint if this outcome cannot be determined or is unavailable for a subject. Every effort will be made to collect the data necessary to evaluate the primary endpoint. Patients who have been lost to follow-up and do not have mechanical leg alignment in HKA frontal plane data at 4-6 weeks will not be included in the primary study analysis.

Sensitivity analyses will be performed to assess the impact of missing data on the primary study analysis. These analyses may include a best-case and worst-case imputation as well as a tipping point analysis.

2.2 Data Analysis

Data will be analyzed using SAS 9.4 or higher. The Type I error rate for the primary study analysis will be 0.05. Comparisons for secondary, exploratory, and safety analyses will be two-sided comparisons using $\alpha = 0.05$, with no adjustment for multiple comparisons.

Primary Analysis: The primary analysis will be conducted on the as-treated data set. In the as-treated-analysis for the primary endpoint, missing data will be treated as described in Section 1.1.

The primary endpoint is to show achievement of mechanical leg alignment in HKA frontal plane (± 3 degrees) with X-PSI Knee System is as accurate as with standard instrumentation at 4-6 weeks post operation. The X-PSI Knee System cohort will be compared with current literature (70% of cases within ± 3 degrees).

To determine the upper and lower limits with 95% confidence that 70% of the X-PSI patients' HKA frontal plane measurements are contained, a 70% tolerance interval will be constructed based on the mean and standard deviation of the HKA frontal plane measurements from patients in the study. A tolerance interval is defined as "a statistical interval within which, with some confidence level, a specified proportion of a sampled population falls". In this study, we will claim with 95% confidence that 70% of the X-PSI patients fall within a computed tolerance interval. This method allows us to state an upper and lower limit in which we can claim 70% of the alignments will fall within with a given confidence (95%).

The upper and lower tolerance limits are defined as

$$Y_L = \bar{Y} - K*s;\ Y_U = \bar{Y} + K*s;$$

where Y_L and Y_U are the lower and upper tolerance limits respectively, $\bar{Y}$ is the sample mean, s is the sample standard deviation and k is defined as

$$K = \sqrt{\frac{v\left(1+\frac{1}{N}\right)z^2_{(1-p)/2}}{X^2_{1-y,v}}}$$

where *p* is the percentage (proportion) of the population we want to claim within the interval, $X^2_{1-y,v}$ is the critical value of the chi-square distribution with degrees of freedom *v* that is exceeded with probability *y*, and $z_{(1-p)/2}$ is the critical value of the normal distribution associated with cumulative probability *(1-p)/2.*

For this study, p = 0.7 (70%), and y = 0.95 (95%). The study will be considered a success if both the upper and lower tolerance limits are within +/- 3 degrees.

Secondary Analysis: Analyses for secondary endpoints will be conducted on the as-treated data set, and will only use those cases with complete data for the endpoint being analysed.

Continuous data (e.g. age, BMI, VAS pain) will be reported using mean, standard deviation, median, and range. Categorical data (e.g. gender) will be reported using frequency and percentage.

2.3 Sample Size

Based on preliminary U.S. IDE data, we estimate the standard deviation to be 1.62. Based on the above formula for calculating tolerance intervals, a sample size of 60 will allow us to claim that 70% of the alignments fall within +/- 2 degrees. The sample size formula plans for +/- 2 degrees to account for the initial IDE data showing the average offset is about -1 degrees and our goal sit to show that 70% or more are within +/- 3 degrees. To account for loss to follow up and patient dropouts, enrolling 70 patients includes a 10% loss to follow-up to ensure there are 60 patients at the end of the study.

2.4 Study Report

The primary analysis will be performed after all patients reach the 4-6 weeks follow up time point. Data will be analysed using the methods described in Section 1.2.