STATISTICAL ANALYIS PLAN (SAP)

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Daniel Lopez Juarez (Statistician)	Signed by: Daniel Lopez Juarez Signer Name: Daniel Lopez Juarez Signing Reason: I am the author of this document Signing Time: 04-Sep-2024 | 20:28:00 BST 9F378CDA0B37457B861C8BF9740D6CE2
Jay Jantz Director of Global Data analytics (Head of Global Biostatistics or designee)	Signed by: Jay Jantz Signer Name: Jay Jantz Signing Reason: I approve this document Signing Time: 05-Sep-2024 | 16:20:08 BST B7D37248838E4CACAE11E7E55198A88D

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1 LIST OF ABBREVIATIONS

Abbreviation	Definition
CORI	REAL INTELLIGENCE™ CORI™
CRF	Case Report Form
PROM	Patient Reported Outcome Measure
SAP	Statistical Analysis Plan
UKA	Unicondylar Knee Arthroplasty

2 INTRODUCTION

The following Statistical Analysis Plan (SAP) details the statistical considerations, including the data presentation methods for the Study Protocol CORI.2019.06 version 4.0-Master. Due early termination of the study on 15th May 2024 with only four subjects enrolled, the contents of this SAP have been reduced and do not fully accomplish the requirements outlined in the Study Protocol. Related documents to this SAP are the Study Protocol, Case Report Form (CRF), and Listings Templates Shells.

3 STUDY DESIGN

Refer to Study Protocol CORI.2019.06 version 4.0-Master.

4 STUDY OBJECTIVES

Refer to Study Protocol CORI.2019.06 version 4.0-Master.

5 STUDY ENDPOINTS

Refer to Study Protocol CORI.2019.06 version 4.0-Master.

6 STATISTICAL CONSIDERATIONS

6.1 Determination of Sample Size

Considering the design and assumptions defined in Study Protocol CORI.2019.06 version 4.0-Master, to demonstrate that the lower limit of the two-sided 95% confidence interval for the proportion of mechanically aligned UKAs exceeds the value reported from literature of 92.1%, 70 knees in each group (140 knees combined, 70 CORI procedure for UKA and 70 Conventional procedures for UKA) will be enrolled into the randomized phase of the study. The required number of knees was defined to achieve 80% of power and account for 10% attrition.

6.2 Randomisation

Subjects will be randomly assigned to the CORI navigational or conventional manual instrumentation groups according to a balanced randomization procedure using a 1:1 allocation ratio.

6.3 Interim Analysis

The Study Protocol CORI.2019.06 version 4.0-Master specifies the incorporation of interim analysis. With study's prematurely termination, interim analysis will be omitted, and the available information will be presented in a final report.

7 STATISTICAL ANALYSIS

7.1 General

Due early termination of the study with 4 subjects enrolled, the statistical analysis specified in the protocol will not be conducted due to insufficient interpretability of the results. Consequently, available data will be presented as listings, which will be created using SAS version 9.4 (or later) and executed by Smith+Nephew's Global Biostatistics group.

7.2 Analysis Populations

Not applicable. Listings will include sufficient information to identify analysis populations presented in Study Protocol CORI.2019.06 version 4.0-Master.

7.3 Handling of Missing, Incomplete and Repeat Data

Not applicable.

7.4 Derived Data

Not applicable, unprocessed responses from subjects will be reported in listings. Derivation of PROMs is included with the purpose of listings interpretation.

KSS Endpoints

According to instructions for the derivation of the KSS endpoints, in an event that there are fewer than 50% missing responses within a domain, imputation with values equal to the average of all of the other items in the same domain will be used otherwise scoring will not be performed (KSS User Manual, 2012) [1]. The Knee Society Score (KSS) comprises information on Objective Knee Indicators (range 0 to over 100 points), Patient Satisfaction (range 0-40), Patient Expectation (range 0-15), and Functional Activities (range 0-100). The KSS endpoints are derived from a series of questions that relate to everyday activities. More elaborate information for deriving the KSS endpoints are described in the publication by Scuderi et al (2012). However, an abbreviated description of the KSS endpoints used in the study is described in this SAP.

- Objective Knee Score (Completed by Physician/Surgeon)

  The objective score allows for more than 100 points in patients with greater than 125° of flexion and a stable painless knee as outlined below.

  - "Alignment" allows for a maximum of 25 points and is determined on a weight-bearing AP radiograph measuring the femoral-tibial (Anatomic) axis.
  - "Instability" allows for a maximum of 25 points for a knee that is stable in the coronal and saggital axis.
  - "Joint Motion" allows one point for each 5° of joint motion with a potential for greater than 25 points to be assigned for patients with greater than 125° of motion. There are deductions for flexion contracture and extension lag.
  - "Instability" has a maximum allowable point allocation of 25+.
  - "Symptoms" category contains two 10-level scales, ranging from "none" to "severe" for each patient to rate pain encountered when walking on level ground and on stairs/inclines. For this, a patient starts with 10 points on each scale for a painless knee with deductions of up to 10 points deductions as indicated by the patient's response on each pain scale. There is an additional question regarding how "normal" the knee feels to the patient. The maximum allowable point is 25.

- Patient Expectations and Satisfaction (Completed by Patient)
    - "Patient Expectations" is a three-question fifteen-point scale that is collected preoperatively and post-operatively. The pre-operative questions reflect a patient's opinion on the extent to which s/he expects that the operation will improve his/her knee pain, and the ability to perform activities of daily living and recreational activities.
    - The post-operative patient expectations questions reflect the extent to which the outcome after the operation has met the patient's pre-operative expectations with respect to pain and function.
    - "Patient Satisfaction" is a five-question 40-point scale that is collected preoperatively and at each follow-up visit.
- Functional Score (Completed by Patient)

  The functional score is composed of the four subgroups and has a maximum score of 100 as follows:

    - "Walking and Standing" has a maximum value of 30 points with deductions for the use of walking aids and supports.
    - "Standard Activities" has a maximum of 30 points and evaluates "standard" activities of daily living. Patients can also respond if they never participate in the activities. Patients who respond "I never do this" receive zero points for that activity.
    - "Advanced Activities" has a maximum of 25 points and evaluates function in performing more vigorous activities ranging from climbing a ladder or step-stool to running. Patients can also respond if they never participate in the activities. Patients who respond "I never do this" receive zero points for that activity.
    - "Discretionary Activities" has a maximum of 15 points and allows patients to select the three activities that they consider most important to them personally from a group of seventeen recreational and exercise activities. Patients who do not participate in any of the discretionary activities will have a functional knee score that is limited to 85 points. The discretionary activities do not need to be identical in the pre-operative and post-operative period.

<u>European QoL (EQ-5D-5L)</u>

The classification system of the EQ-5D-5L is comprised of five dimensions, namely mobility, self care, usual activities, pain/discomfort and anxiety/depression with each of the dimensions having five levels: "no problem" (level 1), "slight problems" (level 2), "moderate problems" (level 3), "severe problems" (level 4), and "extreme problems" (level 5). Hence, the system defines 3125 (55) health states ranging from 11111 to 55555 (i.e. the best possible health state to the worst possible health state).

- The individual domain responses on each of the 5 levels a scale of 1-5 will be combined based on the levels scored combining the domains to form a 5-digit number in the form XXXXX (where X is 1-5) describing the respondent's health state as previously described. The EQ 5D-5L index value would be derived by using the vendor supplied calculator in Microsoft Excel to convert each 5-digit EQ-5D-5L profile.

Forgotten Joint Score (FJS) The FJS-12 is a PROM that assesses joint awareness during the activities of daily living. The FJS-12 comprises of 12 questions with a 5-point Likert response format (0 to 4), where 0 = Never; 1 = Almost Never; 2 = Seldom; 3 = Sometimes and; 4 = Mostly. The 12 questions that joint awareness is based on are as follows:

- Night Symptoms
- Sitting
- Walking
- Bathing
- Travelling
- Stairs
- Walking uneven ground
- Rising
- Standing
- Housework/Gardening
- Walking/Hiking
- Favorite Sport

An overall score based on the sum of all 12 responses (minimum of 0 and maximum of 48) is computed and transformed linearly into a 0 to 100 score. The higher the transformed score the greater is the ability of the subject to forget about the affected/replaced knee during activities of daily living.

<u>Oxford Knee Score (OKS)</u>

The OKS is a PROM that was developed to assess a patient's perspective of outcome following Total Knee Arthroplasty (TKA). The OKS comprises of 12 questions with each question (item) scored from 0 to 4 with 0 being the worst possible outcome and 4 being the best possible outcome on

each question. The scores are then summed to produce an overall score running from 0 (worst possible possible) to 48 (best possible outcome).

7.5 Baseline Data

Demographic and/or baseline variables whose information is available either at the preoperative or at the operative visits will be presented in listings.

7.6 Disposition Data

Not applicable.

7.7 Protocol Deviations

A listing of all protocol deviations reported will be provided.

7.8 Measurement of Treatment Compliance

Not applicable.

7.9 Multiplicity

Not applicable.

7.10 Analysis of Primary Endpoint(s)

Not applicable.

7.11 Analysis of Secondary Endpoint(s)

Not applicable.

7.12 Analysis of Exploratory Endpoint(s)

Not applicable.

7.13 Analysis of Safety Endpoint(s)

A list of the adverse events reported in the study will be provided.

7.14 Other Data Summaries

Not applicable.

7.15 Changes in Analysis Methods Specified in the Protocol

Statistical analysis and summary measures will not be performed for this study. Instead, listings will be provided to fulfil the requirements of Study Protocol CORI.2019.06 version 4.0-Master.

8 REFERENCES

1. Scuderi GR, Bourne RB, Noble PC, Benjamin JB, Lonner JH, Scott WN. The new knee society knee scoring system. Clin Orthop Relat Res 2012; 470: 3-19.