STATISTICAL ANALYIS PLAN (SAP)

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Contents

1 LIST OF ABBREVIATIONS

Abbreviation	Definition
ADE	Adverse Device Effect
AE	Adverse Event
ANCOVA	Analysis of Covariance
ASADE	Anticipated Serious Adverse Device Effect
BMI	Body Mass Index
CI	Confidence Interval
CRF	Case Report Form
EQ-5D-5L	EuroQol (European Quality of Life) five-dimensional Five-level
FAS	Full Analysis Set
HOOS JR	Hip disability and Osteoarthritic Outcome Score for Joint Replacement
HRQoL	Health Related Quality of Life
ITT	Intent to Treat
LL	Lower Limit
LSMean	Least Square Mean
MI	Multiple Imputation
NA or N/A	Not Applicable
N (or n)	Total Sample Size (or subgroup sample size)
NMPA	National Medical Products Administration
PP	Per-protocol Population
PROM	Patient Reported Outcome Measure
QoL	Quality of Life
S&N	<Smith & Nephew Inc.,/T. J. Smith & Nephew Ltd./Smith & Nephew Orthopaedics >
SAP	Statistical Analysis Plan

Abbreviation	Definition
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAF	Safety Analysis Population
SE	Standard Error
TFL	Tables, Figures and Listing
THA	Total Hip Arthroplasty
UL	Upper Limit
USADE	Unanticipated Serious Adverse Device Effect
VAS	Visual Analogue Scale

2 INTRODUCTION

This statistical analysis plan (SAP) is written to specify in greater detail, the statistical analyses that will be carried out as outlined in OR3O study protocol ID: OR3O.2019.10 version 1.0 dated 18-Aug-2020. The contents of this SAP and its accompanying tables, figures and listings (TFLs) mockups will serve as guideline for programming the TFLs that will summarize the study data.

If modifications to the analyses specified herein or additional analyses required prior to reporting, these would be detailed either in an addendum to the SAP or in an amended SAP.

3 STUDY DESIGN

This study is a prospective, multi-center, randomized, controlled, 2-arm study planned to assess safety and efficacy of the OR3O™ Dual Mobility System in Primary THA. Subjects who meet the pre-specified inclusion/exclusion criteria in the protocol will be randomized to receive implantation with either the investigational product or controlled system. Up to 4 sites in China will participate competitive enrolling a total of 170 hips.

The study is expected to enroll all subjects within a 12 month timeframe.

Subjects will be postoperatively followed-up at 6 weeks, 3, 6, 12 and 24 months.

In this study, a summary of 1 year follow-up data will be reported to National Medical Products Administration (NMPA) for regulatory approval and a 2 year follow-up will be sufficient to identify and assess the risk of any associated unacceptable adverse event over this time period. The study duration will be sufficient to allow conclusions about likely safety and efficacy of the OR3O Dual Mobility System in a longer term.

Figure 1 describes and details the different steps of study conduct from screening to enrollment and follow-up while Table 1 provides details of the study's schedule of events.

Figure 1: Study Flowchart

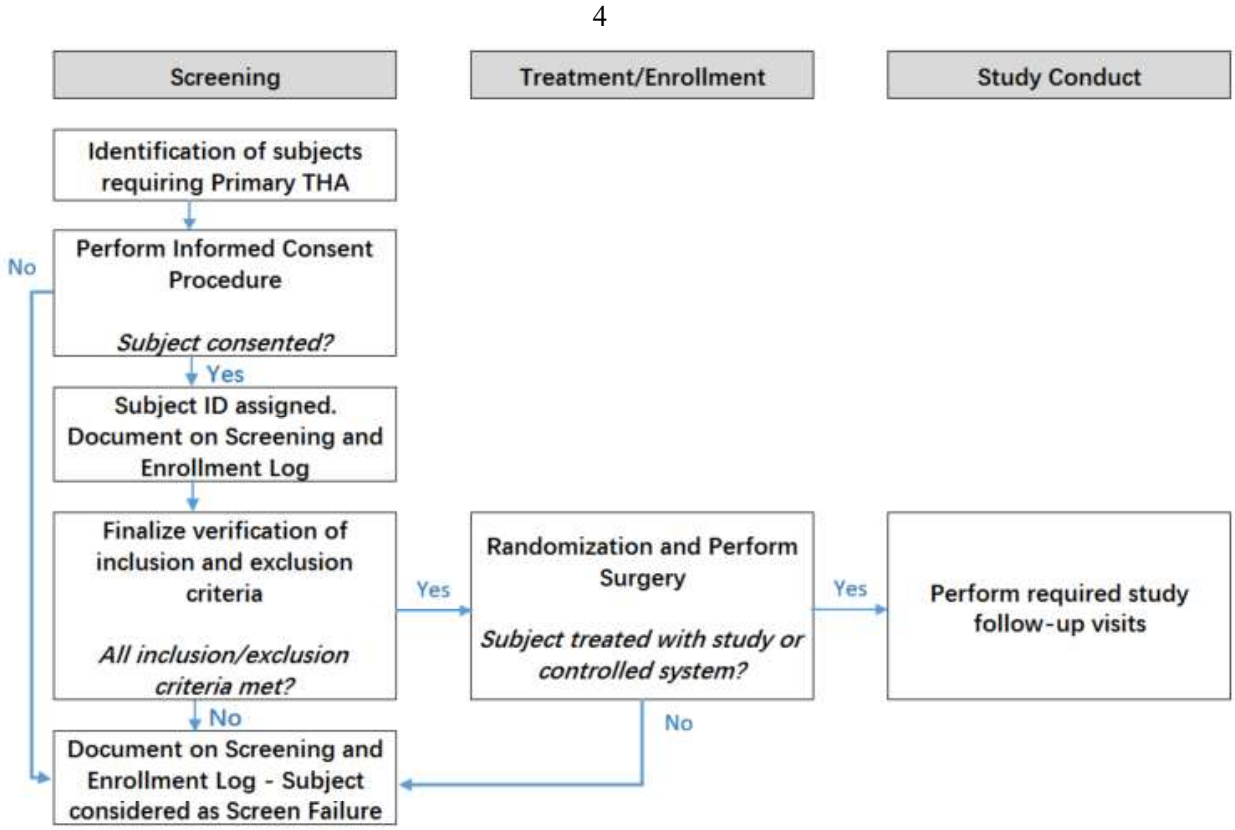

Table 1: Study Schedule of Events

Schedule of events	Pre-Operative Data	Operative / Discharge	6 Weeks (42 – 7/+14 days)	3 mos (90 ± 30 days)	6 mos (180 ± 30 days)	1 yr. (365 ± 60 days)	2 yr. (730 ± 60 days)
Informed Consent	x						
Inclusion/ Exclusion	x						
Demographics	x						
Medical History	x						
Vital Signs	x						
Preoperative Lab Examinations (eg. Blood Routine Examination, Biochemical Examination, Coagulation Examination) [1]	x						
Pregnancy Test[2]	x						
Operative Data		x					
Discharge Data		x					
Implant status			x		x	x	x
HHS	x		x	x	x	x	x
EQ-5D-5L	x		x	x	x	x	x
HOOS JR.	x		x	x	x	x	x
Radiographic Assessment	(x)[3]	(x)[4]	(x)[4]	x	x	x	x
Concomitant Medications[5]		x	x	x	x	x	x
Safety Assessment (AEs, DDs)		x	x	x	x	x	x
End of Study/ Exit		x	x	x	x	x	x

1 If applicable, where, for preoperative lab examinations, only those within Day 0~14 before the operation are acceptable. The Preoperative Lab Examinations required to be performed include:

- Blood routine examination: Haemoglobin, Platelet count, White Blood Cell count, neutrophil count, erythrocyte sedimentation rate
- Coagulation examination: Prothrombin time, activated partial thromboplastin time), thrombin time, D-dimer
- Biochemical examination: Urea or urea nitrogen, creatinine, AST, ALT, blood glucose
- Other examination: Erythrocyte sedimentation rate, C-reactive Protein

2 If applicable, where, the pregnancy test is only suitable for females of child-bearing potential, neither premenstrual females nor sterilized or postmenopausal (i.e., 12-month amenorrhea without alternative medical reasons) females.

3 If X-ray image has been done within 30 days before the Informed Consent Form is signed, and the data is available, they can be used as the data for screening before operation.

4 Radiographic assessment performed at discharge or 6 week follow-up visit only.

5 All combination medications associated with AEs or serious adverse events (SAEs) are reported.

5 STUDY OBJECTIVES

5.1 Primary Objective

The primary objective of this study is to assess safety and efficacy of the OR3O™ Dual Mobility System in Primary THA at 1 year postoperative.

5.2 Secondary Objectives

The secondary objectives of this study are to assess safety and efficacy of the OR3O™ Dual Mobility System and compatible components in Primary THA up to 2 years after surgery.

5.3 Exploratory Objectives

Other objectives of the study are to assess the hip dislocation percentage and hospital readmission percentage (cumulative) up to 2 years after device implantation.

STUDY ENDPOINTS

5.4 Primary Endpoint

The primary endpoint is proportion of excellent (≥ 90) or good (80-89) HHS scores at 12 month postoperative.

5.5 Secondary Endpoints

Safety and efficacy evaluated in this study at baseline, 6 weeks, 3 months, 6 months, 1 year and 2 years after surgery as measured by:

- Survivorship of the OR3O™ Dual Mobility System (no revision due to any reason)
- Survivorship of controlled system (assessed by revision for any reason) (no revision due to any reason)
- Harris Hip Score (HHS)
- EuroQol (European quality of life) five-dimensional Five-level (EQ-5D-5L) score
- Hip Disability and Osteoarthritis Outcome Score for Joint Replacement (HOOS JR.)
- Radiographic Assessment
    - Implant position/Orientation
    - Implant subsidence/migration
    - Periprosthetic fractures
    - Heterotopic ossification
    - Radiolucencies
    - Osteolysis
    - Implant loosening
    - Stress Shielding

5.6 Exploratory Endpoints

The following exploratory endpoints will be collected:

- Dislocation percentage of the hip up to 2 years after device implantation.
- Hospital readmission percentage (cumulative) within 30, 60 and 90 days of discharge due to any reason related to study device or study procedure.

5.7 Safety Endpoints

Safety endpoints include the collection of the following events:

- All adverse events (AEs) occurring from the time of subject enrollment until study termination or study completion including intra-operative adverse events.

- Device Deficiencies.

6 STATISTICAL CONSIDERATIONS

6.1 Determination of Sample Size

Sample size calculation is based on the assumption that in order to be considered of comparable efficacy, study arm (dual mobility cohort) must obtain at least 90% of the efficacy in the controlled arm (conventional cohort). It is expected and further assumed that 95% of the Harris Hip Score at 12 months postoperative will have a rating of good or excellent (80-89, ≥ 90), then 76 evaluable subjects per group would be required to carry out the hypothesis testing at 12 months postoperatively. Assuming an attrition rate of 10% at 1 year, 85 subjects are needed per arm. It is planned to have 4 sites enroll on average, 43 subjects per investigational site and a min. of 20 subjects should be enrolled per site (overall subjects enrolled in the study of 170).

6.2 Randomisation

Subjects meet all inclusion/exclusion criteria will be randomly allocated into any of two study groups (study arm or controlled arm) in a 1:1 allocation ratio. Blocked randomization to balance this allocation ratio by investigational site and overall will be implemented through a network-based randomization system. A randomization number is allocated only when subjects have signed the Informed Consent Form and satisfy all study eligibility criteria.

6.3 Interim Analysis

An interim analysis is planned to be carried out after completion of all 1 year follow-up visits in order to support the China NMPA registration. Additional interim analyses might be performed as and when

needed to support and maintain product registration in different markets globally. At minimum, preoperative, demographic and PROMS data will be summarized for interim analyses.

7 STATISTICAL ANALYSIS

The Full Analysis Set (FAS) population will be used to summarize the primary and all secondary endpoints (excluding radiographic assessments) while the Safety (SAF) population will be used summarize all safety and exploratory endpoints. The SAF population will additionally be used to summarize radiographic assessments The Per Protocol (PP) population will additionally be used to summarize the primary endpoint.

7.1 General

All statistical comparisons of the data will indicate the test statistic used as well as its distributional assumptions. Unless otherwise stated, all statistical significance tests will be two-sided, performed at the 5% significance level (i.e. $\alpha = 0.05$). Where appropriate, the resulting p-values will be quoted and if applicable, the corresponding 95% two-sided confidence intervals (CIs) will also be generated. All p-values will be rounded to three decimal places; p-values less than 0.001 will be presented as '<0.001' in all tables.

For data summaries, categorical and ordinal variables will be summarized using frequency (n) and percent (%). Continuous variables will be summarized using characteristics such as number of observations, mean, median, standard deviation, minimum and maximum values.

7.2 Analysis Populations

The following section details the analysis populations:

Safety (SAF) Population: This is defined as all hips who have been implanted with the OR3O™ Dual Mobility System or controlled system. The SAF population will be based on the device that is implanted into the hip and not the one the hip is randomized to (if different).

Full Analysis Set (FAS) Population: This is defined according to the basic principle of Intent-to-Treat (ITT) principle i.e., all implanted hips with at least one postoperative effectiveness, HRQoL or performance will be included in FAS Population.

Per-Protocol (PP) Population: The PP population is the subset of hips in the FAS population who do not have major protocol deviations and who satisfied all enrollment eligibility criteria. Criteria that can be regarded as major deviations will be formally classified on a case-by-case basis prior to the final study database lock.

7.3 Handling of Missing, Incomplete and Repeat Data

- For the missing primary endpoint, missing values will be imputed by using the postoperative Last Observation Carried Forward (LOCF) method. For the LOCF method, the results at time of discontinuation from study or last postoperative observation will be imputed as described in Table 2 as an illustrative example. If no postoperative data is available to be carried forward, then missing values will be imputed as failures in their response.

Table 2: Example of Last Observation Carried Forward (LOCF) Imputation Method

	Observed Data				**Last Observation Carried Forward**			
Hip ID	Preop	6 Weeks	3 Months	6 Months	Preop	6 Weeks	3 Months	6 Months
1	Preop	X_{12}	Missing	X_{14}	Preop	X_{12}	X_{12}	X_{14}
2	Preop	Missing	Missing	X_{24}	Preop	Fail	Fail	X_{24}
3	Preop	Missing	X_{31}	Missing	Preop	Fail	X_{31}	X_{31}

- Multiple Imputation (MI) will be used for the imputation of missing postoperative HHS (and its subscores), EQ-5D-5L index, EQ-5D-5L VAS and HOOS JR scores. For each of these PROMs, 5 distinct datasets each containing an imputed value sampled from the posterior predictive distribution of the observed data will be generated. Standard errors (SEs) obtained for estimates after MI imputation are smaller than those obtained from single imputation methods, as a result, the CIs obtained become narrower. Thus, the MI method is regarded as a conservative and unbiased missing value imputation method.

7.4 Derived Data

Change from pre to postoperative visits

This will be calculated as:

$$\text{Post} - \text{operative value}_{visit\ n} - \text{Pre} - \text{operative value}_{(Visit\ 1)}\ where\ n > 1.$$

Body Mass Index (BMI)

- BMI = {(Weight in kg)/(Height in m)^2}, if units are in kg for weight and m for height
- BMI = {(Weight in lbs.)x703.07))/(Height in inches)^2}, if units are in lbs. for weight and inches for height (Adjustments made to formula to standardize BMI unit to kg/m^2)

Time to Revision

- Time to revision (in months) = (Revision Date – Operative Date + 1)/30.4375.

Hip disability and Osteoarthritis Outcome Score for Joint Replacement (HOOS JR)

The HOOS JR is a short-form survey based on the HOOS that specifically focuses on the outcome after THA. HOOS JR consists of the following 2 items:

- Pain (2 items) and
- Activities of daily living (4 items).

Each item (question) that is used for scoring the HOOS JR is rated on a scale of 0 to 4 as follows:

- 0 = None; 1 = Mild; 2 = Moderate; 3 = Severe and; 4 = Extreme.
- The range of potential sum of raw scores for all 6 items of the HOOS JR is between 0 and 24 where 0 is the best score and 24 is the worst possible score. The maximum allowable number of missing items on the HOOS JR is 2. If more than 2 of the 6 items are missing, the raw HOOS JR score will not be computed. If 1 or 2 of the item scores are missing, the rounded average of the other non-missing items for that subject will be imputed. An interval score from 0-100 (0 indicating total hip disability and 100 indicating perfect hip health) is extrapolated from the sum of the HOOS JR item scores [1].

Five-level Euro QoL five-dimensional score (EQ-5D-5L)

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 (5^5) 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.

Harris Hip Score (HHS)

The HHS is a joint specific score that consists of 10 items covering domains of pain (1 item, 0-44 points), function (7 items, 0-47 points), absence of deformity (1 item, 0 or 4 points), and hip range of motion (2 items, 0-5 points). The overall HHS ranges from 0 (worst) to 100 (best).

Algorithms used for scoring each of the 10 items (components) of the HHS as well as its domains (pain, function, AoD and ROM) as well as total HHS are summarized in Table 3.

Table 3. Harris Hip Score (HHS) scores per item and domain

Item	Original Response	Likely scores per Item	Domains (Range of Scores)
Pain	None or ignores it	44	**Pain Domain (0 to 44)**
	Slight, minimal, no compromise in activities	40	
	Mild pain, no effect on average activities, rarely moderate pain with unusual activity; may take aspirin	30	
	Moderate pain; tolerable but makes concessions to pain. Some	20	

	limitation of ordinary activity or work. May require occasional pain medication stronger than aspirin		
	Marked pain, serious limitation of activities	10	
	Totally disabled, crippled, pain in bed, bedridden	0	
Limp	None	11	**Function Domain (0 to 47)** **{Sum of all items within subdomain}**
	Slight	8	
	Moderate	5	
	Severe	0	
Support	None	11	
	Single cane for long walks	7	
	Single cane most of the time	5	
	One crutch	3	
	Two canes	2	
	Two crutches or not able to walk	0	
Distance walked	Unlimited	11	
	Six blocks	8	
	Two or three blocks	5	
	Indoors only	2	
	Bed and chair only	0	
Sitting	Comfortably in ordinary chair	5	
	On a high chair for 30 minutes	3	
	Unable to sit comfortably in any chair	0	
Public transportation	Yes, possible	1	
	No, unable	0	
Stairs	Normally without using a railing	4	
	Normally using a railing	2	
	In any manner	1	
	Unable to do stairs	0	
Socks/Shoes	With ease	4	
	With difficulty	2	
	Unable	0	

Range of Motion (ROM)	Flexion = FLEX+EXT-FLEX_ZERO	N/A	
	Movement = ABD+ADD-ABD_ZERO	N/A	
	Rotation = ER+IR-ER_ZERO	N/A	
ROM subscore	Flexion+Movement+Rotation		**Range of Motion Domain (0 to 5))**
	0 to 29	0	
	30 to 59	1	
	60 to 99	2	
	100 to 159	3	
	160 to 209	4	
	≥ 209	5	
Leg Length Difference (in mm)	None	N/A	
	Ipsilateral longer (LL_DIF_LONG)	N/A	
	Ipsilateral shorter (LL_DIF_SHORT)	N/A	
Absence of Deformity (AOD)	IF (FLEX_ZERO = . OR FLEX_ZERO < 31) AND (ABD_ZERO = . OR ABD_ZERO < 11) AND (ER_ZERO = . OR ER_ZERO < 11) AND LL_DIF_LONG < 33 AND LL_DIF_SHORT < 33 THEN AODScore = 4	0 or 4	**Absence of Deformity Domain (0 to 4)**
Total HHS		Sum of all domain scores per subject	**Sum of all domain scores per subject**
Note: The maximum possible score for the HHS is 100.			

7.5 Baseline Data

Preoperative or operative variables will be summarized using descriptive characteristics for continuous[1] or categorical[2] data as applicable.

- Age[1] (in years),
- Sex[2] (males or females),
- Bilateral status (i.e. unilateral or bilateral)[2],
- Body Mass Index (BMI)[1],
- Primary hip diagnosis[2],
- Charnley Co-morbidity Classification[2],
- Components of the device implanted[2].
- Surgical approach used[2].
- Side of implantation (left versus right versus both left and right) [2].

Variables summarized will not only be restricted to the above listed but on all variables deemed pertinent and obtainable preoperatively and operatively.

Additionally, age will be categorically summarized by stratifying into: < 60 years versus ≥ 60 years. BMI will also be categorically summarized by stratifying into: < 30 kg/m^2 versus ≥ 30 kg/m^2.

7.6 Disposition Data

- Subject (and hip) disposition will be summarized after completion of the study using frequency (n) and percentage (%) of subjects (or hips) who completed and who did not complete the study. For those who did not complete the study, the primary reason for discontinuation will additionally be summarized. A listing of subject (and hip) disposition at both interim and at termination visits will be provided.
- Hip accountability information will be tabulated by visit. The information included in this table will include the number of hips that are theoretically due, subjects who are dead, hips revised, hips terminated from the study for any reason. Additional information that will be included on the subject accountability table will include but not limited to the number of hips presenting at each visit, number of hips expected at each visit.

7.7 Protocol Deviations

A listing of deviations encountered on-study will be listed. Major protocol deviations that are deemed significant which will subsequently lead to the exclusion of subjects in the PP population will be appropriately identified and flagged.

7.8 Measurement of Treatment Compliance

Not applicable.

7.9 Multiplicity

The null hypothesis will be rejected for Ha1/Ha2 if the lower bound of the 2-sided 95% CI of p1-p0 is above the respective margin (ie, $-\Delta$ or 0), respectively or both using a stepwise hypothesis

testing approach. This stepwise hypothesis-testing framework would not require any adjustment made to α, thus strongly controlling the overall significance at 0.05.

7.10 Analysis of Primary Endpoint

The analysis of the primary endpoint will utilize hypothesis testing in two steps. First, testing for non-inferiority of P1 versus P0 and secondly if non-inferiority is demonstrated then testing for superiority of P1 to P0 as follows:

H0 (null): $P1 \leq (P0-\Delta)$ versus
Ha1 (alternate 1st stage): $P1 > (P0-\Delta)$ and Ha2 (alternate 2nd stage): $P1 > P0$,

Where Δ is the margin of non-inferiority (9.5%), P1 is the proportion of good to excellent HHS scores at 12 months in the OR3O dual mobility system (test) and P0 is the proportion of good to excellent HHS scores at 12 months in the Conventional, single-bearing design (control).

- The null hypothesis, H0, is rejected in favor of the first alternate hypothesis, Ha1, (i.e. demonstration of non-inferiority) if the lower limit of the 95% Confidence interval for P1-p0 > -Δ) otherwise, H0 will be accepted.
- If the null hypothesis, H0, is rejected and in favor of Ha1, the test for superiority would be performed. If the upper limit of the 95% CI for P0 is less than the lower limit of the 95% CI for P1, then superiority of P1 to P0 is demonstrated, i.e. acceptance of Ha2.. This stepwise hypothesis-testing framework would not require any adjustment made to α, thus strongly controlling the overall significance at 0.05. All 95% CIs generated for P1 and P0 would be calculated using exact methods.

However, as this study has been early terminated the study no longer has sufficient power for this test to be relevant and it will therefore not be performed. Summary statistics for P1 and P0 will be reported.

The primary endpoint will be summarized using the SAF population.

7.11 Analysis of Secondary Endpoints

All secondary endpoints will be summarized using the SAF analysis population. Changes from preoperative to postoperative will not be analysed for PROMs due to early termination of the study. Summary statistics for observed PROMs score would be presented.

Implant Survivorship

- Survivorship of the OR3O Dual Mobility System (assessed by revision for any reason) will be summarized using Kaplan-Meier survival tables and graphs. Time to revision will be the endpoint of interest, for subjects who die, are lost to follow-up or do not encounter the event of interest by the time of study termination would be censored on these dates.
- Survivorship of the controlled system up to 2 years after surgery (assessed by revision for any reason), Kaplan-Meier survival tables analogous to that specified for the OR3O Dual Mobility system will be implemented here as well.

Harris Hip Score (HHS)

- HHS scores for each subject will further be categorized as follows: Excellent (90-100); Good (80-89); Fair (70-79); Poor (60-69) and; Very poor (<60). Shift tables from the preoperative visit to all postoperative visits using these classifications will be generated.
- The total HHS and the scores for each of its following subdomains: pain, function, absence of deformity, and range of motion will be summarized using continuous summary characteristics by preoperatively and postoperatively at 6 weeks, 3 months, 6 months, 1 year and 2 years (i.e. by visit). For the HHS and its subdomain scores, independent repeated measurement Analysis of Covariance (ANCOVA) model (with visit as the repeated term) will be used to model the change from preoperative to postoperative with total HHS (and its

subdomain) scores as dependent variable (s). As a minimum, each model will contain treatment (OR3O dual mobility system i.e. Test, versus Conventional single-bearing design, i.e. Control) and a repeated visit as fixed effect terms. Preoperative prognostic and demographic variables including but not only restricted to type of THA procedure (primary), age, BMI, sex, and investigational site and any other covariate that can be ascertained to be impactful on the total HHS (or its subdomain scores) will be introduced as covariates in the model. These covariates will be added to the model in a stepwise manner and retained in the final model if a p-value of ≤ 0.1 is encountered. Model based means (adjusted means or Least Square Means, LSMeans) and corresponding standard errors associated with the change from preoperative to postoperative HHS (and its subdomain) scores by treatment will be presented. Model based differences (and corresponding standard errors) between treatment as well as their corresponding 95% CIs will additionally be summarized.

- However, as this study has been early terminated there is not sufficient data for the change from baseline analysis. Thus, only summary statistics of the observed score would be presented.

<u>EQ5D-5L Score</u>

- The HRQoL Index score and its VAS component will be sumarized using summary statistics for continuous variables preoperatively and at the postoperative visits: 6 weeks, 3 months, 6 months, 1 year and 2 years (i.e. by visit). Model based repeated measures ANCOVA analysis, which specified for the total HHS and its subdomain scores will be implemented.
- However, as this study has been early terminated there is not sufficient data for the change from baseline analysis. Thus, only summary statistics of the observed score would be presented.

<u>Hip Disability and Osteoarthritis Outcome Score for Joint Replacement (HOOS JR.)</u>

- The transformed (0-100) interval scores will be summarized by visit using descriptive summary characteristics for continuous variables. Changes from preoperative to postoperative follow-up time points will similarly be summarized. Model based repeated measures ANCOVA analysis, the type previously specified for the total HHS (and its subdomain scores) will be implemented.
  - However, as this study has been early terminated there is not sufficient data for the change from baseline analysis. Thus, only summary statistics of the observed score would be presented.

Radiographic Characteristics

- The radiographic characteristics of implant position, implant fixation, heterotopic ossification, radiolucencies, osteolysis, atrophy and hypertrophy will be summarized using descriptive characteristics for continuous or categorical variables as appropriate and relevant by visit.

7.12 Analysis of Exploratory Endpoints

Survivorship of compatible components up to 2 years

Survivorship of acetabular shell, femoral head, and any of the femoral stems will be estimated by cumulative proportion of hips without revision of the respective components due to any reason, up to 2 years. The cumulative implant survival rates will be summarized using KM product limit estimates. This will be summarized using the SAF analysis population.

Dislocation percentage of the hip up to 2 years after device implantation

The cumulative dislocation percentage at the interim visits up to 2 years after device implantation, $p_{dis,i}$ will be compared to a literature specified percentage, $p_{literature}$. These literature-specified

percentages will be specified prior to database lock for final analyses. For the estimation of dislocation rate, a hip with multiple dislocations on-study will be counted only once. Two-sided exact 95% CIs will be estimated for $p_{dis,i}$ where i is the visit at which the cumulative dislocation will be estimated (i.e. at 3months, 6 months, 1 year and 2 years). This will be summarized using the SAF population. One of the following conclusions will be made:

- If the lower limit (LL) of the two-sided 95% CI for $p_{dis,i}$ is > $p_{literature}$, then it is concluded that the dislocation rate on-study is significantly greater than the literature-specified rate.
- If the upper limit (UL) of the two-sided 95% CI for $p_{dis,i}$ < $p_{literature}$, then it is concluded that the dislocation rate on-study is significantly less than than the literature-specified rate.
- If (LL of 95% CI of $p_{dis,i}$ <= pliterature <= UL of 95% CI of $p_{dis,i}$), then the dislocation rate on-study is comparable to that specified in literature.

However, as this study has been early terminated the study no longer has sufficient power for this test to be relevant and it will therefore not be performed. Descriptive summary statistics will be present for $p_{dis,i.}$

Hospital readmission percentage (cumulative) within 30, 60 and 90 days of discharge

The readmission percentage by 30, 60 and 90 days of discharge, p30,60,90 will be descriptively summarized as counts (n) and percentages (%). This will be summarized using the SAF analysis population.

7.13 Analysis of Safety Endpoints

The following summaries will be performed on the safety endpoints:

- The number of adverse events will be reported both overall and by seriousness, relationship to study device and/or study procedure and expectedness.

- The number of subjects experiencing adverse events will be summarised both overall and by seriousness, relationship to study device and/or study procedure and expectedness.
- An overall AE summary table that will summarize as number (n) and percentages (%), the overall incidence according to subjects with at least one AE; subjects with at least one AE by worst severity (mild, moderate, or severe); subjects with at least one AE by worst outcome (resolved, ongoing/unresolved, or death); subjects with an AE that led to study discontinuation and; subjects with at least one AE by worse relatedness to device. Other events such as SAEs, ADEs, SADEs or ASADEs, USADEs will also be similarly summarized using number (n) and percentages (%).
- Incidence of device- or procedure-related re-interventions that occur on-study will be summarized as number (n) and percentages as well as by type.
- Device deficiencies that occur on-study will be listed.

All safety endpoints will be summarized using the SAF analysis population.

7.14 Other Data Summaries

Not applicable

7.15 Changes in Analysis Methods Specified in the Protocol

Statistic testing will not be performed for the endpoints due to premature termination. Descriptive summary statistics will be presented for the endpoints instead.

8 REFERENCES

1. Lyman S, Lee YY, Franklin PD, Li W, Mayman DJ, Padgett DE. Validation of the HOOS, JR: A Short-form Hip Replacement Survey. Clin Orthop Relat Res. 2016; 474(6):1472-82.