Study OCI_2102

"A single center post-market clinical follow up (PMCF) observational study evaluating the clinical performance and the safety profile of the JuniOrtho™ Plating System™ (JPS) for the treatment of congenital deformities and fractures in lower limb of pediatric and adult patients"

Statistical Analysis Plan Final
Version 1.0, 07 December 2023

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Study code: OCI_2102

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STATISTICAL ANALYSIS PLAN APPROVAL SHEET

Version 1.0, 07 December 2023

Study title: A single center post-market clinical follow up (PMCF) observational study evaluating the clinical performance and the safety profile of the JuniOrtho™ Plating System™ (JPS) for the treatment of congenital deformities and fractures in lower limb of pediatric and adult patients

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1 GLOSSARY

Abbreviation	***Explanation***
AE	Adverse Event
CI	Confidence Interval
CRF	Case Report Form
CRO	Contract Research Organization
CV	Curriculum Vitae
DB	Database
IC	Informed Consent
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IEC/IRB	Independent Ethics Committee/Institutional Review Board
JPS	JuniOrtho™ Plating System™
Max	Maximun
MDDs	Medical Device Deficiencies
Min	Minumun
PMCF	Post-Market Clinical Follow-up
QOL	Quality of Life
ROM	Range of Motion
SAE	Serious Adverse Event
SOA	State-of-art
WBI	Weight Baring Index

2 INTRODUCTION

A manufacturer of a medical device must demonstrate that the intended purpose(s) and claim(s) made in relation to safety and performance of a Medical Device are achieved. As a general rule, such demonstration will require clinical data. Clinical data is data which is relevant to the various aspects of the clinical safety and performance of the device. This may include data from prospective and retrospective clinical investigations of the device concerned as well as market experience of the same or equivalent devices and medical procedures and information from the scientific literature.

The aim of the present study is to collect post-market clinical evidence (post-market clinical follow up - PMCF) on the use of the medical device JuniOrtho Plating System (JPS).

2.1 BACKGROUND INFORMATION

Principles of bone fixation through plating systems Plating systems are treatment options for bone fixation, indeed they are intended to provide bone fragments stabilization in case of bone fracture or osteotomy. Fixation works by blocking movements that would prevent the normal biological process of callus formation and consolidation. Excessive movement would otherwise increase the incidence of delayed union or nonunion. The very same principle is exploited when surgical fusion of bone fragments is sought, for example in joint arthrodesis or after surgical osteotomies performed to correct a limb deformity.

The JPS is a complete plating system designed to address the specific demands of advanced deformity and trauma reconstruction of the lower extremities in pediatric population and small stature adults. The system is intended for internal fixation and stabilization of fractures, osteotomies, mal-unions and non-unions of long bones of the lower limb.

Indications (as per IFU)

The JPS is intended for internal fixation and stabilization of fractures, osteotomies, mal-unions and non-unions of long bones of the lower limb.

The JPS is indicated for internal fixation and stabilization of femoral and tibial fractures, osteotomies, mal-unions and non-unions. Indications include:

- Varus, valgus, rotational and/or shortening osteotomies
- Femoral neck and/or pertrochanteric fractures
- Proximal and distal metaphyseal fractures
- Pathological and impending pathological fractures

Use of the JPS JuniOrtho Plating System™ is indicated in pediatric (excluding newborns) and small stature adult patients.

2.2 RATIONALE OF THE CLINICAL INVESTIGATION AND JUSTIFICATION OF VULNERABLE GROUP

Orthofix Srl put the JPS on the European market (2019) by the mean of a pre-market clinical evaluation made under the Medical Device Directive (MDD) requirements that was based on the analysis of the scientific literature of equivalent devices.

This study has been planned as part of the Orthofix Srl post-market active surveillance plan for the collection of data on both the clinical performance and the safety profile of the JPS in a representative population of patients and users.

The rationale of the proposed study is to update and support the pre-market clinical evaluation of the JPS with real-word-evidence clinical data, in order to confirm the benefit/risk ratio of this medical device and to keep the CE mark under Medical Device Regulation (MDR) requirements.

The uniqueness of the pediatric population manifests itself in specific indications for lower extremity reconstruction, mostly due to congenital deformities or conditions; different approach in compliance with postoperative care or need for adaptability to rapid growth and development. The JuniOrtho™ Plating System™ (JPS) is a well established, marketed device, commercially available and used as standard device in orthopedic surgeries.

The post-marketing, retrospective/prospective study with CE-marked device JuniOrtho™ Plating System™ (JPS) is designed for gathering real-world medical data from treatment of congenital deformities and fractures in lower limb of pediatric and in small stature adult patients.

All data will be collected from standard medical documentation of patients who have already been treated with JPS. Additionally, all procedures that patients underwent are justified by standard of care.

Constant identification of serious or unexpected serious risk related to the use of the device, especially in real-world experience may bring additional data, that can contribute to the safety of future patients.

In conclusion, patients will not directly benefit from the participation in this study but no additional risk related to the study participation is to be recognized.

3 PROTOCOL AND CRF VERSION

Protocol version: Version3.1_21/06/2023

CRF version: v.96.11

4 OBJECTIVE AND DESIGN

5 OBJECTIVES OF THE ANALYSIS PLAN

The analysis plan proposed below describes the aspects needed to know about the study and the statistical analysis methods to be used to apply them to the data collected and respond to the study objectives.

6 PRIMARY STUDY OBJECTIVE

The primary objective of the study is to evaluate the safety profile of JPS within the scope of its intended purpose, when used according to the manufacturer IFU on a representative population of subjects and users.

In order to fulfill this objective, the safety profile of JPS will be assessed by the following endpoints:

- percentage (%) of subjects with at least one serious/not serious adverse event certainly related or possibly related to JPS (primary endpoint) at device removal followup (up to 18 months according to site's standard practice).
- percentage (%) of Medical Device Deficiencies (MDDs) at device removal follow-up (up to 18 months according to site's standard practice).

7 SECONDARY STUDY OBJECTIVES

The secondary objective of the study is to evaluate the clinical performance of JPS within the scope of its intended purpose, when used according to the manufacturer IFU on a representative population of subjects and users.

In order to fulfill these objectives the clinical performance of JPS will be assessed by the two following efficacy endpoints:

- percentage (%) of subjects that reached a satisfactory bone consolidation according to investigator's opinion.
- percentage (%) of subjects that maintained bone correction alignment according to investigator's opinion until device removal.

8 STUDY DESIGN

This is a Post Market Clinical Follow-up (PMCF) study which is retrospective and prospective, observational, single-center, not controlled. All data from patients observation are gathered according to the site standard-of-care.

9 STUDY POPULATION

This study will be conducted only on patients with a regular indication for JPS as per IFU (no off-label use will be included): the system is intended in pediatric (excluding newborns) and small stature adult patients. Pediatric patients include infants (greater than 1 month to 1 years of age), children (greater than 1 to 12 years of age) and adolescents (greater than 12 to 18 years of age) and appropriate adults (where according to investigator assessment, the JPS plates fit the treated bone anatomy).

This study includes only one site (monocentric) that is located in Wetter (Germany). The site was chosen for this study due to the number of subject devices already implanted, and the wideness of the indications covered by the surgeries. The site was also positively evaluated by sponsor for the appropriate qualification and competency of the investigator and of the staff, and availability of facilities and equipment.

Sample size calculation:

Assuming the expected proportion of patients with at least one serious/not serious adverse event surely or possibly related to JPS will be 3 %,and assuming the worst case of each patient contributing for only one JPS implant case: 30 subjects was calculated to be the sample size of this study so that the upper limit of the 95 % confidence interval for the primary endpoint, based on the exact binomial method, is under 15 %. Considering that one patient can contribute for ore that one JPS implant, and considering a 10% drop out rate, the site can enrol a maximum of 40 JPS implant cases.

10 STUDY DURATION

The follow-up period considered for this study lasts until the second surgery for JPS removal that, with the exception of clinical complications, is usually scheduled between 9 and 18 months after the surgery. (see table 10.2 “Events and Assessments Schedule” in protocol).

The estimated length of data collection period by the investigator is the time until all data is abstracted from clinical records. The data extraction from clinical record will finish after the plate removal of the last patient is completed.

11 INCLUSION CRITERIA

A patient will be eligible for inclusion in the study if:

- had/has a regular indication for surgical intervention with JPS according to the manufacturer's IFU.
- underwent a surgery for bone deformity correction or trauma reconstruction of the lower extremities performed by JPS.
- the clinical data registered in her/him patient chart are sufficient to assess the safety and efficacy endpoint of the study (for retrospective patients).
- patient (or his/her legally acceptable representative) is capable of understanding the content and is willing to sign the Informed Consent Form (ICF).
- patient is willing and able to participate in the data collection and comply with the protocol requirements.

12 EXCLUSION CRITERIA

A Patient will be excluded from participation in the study if he/she:

- had/has a medical condition that is a contraindication according to the manufacturer's instruction for use leaflet.
- had/has a concomitant not permitted device which cannot be safely removed.
- patient for whom there are other concurrent medical or other conditions that in opinion of the participating investigator may prevent participation or otherwise render patient ineligible for the study.

13 ANALYSIS POPULATION

The classification of the implants based on compliance with the screening criteria is defined below:

- ***Evaluable* implants** are defined as all implants who meet all inclusion criteria and none of the exclusion criteria described in the protocol.
- ***Non-evaluable* implants** are defined as all implants who fail to meet any of the inclusion criteria or meet any of the exclusion criteria.

The CRF contains the screening criteria information in the form of a binary variable (Yes/No) for each item described.

Analyses will be performed on evaluable implants.

14 STATISTICAL ANALYSIS METHODS

The methods of analysis to be used for both objectives of the study and for description of the study variables are detailed below.

Quantitative variables will be described with measures of central tendency and dispersion: mean, median, SD (standard deviation), Q1 (first quartile) and Q3 (third quartile), minimum and maximum. Qualitative variables will be described using absolute and relative frequencies.

In the descriptive analysis of qualitative variables, two percentage columns will be presented, total percentage (%) and valid percentage (% valid), that are respectively, the percentage over the sum of valid responses plus missing values and the percentage over the total of valid responses.

For independent samples, parametric (t-test) or non-parametric (Mann-Whitney) statistical tests will be performed, depending on the distribution of the sample.

These tests will be used in all bilateral cases and with a level of significance of 0.048. In cases where a p-value less than 0.048 appears, it refers to the existence of statistical significance.

Clopper-Pearson confidence intervals will be shown at 95.2%.

Data will be analysed using SPSS v29.0.

An interim analysis, not planned at the start of the study, was performed after at least 20 subjects will be enrolled and completed the “Bone Consolidation” event.

The aim of this interim analysis was to verify the consistency of testing hypothesis and to confirm the historical data on the medical device safety and performance. Interim results were used to prepare the Clinical Evaluation Report (CER).

To preserve the integrity of the study results interpretation, a correction for multiplicity due to two planned analyses (interim+final) was implemented using the approach proposed by O’Brian-Fleming for sequential design (Shein –Chung Chow et Al Sample size calculations in Clinical Research 2003, Christopher Jennison et Al Group Sequential Methods with applications to clinical Trials,2000)

For this purpose, sample size was recalculated using this approach (all details are reported in the cited bibliography):

- The initial sample size was correct by factor 1.008 for a twosided test at 5% level and 80% power. The final sample size is 30*1.008=30.2
- The probability level was correctedcby factor 1.977, at interim the P value was 0.0052 while at the final analysis P value will be 0.048.

The corresponding confidence limits were at interim 99.5% and at final analysis 95.2%

In conclusion, applying the O'Brian-Fleming approach to control the type I error no great impact on sample size is observed and integrity of clinical study is preserved from any interpretation bias.

15 DATABASE LOCK AGREEMENT

If anomalous and/or inconsistent values are detected in any table of results, the database will not be reopened for modification, but instead the anomalous data and the manner in which it was processed will be highlighted (for example, by assigning non-existent data or eliminating the case depending on the statistical method to be used in the analysis in question).

Any modification to this table will be set out in writing in the report, along with the procedure followed (for example, assignment of non-existent data, interpolation, elimination of the case, etc.).

For the final statistical analysis, the database will only be reopened and the study data and tables that could be modified will be re-analysed if, jointly with the sponsor, a rethink of the initial analysis is considered.

16 DESCRIPTIVE STATISTICAL ANALYSIS

16.1 PATIENT DISPOSITION

A summary of patients included in the study, as well as those who are non-evaluable and the reasons for this will be shown.

16.2 ENROLMENT VISIT

16.3 DEMOGRAPHIC DATA BY PATIENT

The categorical variables to be described are, N and (%):

- Number of implants by patient
- Gender (Male / Female)
- Medical conditions by patient (Yes / No):
    - Transient synovitis
    - Septic arthritis
    - Juvenile idiopathic arthritis
    - Cerebral palsy
    - Slipped Capital Femoral Epiphysis SCFE
    - Developmental Dysplasia of the Hip DDH
    - Blounts Disease
    - Neurogenic Hip Dysplasia
    - Ligamentary laxity
    - LeggCalvPerthes disease
    - Spina bifida
    - Down Syndrome
    - Chromosomal aberration
    - Other, specify (other medical conditions will be shown). The sponsor will give an elaboration of the open text with the correct number of other conditions inserted.
- Number of Medical conditions, considering other as one

- History of cardiovascular disease (Yes / No)
- History of diabetes (Yes / No)
- Family history of disease: Renal disease (Yes / No)
- Family history of disease: Deafness (Yes / No)
- Family history of disease: Cardiomyopathy (Yes / No)

- Family history of disease: Encephalopathy (Yes / No)
- Family history of disease: Diabetes Mellitus (Yes / No)
- Family history of disease: Hypertension Cardiovascular disease (Yes / No)
- Family history of disease: Thrombosis (Yes / No)
- Family history of disease: Malignancy (Yes / No)

16.4 DIAGNOSIS & X-RAY IMAGES BY PATIENT

The categorical variables to be described are, N and (%):

- The patient was treated for (Deformity Correction / Fracture)

16.5 DEMOGRAPHIC AND CLINICAL DATA BY IMPLANT

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- Age at surgery (calculated as date of surgery minus date of birth)
- Age at ICF signature (calculated as date of ICF signature minus date of birth)
- Height
- Weight
- BMI

The categorical variables to be described are, N and (%):

- Gender (Male / Female)
- Is this patient already included in this study for a previous JPS implantation? (Yes / No)

16.6 DIAGNOSIS & X-RAY IMAGES BY IMPLANT

The categorical variables to be described are, N and (%):

- The patient was treated for (Deformity Correction / Fracture). In case of fracture the following variables will be described:
    - The date of fracture is available?
    - Type of fracture (neck fracture / Pertochanteric fracture / Methaphyseal fracture / PathologicalImpending pathological fracture / Other (specify)).
- Treated bone (Distal Femur / Distal Tibia / Proximal Femur / Proximal Tibia)
- Body side (Left / Right)
- Body side (Only Left / Only Right / Both). A new variable will be generated based on original variable body side. For implants with only left, with only right and with both the variable “Treated bone (Distal Femur / Distal Tibia / Proximal Femur / Proximal Tibia)” will be described separately.
- Plane(s) of deformity: Frontal
- Plane(s) of deformity: Horizontal
- Plane(s) of deformity: Sagittal
- A new variable will be generated with the different combinations based on Plane(s) of deformity variables. (Frontal / Horizontal / Sagittal / Frontal-Horizontal / Frontal-Sagittal / Horizontal-Sagittal, etc…)
- Intended correction: Varus correction
- Intended correction: Valgus correction
- Intended correction: Rotational correction
- Intended correction: Shortening correction
- Intended correction: Extension correction
- A new variable will be generated with the different combinations based on Intended correction variables.

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- Degree Varus
- Degree Valgus
- Degree antecurvation

The categorical variables to be described are, N and (%):

- Was a software used during pre-planning ? (Yes / No)

- Did the patient refer pain at the affected limb before JPS application? (Not at all / A little bit / Moderately /Quite a bit /Extremely)
- In case of previous question is not equal to 'Not at all' VAS will be described
- In case of previous question is not equal to 'Not at all' VAS Pain Score according to the patient will be described
- Preoperative AP projection X-Ray
- Preoperative ML projection X-Ray

16.7 PRE-OP ROM AND WB BY IMPLANT

The categorical variables to be described are, N and (%):

- Pre operative Weight-bearing Grade (Non-weight-bearing (NWB) / Toe-touch weight-bearing (TTWB) / Partial weight-bearing (PWB) / Full weight-bearing (FWB))
- Which Range of Motion are available for this patient?
    - Knee Flexion
    - Knee Extension
    - Hip Flexion
    - Hip Extension
    - Hip Abduction
    - Hip Internal Rotation
    - Hip External Rotation
    - Ankle Joint Dorsiflexion
    - Ankle Joint Plantarflexion
    - None

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- ROM Knee Flexion
- ROM Knee Extension
- ROM Hip Flexion
- ROM Hip Extension
- ROM Hip Abduction
- ROM Hip Internal Rotation
- ROM Hip External Rotation
- ROM Ankle Joint Dorsiflexion
- ROM Ankle Joint Plantarflexion

17 SURGERY VISIT

17.1 DEVICE APPLICATION SURGERY

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Duration surgery (hours)

The categorical variables to be described are, N and (%):

- How many plates were applied during this same surgery?
- Plate Size (3.0 mm / 3.5 mm / 5.0 mm)
- 3.0 mm Plate Type (Prox. Fem. 90° - 110° / Prox. Fem. 130°)
- 3.5 mm Plate Type (Prox. Fem.90° / 120° / Prox. Fem. 130° / Prox. Fem. 140° / Prox. Fem. 150° / Wide Medial Tibia / Narrow Medial Tibia / Anterolateral Tibia /Distal Femur Plate 3.5 mm)
- 5.0 mm Plate Type (Prox. Fem. 90° / 120° / Prox. Fem. 130° / Prox. Fem. 140° /Prox. Fem. 150° / Distal Fem.)
- If '5.0 mm Plate Type' is equal to 'Prox. Fem. 90° / 120°': Plate holes number will be described
- If '3.5 mm Plate Type' is equal to 'Distal Femur Plate 3.5 mm': Plate holes number will be described
- If '5.0 mm Plate Type' is equal to 'Distal Fem.': Plate holes number will be described

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable by the number of plates that were applied during this surgery:

- Duration surgery (hours)

Comparisons will be performed for this variable described above based on the number of plates using T-Student or U Mann Whitney, ANOVA or Kruskal Wallis, depending on the distribution of the variable.

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable by MDD (Yes / No)[1] present in surgery visit:

- Duration surgery (hours)

Comparisons will be performed for this variable described above based on MDD at surgery using T-Student or U Mann Whitney depending on the distribution of the variable.

[1]This variable will be obtained from Form MDD Description.

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable by MDD (Yes / No)[1] present in surgery visit for each number of plates were applied during surgery separately:

- Duration surgery (hours)

Comparisons will be performed for this variable described above based on MDD at surgery using T-Student or U Mann Whitney depending on the distribution of the variable.

[1]This variable will be obtained from Form MDD Description.

The categorical variable to be described is, N and (%):

- Did the patient receive a blood transfusion? (Yes / No)

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- If 'Did the patient receive a blood transfusion?' is equal to 'Yes': How many BT unit were used will be described

The categorical variables to be described are, N and (%):

- Number of Locking Screws used
- Number of Non-Locking Screws used
- Number of total screws as a sum of Number of Locking Screws+Number of Non-Locking Screws

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- Number of Locking Screws used
- Number of Non-Locking Screws used
- Number of total screws as a sum of Number of Locking Screws+Number of Non-Locking Screws

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Radiant dose

The categorical variables to be described are, N and (%):

- Post operative AP projection X-Ray
- Post operative ML projection X-Ray

17.2 CORRECTION OUTCOME EVALUATION

The categorical variables to be described are, N and (%):

- According to the investigator, was the planned level of correction achieved? (Yes / No / Partially), if yes:
    - Please motivate the answer
    - Is another surgery recommended? (Yes / No)

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- Degree Varus
- Degree Valgus
- Degree antecurvation

18 DISCHARGE VISIT

18.1 DISCHARGE VISIT INFORMATION

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Time from surgery to Discharge (days) (calculated as Date of discharge minus date of surgery)

The categorical variable to be described is, N and (%):

- Time from surgery to Discharge (days) within the time windows estimated in the protocol (5-9 days)? (Yes / No)

18.2 ROM AND WB AT DISCHARGE

The categorical variable to be described is, N and (%):

- Discharge Weight-bearing Grade (Non-weight-bearing (NWB) / Toe-touch weight-bearing (TTWB) / Partial weight-bearing (PWB) / Full weight-bearing (FWB))

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- ROM Knee Flexion
- ROM Knee Extension
- ROM Hip Flexion
- ROM Hip Extension
- ROM Hip Abduction

- ROM Hip Internal Rotation
- ROM Hip External Rotation
- ROM Ankle Joint Dorsiflexion
- ROM Ankle Joint Plantarflexion

19 FIRST CONTROL VISIT

19.1 VISIT GENERAL INFORMATION

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Time from surgery to First control visit (days) (calculated as Date of first control minus date of surgery)

The categorical variable to be described is, N and (%):

- Time from surgery to First control visit (days) within the time windows estimated in the protocol (4-8 weeks)? (Yes / No)

The categorical variables to be described are, N and (%):

- Has the bone reached a satisfactory consolidation? (No / Partially / Yes)
- Comments

The categorical variables to be described are, N and (%):

- Did the patient refer pain at the treated limb ? (Not at all / A little bit / Moderately /Quite a bit /Extremely)
- In case of previous question is not equal to 'Not at all' VAS will be described
- In case of previous question is not equal to 'Not at all' VAS Pain Score according to the patient will be described
- X-ray AP image
- X-ray ML image

19.2 CORRECTION EVALUATION AT FIRST CONTROL

The categorical variables to be described are, N and (%):

- According to the investigator is the level of correction maintained? (No / Partially / Yes), if yes:
  - Please motivate the answer
  - Is another surgery recommended? (Yes / No)

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- Degree Varus
- Degree Valgus
- Degree antecurvation

19.3 ROM AND WB AT FIRST CONTROL

The categorical variable to be described is, N and (%):

- Current Weight-bearing Grade (Non-weight-bearing (NWB) / Toe-touch weight-bearing (TTWB) / Partial weight-bearing (PWB) / Full weight-bearing (FWB))

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- ROM Knee Flexion
- ROM Knee Extension
- ROM Hip Flexion
- ROM Hip Extension
- ROM Hip Abduction
- ROM Hip Internal Rotation
- ROM Hip External Rotation
- ROM Ankle Joint Dorsiflexion
- ROM Ankle Joint Plantarflexion

20 BONE CONSOLIDATION VISIT

20.1 VISIT GENERAL INFORMATION

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Time from surgery to Bone Consolidation visit (months) (calculated as Date of bone consolidation minus date of surgery)

The categorical variable to be described is, N and (%):

- Time from surgery to Bone Consolidation visit (months) within the time windows estimated in the protocol (6-9 months)? (Yes / No)

The categorical variables to be described are, N and (%):

- Has the bone reached a satisfactory consolidation? (No / Partially / Yes)
- Comments

The categorical variables to be described are, N and (%):

- Did the patient refer pain at the treated limb ? (Not at all / A little bit / Moderately /Quite a bit /Extremely)
- In case of previous question is not equal to 'Not at all' VAS will be described
- In case of previous question is not equal to 'Not at all' VAS Pain Score according to the patient will be described
- X-ray AP image
- X-ray ML image

20.2 CORRECTION EVALUATION AT BONE CONSOLIDATION ASS

The categorical variables to be described are, N and (%):

- According to the investigator is the level of correction maintained? (No / Partially / Yes), if yes:
  - Please motivate the answer
  - Is another surgery recommended? (Yes / No)

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- Degree Varus
- Degree Valgus
- Degree antecurvation

20.3 ROM AND WB AT BONE CONSOLIDATION ASS

The categorical variable to be described is, N and (%):

- Current Weight-bearing Grade (Non-weight-bearing (NWB) / Toe-touch weight-bearing (TTWB) / Partial weight-bearing (PWB) / Full weight-bearing (FWB))

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- ROM Knee Flexion
- ROM Knee Extension
- ROM Hip Flexion
- ROM Hip Extension

- ROM Hip Abduction
- ROM Hip Internal Rotation
- ROM Hip External Rotation
- ROM Ankle Joint Dorsiflexion
- ROM Ankle Joint Plantarflexion

21 DEVICE REMOVAL VISIT

21.1 VISIT GENERAL INFORMATION

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Time from surgery to Device removal visit (months) (calculated as Device Removal Surgery Date minus date of surgery)

The categorical variable to be described is, N and (%):

- Time from surgery to Device removal visit (months) within the time windows estimated in the protocol (10-18 months)? (Yes / No)

The categorical variables to be described are, N and (%):

- Has the bone reached a satisfactory consolidation? (No / Partially / Yes)
- Comments

The categorical variables to be described are, N and (%):

- Did the patient refer pain at the treated limb ? (Not at all / A little bit / Moderately /Quite a bit /Extremely)
- In case of previous question is not equal to 'Not at all' VAS will be described
- In case of previous question is not equal to 'Not at all' VAS Pain Score according to the patient will be described

21.2 DEVICE REMOVAL SURGERY INFORMATION

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Duration surgery

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable by the number of plates were applied during device **application** surgery:

- Duration surgery (hours)

Comparisons will be performed for this variable described above based on the number of plates using T-Student or U Mann Whitney, ANOVA or Kruskal Wallis, depending on the distribution of the variable.

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable by MDD (Yes / No)[1] present in device removal visit:

- Duration surgery (hours)

Comparisons will be performed for this variable described above based on MDD at surgery using T-Student or U Mann Whitney depending on the distribution of the variable.

[1]This variable will be obtained from Form MDD Description.

The categorical variable to be described is, N and (%):

- Did the patient receive a blood transfusion? (Yes / No)

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Radiant dose

The categorical variables to be described are, N and (%):

- Post removal AP projection X-Ray
- Post removal ML projection X-Ray

21.3 CORRECTION EVALUATION AT DEVICE REMOVAL

The categorical variables to be described are, N and (%):

- According to the investigator is the level of correction maintained? (No / Partially / Yes), if yes:
    - Please motivate the answer
    - Is another surgery recommended? (Yes / No)

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- Degree Varus
- Degree Valgus
- Degree antecurvation

21.4 ROM AND WB AT DEVICE REMOVAL

The categorical variable to be described is, N and (%):

- Current Weight-bearing Grade (Non-weight-bearing (NWB) / Toe-touch weight-bearing (TTWB) / Partial weight-bearing (PWB) / Full weight-bearing (FWB))

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variables:

- ROM Knee Flexion
- ROM Knee Extension
- ROM Hip Flexion
- ROM Hip Extension
- ROM Hip Abduction
- ROM Hip Internal Rotation
- ROM Hip External Rotation
- ROM Ankle Joint Dorsiflexion
- ROM Ankle Joint Plantarflexion

22 EXIT VISIT

The categorical variables to be described are, N and (%):

- Reason for study exit
- Please explain why the investigator withdrew the subject
- Please specify the reason

23 PRIMARY OBJECTIVE

The primary objective of the study is to evaluate the safety profile of JPS within the scope of its intended purpose, when used according to the manufacturer IFU on a representative population of subjects and users.

In order to fulfill this objective, the safety profile of JPS will be assessed by the following endpoints:

- percentage (%) of subjects with at least one serious/not serious adverse event certainly related or possibly related to JPS (primary endpoint) at device removal follow-up (up to 18 months according to site's standard practice).
- percentage (%) of Medical Device Deficiencies (MDDs) at device removal follow-up (up to 18 months according to site's standard practice).

23.1 ADVERSE EVENTS

The categorical variables to be described are, N and (%) and Clopper-Pearson confidence intervals will be shown at 95.2% as well:

- Implants with at least one adverse event
- Implants with at least one serious adverse event
- Patients with at least one adverse event
- Patients with at least one serious adverse event

23.1.1 ADVERSE EVENTS DESCRIPTION

The categorical variables to be described are, N and:

- Adverse Event Description by implant
- Adverse Event Description by patient
- The detailed description of the AE for each Adverse Event Description by implant

23.1.2 ADVERSE EVENTS SERIOUSNESS

The categorical variables to be described are, N and:

- The detailed description of the AE for each: Seriousness / Not seriousness

23.1.3 ADVERSE EVENTS POTENTIALLY LINKED TO JPS MD?

The categorical variables to be described are, N and (%) and Clopper-Pearson confidence intervals will be shown at 95.2% as well:

- According to the investigator, is this AE potentially linked to JPS Medical Device? by implants
- According to the investigator, is this AE potentially linked to JPS Medical Device? by patients
- Is this AE linked to a Medical Device Deficiency? by implants
- Is this AE linked to a Medical Device Deficiency? by patients

23.1.4 ADVERSE EVENTS LIST

A list with adverse events collected and its characteristics will be shown.

23.2 MEDICAL DEVICE DEFICIENCIES (MDD)

The categorical variables to be described are, N and (%) and Clopper-Pearson confidence intervals will be shown at 95.2% as well:

- Implants with at least one MDD
- Patients with at least one MDD

23.2.1 MEDICAL DEVICE DEFICIENCIES (MDD) TYPES AND DESCRIPTION

The categorical variables to be described are, N and (%):

- Types of MDD by implant
- Types of MDD by patient
- For each type of MDD description will be shown by implant

23.2.2 MEDICAL DEVICE DEFICIENCIES (MDD) RESULTED IN AN ADVERSE EVENT FOR THE PATIENT

The categorical variables to be described are, N and (%) and Clopper-Pearson confidence intervals will be shown at 95.2% as well:

- Did this MDD resulted in an Adverse Event for the patient? by patient
- Did this MDD resulted in an Adverse Event for the patient? by implant

23.2.3 MEDICAL DEVICE DEFICIENCIES (MDD) LIST

A list with MDD collected and its characteristics will be shown.

24 SECONDARY OBJECTIVES

The secondary objective of the study is to evaluate the clinical performance of JPS within the scope of its intended purpose, when used according to the manufacturer IFU on a representative population of subjects and users.
In order to fulfill these objectives the clinical performance of JPS will be assessed by the two following efficacy endpoints:

- percentage (%) of subjects that reached a satisfactory bone consolidation according to investigator's opinion;
- percentage (%) of subjects that maintained bone correction alignment according to investigator's opinion until device removal.

24.1 SATISFACTORY BONE CONSOLIDATION

The categorical variables to be described are:

- Number of Implants that reached a satisfactory bone consolidation according to investigator's opinion in any visit
- Number of patients that reached a satisfactory bone consolidation according to investigator's opinion in any visit or implant

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Time to full consolidation from surgery (months), per implant, considered at the first visit in which the answer is "Yes" in "Has been reached a satisfactory consolidation?" variables. Calculated as date of first satisfactory consolidation minus date of surgery.

  A list will be made to identify possible outliers from the "time to full consolidation from surgery" in order to verify if there are any. In case any outliers descriptive of "time to full consolidation from surgery" will be repeated without the outlier data.

A list with satisfactory bone consolidation variables will be shown.

24.2 MAINTAINED BONE CORRECTION

This analysis will be performed for cases that have indicated: Deformity Correction.

The categorical variables to be described are:

- Number of Implants that according to the investigator is the level of correction maintained until last visit performed
- Number of Patients that according to the investigator is the level of correction maintained until last visit performed

A list with maintained bone correction variables will be shown.

24.3 WEIGHT BEARING GRADE

The categorical variables to be described are:

- Number of Implants that reached a Full weight-bearing (FWB) from surgery in any visit
- Number of Patients that reached a Full weight-bearing (FWB) from surgery in any visit or implant

The descriptive statistic (Mean, SD, Median, Q_1, Q_3, Min, Max) will be shown for the following continuous variable:

- Time to Full weight-bearing from surgery (months), per implant, considered at the first visit in which the answer is "'Full weight-bearing (FWB)" in "Weight-bearing Protocol" variables. Calculated as date of the first visit of Full weight-bearing minus date of surgery.

  A list will be made to identify possible outliers from the "time to full weight-bearing" in order to verify if there are any. In case any outliers descriptive of "time to full weight-bearing" will be repeated without the outlier data.

A list with Weight bearing grade variables will be shown.

25 CONCOMITANT MEDICATION

The type of drug group by patient will be described (N, %) considering the patient has taken at least once.

MARTOM_ORTHOFIX_JPS_Statistical Analysis Plan SAP_ver1.0

Final Audit Report 2024-04-11

Created:	2024-04-11
By:	Eco Sign QA (esign-qa@orthofix.com)
Status:	Signed
Transaction ID:	CBJCHBCAABAAvRfl_dGQaDLmrimTp8MwMoQFBNE6_vbu

"MARTOM_ORTHOFIX_JPS_Statistical Analysis Plan SAP_ver1.0" History

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Document created by Eco Sign QA (esign-qa@orthofix.com)
2024-04-11 - 08:28:12 GMT- IP address: 193.17.45.5

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