



CLINICAL STUDY RESULT SUMMARY

Study Title	A single center post-market clinical follow-up (PMCF) observational study evaluating the clinical performance and the safety profile of the JuniOrtho™ Telescopic Intramedullary Nail (JTIN) for the treatment of pediatric patients suffering from Osteogenesis Imperfecta
Clinical Investigation Plan Number	OCI_2201
Public Database Registration Number	NCT05612139 (clinicaltrials.gov)
Indication	Treatment of fractures and limb deformities in pediatric patients with Osteogenesis Imperfecta
Study Design	Apparent from the title
Sponsor	Orthofix S.r.l., Via Delle Nazioni 9, 37012 Bussolengo Verona, Italy
Coordinating Investigator	Dr. Zagorka Pejin; Pediatric Orthopedic Surgeon
Study Initiation	27 August 2024
Study Completion:	
<i>Defined as Last Patient Last Visit</i>	20 February 2025
<i>Close Out Visit</i>	19 March 2025

Statement of Compliance:

This study was conducted according to [the principals of ISO 14155:2020, and further updates, for the clinical investigation of medical devices for human subjects, and Good Clinical Practice (ICH-GCP (E6)).

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Synopsis

Study Product(s):	INVESTIGATIONAL PRODUCT: The JuniOrtho™ Telescopic Intramedullary Nail (JTIN) system consists of components classified as IIb, IIa, Ir and Is. The nail is designed for self-extension, adjusting the length of the device, in order to follow the patient growth as it occurs. JTIN is a CE marked device under European Union MDD 93/42 amended by 2007/47/EC. CONTROL: N.A.	
Indication:	The JTIN is indicated for fractures, osteotomies/deformities treatment, malunions and non-unions in femur and tibia in pediatric patients (> 18 month and < 18 years) at the time of surgery, suffering from osteogenesis imperfecta.	
Study Center(s):	Hôpital Necker-Enfants maladies, Paris - France	
Publications:	None to date	
Study Registration:	ClinicalTrials.gov Identifier NCT05612139	
Study Period:	<u>Date of First Subject Enrolled:</u> 23 Sep 2024 <u>Date of Enrollment Completion:</u> 21 Feb 2025 <u>Date of Final Closeout Visit:</u> 19 Mar 2025	<u>Study Duration:</u> The total duration of the conducted study was 6 months.
Study Type & Methodology:	The OCI-2201 study is a Post Market Clinical Follow-up (PMCF) prospective and retrospective, observational, not controlled, non-randomized, single-center, one country, study. All data from patients'/ procedures' observation are collected according to the site standard-of-care.	
Study Objectives:	Primary: The primary objective of the study was to evaluate the safety of JTIN, in terms of percentage of procedures with at least one serious/not serious adverse event certainly or possibly related to JTIN up to 1 year follow-up. Secondary: The secondary objectives of this study were to: evaluate clinical safety and performance of the JTIN, in terms of: 1. Safety: implant survival 2. Performance: 2.1. bone union achievement 2.2. fracture-free survival Exploratory: The exploratory objectives of this study were to: Evaluate functional changes after treatment, by the Gillette Functional Assessment Questionnaire.	
No. of Procedures:	<u>Planned:</u> 25 surgical procedures <u>Screened:</u> 14 subjects corresponding to 25 procedures	

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	Enrolled & Analyzed: 14 subjects corresponding to 25 procedures
Introduction:	The hallmark feature of Osteogenesis imperfecta (OI) is bone fragility, with susceptibility to fracture from minimal trauma, as well as bone deformity and growth deficiency. OI manifestation is ranging from perinatal lethality, severe skeletal deformities, mobility impairments, very short stature to nearly asymptomatic individuals. Fractures can occur in any bone but are most common in the limbs. Intramedullary nails have an important role for bone stabilization and fracture prevention in patients with OI, who suffer from bone fragility and recurrent fractures. The JuniOrtho™ Telescopic Intramedullary Nail (JTIN) is an established, marketed device, commercially available and used as standard device in orthopedic surgeries. The post-marketing, prospective study with CE-marked device JuniOrtho™ Telescopic Intramedullary Nail (JTIN) reported, was designed for gathering real-world medical data from treatment of fractures, osteotomies/ bone deformities, malunions and non-unions in femur and tibia in pediatric patients (older than 18 months) suffering from osteogenesis imperfecta.
Diagnosis and Main Criteria for Inclusion:	Patients were enrolled in this study if they meet all of the following inclusion criterion: 1. is in pediatric age (> 18 month and < 18 years) at the time of surgery; 2. is skeletally immature; 3. has a diagnosis for OI; 4. has a regular indication for surgical intervention with JTIN to treat femoral and/or tibial fractures, osteotomies, malunions and non-unions; 5. Patient and/or legal representative is duly informed and doesn't oppose to participation.
Main Criteria for Exclusion:	Patients were enrolled in this study if they meet the following non-inclusion criterion: 1. has a medical condition that is a contraindication according to the manufacturer's instruction for use; 2. has any conditions that in the Investigator's opinion may interfere with the study execution or due to which the patient should not participate for safety reasons; 3. requires the application of, or has already in-situ the application of concomitant devices that cannot be safely removed (except for permitted concomitant devices Paragraph); 4. is participating in other clinical trials or has taken part in any clinical study in the last 3 months with exception of analytical trials on genetics study related to OI (i.e. studies that do not include an investigational treatment for the patient such as new drugs or other medical devices); 5. is likely to be lost to follow up, according to Investigator's opinion.

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Study Endpoints:	Safety endpoints: The safety profile of JTIN will be assessed by the following safety endpoints: • Percentage (%) of procedures with at least one serious/not serious adverse event certainly or possibly related to JTIN up to 1 year follow-up (primary); • Implant survival rate: it is the percentage of not exchanged nails up to 1 year follow-up. Efficacy endpoints: the clinical performance of the JTIN will be assessed by the means of the: • Bone union achieved; • Post-treatment fracture-free survival up to 1 year follow-up. Exploratory endpoint was assessed by: • Change in Gillette Functional Assessment Questionnaire from Pre-operative to bone consolidation assessment visit and to 1 year follow up.
Statistical Methods:	Quantitative variables are 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 are described using absolute and relative frequencies. In the descriptive analysis of qualitative variables, two percentage columns are 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. Clopper-Pearson confidence intervals at 95.0% will be shown for the primary and secondary objectives. For time-to-event variables (i.e. fracture free-survival) are analyzed using the Kaplan-Meier method. The median and the 95% CI as well as the number of events and patients censored are provided. Error standard is estimated per the method Greenwood (Greenwood, 1926). KM graphs are presented along with the number of case-at-risk at exact time points. Change in Gillette Functional Assessment Questionnaire from Screening to 1 year follow up is analyzed by means of descriptive statistics as a continuous variable. Comparisons are performed by means of paired t-test (parametric) or Wilcoxon (non-parametric) depending on the distribution of the sample. These tests are used in all bilateral cases and with a level of significance of 0.05. In cases where a p-value less than 0.05 appears, it refers to the existence of statistical significance. <u>Analysis Populations:</u> This study examined 14 patients contributing a total of 25 surgical procedures performed in pediatric patients who had a regular indication for surgical intervention with the JTIN. The Full Analysis Set (FAS) population consisted of all enrolled patients treated by the means of JTIN application and who didn't oppose to study participation. The FAS population was used for all the analyses of the study that are presented at subject level. FAS resulted from this study: N=14 The Full Analysis Implant Set (FAIS) population consisted of all JTIN applications performed on subjects belonging to the FAS population. The FAIS population

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	was used for all the analyses of the study that are presented at implant level. FAIS resulted from this this study: N=25 The CRF contains the selection criteria information in the form of a binary variable (Yes/No) for each element described. Patients were considered to belong to the FAS and FAIS populations if they indicate that they met the selection criteria in the previously mentioned binary variables.
Summary of Results:	Study Population: The study was performed in 14 pediatric patients who had a regular indication for surgical intervention with JTIN and in this document are reported the results obtained in 25 surgical procedures. The study design was observational, prospective and retrospective. The study population included 14 patients, each of whom could contribute for one or more than one JTIN implants. When assessed by patient, the population consisted of 9 males (64.3%) and 5 females (35.7%). When assessed by implant, the distribution was 14 male-contributed implants (56.0%) and 11 female-contributed implants (44.0%). Other demographic data and anamnesis, collected before surgery, for each patient at first implant were: mean age 5.4 ± 3.0 years (minimum 1.6 and maximum 10.0 years); mean weight 15.9 ± 7.3 kg (minimum 7.5 and maximum 32.0 kg); mean height 97.4 ± 22.1 cm (minimum 60.0 and maximum 132.0 cm); BMI 17.4 ± 3.9 kg/m² (minimum 13.4 and maximum 27.3 kg/m²). The demographic data per implant are: mean age 4.9 ± 2.9 years (minimum 1.6 and maximum 10.0 years); mean weight 14.5 ± 5.9 kg (minimum 7.5 and maximum 32.0 kg); mean height 91.2 ± 18.4 cm (minimum 60.0 and maximum 132.0 cm); BMI 17.3 ± 3.7 kg/m² (minimum 13.4 and maximum 27.3 kg/m²). Eight medical conditions were recorded in 8 patients and 2 medical conditions were recorded in 1 patient; no medical conditions were recorded in 5 patients. Family history of Osteogenesis Imperfecta was recorded in 3 patients (21,4%). Twelve patients (85,7%) were taking medication before the surgery. At surgery, all patients were treated, according to IFU, with 1 or more than one JTIN implants for treatment of fractures (10 implants, 40.0%) osteotomy fixation (14 implants, 56.0%) or malunion (1 implant, 4.0%). In total 14 patients were treated whit 25 implants; 7 patients received 1 implant, 5 patients 2 implants and 2 patients 4 implants The surgery duration was, in mean, 1.7 hours. Safety Results: <i>Primary Endpoint:</i> the CIP primary safety end point has been evaluated. At least one adverse event was recorded in 18 (72.0%) procedures and in 13 patients (92.9%) treated with JTIN. At least one serious adverse event occurred in 10 (40.0%) implants and 9 in (64.0%) patients. At least one serious adverse event, considered by Investigator as possibly related, occurred 1 implant (4.0%) and in 1 patient (7.1%). In total 31 AEs occurred, 21 of them, in Investigator's opinion, not serious and 10 considered serious. In 1 implant (4.0%) on 1 patient (7.1%), the occurred AE, device malfunction, was classified, in Investigator's opinion, as

	possibly related to the JTIN. Five MDDs occurred during study 1 of them, reported as device malfunction in 4.0% of the 25 implants performed and in 7.1% of the patients included. The study reported showed that 1 (4.0%) implant had an SAE related to JTIN. The serious event occurred was caused by an MDD, device malfunction, that required a reoperation after IMD implantation for replacement of the proximal female screw of the telescopic nail in the left femur, following migration of the component. Results obtained indicated that only 1 (4.0%) of the procedures performed reported one serious adverse event possibly related with JTIN versus the estimated mean of 31.0% (ranging from 9% to 60%) derived from data reported in the available literature for implants performed in patients with similar disease. No complications associated with the retrograde technique in femurs were observed in this study population. The result obtained is lower than the lowest values reported in literature. <u>Safety and efficacy Results:</u> <i>Secondary Endpoint:</i> The results obtained by the analysis of the secondary safety objectives “Implant survival rate: percentage of not exchanged nails up to 1 year follow-up” and “Bone union achievement”, indicate that no one of the 25 (100%) nails implanted was removed, and that all the 25 implants (100%) and all the 14 patients (100%) included reached and maintained bone union until study end. The time to full satisfactory bone consolidation, reported for 25 implants, was, in mean, 1.5 ± 0.9 months after surgery. The OI severity type did not affect bone union process that was rapid and effective. The results obtained from the evaluations of the secondary performance objectives: “post-treatment fracture-free survival up to 1 year follow-up” indicate that 5 adverse events in 5 treated bone, 20% of the implants, reported fracture on the implanted limb. The estimate average time of post-treatment fracture-free survival was about 17.05 ± 0.88 months. Fractures occurred during study were expected and are consistent with the patients’ rare disease. <u>Exploratory endpoint:</u> assessed by means of the Gillette Functional Assessment Questionnaire. Due to the small number of implants examined (19) and the high results variability a clear assessment, it seems that the values at the pre-surgery visit and at the final visit are similar.
Conclusion:	In terms of safety profile, results obtained indicated that only 1 (4.0%) of the procedures performed reported one serious adverse event possibly related with JTIN while the estimated mean of 31.0% (ranging from 9% to 60%) derived from data reported in the available literature for implants performed in similar population of pediatric patient with osteogenesis imperfecta. No complications associated with the retrograde technique in femurs were observed in this study population.

	The implant survival rate, assessed as secondary safety profile, indicate that none of the implants performed was removed. Bone union, assessed as secondary performance profile, was reached by all implants and maintained until last study visit. Post-treatment fracture, on the implanted limb, occurred in 5 of the total implants performed and fracture-free survival time was estimated on 17.05 months. The free-survival time reflects the clinical complexity and inherent bone fragility characteristic of the osteogenesis imperfecta (OI) population and is consistent with the pathology under study and does not contradict the study findings. The functional recovery evaluation (FWB) reports a consistent increase of implants with Full weight-bearing or Partial weight-bearing. The improvement is less consistent in patient with Highly Severe/Progressively deforming (Type III, Type VII, Type VIII) OI. Obtained results confirms that the JTIN nail could be a safe and an effective method of treatment of fractures, osteotomies, malunions and non-unions in femur and tibia in pediatric patients suffering from osteogenesis imperfecta, when used according to the manufacturer's IFU and in line with the instructions provided by Orthofix Srl to carry out JTIN[®] Medical Device implantation procedures.
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