OrthoCor Medical
Statistical Analysis Plan (SAP)

Study Number: OCM-OAS-01

Study Title:

Prospective, Multi-Center, Randomized Study to Evaluate the OrthoCor Active System for Pain Relief

Investigational Product:	**OrthoCor Active System**
Protocol Number:	**OCM-OAS-01 Version 3.0**
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1. DOCUMENT INFORMATION

Document Details	Information
Study Number	OCM-OAS-01
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2. DOCUMENT HISTORY

Version	Effective Date	Changes	Reason for Changes	Author
1.0	23-Mar-2022	Original	N/A	Adelina Paunescu
2.0	23-Sep-2022	Administrative / formatting changes made throughout various sections to better align with protocol. No statistical analysis measurement details / information changed from v1.0.	Review SAP with amendment 2 to protocol OCM-OAS-01 v3.0	Adelina Paunescu
3.0	27-Nov-2023	Correction of typo in the PP Population definition	Error in treatment duration	Adelina Paunescu

3. INTRODUCTION

The purpose of this Statistical Analysis Plan (SAP) is to describe the operational aspects of statistical analysis of the efficacy and safety data to ensure endpoint analysis for primary, secondary endpoints and safety.

The objective of this study is to evaluate the OrthoCor Active System in individuals prescribed its use in comparison with Standard of Care (SOC) intervention. Pain assessments will be conducted utilizing the Mankoski Pain Scale.

4. STUDY DESIGN

This is a prospective, multi-center, randomized, open label study that will enroll up to100 subjects. Subjects will consist of both males and females, presenting to the designated study sites with pain in superficial soft tissue, such as in the ankle, back, knee, wrist, elbow, shoulder, foot, or neck who are prescribed the use of the OrthoCor Active System or Standard of Care (SOC) intervention.

Patients will be enrolled consecutively at each participant site until up to 50 using the OrthoCor Active System and up to 50 using the Standard of Care (SOC) intervention have enrolled. The CRO will stratify the arms (OrthoCor Active System vs SOC) by selecting the arm alternatively. The patients will be enrolled consecutively at the participant site until enrollment is met.

As part of exploratory research extension, patients using the OrthoCor Active system will have the opportunity to continue the trial for an additional 2 weeks. Participants assigned SOC will have the opportunity to cross-over using the OrthoCor Active system for the additional 2 weeks. Participation in the exploratory extension is optional.

5. STUDY OBJECTIVES AND ENDPOINTS

The primary safety and efficacy objectives are:

Safety endpoint of this study will be the adverse events reported with the OrthoCor Active System after 2 weeks of use.

Efficacy endpoint of this study will be the comparison of the OrthoCor Active System pain assessment scores to the Standard of Care (SOC) intervention after 2 weeks of use. The primary effectiveness endpoint of this study is the change from baseline of the OrthoCor Active System compared to the SOC intervention.

The exploratory objectives, for publication only, are comparison of the performance of the OrthoCor Active System to standard of care after additional 2 weeks of use.

6. SUBJECT POPULATION

The target population is both female and male, over the age of 18 years pain in the superficial tissue at sites such as ankle, back, knee, wrist, elbow, shoulder, foot, or neck who meet inclusion criteria and do

not meet any exclusion criteria from the protocol. The participants will be selected from the population selected by the Principal Investigator at each of the 5 participant US sites after passing the screening and eligibility assessments per protocol.

As part of exploratory research extension, patients using the OrthoCor Active system will have the opportunity to continue the trial for an additional 2 weeks. Participants assigned SOC have the opportunity to cross-over using the OrthoCor Active system for the additional 2 weeks. Participation in the exploratory extension is optional.

7. SAMPLE SIZE

The sample size estimates are calculated assuming a binomially distributed response of improvement or no improvement. Without any a priori estimates, the most conservative estimate (widest interval) is using a baseline for the standard of care (SOC) of 50% improvement. The null hypothesis for a non-inferiority study is that the experimental treatment is inferior to the standard of care. The alternative hypothesis is that the experimental treatment is non-inferior to the standard of care.

The sample size per group is based on the comparison of two proportions with baseline proportion of 50% for the experimental treatment assuming a 50% response for SOC and a non-inferiority margin of 10% assuming 90% power. The assumed confidence is 95% or a type 1 error rate of 5%.

The study will enroll 100 subjects, up to 50 using the OrthoCor Active System and up to 50 using the Standard of Care (SOC) intervention. The patients will be enrolled consecutively at the participant site until enrollment is met. The CRO will stratify the arms (OrthoCor Active System vs SOC) by selecting the arm alternatively.

For the exploratory assessments, the 50 subjects who received SOC will have the opportunity to cross-over and use the OrthoCor Active system.

8. RANDOMIZATION

The study will use simple randomization in two groups: OrthoCor Active System and SOC. The randomization schema utilized will be consecutive enrolment at each site, alternatively in each group.

9. BLINDING

The study is not blinded.

10. STUDY ASSESSMENTS

Mankoski Pain Scale assessments are conducted during the study for a period of 2 weeks of treatment with OrthoCor Active system or Standard of Care. The enrolled participant will have a treatment period from Day 0 through Day 14 when the study ends, and a research extension period and assessments are conducted for a period of additional 2 weeks (see Table 1. Schedule of Assessments in protocol).

The primary endpoints as well as safety analyses will be evaluated at study end.

Exploratory analyses will be assessed after the extension period of additional 2 weeks.

11. GENERAL CONSIDERATIONS

11.1. General Methods

A repeated measures ANOVA will be utilized to assess statistical differences between the active and sham devices. A test of normality will be performed. If the data is not shown to be normally distributed, nonparametric methods may be used. All hypotheses are performed at an alpha equal to 0.05.

11.2. Analysis Population

The following analysis populations will be defined for the study:

Intent-to-Treat (ITT) Population – The ITT population will consist of all enrolled subjects that completed any treatment.

Per-Protocol (PP) Population – The PP population will consist of all enrolled subjects with 2 weeks of treatment and without any critical data missing and data collected per protocol.

Safety Population – The safety population will consist of all enrolled subjects that have had treatment with active OrthoCor Active System.

The analysis of efficacy data will be conducted on the ITT and PP populations.

All safety analyses will be performed on the safety population.

11.3. Timing of Analyses

The final analysis will be performed after all enrolled participants have completed the 2 weeks treatment period.

The additional analysis for exploratory research will be performed after all enrolled participants completed the 2 weeks of treatment and any of the additional exploratory days and up to 2 weeks.

12. STATISTICAL ANALYSIS

The data consists of multiple repeated measures and will be checked for normalcy and sphericity, and primary analysis will consist of ANOVAs for repeated measures and with other secondary analysis as appropriate for secondary hypotheses. Nonparametric methods will be used if the data is not normally distributed.

12.1. Primary Endpoints

The primary endpoints of this study will be to compare the reduction of pain symptoms from baseline on the Mankoski Pain Scale after 2 weeks of treatment with the OrthoCor Active System device and Standard of Care.

12.2. Exploratory Endpoints

The exploratory endpoints of this study will be to compare the reduction of pain symptoms from baseline on the Mankoski Pain Scale after 4 weeks of treatment with the OrthoCor Active System device and Standard of Care.

Usage (device records use), feedback via participant diaries, usability assessment, user preferences will be summarized as descriptive statistics.

12.3. Safety Variables

This is a non-significant risk study. Because no procedures are required to perform the investigational study, safety will be monitored via the reported Adverse Events, in this study. The descriptive table of Adverse Events, within protocol, will be the extent of safety reporting.

12.4. Handling Missing Data

Only participants with complete available data will be used in the statistical analysis, i.e., a complete case analysis. For missing visits, an imputation of last visit carried forward will be considered.

12.5. Protocol Deviations

Important Protocol Deviations will be summarized. The MEDIcept team will identify important protocol deviations and will be reviewed prior to database lock.

12.6. Subject Disposition

Subjects who have signed the Informed Consent Form with available data for the will be used in the statistical analysis, i.e., a complete case analysis, for Per Protocol analysis. All subjects will be included in the Intent to Treat (ITT) analysis.

12.7. Demographics

Subject demographics will be summarized using descriptive statistics (mean, median, Standard Deviation (SD), minimum, maximum), number of subjects for continuous variables (e.g., age), and frequency distributions (number and percentage of subjects) for categorical variables (e.g., sex at birth, race, and ethnicity).

12.8. Safety

All adverse events for participants in the safety population will be reported.

- Serious Adverse Events
- Non-serious Adverse Events Device Related Adverse Event
- Device Related Serious Adverse Events

Results will include the number of participants experiencing each type of event as well as the number of events.

12.9. Concomitant Medication

All concomitant medication for pain will be recorded. A medication is considered concomitant if the start date is before the informed consent and there is no stop date, or the stop date is after the end of study treatment.

13. CHANGE FROM ANALYSES PLANNED IN THE PROTOCOL

This statistical analysis plan is based on protocol.