CLINICAL PROTOCOL

WALTZ: a prospective, non-significant risk, feasibility study to evaluate serial 90-minute applications of VibratoSleeve therapy to acutely increase the perfusion in peripheral arterial disease (PAD) subjects 65 years of age and older.

STUDY NO: 022-01 VER 1.0

NCT05888740

AUGUST 18, 2022

STUDY SPONSOR

Vibrato Medical, Inc.

1. PROTOCOL SYNOPSIS

Title:	WALTZ: a prospective, non-significant risk, feasibility study to evaluate serial 90-minute applications of VibratoSleeve therapy to acutely increase the perfusion in peripheral arterial disease (PAD) subjects 65 years of age and older.
Design:	Prospective, single arm, open-label clinical trial to evaluate the feasibility of TUS in the treatment of early stage (Rutherford Class 1-3) PAD. The results of this study will be used to support future studies.
Device Name and Intended Use:	VibratoSleeve is an array of single element ultrasound transducers, driven in a phased manner, and held in place externally by an adjustable sleeve. In this study, the VibratoSleeve will be applied in clinic and will be tested to demonstrate evidence of an increase in distal limb perfusion in adults with PAD.
Visit Schedule:	Visits will occur at screening (baseline data) and at three in-clinic treatment sessions, each separated by at least a 1-week interval.
Study Objectives:	The objectives of this study are: • To determine the feasibility of VibratoSleeve therapy to acutely increase distal perfusion in peripheral arterial disease (PAD) subjects 65 years of age and over. • Collect data on tolerable acoustic dose of serial 90-minute TUS therapy in the treatment of early stage (Rutherford Class 1-3) PAD. • Evaluate subject feedback on wearability and tolerability of serial 90-minute TUS therapy. • Evaluate the nature, incidence, timing and resolution of all adverse events in subjects treated with VibratoSleeve as compared with historical data on current standard of care treatments for PAD.
Number of Subjects and Defined Point of Enrollment	A total of up to 12 subjects will be required to receive VibratoSleeve therapy. The point of enrollment is defined as the time the subject signs the Informed Consent Form (ICF) to undergo screening procedures to ascertain eligibility. It is anticipated that up to 50% of subjects enrolled in the study will meet the inclusion/exclusion criteria. Given the screen success rate, it is anticipated that approximately 24 subjects could be enrolled in the study to have 12 evaluable subjects qualified for the treatment and evaluation.

Inclusion Criteria	1. Age ≥ 65 2. Diagnosis of PAD. 3. Claudication symptoms in Rutherford class 1, 2, or 3 as determined by the investigator.
Exclusion Criteria	1. Prior stenting in posterior tibial artery. 2. Re-vascularization procedure within 30 days prior to enrollment in the study. 3. Ulcers, cellulitis, or skin breakdown in treatment areas (posterior calf). 4. History or diagnosis of severe chronic venous insufficiency. 5. Acute limb ischemia within 30 days prior to treatment. 6. History or diagnosis of deep venous thrombosis below the knee in treatment leg. 7. Any conditions that, in the opinion of the investigator, may render the subject unable to complete the study or lead to difficulties for subject compliance with study requirements, or could confound study data. 8. Subject's enrollment in another investigational study that has not completed the required primary endpoint follow-up period.
Safety Endpoint	All device and procedure related adverse clinical events experienced by subjects will be collected. Summaries of adverse events will be provided on a per subject and a per device basis. Severity and method of resolution will also be summarized. The number and primary reasons for medical or surgical interventions to treat device related adverse events will be summarized. This study is not powered to definitively evaluate the safety of the investigational device as compared to the historical data of comparable treatments for PAD.
Efficacy Endpoints	The following parameters will be evaluated to assess performance of the VibratoSleeve TUS: • The mean improvement in FlowMet perfusion rate as measured by the noninvasive FDA-approved imaging system FlowMet. Each subject's pre-treatment baseline perfusion rate will be calculated from at least 5 minutes (mean of 300 FlowMet measurements which are taken once a second) as Baseline period. The mean of the 90 minutes of the treatment period will then be normalized to the pre-treatment baseline to determine the percentage change in perfusion rate. • Tissue oxygen saturation and hemoglobin content as measured by the noninvasive FDA-approved imaging system Clarifi (StO_2). . Clarifi measurements will be taken before (baseline), during and after treatment.

	• Ankle and Toe Brachial Indices (ABI, TBI). Improvement in ABI, TBI will be similarly compared for all subjects. ABI and TBI will be taken before and after each treatment • Quality of Life with VascuQoL and Walking Impairment Questionnaires Mean changes of all these endpoints from baseline during the treatment and to post-treatment will be analyzed.
Treatment	In this protocol, therapy will be delivered at VISOC clinic during 3 separate visits with at least 1-week interval between each visit. TUS therapy will last for 90 minutes during each treatment visit. Each subject will receive either low, medium or high acoustic intensity (varying peak negative pressure) of TUS at a treatment visit and all subjects will receive all 3 levels of intensity during the study. Regular monitoring will be conducted to ensure subject compliance with therapy during treatment. Subjects will be discharged from the study after Treatment Visit 3 or until any device or procedure adverse events are resolved or remain stable.
Statistical Hypothesis	Statistical hypotheses will not be applied in this pilot study. Tables and descriptive statistics of the subject demographic data, treatment parameters, and outcome variables will be generated at the completion of the study. Information collected during the study may be used to support a 510(k) application as well as to select the endpoints and determine sample sizes for future trials.
Study Duration	The Sponsor expects the trial to last six months from the time the first subject enrolls until the time of the last visit.