PROTOCOL SYNOPSIS COVER PAGE

A Prospective Single-Arm Multicenter StuDy of the BarE TEmporary SPur StEnt System foR the tREatment of Vascular lesions located in the infrapoplitEal Arteries beLow the knee (DEEPER REVEAL)

Protocol ID: CP-007

NCT Identification Number: NCT05358353

Date of Document: 01 December 2022

1 PROTOCOL SUMMARY

1.1 Protocol Synopsis

Title:	A Prospective Single-Arm Multicenter Stu**D**y to Evaluate the Performance of the Bar**E** T**E**mporary S**P**ur St**E**nt System fo**R** the t**RE**atment of **V**ascular lesions located in the infrapoplit**E**al **A**rteries be**L**ow the knee **(DEEPER REVEAL)**
Short Title:	**DEEPER REVEAL**
Protocol Number:	CP-007
Revision and Date:	Rev B, 01 December 2022
Test Device	The Bare Temporary Spur Stent System manufactured by Reflow Medical
Device Classification	II
Control Device	None
Trial Registration	NCT05358353
Study Design	This is a prospective, multicenter, single arm study designed to evaluate the safety and efficacy of the Temporary Bare Spur Stent System (Spur Stent System).
Intended Use	The Bare Temporary Spur Stent System is intended for use in the infrapopliteal arteries ranging in diameter from 2.5mm to 4.5mm for the treatment of critical limb ischemia (CLI).
Planned Number of Subjects	Up to 130 subjects will be enrolled at up to 50 investigational centers in the US and outside of the US. A minimum of 50% of subjects will be enrolled at US sites, and no single site will be permitted to enroll more than 20% of all subjects.
Study Objectives	*Primary Objective:* To compare the safety and efficacy of the Bare Temporary Spur Stent System in subjects with infrapopliteal critical limb ischemia (CLI) to a pre-defined performance goal (PG) based on standard percutaneous transluminal balloon angioplasty (PTA). *Secondary Objective:* To gather data on objective and subjective measures of clinical outcomes in this population.
Primary Endpoints:	***Primary Efficacy Endpoint*** Technical success, defined as <30% residual stenosis within the treated lesion area by visual estimate on completion angiography. ***Co-Primary Safety Endpoint*** Freedom from the occurrence of major adverse limb events (MALE) [evaluated at 30 days post procedure] and peri-

	operative death (POD) [defined as all-cause mortality within 30 days post procedure]. MALE is defined as: • Above-the-ankle amputation of the index limb • Major reintervention (new bypass graft, jump/interposition graft revision, or thrombectomy/thrombolysis) of the index limb involving the infrapopliteal arteries.
[redacted]	[redacted]
[redacted]	[redacted]

	[redacted]
Principal Investigators and Study Sites:	Co-Principal Investigators Principal Investigator: Dr. Jihad Mustapha Principal Investigator: Dr. Jay Mathews Principal Investigator: Dr. Mahmood Razavi
DSMB and CEC	An independent Data Safety Monitoring Board (DSMB) will perform study oversight, review primary safety endpoint data for all subjects [redacted] An independent Clinical Events Committee (CEC) will adjudicate MALE, limb salvage and primary patency events, unanticipated serious adverse device effects (USADE), device deficiencies, and all deaths as reported by the trial investigators.
Core Laboratories	• Angiographic: to adjudicate angiograms taken during the index procedure for all subjects and in follow up for CD-TLR adjudication, and/or primary patency evaluation as applicable. • Ultrasound: to adjudicate ultrasounds taken during the follow-up period for lesion patency. • Wound: to adjudicate wound pictures and documentation taken at baseline and during the follow up period for wound healing.

Study Population	The study population consists of those with infrapopliteal CLI, Rutherford class 4-5, that in the opinion of the investigator are not amenable to conservative medical therapy (lifestyle changes, medication) and require endovascular intervention for alleviation of symptoms and tissue preservation. Subjects must be ≥ 18 years of age, with a life expectancy of greater than 1 year and are eligible for enrollment if all inclusion criteria are met and none of the exclusion criteria are met.
Description of Study intervention	The Bare Temporary Spur Stent System is a temporary endovascular stent integrated with a balloon catheter intended for use as a primary treatment of the infrapopliteal arteries, in subjects with critical limb ischemia. The Bare Temporary Spur Stent System consists of a stent and balloon that is retrievable after delivery of the stent system. • [redacted]
Study Duration	Active enrollment for at least 12 months Enrollment initiation date: Q3 2022 Follow up anticipated completion date: Q2 2024
Participant Duration	Follow up dates: 2 weeks (for Rutherford 5 patients) 30 days 3 months 6 months 12 months
Inclusion Criteria:	**Pre-Procedure Inclusion Criteria:** 1. Subject willing and able to provide informed consent and able to comply with the study protocol and follow up. Subjects who are unable to sign due to a physical limitation may have a Legally Authorized

	Representative (LAR), including a family member, sign on their behalf. 2. Life expectancy greater than 1 year in the investigator's opinion. 3. Male or non-pregnant female ≥18 years of age at time of consent. 4. Subjects must have chronic (greater than 14 days) symptoms of limb ischemia, determined by clinical symptoms of Rutherford class 4-5, rest pain (R 4), and/or minor tissue loss (R5), that in the opinion of the investigator are not amenable to conservative medical therapy and require endovascular intervention for alleviation of symptoms and tissue preservation. 5. For subjects with bilateral disease, planned treatment of the contralateral limb must either be performed greater than or equal to 3 days prior to the index procedure or greater than or equal to 7 days following the index procedure. **Angiographic Inclusion Criteria**: 1. Stenotic, restenotic, or occlusive lesions located in the infrapopliteal vessels, with target lesion that can be successfully crossed via the true lumen with a guidewire (no subintimal crossing). 2. Iliac, SFA and popliteal inflow lesions can be treated using standard of care during the index procedure. *Note:* a) Inflow lesions treated intraprocedure must be treated first, prior to consideration of treatment of infrapopliteal lesions. b) Treatment of in-stent restenosis in inflow treatment is permitted, provided that stents are not fractured or otherwise compromised. c) Distal embolic protection is strongly encouraged in cases where atherectomy is used. d) Inflow lesions must have a healthy vessel segment of greater than 30 mm between the study lesion and the treated segment, defined as less than 50% stenosis without aneurysmal segments. e) Inflow treatment must be successful, prior to treatment of the target lesion, resulting in stenosis less than or equal to 30%, without

	resulting flow limiting dissection, thrombus, or aneurysm by angiography. 3. Target vessel(s) reconstitute(s) at or above the ankle, with the target treated segment ending at least 10 mm above the ankle joint. *Note*: a) If the anterior tibial or posterior tibial arteries are treated, there must be inline flow to the foot. b) If the peroneal artery is treated, there must be at least one collateral supplying the foot. c) In all cases, patent runoff (no lesions with greater than 50% stenosis) must be present via the dorsalis pedis and/or plantar arteries 4. Target lesion must be located in the tibial arteries. If vessel sizing remains appropriate, treatment may extend into the distal popliteal (P3) segment. 5. Target vessel reference diameter is measured to be between 2.5 to 4.5 mm in diameter assessed by one of the following methods after successful completion of guidewire crossing of the lesion site: a. Intravascular Ultrasound (IVUS) (primary) b. Visual estimate using Angiography (secondary) 6. Target lesion length is less than or equal to 210mm in length. Tandem lesions that are less than or equal to 4 cm should be treated as one lesion. Multiple discrete lesions may be treated provided cumulative length is less than or equal to 210 mm. 7. Successful predilatation of the target lesion without resulting flow limiting dissection, thrombus, or aneurysm by angiography prior to the insertion of the Bare Temporary Spur Stent System. 8. Only one limb and one contiguous vessel may be enrolled per subject. If required, a second modality may be used for treatment in the non-target infrapopliteal vessel. Note: a) Distal embolic protection is strongly recommended in cases using atherectomy. b) Treatment of the target vessel/lesion may be performed only if treatment of the non-target lesion is successful without resulting flow limiting (Type D or greater) dissection, thrombus, or aneurysm by angiography.

	c) Treatment of non-target lesions must be parallel to, and not contiguous with, the target lesion. 9. If pre-screening with duplex ultrasound, angiography, CTA, or MRA has been performed less than or equal to 365 days prior to the procedure, intra-procedure angiography of the aorto-iliac vasculature is not required, however, the femoropopliteal inflow must still be imaged using angiography during the index procedure. 10. Retrograde access (in the infrapopliteal arteries) is permitted for lesion crossing; however, the Bare Temporary Spur Stent System must be deployed from antegrade (above the knee, either ipsilateral or contralateral) access.
Exclusion Criteria:	**Pre-procedure Exclusion Criteria:** 1. Subject unwilling or unlikely to comply with the 1-year duration of the study in the opinion of the investigator. 2. Subject is pregnant or planning to become pregnant during the course of the trial. 3. Subject has an active systemic infection that is not controlled at the time of the procedure, including septicemia or bacteremia. 4. Subject has osteomyelitis proximal to the phalanges. Osteomyelitis in the digit(s) of the target foot is permitted. 5. Wounds must be confined to the foot below the ankle. Heel wounds are excluded. 6. Planned major (above the ankle) amputation of the target limb. A planned or previous minor (trans metatarsal amputation or digit amputation) is permitted. 7. Myocardial infarction (MI) or stroke within 90 days prior to the index procedure. 8. Symptomatic acute heart failure NYHA class III or greater. 9. Impaired renal function (eGFR less than or equal to 25 mL/min) within 30 days of procedure or end stage renal disease on dialysis. 10. Inability to tolerate dual antiplatelet and/or anticoagulation therapy, including a history of severe bleeding or coagulopathy. 11. Known allergies or sensitivities to heparin, antiplatelet drugs, other anticoagulant therapies which could not be

	substituted, or an allergy to contrast media that cannot be adequately pre-treated prior to the index procedure. 12. The subject is currently enrolled in another investigational device or drug trial that interferes with the study endpoints. 13. Known allergy to nitinol or nickel. 14. Bypass surgery of the target vessel(s). Prior bypass above the level of the infrapopliteal arteries is permitted. **Angiographic Exclusion Criteria** 1. Target lesion is located within an aneurysm or associated with an aneurysm in the vessel segment either proximal or distal to the target lesion. Inflow must also be free of aneurysmal segments. 2. Fractured or otherwise compromised stents or dissection repair devices in the target vessel or inflow vessel. 3. In-stent restenosis in the target vessel, including restenosis of dissection repair devices. 4. Previous treatment of the target vessel less than or equal to 90 days prior to index procedure. 5. Angiographic evidence of thrombus within target limb. 6. Extremely severe calcification that, in the investigator's opinion, would not be amenable to PTA. 7. Type D dissections or greater incurred during CTO crossing (see Appendix I for definitions). 8. Significant (greater than or equal to 50%) stenosis of inflow arteries or unsuccessful treatment of inflow lesions. 9. Distance from access to lesion is too long for a 135 cm working length of the Bare Temporary Spur Stent System catheter.
Analysis Plan	**Primary Efficacy Endpoint** The primary efficacy endpoint hypothesis is that technical success (defined as <30% residual stenosis in subjects treated with the Bare Temporary Spur Stent System) meets a performance goal [redacted] based on historical technical success rates with percutaneous transluminal balloon angioplasty (PTA) for below-the-knee infrapopliteal artery disease. A sample size of 130 evaluable subjects provides [redacted] power to demonstrate that the PG has been met at a 1-sided alpha of 0.05 using the Exact Binomial Test, assuming that the observed

technical success in Bare Temporary Spur Stent System treated subjects [redacted]

The primary analysis will be performed in the Full Analysis Set (FAS), defined as all subjects enrolled in the study and treated with the study device.

A secondary analysis will be performed in the Per Protocol (PP) analysis set, defined as all FAS subjects in whom the Bare Temporary Spur Stent System was used to treat at least one lesion and who did not have major protocol deviations.

Co-Primary Safety Endpoint

The primary safety endpoint hypothesis is that the primary safety endpoint of freedom from composite of MALE and POD at 30 days in subjects treated with the Bare Temporary Spur Stent System meets a PG of [redacted] based on historical outcomes with PTA for below-the-knee infrapopliteal artery disease.

A sample size of 123 evaluable subjects would provide [redacted] power to demonstrate that the PG has been met at a 1-sided alpha of 0.05 using the Exact Binomial Test, assuming that the observed freedom from composite of MALE and POD in Bare Temporary Spur Stent System treated subjects is [redacted]. With 130 total subjects, the sample size allows for up to [redacted] loss to follow-up at 30 days.

The primary safety analysis will be performed in the FAS. A secondary analysis will be performed in the PP analysis set.

Study success requires that the PG is met for both primary endpoints.

Secondary Powered Efficacy Endpoint

If both primary endpoints are met, the secondary powered efficacy endpoint of limb salvage and primary patency at 6 months will be tested sequentially. The secondary powered efficacy endpoint hypothesis is that secondary efficacy endpoint of limb salvage and primary patency at 6 months in subjects treated with the Bare Temporary Spur Stent System meets a PG of [redacted].

A sample size of [redacted] demonstrate that the PG has been met at a 1-sided alpha of 0.05 using the Exact Binomial Test, assuming that the observed limb salvage and primary patency rate in Bare Temporary Spur Stent System treated subjects is [redacted]. With

	130 total subjects, the sample size allows for up to [redacted] The primary analysis will be performed in the FAS analysis set. A secondary analysis will be performed in the PP analysis set. **Other Secondary Endpoints** All other secondary endpoints will be reported using appropriate descriptive statistics. In general, statistics for continuous variables will include mean, median, quartiles, standard deviation, minimum, maximum, and sample size. Categorical variables will be summarized using frequencies, percentages, and sample size. The primary analysis population for secondary endpoints is the FAS. **Interim Analysis** An interim analysis for futility is planned when 50% of subjects have reached 30 days follow-up. [redacted]
Measurements and Procedures:	Visit 1 (baseline visit; may be combined with index procedure), will consist of: • Inclusion and Exclusion criteria (pre-procedure) • Ankle Brachial Index (ABI) and Toe Brachial Index (TBI) • Medical History, including medications • Wound evaluation, including pictures if applicable • Rutherford score • Vital signs • VascuQOL-25 • EQ-5D • Blood draw (within 30 days prior to the procedure), including creatinine, eGFR, platelet count, white blood cell count, hemoglobin, and pregnancy (if applicable) Visit 2 (index procedure), will consist of: • Inclusion and Exclusion criteria (angiographic) • Interventional procedure

	• Initiation of dual antiplatelet therapy (DAPT), if not already started • Adverse event assessment • Device deficiency assessment Visit 3a [2 weeks] (for Rutherford 5 subjects only), will consist of: • Wound evaluation, including pictures • Adverse event assessment Visits 3b-6 (1, 3, 6, 12 months), will consist of: • Ankle Brachial Index (ABI) and Toe Brachial Index (TBI) • Medications, including DAPT • Wound evaluation, including pictures, if applicable • Rutherford score • Adverse event assessment • VascuQOL-25 at 1, 6, 12 months • EQ-5D at 1, 6, 12, months • Blood draw within 1 month post-procedure, including creatinine, eGFR, hemoglobin level, white blood cell count, and platelet level. • Duplex ultrasound of index limb at 1, 3, 6, and 12 months ***NOTE:** Subjects in whom Bare Temporary Spur Stent System was introduced, but was not ultimately used to treat a lesion, will be followed to 30 days for safety.
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