A Prospective, Multi-Center, Single-Arm Study to Assess the Safety and Performance of the Surmodics Drug Coated Balloon in the Treatment of Subjects with Obstructive Lesions of Arteriovenous Fistulae for Hemodialysis, Including Native or Synthetic Grafts (AVess FIH Study)

CLINICAL PROTOCOL SUR18-001

Version: 2.0

Date: 15 January 2020

Investigational Device: Surmodics SurVeil™ Drug Coated Balloon (SurVeil DCB)

Sponsored By

Surmodics, Inc.

9924 West 74th Street

Eden Prairie, MN 55344 USA

Protocol Synopsis

<table>
<tr><td>Sponsor</td><td>Surmodics, Inc.</td></tr>
<tr><td>Protocol Title</td><td>A Prospective, Multi-Center, Single-Arm Study to Assess the Safety and Performance of the Surmodics Drug Coated Balloon in the Treatment of Subjects with Obstructive Lesions of Arteriovenous Fistulae for Hemodialysis, Including Native or Synthetic Grafts (AVess FIH Study)</td></tr>
<tr><td>Protocol Number</td><td>SUR18-001</td></tr>
<tr><td>Test Device</td><td>SurVeil™ Drug Coated Balloon (SurVeil DCB)</td></tr>
<tr><td>Device Sizes</td><td>
<table>
<tr><th rowspan="2">Working Length (cm)</th><th rowspan="2">Balloon diameter (mm)</th><th colspan="2">Balloon length (mm)</th><th rowspan="2">Rate Burst Pressure (atm)</th><th rowspan="2">Minimum Introducer</th></tr>
<tr><th>40</th><th>80</th></tr>
<tr><td rowspan="3">135</td><td>5.0</td><td>X</td><td>X</td><td>14</td><td>6Fr</td></tr>
<tr><td>6.0</td><td>X</td><td>X</td><td>12</td><td>6Fr</td></tr>
<tr><td>7.0</td><td>X</td><td>X</td><td>10</td><td>7Fr</td></tr>
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</td></tr>
<tr><td>Indication</td><td>The SurVeil DCB will be indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of obstructive lesions of native or synthetic arteriovenous dialysis fistulae.</td></tr>
<tr><td>Study Design</td><td>Prospective, multi-center, single arm, first-in-man feasibility study</td></tr>
<tr><td>Study Size</td><td>Up to 15 subjects will be enrolled in the study. At up to 3 sites in Australia, New Zealand and/or Europe.</td></tr>
<tr><td>Study Population</td><td>Subjects with obstructive lesion of native arm arteriovenous fistulae for hemodialysis intended with treatment with balloon angioplasty.</td></tr>
<tr><td>Study Purpose</td><td>To evaluate the safety and performance of the SurVeil DCB in subjects with obstructive lesions of arteriovenous fistulae for hemodialysis.</td></tr>
<tr><td>Study Endpoints</td><td>Primary Endpoints:
1. Target Lesion Primary Patency at 6 months post procedure

Secondary Endpoints:
1. Absence of all-cause death up to 30 days.
2. Rate of device and procedure related adverse events through 30 days.
3. Secondary Patency: defined as supporting hemodialysis with a pump speed of at least 300ml/min through 6 months.
4. Patency of Target Lesion as defined by duplex ultrasound at 30 days, 6 months, 9 months and 1 year.
5. Number of interventions required to maintain target lesion patency at 30 days, 6 months, 9 months and 1 year.</td></tr>
<tr><td>Statistical Considerations</td><td>The sample size for this feasibility study is based on clinical considerations and not power requirements for a formal statistical hypothesis test. All calculated p-values will be nominal. The data from this FIH study will be utilized to inform the sample size for future larger studies.</td></tr>
<tr><td>Inclusion Criteria</td><td>1. Subjects must be ≥18 years of age.
2. Native AV fistula has been created ≥60 days prior to the index procedure.
3. AV fistula, located in the arm, has undergone one or more successful hemodialysis sessions.</td></tr>
</table>

	4. Target de novo or non-stented restenotic lesion consisting of a ≥50% stenosis by operator visual estimate. 5. Fistula vessel diameter ≥5 mm and ≤7 mm by operator visual estimate. 6. Target lesion or tandem lesion ≤120 mm in total length by operator visual estimate. NOTE: Only 2 tandem lesions permitted. Tandem lesions must be able to be treated as a single lesion and separated by a gap of ≤30 mm. The total combined lesion length including the gap must be ≤120 mm in length by operator visual estimate. 7. Successful pre-dilatation of the target lesion. Defined as crossing of the guide wire AND pre-dilatation with a PTA balloon resulting in: a. Residual stenosis of ≤30%, AND b. Dissection ≤ Grade B 8. Subject has provided written informed consent and is willing to comply with study follow-up requirements. 9. Subject has a life expectancy of ≥1 year.
Exclusion Criteria	1. Subject has a synthetic AV graft. 2. Determined by operator to have a lesion that prevents complete inflation of an angioplasty balloon. 3. Presence of pseudoaneurysm or aneurysm requiring treatment at the lesion site. 4. Target lesion is located <30 mm from any stent. 5. Thrombosis of the access site 30 days prior to procedure. 6. Surgical revision of the access site planned within 30 days of procedure. 7. Blood coagulative disorder, sepsis, or current AV access infection (white blood count ≥12,000). 8. Known contraindication (including allergic reaction) or sensitivity to antiplatelet therapy, anticoagulation therapy or paclitaxel (mild to severe cases), that cannot be adequately managed with pre-and post-procedure medication. 9. Subjects who are taking immunosuppressive therapy or are routinely taking ≥10mg of prednisone per day. 10. Scheduled for kidney transplant or peritoneal dialysis within the next 6 months post procedure. 11. Myocardial infarction 30 days prior to procedure. 12. Stroke or TIA 90 days prior to procedure. 13. Women who are pregnant, breast-feeding or intend to become pregnant or men who intend to father children during the time of the study. 14. Subject is participating in any other investigational study that has not completed primary endpoint(s) evaluation or that clinically interferes with the endpoint from this study.
Subject screening and enrollment process	Subjects with signed informed consent who meet ALL inclusion and NONE of the exclusion criteria and attempted treatment with investigational device will be considered enrolled into the study.
Follow-up Schedule	Preoperative, Intra-Procedure, Post-Procedure, 30 days and at 6, 12, 24, 36, 48, and 60 months.
Enrollment and Study Duration	The enrollment period is expected to last approximately 6 months and study duration isexpected to be approximately 66 months from study initiation.