Micro Therapeutics, Inc. d/b/a ev3 Neurovascular
Helen Chow, PhD, RAC
Senior Specialist, Regulatory Affairs
9775 Toledo Way
Irvine, California 92618

March 6. 2019

Re: K181807
Trade/Device Name: Solitaire™ 2 Revascularization Device, Solitaire™ Platinum Revascularization Device (Solitaire™ Revascularization Device)
Regulation Number: 21 CFR 882.5600
Regulation Name: Neurovascular Mechanical Thrombectomy Device for Acute Ischemic Stroke Treatment
Regulatory Class: Class II
Product Code: POL, NRY
Dated: February 1, 2019
Received: February 4, 2019

Dear Helen Chow, PhD, RAC:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal

statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

John Marler -S

Digitally signed by John Marler -S
Date: 2019.03.06 19:37:30 -05'00'

For Carlos L. Peña, PhD, MS
Director
Division of Neurological
and Physical Medicine Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K181807

Device Name
Solitaire™ 2 Revascularization Device, Solitaire™ Platinum Revascularization Device
(Solitaire™ Revascularization Device)

Indications for Use *(Describe)*

1. The Solitaire™ Revascularization Device is indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion, and smaller core infarcts who have first received intravenous tissue plasminogen activator (IV t-PA). Endovascular therapy with the device should be started within 6 hours of symptom onset.

2. The Solitaire™ Revascularization Device is indicated to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset. Patients who are ineligible for IV t-PA or who fail IV t-PA therapy are candidates for treatment.

3. The Solitaire™ Revascularization Device is indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion of the internal carotid artery (ICA) or middle cerebral artery (MCA)-M1 segments with smaller core infarcts (< 70 cc by CTA or MRA, < 25 cc by MR-DWI). Endovascular therapy with the device should start within 6-16 hours of time last seen well in patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(K) Summary - K181807

510(k) Owner:	Micro Therapeutics, Inc. d/b/a ev3 Neurovascular 9775 Toledo Way Irvine, CA 92618 Establishment Registration No. 2029214
Contact Person:	Jennifer Correa Program Manager, Regulatory Affairs Telephone: (949) 297-5494 E-mail: jennifer.l.correa@medtronic.com
Alternate Contact:	Helen Chow Sr. Specialist, Regulatory Affairs Telephone: (949) 297-5474 E-mail: helen.h.chow@medtronic.com
Date Summary Prepared:	March 5, 2019
Trade Name of Device:	Solitaire™ 2 Revascularization Device, Solitaire™ Platinum Revascularization Device (Solitaire™ Revascularization Device)
Common Name of Device:	Neurovascular Mechanical Thrombectomy Device for Acute Ischemic Stroke Treatment
Classification of Device:	Class II, 21 CFR 882.5600, 21 CFR 870.1250
Product Code:	POL, NRY
Predicate Devices:	Solitaire™ 2 Revascularization Device (K162539),
Reference Devices:	Solitaire™ Platinum Revascularization Device (K153071, K160641, K161879)

Device Description:

The Solitaire™ Revascularization Device is designed to restore blood flow in patients experiencing ischemic stroke due to large intracranial vessel occlusion in the neurovasculature such as the Internal Carotid Artery (ICA), M1 and M2 segments of the middle cerebral artery, basilar, and the vertebral arteries. The distal nitinol portion of the Solitaire™ Revascularization Device facilitates clot retrieval and has Platinum/Iridium radiopaque markers on the proximal and distal ends. The Solitaire™ Platinum Revascularization Device also features radiopaque markers along the circumference of the working length of the device. The devices are supplied sterile and intended for single-use only.

There have been no changes to the design of the Solitaire™ Revascularization Device from the currently cleared device (K153071, K160641, K161879, K162539) to support the proposed additional indication. The currently cleared Solitaire™ 2 Revascularization Device is used as a predicate device and the Solitaire™ Platinum Revascularization Devices are used as a reference device for previously completed bench, animal, and clinical data.

Indications for Use:

1. The Solitaire™ Revascularization Device is indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion, and smaller core infarcts who have first received intravenous tissue plasminogen activator (IV t-PA). Endovascular therapy with the device should be started within 6 hours of symptom onset.
2. The Solitaire™ Revascularization Device is indicated to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset. Patients who are ineligible for IV t-PA or who fail IV t-PA therapy are candidates for treatment.
3. The Solitaire™ Revascularization Device is indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion of the internal carotid artery (ICA) or middle cerebral artery (MCA)-M1 segments with smaller core infarcts (< 70 cc by CTA or MRA, < 25 cc by MR-DWI). Endovascular therapy with the device should start within 6-16 hours of time last seen well in patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy.

Device Comparison:

A comparison of the technological characteristics of the subject Solitaire™ Revascularization Device and the predicate Solitaire™ 2 Revascularization Device (K162539) is provided in **Table 1**. The subject Solitaire™ Revascularization device is identical to the predicate Solitaire™ 2 Revascularization Device and reference Solitaire™ Platinum Revascularization Device, apart from the expanded indications for use.

Table 1: Device Comparison

	Predicate Solitaire™ 2 Revascularization Device (K162539)	**Subject Solitaire™ Revascularization Device**	**Rationale for Difference (if applicable)**
Indication for Use	1. The Solitaire™ Revascularization Device is indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion, and smaller core infarcts who have first received intravenous tissue plasminogen activator (IV t-PA). Endovascular therapy with the device should be started within 6 hours of symptom onset.	1. The Solitaire™ Revascularization Device is indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion, and smaller core infarcts who have first received intravenous tissue plasminogen activator (IV t-PA). Endovascular therapy with the device should be started within 6 hours of symptom onset.	The DEFUSE 3 study data analysis has demonstrated that the expanded indications for use does not raise any new or different questions of safety or effectiveness.

Table 1: Device Comparison			
	Predicate Solitaire™ 2 Revascularization Device (K162539)	**Subject Solitaire™ Revascularization Device**	**Rationale for Difference (if applicable)**
	2. The Solitaire™ Revascularization Device is indicated to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset. Patients who are ineligible for IV t-PA or who fail IV t-PA therapy are candidates for treatment.	2. The Solitaire™ Revascularization Device is indicated to restore blood flow by removing thrombus from a large intracranial vessel in patients experiencing ischemic stroke within 8 hours of symptom onset. Patients who are ineligible for IV t-PA or who fail IV t-PA therapy are candidates for treatment. 3. The Solitaire™ Revascularization Device is indicated for use to restore blood flow in the neurovasculature by removing thrombus for the treatment of acute ischemic stroke to reduce disability in patients with a persistent, proximal anterior circulation, large vessel occlusion of the internal carotid artery (ICA) or middle cerebral artery (MCA)-M1 segments with smaller core infarcts (< 70 cc by CTA or MRA, < 25 cc by MR-DWI). Endovascular therapy with the device should start within 6-16 hours of time last seen well in patients who are ineligible for intravenous tissue plasminogen activator (IV t-PA) or who fail IV t-PA therapy.	
Principles of Operation	The device is used in the neurovasculature to restore blood flow for treatment of acute ischemic stroke	Same	N/A
Dimensions and Materials			
Device Size(s)	4-15 mm 4-20 mm 4-40 mm 6-20 mm 6-30 mm	4-15 mm 4-20 mm 4-40 mm 6-20 mm 6-30 mm 4-20-05 mm 4-20-10 mm 4-40-10 mm 6-20-10 mm 6-24-06 mm	The subject device includes sizes cleared in both the predicate Solitaire™ 2 and reference Solitaire™ Platinum Revascularization Device

Table 1: Device Comparison			
	Predicate Solitaire™ 2 Revascularization Device (K162539)	**Subject Solitaire™ Revascularization Device**	**Rationale for Difference (if applicable)**
		6-40-10 mm	
Device Materials	Stent: Nitinol Pushwire: Nitinol Markers: 90% Platinum/ 10% Iridium Push-wire shrink Tubing: PTFE Introducer Sheath: PTFE/Grilamid	Same	N/A
Sterilization and Packaging			
Packaging Materials	Stored within dispenser coil, Tyvek pouch, and shipping carton.	Same	N/A
Sterilization Method	Ethylene Oxide	Same	N/A
How Supplied	Sterile, Single Use	Same	N/A

Leveraged Non-Clinical Data:

There are no changes to the subject Solitaire™ Revascularization Device in design, manufacturing process, sterilization, material formulation, principles of operation, or fundamental scientific technology. The only change is the expanded Indications for Use. Therefore, no new or additional non-clinical testing was required or performed.

Performance Testing – Clinical:

Clinical data from the Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke (DEFUSE 3) study[1] was used to support the expanded indication for the subject Solitaire™ Revascularization Device. The DEFUSE 3 study allowed the use of various cleared endovascular therapy devices. To support substantial equivalence of the subject Solitaire™ Revascularization Device, a sub-analysis of the DEFUSE 3 study data was performed and was limited to subjects treated with the Solitaire™ Revascularization Device in the endovascular plus standard medical therapy (endovascular therapy group) vs. those treated with standard medical therapy alone (control/medical-therapy group).

Study Design

The DEFUSE 3 study was a multicenter, randomized, open-label trial, with blinded outcome assessment, of thrombectomy in subjects 6 to 16 hours after they were last known to be well and who had remaining ischemic brain tissue that was not yet infarcted. Subjects with proximal middle-cerebral-artery or internal-carotid-artery occlusion, an initial infarct size of less than 70 ml, and a ratio of the volume of ischemic tissue on perfusion imaging to infarct volume of 1.8 or more were randomly assigned to endovascular therapy (thrombectomy) plus standard medical therapy (endovascular-therapy group) or standard medical therapy alone (control/medical-therapy group). The primary outcome was the ordinal score on

[1]Albers GW, Marks MP, Kemp S, et al. Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging. *The New England journal of medicine.* Feb 22 2018;378(8):708-718.

the modified Rankin scale (range, 0 to 6, with higher scores indicating greater disability) at day 90.

Sample Size

The DEFUSE 3 Study was designed to assess the safety and effectiveness of endovascular therapy using FDA cleared mechanical thrombectomy devices, and was not designed to assess a specific neurothrombectomy device. The DEFUSE 3 study included a total of 182 subjects (92 in the endovascular therapy group and 90 in the control group). Solitaire was the first device used amongst all mechanical thrombectomy devices for 38 subjects in the endovascular therapy group.

Statistical Analysis

A subgroup analysis was conducted including all subjects randomized to endovascular intervention and in whom Solitaire was the first device used amongst all mechanical thrombectomy devices, and all subjects randomized to the control group. Results between the two groups thus defined were summarized and compared, including formal statistical hypothesis testing on the primary efficacy endpoint.

All analyses were carried out consistent with the principle of intention-to-treat in that the randomized assignments in DEFUSE 3 as a whole were preserved in making group assignments, and in whom Solitaire was the first device used amongst all mechanical thrombectomy devices (that is, intention-to-treat with Solitaire) constitute the Analysis Cohort. The intention-to-treat (ITT) Analysis Cohort is thus comprised of 90 in the control group and 38 in the Solitaire group.

The DEFUSE 3 study allowed IV t-PA use beyond 3 hours, although IV t-PA is not approved in the United States beyond 3 hours. A total of 11 subjects (5 from the control group and 6 from the Solitaire group) were excluded from the primary and secondary efficacy endpoint analyses due to receiving IV t-PA beyond 3 hours and/or carotid stenting. Therefore, the primary and secondary efficacy endpoint analyses consist of 117 subjects (Analysis Cohort - mITT). In the mITT Analysis Cohort, subjects with multiple interventions (n=8) were treated as failures. All analyses presented for the Analysis Cohort (ITT and mITT) are post-hoc analyses. As such, there may be uncertainty in the interpretation of the clinical study results and any statistically meaningful conclusions due to the post-hoc nature of the analyses, limitations in sample size, and lack of pre-specified hypothesis testing.

Study Endpoints

The primary efficacy outcome was the ordinal score on the modified Rankin scale (range, 0 [no symptoms] to 6 [death]) at day 90. The primary safety outcomes were death within 90 days and the occurrence of symptomatic intracranial hemorrhage (sICH) within 36 hours, defined as an increase of at least 4 points in the NIHSS score that was associated with brain hemorrhage on imaging within 36 hours after symptom onset.

Imaging outcomes were:

- infarct volume measured at 24 hours (with a window of ± 6 hours) after randomization;
- lesion growth (increase in volume of the infarct) between baseline imaging and 24 hours;

- reperfusion, defined as a greater than 90% reduction in the region of perfusion delay (Tmax of > 6 seconds) between baseline and 24 hours; and
- complete recanalization of the primary arterial occlusive lesion at 24 hours on CTA or MRA.

The technical efficacy of the endovascular procedure in establishing reperfusion was defined in the endovascular-therapy group by a modified Thrombolysis in Cerebral Infarction (mTICI) score of 2b (50 to 99% reperfusion) or 3 (complete reperfusion).

Inclusion Criteria

Clinical inclusion criteria:

1. Signs and symptoms consistent with the diagnosis of an acute anterior circulation ischemic stroke
2. Age 18-90 years
3. Baseline NIHSS is ≥ 6 and remains ≥ 6 immediately prior to randomization
4. Endovascular treatment can be initiated (femoral puncture) between 6 and 16 hours of stroke onset. Stroke onset is defined as the time the patient was last known to be at their neurologic baseline (wake-up strokes are eligible if they meet the above time limits).
5. Modified Rankin Scale (mRS) less than or equal to 2 prior to qualifying stroke (functionally independent for all ADLs)
6. Patient/Legally Authorized Representative has signed the Informed Consent form.

Neuroimaging inclusion criteria:

- ICA or MCA-M1 occlusion (carotid occlusions can be cervical or intracranial; with or without tandem MCA lesions) by MRA or CTA

AND

- Target Mismatch Profile on CT perfusion or MRI (ischemic core volume is < 70 ml, mismatch ratio is > 1.8 and mismatch volume* is > 15 ml)

*Notes: The mismatch volume is determined by the RAPID software in real time based on the difference between the ischemic core lesion volume and the Tmax > 6s lesion volume. If both a CT perfusion and a multimodal MRI scan are performed prior to enrollment, the later of the 2 scans is assessed to determine eligibility. Only an intracranial MRA is required for patients screened with MRA; cervical MRA is not required. Cervical and intracranial CTA are typically obtained simultaneously in patients screened with CTA, but only the intracranial CTA is required for enrollment.

Alternative neuroimaging inclusion criteria (if perfusion imaging or CTA/MRA is technically inadequate):

A. If CTA (or MRA) is technically inadequate:
   Tmax>6s perfusion deficit consistent with an ICA or MCA-M1 occlusion

AND

   Target Mismatch Profile (ischemic core volume is < 70 ml, mismatch ratio is >1.8 and mismatch volume is >15 ml as determined by RAPID software)

B. If MRP is technically inadequate:

ICA or MCA-M1 occlusion (carotid occlusions can be cervical or intracranial; with or without tandem MCA lesions) by MRA (or CTA, if MRA is technically inadequate and a CTA was performed within 60 minutes prior to the MRI)

AND

MR Diffusion Weighted Imaging (DWI) lesion volume < 25 ml

C. If CTP is technically inadequate:
Patient can be screened with MRI and randomized if neuroimaging criteria are met.

Exclusion Criteria

Clinical exclusion criteria:

- Other serious, advanced, or terminal illness (investigator judgment) or life expectance is less than 6 months.
- Pre-existing medical, neurological or psychiatric disease that would confound the neurological or functional evaluations
- Pregnant
- Unable to undergo a contrast brain perfusion scan with either MRI or CT
- Known allergy to iodine that precludes an endovascular procedure
- Treated with t-PA > 4.5 hours after time last known well
- Treated with t-PA 3-4.5 hours after last known well AND any of the following: age > 80, current anticoagulant use, history of diabetes AND prior stroke, NIHSS >25
- Known hereditary or acquired hemorrhagic diathesis, coagulation factor deficiency; recent oral anticoagulant therapy with INR > 3 (recent use of one of the new oral anticoagulants is not an exclusion if estimated GFR > 30 ml/min).
- Seizures at stroke onset if it precludes obtaining an accurate baseline NIHSS
- Baseline blood glucose of < 50 mg/dL (2.78 mmol) or > 400mg/dL (22.20 mmol)
- Baseline platelet count < 50,000/uL
- Severe, sustained hypertension (Systolic Blood Pressure >185 mmHg or Diastolic Blood Pressure > 110 mmHg)
- Current participation in another investigational drug or device study
- Presumed septic embolus; suspicion of bacterial endocarditis
- Clot retrieval attempted using a neurothrombectomy device prior to 6 hours from symptom onset
- Any other condition that, in the opinion of the investigator, precludes an endovascular procedure or poses a significant hazard to the subject if an endovascular procedure was performed

Neuroimaging exclusion criteria:

- ASPECT score < 6 on non-contrast CT (if patient is enrolled based on CT perfusion criteria)
- Evidence of intracranial tumor (except small meningioma) acute intracranial hemorrhage, neoplasm, or arteriovenous malformation
- Significant mass effect with midline shift
- Evidence of internal carotid artery dissection that is flow limiting or aortic dissection
- Intracranial stent implanted in the same vascular territory that precludes the safe deployment/removal of the neurothrombectomy device

- Acute symptomatic arterial occlusions in more than one vascular territory confirmed on CTA/MRA (e.g., bilateral MCA occlusions, or an MCA and a basilar artery occlusion).

Demographic and other Baseline Characteristics (Analysis Cohort - ITT)

Subject demographics and baseline characteristics are presented in **Table 2**. Subject age, gender, race, ethnicity, baseline NIHSS, systolic blood pressure and diastolic blood pressure did not differ significantly between the Solitaire and control groups. Median age was 71 years in each treatment group, while gender was similarly balanced with a total of 54% (69/128) females. The majority of the subject population was non-Hispanic and white. Baseline median NIHSS scores were 17 in the Solitaire group and 16 in control, indicating a moderate to severe stroke population.

Table 2: Demographics and Baseline Characteristics (Analysis Cohort - ITT)

Outcome	Solitaire Mean ± SD (N) [Median] (IQR) or % (n/N)	Control Mean ± SD (N) [Median] (IQR) or % (n/N)	p-value	All Mean ± SD (N) [Median] (IQR) or % (n/N)
Age (years)	68.2 ± 13.0 (38) [71.0] (58.3,76.8)	68.9 ± 13.4 (90) [71.0] (59.3,80.0)	0.797	68.7 ± 13.2 (128) [71.0] (59.0,79.0)
Gender			0.329	
Male	39.5% (15/38)	48.9% (44/90)		46.1% (59/128)
Female	60.5% (23/38)	51.1% (46/90)		53.9% (69/128)
Race			0.765	
American Indian or Alaska Native	0.0% (0/38)	1.1% (1/90)		0.8% (1/128)
Asian	2.6% (1/38)	3.3% (3/90)		3.1% (4/128)
Black or African American	10.5% (4/38)	5.6% (5/90)		7.0% (9/128)
White	86.8% (33/38)	88.9% (80/90)		88.3% (113/128)
Unknown	0.0% (0/38)	1.1% (1/90)		0.8% (1/128)
Ethnicity			0.266	
Hispanic or Latino	18.4% (7/38)	11.1% (10/90)		13.3% (17/128)
Not Hispanic or Latino	81.6% (31/38)	88.9% (80/90)		86.7% (111/128)
NIHSS at baseline	16.5 ± 5.4 (38) [17.0] (14.3,20.0)	16.9 ± 6.4 (90) [16.0] (12.0,21.0)	0.749	16.7 ± 6.1 (128) [17.0] (12.0,21.0)
Systolic blood pressure (mmHg)	140.8 ± 23.7 (38) [139.5] (123.3,158.0)	145.5 ± 19.5 (90) [147.0] (130.5,159.0)	0.255	144.1 ± 20.9 (128) [146.0] (130.0,159.3)
Diastolic blood pressure (mmHg)	74.8 ± 12.9 (38) [74.0] (68.0,82.0)	79.3 ± 15.9 (90) [81.0] (67.0,88.8)	0.122	78.0 ± 15.1 (128) [77.0] (67.0,87.0)

Procedural Characteristics (Analysis Cohort - ITT)

Procedural characteristics are summarized in **Table 3**. Among both treatment groups, a majority of subjects were transferred to the endovascular enrolling hospital from an external facility. In the Solitaire group, IV t-PA was administered for 18.4% (7/38) of subjects and general anesthesia was administered in 36.8% (14/38) of subjects. The median time from arrival at the enrolling hospital to arterial puncture was 118.5 minutes, with a median of 65.5 minutes from imaging to arterial puncture. The median time from symptom onset to emergency department

(ED) arrival was 530.0 minutes. Workflow intervals between stroke onset and randomization, ED arrival, arterial puncture and reperfusion times are also provided.

Table 3: Procedural Characteristics (Analysis Cohort - ITT)		
Outcome	**Solitaire Mean ± SD (N) [Median] (IQR) or % (n/N)**	**Control* Mean ± SD (N) [Median] (IQR) or % (n/N)**
Transfer Subject	68.4% (26/38)	70.0% (63/90)
IV t-PA Administration	18.4% (7/38)	8.9% (8/90)
General Anesthesia	36.8% (14/38)	-
Onset to randomization (min)	631.2 ± 162.2 (38) [644.5] (474.5,742.0)	653.0 ± 153.5 (90) [644.5] (522.8,780.8)
Onset to arterial puncture (min)	667.9 ± 160.1 (38) [674.5] (527.8,778.0)	-
Time of onset to ED arrival (min)	520.7 ± 162.6 (38) [530.0] (405.5,637.8)	-
ED arrival to arterial puncture (min)	147.2 ± 120.8 (38) [118.5] (80.8,156.8)	-
Imaging to arterial puncture (min)	69.9 ± 31.3 (38) [65.5] (46.0,86.8)	-
Onset to reperfusion (min)	719.0 ± 167.5 (34) [708.0] (569.8,855.2)	-
*Note: Data provided for control group where available		

Primary Efficacy Outcomes

In the DEFUSE 3 endovascular-therapy group, treatment was associated with a favorable shift in the distribution of mRS scores at 90 days compared to the control group. Similarly, in the modified ITT Analysis Cohort, the Solitaire cohort shows a favorable shift in the distribution of mRS scores at 90 days compared to the control (p-value=0.014), as presented in **Table 4**. The shift toward better outcomes was consistent in direction across all levels of the mRS (**Figure 1**).

Table 4: Primary Effectiveness Endpoint (Analysis Cohort – mITT)			
mRS Score at 90 days	**Solitaire Mean ± SD (N) [Median] (IQR) or % (n/N)**	**Control Mean ± SD (N) [Median] (IQR) or % (n/N)**	**p-value**
-	3.2 ± 1.7 (32) [3.0] (2.0,4.0)	4.0 ± 1.8 (85) [4.0] (3.0,6.0)	0.014
0	6.2% (2/32)	8.2% (7/85)	
1	12.5% (4/32)	3.5% (3/85)	
2	12.5% (4/32)	3.5% (3/85)	
3	25.0% (8/32)	15.3% (13/85)	
4	21.9% (7/32)	27.1% (23/85)	
5	9.4% (3/32)	15.3% (13/85)	
6	12.5% (4/32)	27.1% (23/85)	-

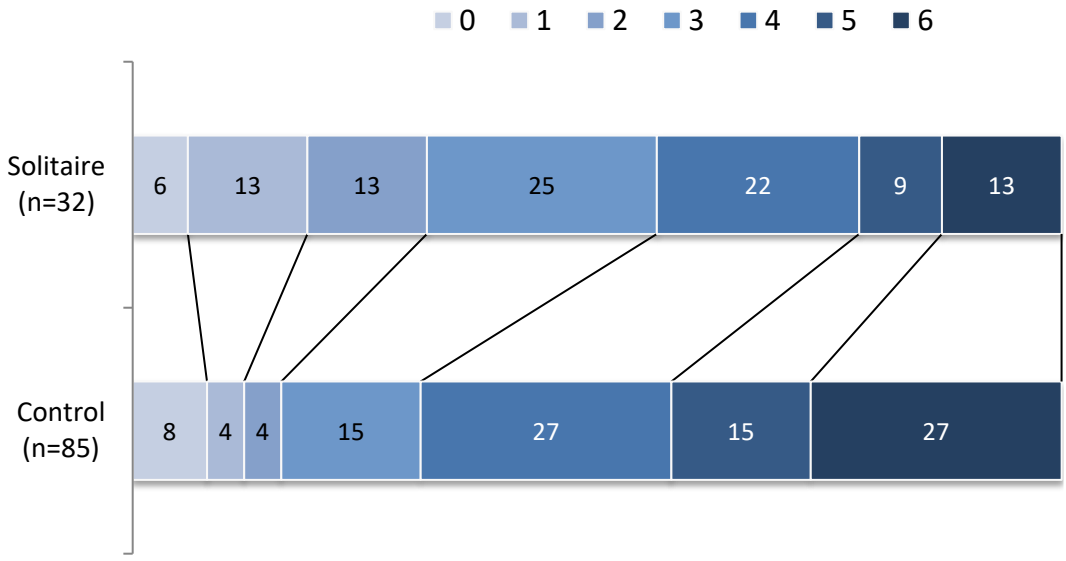

Figure 1: mRS at 90 days (Analysis Cohort – mITT)

Secondary Efficacy Outcome

The proportion of subjects functionally independent at 90 days (mRS 0-2) favors the Solitaire group over control (31.2% vs 15.3%). Results are presented in **Table 5**.

Table 5: Secondary Efficacy Endpoint, mRS 0-2 at 90 days (Analysis Cohort – mITT)		
Outcome	**Solitaire % (n/N)**	**Control % (n/N)**
Functional Independence (mRS 0-2) at 90 days	31.2% (10/32)	15.3% (13/85)

Additional Efficacy, Imaging and Technical Efficacy Outcomes

Early neurological improvement was defined as a > 8-point improvement in NIHSS from baseline to the 24-hour visit, or an NIHSS score of 0-1 attained at the 24-hour visit irrespective of the baseline value of NIHSS. Results are presented in **Table 6**.

Table 6: Early neurological improvement at 24 Hours (Analysis Cohort – ITT)		
Outcome	**Solitaire % (n/N)**	**Control % (n/N)**
Early neurological improvement	31.6% (12/38)	5.6% (5/89*)
*Note: NIHSS at 24 hours, which is needed to compute early neurological improvement, was available for 89 of 90 subjects in the control group.		

In the Solitaire group, arterial reperfusion as measured by the modified TICI score by the central reader, was assessed immediately post-procedure. Results are presented in **Table 7**.

Table 7: TICI Immediate Post-Procedure* (Analysis Cohort – mITT)	
Outcome	**Solitaire % (n/N)**
TICI post-procedure (central reading)	
0	21.9% (7/32)
2a	12.5% (4/32)
2b	43.8% (14/32)
3	21.9% (7/32)
TICI≥2b post-procedure	65.6% (21/32)
*TICI was not assessed for Control Group immediately post-procedure	

Reperfusion was analyzed both as a continuous metric and dichotomized to define successful reperfusion (> 90% reperfused) at 24 hours post-procedure. Complete recanalization of the primary arterial occlusive lesion was assessed on CTA or MRA at 24 hours post-procedure. Results are presented in **Table 8**.

Table 8: Reperfusion and Recanalization 24 hours Post-Procedure* (Analysis Cohort – mITT)		
Outcome	**Solitaire Mean ± SD (N) [Median] (IQR) or % (n/N)**	**Control Mean ± SD (N) [Median] (IQR) or % (n/N)**
Reperfusion rate (%)	92.6 ± 20.2 (24) [100.0] (99.0,100.0)	48.7 ± 46.0 (63) [53.8] (24.7,84.7)
Successful reperfusion (>90%)	83.3% (20/24)	17.5% (11/63)
Complete recanalization at 24h	82.8% (24/29)	19.2% (14/73)
* Results are presented for subjects in the mITT analysis cohort with available data. Reperfusion percentage and successful reperfusion were available on 24 of 32 subjects in the Solitaire group, and 63 of 85 subjects in the control group. Complete recanalization was available on 29 of 32 subjects in the Solitaire group and 73 of 85 subjects in the control group.		

Additional imaging endpoints at 24 hours post procedure were assessed by the core lab and are presented in **Table 9**.

Table 9: Imaging Endpoints (Analysis Cohort – ITT)		
Imaging Outcomes*	**Solitaire Mean ± SD (N) [Median] (IQR)**	**Control** Mean ± SD (N) [Median] (IQR)**
Infarct volume (ml) at 24h per core lab	64.5 ± 67.2 (38) [35.0] (18.6,81.2)	74.3 ± 80.7 (89) [41.0] (25.4,106.2)
Infarct growth (ml) at 24h per core lab	48.6 ± 61.4 (38) [19.9] (3.4,79.9)	57.6 ± 70.6 (89) [32.8] (18.3,74.8)
Tmax6 volume (ml) at 24h per core lab	9.2 ± 32.5 (30) [0.0] (0.0,0.0)	59.5 ± 59.6 (68) [46.6] (11.1,78.7)

*Measured by Rapid Software

**One subject in the control group was missing imaging data 24-hours post-procedure.

Primary Safety Outcomes

All-cause mortality at the 90-day follow-up visit was less frequent in the Solitaire group compared to control (10.5% vs 25.6%). The rate of sICH was low in both study groups, with a rate of 2.6% (1/38) with Solitaire and 4.4% (4/90) in control. Results are presented in **Table 10**.

Table 10: Primary Safety Outcomes (Analysis Cohort – ITT)		
Outcome	**Solitaire % (n/N)**	**Control % (n/N)**
All-cause mortality	10.5% (4/38)	25.6% (23/90)
Symptomatic ICH	2.6% (1/38)	4.4% (4/90)

Additional Important Safety Results

Procedural complications for the Solitaire group were reported by the clinical site and are presented in **Table 11**.

Table 11: Procedural Complications (Analysis Cohort – ITT)	
Outcome	**Solitaire % (n/N)**
Arterial dissection (per site)	0.0% (0/38)
Access site complication requiring surgical repair or transfusion (per site)	0.0% (0/38)
Embolization to previously unaffected territory (per site)	0.0% (0/38)
Vessel perforation (per site)	2.6% (1/38)

Adverse events observed during the study were reported and coded via the MedDRA classification system and are presented in **Table 12** through **Table 14**.

Table 12: Procedure Related Adverse Events by MedDRA Classification (Analysis Cohort – ITT)		
System Organ Class	**Solitaire % (n/N) [events]**	**Control % (n/N) [events]**
TOTAL	28.9% (11/38) [14]	4.4% (4/90) [4]
Cardiac disorders	2.6% (1/38) [1]	1.1% (1/90) [1]
Injury, poisoning and procedural complications	2.6% (1/38) [1]	-
Nervous system disorders	23.7% (9/38) [10]	1.1% (1/90) [1]
Vascular disorders	5.3% (2/38) [2]	-
General disorders and administration site conditions	-	1.1% (1/90) [1]
Investigations	-	1.1% (1/90) [1]

Table 13: All Adverse Events by MedDRA Classification (Analysis Cohort – ITT)		
System Organ Class	**Solitaire % (n/N) [events]**	**Control % (n/N) [events]**
TOTAL	78.9% (30/38) [97]	86.7% (78/90) [229]
Blood and lymphatic system disorders	5.3% (2/38) [2]	6.7% (6/90) [7]
Cardiac disorders	21.1% (8/38) [10]	16.7% (15/90) [19]
Gastrointestinal disorders	21.1% (8/38) [11]	12.2% (11/90) [11]
General disorders and administration site conditions	13.2% (5/38) [5]	12.2% (11/90) [12]
Infections and infestations	10.5% (4/38) [4]	24.4% (22/90) [28]
Injury, poisoning and procedural complications	7.9% (3/38) [3]	4.4% (4/90) [4]
Investigations	5.3% (2/38) [2]	5.6% (5/90) [5]
Metabolism and nutrition disorders	13.2% (5/38) [7]	14.4% (13/90) [17]
Musculoskeletal and connective tissue disorders	7.9% (3/38) [3]	4.4% (4/90) [5]
Nervous system disorders	42.1% (16/38) [22]	58.9% (53/90) [64]
Psychiatric disorders	13.2% (5/38) [5]	4.4% (4/90) [4]
Renal and urinary disorders	10.5% (4/38) [4]	4.4% (4/90) [5]
Respiratory, thoracic and mediastinal disorders	13.2% (5/38) [5]	25.6% (23/90) [29]
Skin and subcutaneous tissue disorders	2.6% (1/38) [1]	-
Vascular disorders	26.3% (10/38) [13]	16.7% (15/90) [16]
Congenital, familial and genetic disorders	-	1.1% (1/90) [1]
Eye disorders	-	1.1% (1/90) [1]
Product issues	-	1.1% (1/90) [1]

Table 14: Serious Adverse Events by MedDRA Classification (Analysis Cohort -ITT)		
System Organ Class	**Solitaire % (n/N) [events]**	**Control % (n/N) [events]**
TOTAL	47.4% (18/38) [26]	53.3% (48/90) [68]
Cardiac disorders	5.3% (2/38) [2]	4.4% (4/90) [5]
Gastrointestinal disorders	7.9% (3/38) [4]	3.3% (3/90) [3]
General disorders and administration site conditions	2.6% (1/38) [1]	1.1% (1/90) [1]
Infections and infestations	2.6% (1/38) [1]	7.8% (7/90) [8]
Nervous system disorders	23.7% (9/38) [10]	31.1% (28/90) [30]
Psychiatric disorders	2.6% (1/38) [1]	-
Renal and urinary disorders	5.3% (2/38) [2]	-
Respiratory, thoracic and mediastinal disorders	10.5% (4/38) [4]	14.4% (13/90) [15]
Vascular disorders	2.6% (1/38) [1]	3.3% (3/90) [3]
Injury, poisoning and procedural complications	-	2.2% (2/90) [2]
Product issues	-	1.1% (1/90) [1]

Conclusion

The DEFUSE 3 study was a multicenter, randomized, open-label trial, with blinded outcome assessment, of thrombectomy in patients 6 to 16 hours after they were last known to be well and who had remaining ischemic brain tissue that was not yet infarcted.

The primary effectiveness endpoint (90-day mRS shift) in the Solitaire group when compared to the control group demonstrates a favorable shift of reduced post-stroke neurological disability over the entire outcome range (p-value=0.014). When combined with the safety findings of a low symptomatic intracranial hemorrhage and all-cause mortality rates of 2.6% and 10.5%, respectively, these provide clinical evidence for the safe and effective use of the Solitaire™ Revascularization Device in this late-window (6-16 hours from last seen well) AIS population.

Summary of Substantial Equivalence:

The subject Solitaire™ Revascularization device is identical to the predicate Solitaire™ 2 Revascularization Device and reference Solitaire™ Platinum Revascularization Device, except for the expanded indications for use. The DEFUSE 3 study data analysis demonstrates that the expanded indications for use does not raise any new or different questions of safety or effectiveness of the Solitaire™ Revascularization Device in the late-window (6-16 hours from last seen well) AIS population. Therefore, the subject Solitaire™ Revascularization device is substantially equivalent to the to the cleared predicate Solitaire™ 2 Revascularization device.