PRIMO Study Protocol

Protocol Number: CDC-00031

NCT04843436

SPONSOR DOCUMENT APPROVALS

Role	Name / Function
Issuer	Chloe Hacker Clinical Operations Project Manager, Clinical Affairs
Reviewer & Approver	Jake Gilson Associate Director, Clinical Affairs
Reviewer & Approver	Mauro Ercolani VP, Regulatory Affairs

Reference ARENA PLM for document approvals and approval date.

Revision History		
REV	**DATE**	**DESCRIPTION**
00	10MAR2020	N/A, first issue
1.0	17NOV2020	Modified from Observational to Post-market clinical study
2.0	20OCT2021	Updates in accordance to EU MDR 2017/745 and ISO 14155:2020; Follow-up visit for free flap, replantation and other procedures extended to 30±7 days
3.0	11AUG2022	Addition of protocol description

PRIMO: **P**ost-Market, Non-**R**andomized, Mult**i**centre PMCF Study To **Mo**nitor The Safety And Performance Of Symani System In Microsurgical Reconstructive Procedures In A Real Life Setting

Protocol Synopsis

Study Objectives	The objective of this PMCF study is to monitor the safety, usability, performance and long-term efficacy of the Symani System.
Study Device	Symani System for Microsurgery (Symani)
Indication for Use	The Symani System is a CE-marked device and it is intended for soft tissue manipulation to perform microsurgery techniques such as anastomosis, suturing, and ligation on small anatomical structures, including blood vessels and lymphatic ducts, in open surgery procedures. The Symani System teleoperated-instruments are indicated for use during microsurgical procedures when use of a motion scaling function is deemed appropriate by the surgeon. The Symani System is not intended for use on the heart, central circulatory system, central nervous system, or the eye. The system is indicated for adult and pediatric use, even if in the present study, only adult population will be enrolled. It is intended to be used by trained physicians in an appropriate operating environment in accordance with the Instructions for Use.
Study Design	A prospective, single-arm, open-label, clinical study designed to evaluate the Symani System safety and effectiveness for microsurgical anastomosis. The study will be conducted in at least 3 centers in Europe.
Target Population and sample size	The patients selected for this PMCF activity will be adults (over 18 years) requiring microsurgical reconstructive procedures applied to arterial, venous, neural or lymphatic anastomosis. The planned minimum sample size is 402 patients to ensure lower 95% confidence limit for the Primary Endpoint. A drop out rate of 5% will allow to include a total of 420 subjects. All subjects will be enrolled and followed in at least 3 EU centres until the sample size is reached.

Duration of Study	Each enrolled subject will be followed through the first 30±7 days post-operatively or 24 weeks post-operatively (according to the procedures) per the follow-up schedule reflecting the standard of care.
Primary Endpoint	The primary endpoint will be defined as the ability to complete the surgical task with Symani as intended by the surgeon. This endpoint will be referred to as “Procedure Robotic Success”.
Secondary Endpoints	The main secondary endpoint will be the rating of the surgeon experience of robot usability, which will be assessed using a questionnaire. Further secondary endpoints will be assessed regarding the clinical outcome of the procedures. These criteria will differ depending on the procedure performed being a replantation, free flap surgery, lymphatic surgery or other. Replantations • Time for each anastomosis execution and warm ischemia time (minutes) • Intraoperative need to redo the anastomosis (yes or no) • Postoperative need to redo within 7 days (complication and need to return to the operating room to explore anastomosis: yes or no) • Complications • Replantation Failure or Loss (subsequent amputation) Free Flaps • Time for each anastomosis execution and warm ischemia time (minutes) • Intraoperative need to redo the anastomosis (yes or no) • Postoperative need to redo within 7 days (complication and need to return to the operating room to explore anastomosis: yes or no) • Complications • Flap Failure or Loss (yes or no) Lymphatic Surgery • Time for each anastomosis execution (in minutes) • Intraoperative need to redo based on ICG Patency (yes or no) • Postoperative need to redo based on ICG Patency (yes or no) • Complications • Limb volume reduction

	Immediate and postoperative complications including arterial insufficiency, venous congestion, thrombosis, need for surgical re-exploration of anastomosis, partial flap necrosis or flap loss will be recorded. In the case of lymphatic surgery, the Surgeon will use volumetric measurement to assess the procedure impact on lymphedema. All adverse events will be collected from the procedure date to the study exit of each subject enrolled.
Analysis	The full analysis set (FAS) is defined as all patients enrolled onto the registry who underwent surgery with Symani. The FAS will be sub-divided into three distinct cohorts, depending on the surgery performed (replantation, free flaps, lymphatic surgery).
Follow-Up Schedule	Assessments will be made intraoperatively and at regular intervals during hospitalization. The study will be considered complete after all patients have completed their follow-up visits as described in the study protocol.
Inclusion and Exclusion Criteria	**Inclusion criteria** 1) Male and female patients aged >18 2) Patients who need a reconstructive procedure and a microsurgical reconstruction is deemed the best option by the plastic, orthopedic or other surgeon in response to a post-oncological, post-traumatic or congenital tissue defect or to treat lymphedema. 3) Patients who have been selected by the PI at the Clinical Center as appropriate candidates for treatment with Symani System in accordance with the IFU. 4) Subjects who fit the criteria to perform surgery requiring reconstructions using free flaps, replantation, lymphatic reconstructions. 5) Subjects who agree to have the surgery and the anaesthesia. 6) Subjects who voluntarily decide to participate in this study with the surgery performed with the aid of the Symani System and sign the Informed Consent Form. **Exclusion criteria** 1) Subjects who have bleeding or coagulation disorders in the past or present. 2) Any criteria that preclude prolonged anesthesia. 3) History of anaphylaxis or severe complicated allergy symptoms.

	4) Clinically significant cardiovascular, digestive, respiratory, endocrine, or central nervous system disorders or previous mental disorders that may significantly affect the data collection or the ability to comply with the protocol. 5) Evidence or history of autoimmune disease or compromised immune system. 6) Participation in another clinical trial within 4 weeks prior to participation in the study. 7) Subjects belonging to vulnerable populations or ineligible to participate for other reasons by the PI at a Clinical Center. 8) Subjects with pacemaker.