Statistical Analysis Plan for:

Contour Neurovascular System™
European Pre-Market Unruptured Aneurysm Study (CERUS)
Protocol DNX099-01

NCT Number: 03680742

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1 Purpose

This document outlines the data handling and planned analyses for Contour Neurovascular System™ European Pre-Market Unruptured Aneurysm Study (CERUS).

2 Reference Documents

- Protocol DNX099-01 Contour Neurovascular System™ European Pre-Market Unruptured Aneurysm Study (CERUS)
- DNX099-06 Data Management Plan

3 Acronyms

The following list provides acronyms used in this document and their meaning:

AE	Adverse Event
CDP	Clinical Discovery Platform = web-based database
CEC	Clinical Events Committee
DSMB	Data Safety Monitoring Board
EDC	Electronic Data Capture
ITT	Intent-to-treat
PP	Per Protocol
SAE	Serious Adverse Event

4 Protocol Summary

Study Title:	**Contour Neurovascular System™ European Pre-Market Unruptured Aneurysm Study (CERUS)**

Study Purpose:	Cerus Endovascular is sponsoring a prospective, multi-center trial to document the safety and performance of the Contour Neurovascular System™ ("Contour"). The purpose of the study is to document safety and performance of the Contour in treatment for patients with intracranial aneurysms (IA). The data from the study will be reported as a Pre-Market study to the Notified Body to support CE Mark approval.
Study Design:	The study is a prospective, single arm, multi-center study.
Objective and Endpoints:	The primary objective of this study is to document the safety and performance of the Contour Neurovascular System. The data from the study will be reported as a Pre-Market study to the Notified Body to support CE Mark approval. In addition, the data may be used to support US approval by the Food and Drug Administration (FDA) to market the Contour device in the United States. **1. Primary Safety Endpoint:** The proportion of subjects with death of any non-accidental cause or any major disabling stroke within the first 30 days after treatment or major disabling stroke or death due to neurological cause from day 31 to 6 months after treatment. Note: Major Disabling Stroke is defined as an episode of neurological signs or symptoms that persist beyond 24 hours accompanied with evidence of ischemia/infarction on imaging that results in an increase of NIHSS from baseline by ³ 4 points and/or an increase from mRS baseline by >2. **2. Primary Performance Endpoint:** To demonstrate the occlusion rate on the 6 month angiogram as adjudicated by a core laboratory. Success will be defined as complete occlusion demonstrated by a Grade 1 using the Raymond Roy Scale.

Secondary Measures	Additional measures will be summarized: **Secondary Safety**: • Serious Adverse Events (SAE) associated with the procedure or device • All serious neurological adverse events **Secondary Performance**: • Detailed assessment of aneurysm occlusion from post procedure to 6months provided by the core lab review of the angiogram (DSA) including the following: - Raymond Roy scale - Modified Web Occlusion Scale - Percent Occlusion - Device Stability • Rate of retreatment • Summary of device performance including the following: - Time required for implantation of the Contour - Device sizes used - Number of attempts to deploy the device - Number of failed implant attempts - Any reports of device deficiencies
Number of Sites:	A maximum of 10 European investigational sites will participate.
Sample Size:	A maximum of 35 subjects will be enrolled to obtain follow-up data for the primary analysis for 30 subjects while allowing for attrition to be submitted for CE Mark application.
Patient Population:	The patient is enrolled at the time of consent and is considered a study subject in the reporting analysis group only when the patient is fully qualified and at least one Contour device has been placed into the patient's body.
Study Visits:	Baseline, procedure, discharge, 1 month, 6 months and 12 months.

Study Oversight:	Both a CEC and DSMB will be employed for study oversight and will meet as a combined committee. The CEC will review and classify all neurologic, devicerelated and procedure-related SAEs to ensure they are reported accurately. The DSMB will review the study data after enrollment of the first five patients. Enrollment of further patients will occur as the DSMB reviews the data. The DSMB will provide a report following the review and advise Cerus Endovascular for any modifications or concerns that may be necessary. The DSMB will provide further evaluation at least twice per year and after the first 5 patients are enrolled. If slow enrollment occurs, the DSMB may meet less frequently.

5 Analysis Population

Two patient populations will be considered in the analyses, an Intent-to-Treat (ITT) population and a Per Protocol population (PP). The ITT population includes all patients. The PP population will include subjects who complete 6 months of follow-up, die prior to their 6-month clinic visit, or are study failure (withdrawal from study to obtain alternate treatment). The PP will exclude patients with any major protocol violation that affects proper study inclusion or significant outcomes. Endpoints will be evaluated in the PP and ITT populations.

Any patient for whom a failed implant attempt is performed will be followed for 1 month, or until resolution of any potential device or implanted related adverse events, whichever occurs last.

Any patient who is consented but has no implant attempt will be study exited.

6 General Statistical Principles

The analysis for all primary and secondary study endpoints and baseline, procedural and follow-up characteristics will be performed on an intent-to-treat analysis population which will include all available data for all enrolled subjects. Standard summary statistics will be calculated for all study variables. For continuous variables, statistics will include means, standard deviations, medians and ranges. Categorical variables will be summarized in frequency distributions. Missing data will not be imputed. The number of data values available for each analysis will be reported so that the impact of missing data can be seen.

Statistical analyses will be conducted in SAS version 9.4 or above (SAS Institute, Cary, N.C.).

7 Analysis of Study Endpoints

Primary Safety Endpoint

The primary safety endpoint will be calculated as the proportion of subjects with death of any nonaccidental cause or any major disabling stroke within the first 30 days after treatment or major disabling stroke or death due to neurological cause from day 31 to 6 months after treatment.

Where "Major Disabling Stroke" is defined as an episode of neurological signs or symptoms that persist beyond 24 hours accompanied with evidence of ischemia/infarction on imaging that results in an increase of NIHSS from baseline by ³ 4 points and/or an increase from mRS baseline by >2.

Primary Performance Endpoint

The primary performance endpoint will be calculated as the proportion of subjects with complete occlusion demonstrated with a Grade 1 on the Raymond Roy Scale at 6 months. The data will be as reported as analyzed by the core laboratory.

Secondary Safety Endpoints

- Serious Adverse Events (SAE) associated with the procedure or device will be calculated as the proportion of subjects with at least one SAE and each individually reported SAE. Event counts will also be reported.

- Serious neurological adverse events will be calculated as the proportion of subjects with at least one serious neurological AE and each individually reported neurological AE. Event counts will also be reported.

Secondary Performance Endpoints

The secondary performance endpoints will be reported as analyzed by the core laboratory. The endpoints will be analyzed at the the 6-month post implant timepoint unless procedure-related.

- Raymond Roy scale: the endpoint will be calculated as the proportion of subjects with each category
- Modified Web occlusion scale: the endpoint will be calculated as the proportion of subjects with each category

- Percent occlusion: the endpoint will be calculated as the mean and standard deviation or median and range depending on the normality of the data of the measured occlusion
- Device stability: the endpoint will be calculated as the proportion of subjects with stable device placement
- Retreatment: the endpoint will be calculated as the proportion of subjects with retreatment of the target aneurysm between the implant procedure and 6 month post implant timepoint
- Time required for implantation of the Contour: the endpoint will be calculated as the mean and standard deviation or median and range depending on the normality of the data
- Device size: the endpoint will be calculated as the proportion of subjects with each size of implanted Contour device
- Number of attempts to deploy the device: the endpoint will be calculated as the proportion of subjects with each number of implant attempts (e.g. 1, 2, 3)
- Number of failed attempts to deploy the device: the endpoint will be calculated as the proportion of subjects with each number of failed attempts (e.g. 1, 2, 3)
- Device deficiencies: the endpoint will be calculated as the proportion of subjects experiencing a device deficiency. Individual deficiency category counts will also be reported.

8 Additional Analyses

Subject accountability and discontinuation will be summarized for all subjects who are enrolled in the study.

A summary of subjects with protocol deviations will be reported but those subjects will be included in all analyses although endpoints may be summarized without the subjects (per-protocol analysis group) to provide additional information but not for the primary analysis.

Applicable summary tables of baseline and follow-up data points not included in the endpoint analyses as well as subject listings will be provided in summary reports.

No interim analyses are planned. Summary reports will be created to comply with regulatory requirements.

9 Data Acquisition

Details for the data acquisition via an electronic database (EDC) are contained in the study-specific Data Management Plan.

10 Revision History

Rev	DCO	Change Description	Release Date
A	0458	Initial Release	01 Feb 2019