FDA Executive Summary

Elana Surgical Kit HUD

Elana, Inc.

H080005

Prepared for the

Pediatric Advisory Committee
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Introduction

In accordance with the Pediatric Medical Device Safety and Improvement Act, this review provides a status update regarding the post-marketing experience with the use of Elana Inc.'s Elana (Excimer Laser Assisted Non-occlusive Anastomosis) Surgical KitHUD in pediatric and adult patients since approval.
The device was approved in March, 2011 by the Center for Devices and Radiological Health (CDRH) under Humanitarian Device Exemption (HDE) application H080005.

There has been no use of this device since 2013 and those attempted to be treated with the device prior to 2013 after approval were all adult patients. Details are below.

This memorandum will include summaries of the post-market medical device reporting (MDR) for adverse events, post-approval studies, and the peer-reviewed literature associated with the device.

Clinical Background

The clinical course may be poor for patients with an aneurysm or a skull base tumor affecting a large, intracranial artery that failed balloon test occlusion, that cannot be sacrificed, or that cannot be treated with conventional means due to local anatomy or complexity. When left untreated, subjects with these lesions can reach morbidity and mortality rates of up to 50% in the first year after diagnosis (Langer, 2005). Bypass grafting to large intracranial arteries is a complex surgery, generally performed on subjects with tumors and aneurysms involving the large feeding arteries of the brain. The associated creation of a distal anastomosis using conventional bypass techniques carries the risk of severe complications related to temporary occlusion of the recipient artery and microvascular suturing. The patient is at high risk for ischemic stroke and peri-operative mortality, particularly during temporary occlusion of the recipient artery. Non-fatal stroke can result in significant morbidity. Neurologic events may include deficits of various nerves, hemiparesis, hemiplegia, ataxia, loss of hearing or vision, and/or aphasia.

Indications for Use

The Elana Surgical KitHUD, when connected to the Spectranetics Xenon-Chloride Laser Model CVX-300, is indicated for creating arteriotomies during an intracranial vascular bypass procedure in subjects 13 years of age or older with an aneurysm or a skull base tumor affecting a large [> 2.5 mm], intracranial artery that failed balloon test occlusion, cannot be sacrificed, or cannot be treated with conventional means due to local anatomy or complexity.

Post-Market Data

Medical Device Reports (MDRs) Received by FDA

The MDR database was searched on July 14, 2017, to identify any MDRs associated with the Elana device. The database was searched by brand name, product code and manufacturer name with no date range. No MDRS associated with the Elana device were identified.

Post-Market Data: Post-Approval Study (Pas)

As a condition of approval, the sponsor was required to conduct a post-approval study (PAS) due to concerns about flap retention and real world safety.

Overview of the Study

The aim of this PAS is to collect information about Elana performance in a post approval setting with special attention to flap retention rate, mortality and stroke. The study will be performed in the form of a registry that includes all patients who receive the procedure. This is an 'all comers' registry with no inclusion or exclusion criteria. The study will be conducted only at sites that have a stroke unit and all necessary medical devices/equipment available. Furthermore, the neurosurgeons are required to have experience in micro-vascular surgery and will undergo mandatory training on how to use the Elana Surgical Kit.

The study was designed to collect information pre-operatively, during the operation and at one post-operative follow up >25 days. The latter follow up is required to collect the modified Rankin score (mRs) to be able to define non-fatal stroke.

Progress reports were to be required every six months during the first 2 years of the registry and annually thereafter. Due to the limited clinical indications for this device and the availability of new surgical alternatives, a limited number of patients can be expected on a six months basis. The total numbers per six months were anticipated to be not higher than 12-18 patients.

Endpoints

The primary endpoint will be the ability of the Elana Surgical Kit to retrieve a flap on the tip of the Elana Catheter while creating an arteriotomy. The flap retrieval will be judged successful if the flap is retrieved on the tip of the Elana Catheter. The flap retrieval will be judged unsuccessful if the flap was either manually retrieved or not retrieved (= flap retention).

A total of 80 device uses will provide 80% power for showing the flap retention rate does not exceed 38% under the assumption that the true rate is 22%. The true flap retention rate of 22% is based on the results of the IDE study on 37 device uses. It is expected that each site can enroll between 3-5 patients on an annual basis. The total expected number of sites in the USA is around 10-15. The total sample size for this registry will be 80 device uses.

Mortality and non-fatal strokes will be recorded as secondary measures, but no statistical analyses beyond summarization of these events will be reported.

Registry Data to be Collected

Data collection summary per patient for this registry includes the following:

Data collection	Rationale
Name hospital	To determine number of patients per hospital and to relate patient success to site
Name treating physician	To check physician is indeed trained and to evaluate if there is a difference between physicians if there is more than 1 treating physician per hospital
Number of prior surgeries performed by physician	To evaluate the potential learning curve effect
Age and gender	Descriptive for patient population
Indication for bypass	Descriptive for patient population
Type of bypass (EC/IC)	Descriptive for procedure
Location of lesion Anterior/posterior)	Descriptive for patient population
Location of anastomosis and type of graft vessel	Descriptive for procedure
Flap retention	Measure if a flap was retrieved on catheter, manually retrieved or not retrieved to determine flap retention rate and corresponding learning curve
Mortality	Measure of safety and mortality rates will be reported
Non-fatal stroke	Measure of safety and total non-fatal stroke incidence will be reported
Modified Rankin score	Scoring used in order to be able to define stroke and patient outcome

Study Status

As of May 2017, a total of 20 devices were shipped to 8 sites and only one site has used one device (use occurred in April of 2013). No device has been shipped to any site or used in any patient since the last PAC (2016) meeting. Three adult patients were enrolled (none pediatric) in this study from 2012 until May 2017 In brief, of these three patients, the device was used successfully in only one patient. In the other two patients the procedure was aborted and the device was not used- A clinical summary of these three patients is provided in the table below.

	Subject (b) (6)	Subject (b) (6)	Subject (b) (6)
Pre-operative			
Demographic	Female, 66yr old	Male, 52yr old	Female, 56yr old
Reason for bypass	Giant Aneurysm of LICA, partially thrombosed, symptomatic	Aneurysm- large calcified paraclinoid carotid aneurysm	Aneurysm, sacrifice of right posterior cerebral artery
mRankin score pre-op	1	2	1
Surgery			
Bypass graft	Autologous Saphenous Vein	Autologous Saphenous Vein	Radial artery
Bypass type	Replacement	Replacement	Replacement
Distal Anastomosis			
Type of anastomosis	Elana. Graft was inadvertently pulled. Elana was aborted due to carotid laceration.	Elana	Conventional
Arteriotomy successful?	n/a	Yes, retrograde flow from recipient	n/a
Flap retrieval	n/a	Yes Flap retrieved on catheter	n/a
Complications in creating the arteriotomy	No	No	No
Proximal Anastomosis			
Type of anastomosis	Conventional	Conventional	Conventional. Elana ring was sewn but felt to be slightly too large therefore a conventional bypass was performed.
Complications in creating the anastomosis	none	none	none
Post- OP Evaluation			
Follow-up 25-40 days post-op	mRs: 4 (3 weeks post-op); mRs: 6 (on 17 Nov 12)	mRs: 2 (on 25 Feb 13)	mRs: 0
Non-fatal stroke/death?	Non-fatal stroke, Death due to mesenteric ischemia 4 weeks after surgery.	No	No new neurological deficit
Serious Adverse Events			
Mesenteric Ischemia/Acute Abdomen	Definitely not device related	None	None

The sponsor has indicated that completing this PAS would be difficult due to recently available alternative options (e.g., flow diversion devices). High flow bypass surgeries being, including bypass surgeries with the Elana Surgical Kit are essentially no longer performed. Approximately 90% of the (already limited) number of cases that used to be treated with the Elana technique are now being treated endovascularly. They have stated the use of their device is at the end of the treatment ladder. Because of the fact that more treatment options have become available, they have stated their device is/will mainly be used as a last-resort option.

Due to these reasons listed above and the limited sales and use within the US to date, the PAS was suspended by the FDA. The sponsor is not required to continue the PAS. However, through required HDE annual reports submitted by the sponsor to the FDA that summarizes sales and use, if it is observed that use of the device increases, the PAS would be reinstated and the sponsor would be responsible for recommencing the PAS.

Post-Market Data: Literature Review

Updated Literature Review Presented for the 2017 PAC

A PubMed and EMBASE search was conducted there were no results retrieved for Elana surgical kit -human studies within the period June 1, 2016 to June 6, 2017 using the defined criteria: ELANA OR Arteriotomy OR "Excimer Laser- Assisted Non-occlusive Anastomosis." This search was consistent with the search performed last year (no results retrieved).

Summary

A total of 20 devices have been distributed in the U.S since HDE approval. The device has only been used in one adult patient at the time of this Executive Summary. In two other patients, intent to use the ELANA was aborted and the device was not used. All three patients (the one successful use and two intended use) were adults and these three were enrolled in the post-approval study. Due to limited use of this device, the post-approval study has been suspended. Should use increase, the sponsor would be required to recommence the study. There were no articles published since last year's literature review and no MDRs were reported to the FDA, therefore there are new safety concerns identified in the past year.

Therefore, FDA recommends continued surveillance and will report the following to the PAC in 2018:

- Annual distribution number
- PAS follow-up results
- Literature review
- MDR review