

FDA Executive Summary

Prepared for the
September 23, 2014 meeting of the
Pediatric Advisory Committee

H080005

Elana, Inc.
Elana Surgical KitHUD

Introduction

In accordance with the Pediatric Research Equity 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 under Humanitarian Device Exemption (HDE) application H080005.

This memorandum will include summaries of the pre-market clinical study, postmarket medical device reporting (MDR) for adverse events, post-approval studies, and the peer-reviewed literature associated with the device. At the panel meeting, the Agency will ask for your recommendations regarding the need for continued monitoring of safety and the appropriateness of the profit-making exemption.

Clinical Background

The clinical course is 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, and 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. Particularly during temporary occlusion of the recipient artery, the patient is at high risk for ischemic stroke and peri-operative mortality. 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.

POSTMARKET DATA MEDICAL DEVICE REPORTS (MDRs) RECEIVED BY FDA

The Manufacturer and User Facility Device Experience (MAUDE) database was searched August 1st, 2014, to identify any Medical Device Reports (MDRs) associated with the Excimer Laser Assisted Non-occlusive Anastomosis (ELANA) device which had been reported to FDA. The first MAUDE search criteria included Brand name (Variations of %Elana% and %Excimer%Laser%) and did not identify any reports associated with the Elana Arteriotomy Kit_{HUD}. A second MAUDE search was performed using Manufacturer name (Variations of %Elana%) which also did not identify any reports associated with the Elana device. Based on these MAUDE searches, there are currently no MDRs within the MAUDE database associated with the Elana device.

POSTMARKET 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 surgeries	Necessary to help 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 used	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 Presented to the 2013 PAC

As of March 6, 2013, the sponsor stated that seven (7) study sites and two subjects – both adults – had been enrolled into the PAS.

In one PAS patient, a 66 year-old female with a giant aneurysm, the ELANA device was actually not used when the bypass graft was inadvertently pulled by a scrub nurse causing a carotid laceration, and a conventional autologous saphenous vein was used as a bypass. The patient died from a mesenteric ischemia 4 weeks after surgery (considered not device-related).

The second PAS subject was a 52 year old male with a large calcified paraclinoid carotid aneurysm which was treated with an autologous saphenous vein that was used as a bypass graft replacement after a successful arteriotomy. The flap was retrieved with the catheter in this subject. Follow-up MRS was 2 and no serious adverse events were reported.

Updated PAS Status and Results as of March 6, 2014

The database closing for the most recent report was March 6, 2014. At that time, a total of 18 devices had been shipped to 8 sites and only one site had used the device. One additional subject (an adult) has been enrolled since the last report for a total of three (3) subjects.

In that newly enrolled PAS patient, a 56 year old female with posterior cerebral artery aneurysm, there was an attempt to use the ELANA surgical Kit during surgery, however intra-operatively the size of the Elana ring was found to be too large for the vessel. Therefore, the device was not used and a conventional bypass was performed. There were no neurological deficits or adverse events.

The sponsor has attributed the slow study progress to factors including reductions in the number of high flow pass surgeries being performed in the US, the need for highly surgical skill in the use of this device and availability of other treatment options.

POSTMARKET DATA: LITERATURE REVIEW

Literature Review Presented at the 2013 PAC

In preparation for the 2013 PAC meeting, a search of the literature was conducted on July 23, 2013. No new articles were found for the period between March 10, 2011 and July 23, 2013 that were not already included in the previous literature search presented at the 2012 PAC. The results of that search are detailed below. A search of the literature from March 11, 2011-August 3, 2012 was conducted to identify all research studies. This search revealed seven articles including two animal studies, two laboratory studies, and three human studies. Of the three human studies, two were interdependent clinical studies and the third was an oral presentation of the findings of the IDE study. All of the human studies were conducted prior to device approval and none included a pediatric population, one did not give ages and the other reported a median age of 54 +/- 13. Among the three clinical studies (which includes the FDA-IDE), patency was achieved in 85-94% of patients and improvement as measured by Rankin score, was observed in 77-86% of patients. Thirty-day mortality was 6-12% and one study (van Doormaal et al 2011) reported 14% strokes, but 92% of patients with no major complications.

Updated Literature Review for the 2014 PAC

A search of the literature was conducted on July 15, 2014 for articles published since the previous literature search conducted on July 23, 2013. A total of 3 articles were found. The titles and abstracts were reviewed and two articles that were related to animal models were excluded. The full text of the remaining article on human subjects by Abla et al 2014 was reviewed and

assessed for eligibility in the analysis. This article presents a surgeons experience with bypass surgeries for complex anterior cerebral artery (ACA) aneurysms in ten patients and a literature review of publications on various bypass techniques for revascularization of ACA aneurysms. In their literature review, the article cited a publication by Brilstra et al 2002, in which the Excimer laser-assisted anastomosis [ELANA] technique was used to construct high flow bypass surgeries in the treatment of cerebral aneurysms. No information on device safety and effectiveness was mentioned. This recent literature search did not yield any recent publications that pertain to the ELANA device safety and effectiveness.

SUMMARY

A total of 18 devices have been distributed in the U.S since HDE approval, although the device has been successfully used in only one subject at the time of this Executive Summary. In two other subjects, intent to use the ELANA was aborted and the device was not used in the subjects. All three subjects (the one successful use and two intended use) were adults and these three were enrolled in the post-approval study. Only one new article has been published since last year's literature review in which it provided no new information on the safety or effectiveness of the ELANA device. In large part due to the limited use of the device since approval, no new safety issues have been identified.

REFERENCES

1. Abla AA, Lawton MT. Anterior cerebral artery bypass for complex aneurysms: an experience with intracranial-intracranial reconstruction and review of bypass options. *J Neurosurg.* 2014 Jun;120(6):1364-77.
2. van Doormaal TP, van der Zwan A, Redegeld S, Verweij BH, Tulleken CA, Regli L. Patency, flow, and endothelialization of the sutureless Excimer Laser Assisted Non-occlusive Anastomosis (ELANA) technique in a pig model. *J Neurosurg.* 2011 Dec;115(6):1221-30. Epub 2011 Jul 22.