FDA Executive Summary

Prepared for the
September 2018 meeting of the
Pediatric Advisory Committee

H080005

Elana, Inc.
Elana Surgical KitHUD

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 Anastamosis) 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 recipientartery 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 MDR database was searched on August 1st, 2018, 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

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
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
Mortality	Measure of safety and mortality rates will be reported
Non-fatal stroke	Measure of safety and total non-fatal stroke incidence will be
Modified Rankin score	Scoring used in order to be able to define stroke and patient outcome

Study Status Presented to the 2014 PAC

As of March 2014, a total of 18 devices had been shipped to 4 sites. Three other enrolled sites had not received any shipment. One patient was enrolled during the reporting period (March 2013 to March 2014) for a total of three patients -all adult patients.

This third patient was 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.

<u>Updated PAS Status and Results as of March 4, 2018</u>

The database closing for the most recent report was March 5, 2018. As of the 2014 PAC presentation, two additional devices had been shipped to one site for a total of 21 devices to 4 sites. Only one site has used the device to date. No additional patient was enrolled since the last report in March 2017.

A total of three patients have been enrolled to date (all adult patients) and the device has been successfully used in one patient. 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. The sponsor stated that because of other available treatment options, the ELANA surgical kits is or will mainly be used as a last resort option, and indicated that surgeons who use the device believe the ELANA surgical kit should be available for the few patients with no alternative treatment option. The firm reiterated that surgeons prefer to keep the device available during a conference call with FDA on August 27, 2015.

POSTMARKET DATA: LITERATURE REVIEW

On July 6th, 2018 a search was conducted within PubMed and EMBASE, using the same search criteria used in previous systematic literature reviews:

"ELANA OR Arteriotomy OR "Excimer Laser- Assisted Non-occlusive Anastomosis."

The PubMed search was limited to articles published in English language, humans, and published within June 6, 2017 to June 6, 2018. The EMBASE search was limited to English language, humans and by year of publication "2017-2018". EMBASE cannot filter by month for publication date. This includes January 1, 2017 to June 6, 2017 which overlaps with last year's search from June 1, 2016 to June 6, 2017. Therefore, EMBASE results were manually evaluated for eligibility via publication date to refine the results to publications between June 6, 2017 to June 6, 2018 if the article was relevant in content.

To determine eligibility of the articles for inclusion, the following process was conducted in sequence:

1. Titles and abstracts were first screened for relevancy.
2. If the previous step was insufficient, the relevant full text article was screened.
3. If the article was deemed relevant, publication date was evaluated.
4. If the publication date was within the expected time frame, the relevant full text article was selected and reviewed for data extraction and synthesis.

Articles were excluded based on the following reasons listed below:

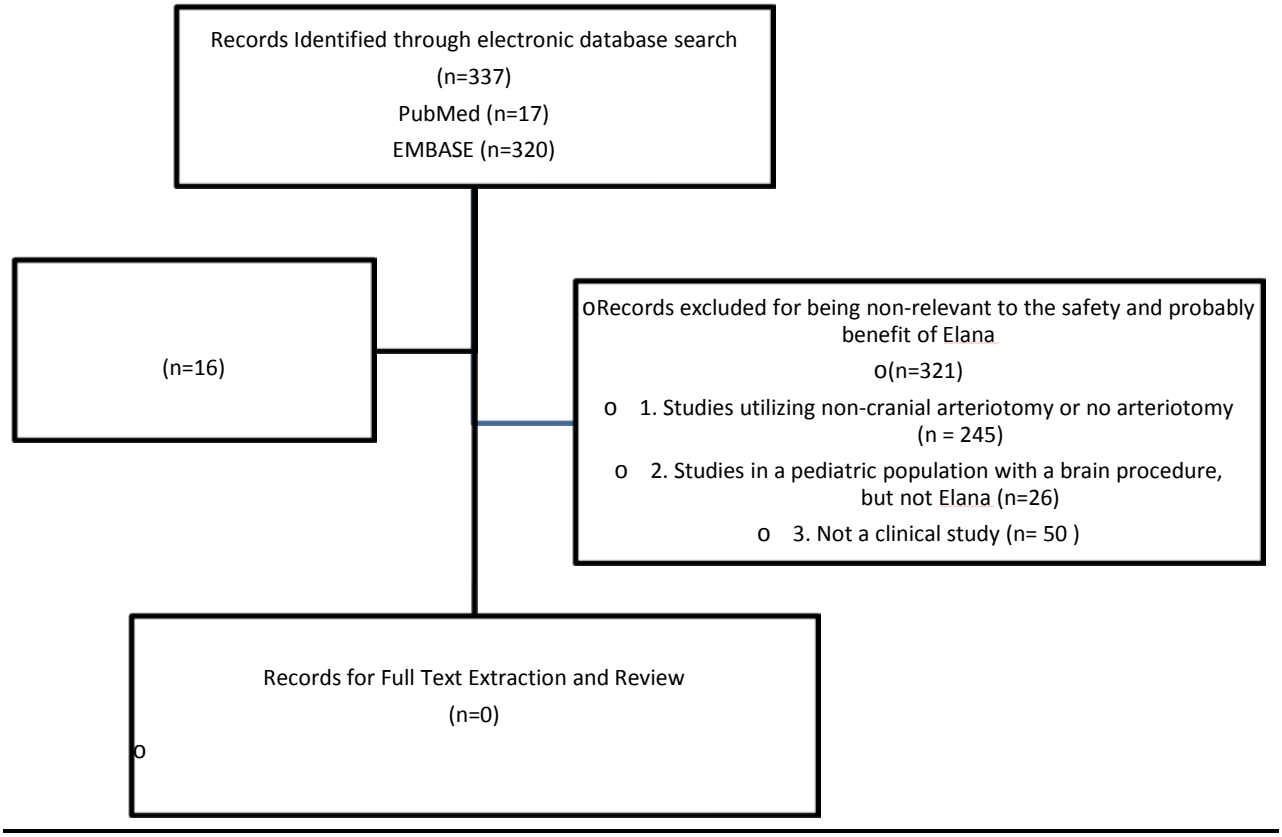
1. Studies utilizing non-cranial arteriotomy or no arteriotomy: listed in Endnote as [**NOTINTRACRANEAL**]
2. Studies in a pediatric population with a brain procedure but **not Elana** listed in Endnote as [**NOTELANA**]
3. Not clinical studies (e.g. training study, in-vitro, in-vivo, etc) listed in Endnote as [**NOTCLINICAL**]

4. Studies published before June 6, 2017 and after June 6, 2018 listed in Endnote as [**DATE**]

Study Selection

Figure 1 presents the diagram of article retrieval and selection including the criteria for exclusion. The EMBASE search yielded 320 articles and the PubMed search yielded 17 articles. After removing 16 duplicate records between the two search results, 321 unique records were subjected to review and screening for eligibility. After exclusion, no article was retained for full text extraction and qualitative synthesis for Elana surgical kit-human studies.

Figure 1: Flow Diagram of the Article Retrieval and Study Selection



Conclusion

The systematic literature review did not find new publications reporting on the safety or probable benefit of the ELANA among pediatrics.

SUMMARY

A total of 21 devices have been distributed in the U.S since HDE approval, although the device has been successfully used in only one 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 no use of this device, the post-approval study has been suspended. Should use resume, 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 no new safety concerns identified in the past year.