FDA Executive Summary

Prepared for the
September 20, 2013 meeting of the
Pediatric Advisory Committee

H080005

Elana, Inc.
Elana Surgical Kit$_{HUD}$

NOTE TO PANELISTS: **This is the 2nd consecutive year CDRH is presenting an annual HDE review for the Elana Surgical Kit device to the PAC. As such, the majority of this Executive Summary is identical to the Summary provided last year. New information obtained since the last PAC meeting is provided on the following pages/sections**

- **Page 11: Distribution of the device in the U.S.**
- **Page 12: Summary of Medical Device Reports (MDRs) received since last PAC**
- **Page 13: Updated status and Summary of Post-Approval Study**
- **Page 14: Updated summary of relevant literature published since last PAC**

INTRODUCTION AND BACKGROUND

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 Kit$_{HUD}$ 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 input on whether the probable benefit/risk profile of the device for the pediatric population continues to support the HDE for which the exemption was granted.

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.

Device Description

The Elana Surgical Kit_{HUD} consists of the Elana Arteriotomy $System_{HUD}$ and extension tubing for connection to a vacuum source. The Elana Arteriotomy $System_{HUD}$ is comprised of the Elana Ring and the Elana Catheter. The Elana Surgical Kit_{HUD} should only be used with the US legally marketed Spectranetics XeCl (Xenon-Chloride) Excimer Laser System, Model CVX-300.

Elana Ring

The Elana Ring is a flat ring implant constructed of platinum and available in 2 configurations: Model 2.6 has an inner diameter of 2.6 mm and an outer diameter of 3.1 mm, while Model 2.8 has an inner diameter of 2.8 mm and outer diameter of 3.3 mm. The Elana Ring is designed to define the exact location of the arteriotomy site on the recipient vessel and is connected along with a donor graft to the recipient artery wall using conventional micro-neurosurgery suturing techniques. The Ring helps to ensure a flush interface between the laser tip and the arteriotomy site, and thereby allows the laser tip to broach the arterial wall along the Ring's circumference.

Elana Catheter 2.0

The Elana Catheter 2.0 is a catheter that provides vacuum through the central lumen, and delivers laser light to cut an arteriotomy. The catheter is 130 inches long with an outer diameter of 2.0 mm at the distal tip. The catheter has a stainless steel distal tip with silica glass laser fibers configured in a ring around the distal tip. The Elana Catheter 2.0 is attached to the Spectranetics XeCl (Xenon-Chloride) Excimer Laser System, Model CVX-300.

An overview of the operating steps for the ELANA Surgical Kit_{HUD} are provided below:

- After preparation and selection of an anastomosis site on one of the major cerebral arteries, the surgeon places the Elana Ring onto the artery wall (See Figures A, B, C below) to confirm the suitability of the site.
- The surgeon attaches the Elana Ring together with the donor graft to the artery wall (See Figure D below) using a fine suture.
- The connection of the graft to the artery is checked for leakage using saline solution and tightened further with additional suture if required.
- The surgeon points the distal tip of the catheter at the center of the energy detector,1-2 inches away, to calibrate the laser and ensure that 10mJ of laser light per pulse at 40 Hz is

emitted. The catheter is connected to an aspiration system. After activating aspiration, the surgeon covers the catheter tip and gently lifts it to confirm vacuum.

- The surgeon inserts the distal end of the Elana Catheter into the donor graft until the tip evenly touches the artery wall inside the Elana Ring (See Figure E below).
- After 2 minutes of suction application, the surgeon activates the Excimer laser (by footswitch). As a result, a train of 200 pulses is delivered (5 seconds at 40Hz) accordingly. When 200 pulses are delivered, the laser will stop automatically
- After the laser has stopped, the surgeon slowly removes the Elana Catheter (see Figure F below) while not exerting force onto the artery or the graft.
- The surgeon checks for retrograde blood flow through the donor graft before occluding it.

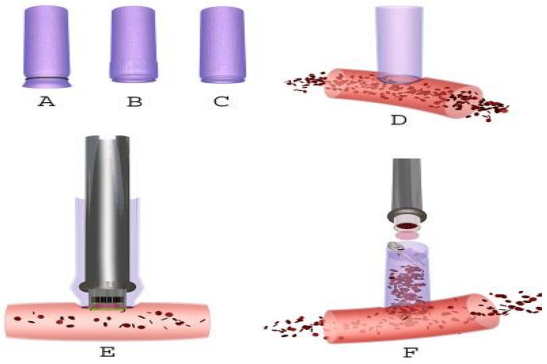

Figure: Operating Steps

PREMARKET DATA: THE IDE CLINICAL STUDY

The clinical information presented to FDA in support of the safety and probable benefit of the Elana Surgical Kit_{HUD} was comprised of two datasets, including prospectively collected data from 7 centers in the United States and Europe ("IDE data"). This dataset comprised 32 adult subjects and one (1) pediatric patient, a male aged 17 years.

Study Overview

This was a prospective, non-randomized, international, multicenter study. Participating centers enrolled subjects who required a temporary (protective bypasses that are required during surgery only) or permanent bypass to be connected to one or more unoccluded intracranial vessel(s) for an established indication and for whom the responsible surgeon felt they could not be safely treated otherwise, e.g., because of a lesion not ideal for coiling or clipping or excision, or temporary or permanent occlusion of a vessel, without the temporary or permanent creation of a bypass. Subjects with a preoperative modified Rankin score of 4 or 5 were excluded.

Study Endpoints

The primary endpoints of the IDE study were flow through the bypass graft and no device-related adverse events. Flow was judged by evaluating graft patency intra-operatively and at 7 ($\pm$2) days follow-up for permanent bypasses, while only intraoperatively for temporary bypasses.

The safety endpoint was the rate of mortality and non-fatal strokes at a 30 (+10/-3) day follow-up period. Neurological state and functional outcome using mRS at the 30 day follow-up visit were also evaluated for safety. Safety of Elana was compared to historically-derived information from

the literature. Historical control was deemed appropriate because it can determine if graft bypasses created with the Elana Surgical Kit present the same type and incidence of adverse events typically seen in these procedures.

Effectiveness Results

Table 1 provides a summary of the outcomes for the 33 IDE subjects. The results in the table are distinguished by bypass procedures involving the anterior and posterior circulation because bypass procedures grafting to the posterior circulation (basilar artery, vertebral arteries, posterior cerebral arteries and posterior communicating arteries) carry a significantly higher risk of serious adverse events than those grafting to the anterior circulation.

Table 1: Primary Effectiveness Results for the IDE Study

Total Device Uses:	37
Total Subjects:	33 Anterior: 32/33 (97%) Posterior: 1/33 (3%)
Bypass patent at end surgery:	31/33 (94%) Anterior: 30/32 (94%) Posterior: 1/1 (100%)
Bypass patent at 7 days post-op:	22/31 (71%) Anterior: 24/30 (73%) Posterior: 0/1 (0%)

Safety Results

Table 2 provides information regarding major safety outcomes from the IDE study. The mortality rate was 9%, and the peri-operative non-fatal stroke rate was 15%.

Table 2: Safety Results for the IDE Study

Total Device Uses	37
Total Subjects:	33 Anterior: 32/33 (97%) Posterior: 1/33 (3%)
All moderate/severe adverse events:	15/33 (45%) Anterior: 14/32 (44%) Posterior: 1/1 (100%)
Mortality:	3/33 (9%) Anterior: 2/32 (6%) Posterior: 1/1 (100%)
Non fatal stroke with permanent deficits at 30 days:	5/33 (15%) Anterior: 5/32 (16%) Posterior: 0/1 (0%)

Adverse Events

All 33 subjects completed their 30 day post-bypass follow-up per protocol. An independent Clinical Events Committee adjudicated all serious adverse events. Severity was defined as:

1. Mild: Noticeable to the subject. The mRS (modified Rankin Scale) may temporarily be increased but returns to the state prior to the surgery.
2. Moderate: Interferes with the subject's activities in the long term. The mRS may permanently be increased compared to pre-operation, but is still well acceptable in proportion to the condition before the operation and the threat posed by this condition.
3. Severe: Causes death or severe/permanent disability

A Serious Adverse Event (SAE) was defined as an event that led to death or led to a serious deterioration in the health of the patient that:

- Resulted in life-threatening illness or injury
- Resulted in permanent impairment of a body structure or a body function
- Required in-patient hospitalization or prolongation of existing hospitalization
- Resulted in medical or surgical intervention to arrest permanent impairment to body structure or a body function
- Led to fetal distress, fetal death or a congenital abnormality or birth defect

There were a total of three device-related severe or moderate adverse events which included

- diffuse subarachnoid hemorrhage and thrombosis of basilar aneurysm with compression of the ventral pons (1),
- bypass occlusion (1), and
- aneurysm rupture during manipulation of distal anastomosis and subsequent stroke (1).

There were three deaths. One case was determined to be definitely not device related, one case was likely device related and definitely procedure related, and the third case was one moderate adverse event likely device related.

There were five non-fatal strokes, one of which was determined to be likely device related.

Table 3 below summarizes the serious adverse events – regardless of the relationship to the device and table 4 summarizes other adverse events which occurred two or more times.

Table 3: Serious Adverse Events in the IDE Study
DEVICE and NON-DEVICE RELATED

Serious Adverse Event	N	Severity
• aneurysm: Brainstem infarction / diffuse subarachnoid hemorrhage / thrombus of basilar aneurysm with compression of the ventral pons • aneurysm: Intra-operative subarachnoid hemorrhage/large • pseudoaneurysm of basilar artery / massive brain edema tumor: Stroke	3	Severe (3)
Non fatal Stroke	5	Severe: 3 Mild: 2
Right SVG, wound dehiscence, infection → bacteremia, fever	1	Severe
Intracerebral hemorrhage under heparinization and hypertension	1	Moderate
Dissection of left common carotid artery during angiogram	1	Mild
Left femoral and lower extremity DVT	1	Mild
Aneurysm bleeding	1	Mild
Increased brain swelling in the frontal lobe	1	Severe
Intracerebral hemorrhage and cerebral edema	1	Severe
Unable to complete bypass (due to aneurysm rupture)	1	Severe
Right hip fracture	1	None

Table 4: Other Adverse Events in the IDE Study*

Adverse Event	N
Bypass occluded	4
Aphasia(Motor)	2
Hydrocephalus	2
Hemiparesis	3
Urinary tract Infection	3
Change in neurological status/exam	3
Worsening speech difficulties	2
Expressive aphasia	2
Pulmonary edema	2
Reduced hemoglobin/hematocrit	2
Anemia	2

*All events were mild or moderate except one case of bypass occlusion (severe).

Results for Pediatric Patient

One pediatric patient (age 17), was treated for a fast growing aneurysm. Preoperative mRS was a 2 and the postoperative mRS was a 1. The bypass was patent at 7 days postoperative. A flap (see below) occurred and was manually retrieved in the single pediatric subject (aged 17) in this study. The retrieval did not result in any adverse events.

PREMARKET DATA: RETROSPECTIVE EUROPEAN CLINICAL DATA

The HDE application was also supported by retrospectively collected data on 30 subjects from 7 European centers from 1993 through 2006. Data analyzed included bypass patency, mortality and non-fatal stroke rates. Ninety-three per cent (93%) of the subjects were followed for more than 30 days. The surgical indications were aneurysm in 72% and ischemia in 24%. There were a total of 4 pediatric subjects included (ages 10, 13, 18, and 18), three of whom had aneurysms while one 18 year old had an anomaly in the carotid artery.

Effectiveness Results

Table 5 provides effectiveness results of the retrospectively collected EU data. The 7 day post-op bypass patency was not examined in the retrospectively collected EU experience.

Table 5: Retrospective European (EU) Clinical Data
Effectiveness Data – All Subjects

Total Device Uses:	375
Total Subjects:	330 Anterior: 307/330 (93%) Posterior: 23/330 (7%)
Bypass patent ≥ 0 days post-op:	255/330 (77%) Anterior: 235/307 (77%) Posterior: 20/23 (87%)

Safety Results

The mortality rate was 7%, and the non-fatal stroke rate was 5% in the EU data.

Table 6: Retrospective European (EU) Clinical Data Safety Data – All Subjects

Total Device Uses	375
Total Subjects:	330 Anterior: 307/330 (93%) Posterior: 23/330 (7%)
All moderate/severe adverse events:	52/330 (16%) Anterior: 38/307 (12%) Posterior: 14/23 (61%)
Mortality:	24/330 (7%) Anterior: 16/307 (5%) Posterior: 8/23 (21%)
Non fatal stroke:	17/330 (5%) Anterior: 12/307 (4%) Posterior: 5/23 (21%)

Adverse Events

Table 7 below describes adverse events in the European Cohort in the period 1993-2006 which occurred two or more times (regardless of severity) and/or at least once but with a severe rating. The events may have been device related or not.

Table 7: Adverse Events

Adverse Event	N	Severity
Hemiparesis	26	Severe: 5/Moderate: 10/Mild: 11
Bypass occlusion	20	Severe: 9/Moderate:3/Mild: 8
(Brain) Edema	13	Severe: 9/Moderate: 2/Mild: 2
High intracranial pressure	8	Severe: 7/Mild: 1
Brain infarction / stroke	8	Severe:6/Moderate: 2
Subdural/epidural hematoma	6	Severe: 5/Mild: 1
Hydrocephalus	5	Severe: 3/Mild: 2
SAH	5	Severe: 3/Moderate: 1/Mild: 1
Aneurysm bleeding	4	Severe:3/Moderate: 1
Intracranial hemorrhage.	4	Severe:4
Intracerebral hematoma	3	Severe:2/Moderate: 1
Brain stem compression	2	Severe:2
Thrombosis of basilar artery	2	Severe: 2
Intraventricular hemorrhage.	1	Severe
Bypass torn off from vessel wall.	1	Severe
Gastric perforation.	1	Severe
Bypass abandoned	1	Severe
Pneumonia	1	Severe
Progressive anterolateral ischemia	1	Severe
Incontrollable blood pressure changes	1	Severe
Clot in bypass	1	Severe
Brain stem compression after coiling aneurysm.	1	Severe
Basilar syndrome	1	Severe
Thrombi in M1, M2 causing ischemia	1	Severe
Hemi paralysis	1	Severe
Severe coagulation problems	1	Severe
Air embolus in superior sagital sinus	1	Severe
Thrombosis of stent	1	Severe
Diffuse hemorrhage	1	Severe
Brain stem ischemia	1	Severe
Aneurysm rupture	1	Severe
Dysphasia	10	Moderate: 5/Mild: 5
Aphasia	6	Moderate: 2/Mild: 4
Bone flap infection	4	Moderate: 1/Mild:3
Hemiplegia	2	Moderate: 1/Mild: 1
Hemorrhage due to retraction	2	Mild

Results for Pediatric Patients

All 4 pediatric subjects had favorable post-operative mRs scores and no adverse events were noted. One pediatric subject (aged 18) had a patent bypass postoperatively; however, at one year the bypass was occluded. This was a patient from the ENT department and the doctor had made a radical cavity, a canal wall down mastoidectomy. However, there was an anomaly in the carotid artery; the carotid artery went through the radical cavity (instead of the skull base). Therefore it was decided to make a bypass and to close-off the carotid artery

PREMARKET DATA: ADDITIONAL RETROSPECTIVE EU DATA

In addition to the pediatric subjects included in the retrospective EU cohort (collected between 1993 and July 2006), data on 3 additional pediatric subjects age 6, 14, 17 years (collected from the Netherlands August, 2006- March 2009) were provided. All 3 were treated for aneurysms and had favorable post-operative mRs scores and bypass patency post operatively. Data on adverse events experienced by these subjects was not available.

PREMARKET DATA: "FLAP RETENTION" DATA

Following use of the Elana Arteriotomy System, there is a potential for the laser perforation not to be complete and result in a circular disk of tissue (or "flap") being retained on the artery wall. This condition may occur if the Catheter does not completely contact the artery wall within the Ring or if the suture exerts uneven or excessive tension on the artery wall within the Ring. There is a potential for the retained flap to embolize when it is not removed manually. In order to remove the flap, the artery must be occluded.

The rate of flap retention in the IDE clinical study was 22% (8/37 device uses in 33 subjects). In 5 of those 8 subjects with a retained flap, the flap was manually retrieved and in 3 cases no flap was retrieved. In the 5 cases of manual flap retrieval, there was 1 severe adverse event - a diffuse subarachnoid hemorrhage and thrombosis of basilar aneurysm with compression of the ventral pons. In the 5 cases of manual retrieval, the average arterial occlusion time was 8 minutes (5-11 minutes). A flap occurred and was manually retrieved in the single pediatric subject (aged 17) in this study. The retrieval did not result in any adverse events. In the 3 cases where no flap was retrieved, there was one severe adverse event consisting of an aneurysm rupture during manipulation of the distal anastomosis with subsequent stroke. In another case the flap dissolved and the arteriotomy was successful (patent bypass at seven (7) days post-op). In the 3rd case the investigators decided to abandon the anastomosis and bypass.

The rate of flap retention in the retrospectively evaluated European (EU) cohort was 26% (96/375 device uses). Data on flap retention were lacking in 4% of the total devices used. Manual flap retrieval was not performed in Utrecht from 1993 to 2003, as their protocol defined that when no flap was retrieved on the catheter (i.e., flap still attached to the artery wall), the bypass was abandoned unless it showed a bypass flow of at least 50 ml/min. Surgeons began to manually retrieve flaps in 2004; therefore, manual flap retrieval has been performed in only 2% (9/375) of device uses in the retrospective EU experience. In 1 of 330 of the European cases, embolization of a retained flap could not be excluded but the subject improved markedly and was active walking (with aid), and talking but was still experiencing severe weakness of the right hand and arm. No pediatric subjects in the EU cohort had flap retention.

PREMARKET DATA: HISTORICAL COMPARISON

Historical data were found via a literature search to identify conventional extracranial to intracranial (EC-IC) bypass operations to a major intracranial artery. Only series with at least 5 subjects with vein grafts and those that presented safety data were included. No prospective study on conventional EC-IC bypass operations could be found. One publication (Amin-Hanjan et al., 2005) used population based methods to analyze a representative sample of the U.S. medical community. The remaining articles present single-center retrospective experience. Only the Mayo clinic experience (Regli et al., 1995) analyzes a large series over a long period of time with operations by several surgeons and includes the initial learning curve. It provided the most reliable comparison for mortality and non-fatal stroke. The data within this article fell within the range of the average from all other literature articles. Table 8 compares the IDE data, the EU data and the Mayo clinic experience (Regli et al., 1995) literature article.

Table 8: Elana Arteriotomy System$_{HUD}$ Data versus Literature

Summary	**IDE data**	**EU data**	**Literature** (Regli et al., 1995)
Total device uses	37	375	n/a
Total subjects:	33	330	202
Anterior	32/33 (97%)	307/330 (93%)	104/202 (51%)
Posterior	1/33 (3%)	23/330 (7%)	98/202 (49%)
Bypass patent 0/7/30 days post-op:	7 days [1,2]**:**	$\geq$ 0 days	30 days
Anterior	22/30 (73%)	235/307 (77%)	87/104 (83%)
Posterior	0/1 (0%)	20/23 (87%)	86/98 (88%)
Total	22/31 (71%)	255/330 (77%)	173/202 (86%)
Mortality:			
Anterior	2/32 (6%)	16/307 (5%)	11% (11/104)
Posterior	1/1 (100%)	8/23 (35%)	19% (19/98)
Total	3/33 (9%)	7% (24/330)	15% (30/201)
Non fatal stroke:	with permanent deficits at 30 days		
Anterior	5/32 (16%)	12/307 (4%)	Estimated[3] 13%
Posterior	0/1 (0%)	5/23 (22%)	Estimated[3] 23%
Total	5/33 (15%)	17/330 (5%)	Estimated[3] 18%

[1] includes subjects that expired within 7 days (no patent bypass at 7 days)

[2] excluded 2 subjects with protective bypass

[3] The Mayo Clinic experience [Regli et al, see footnote 8] includes 21 cases of neurological worsening due to early graft occlusion. The report does not report intra-operative stroke from other reasons. In 8/21 cases, the subjects subsequently died, leaving 13 nonfatal strokes from graft occlusion. Other causes (thrombosis, hemorrhage) that also cause non-fatal strokes are fatal 1.8 times as frequent as graft occlusion. The assumption that hemorrhage and thrombosis cause nonfatal strokes in the same ratio as they caused fatal strokes thus leads to an estimated total of 36/201 (18%) non-fatal strokes. Along the same lines, non-fatal stroke for the posterior circulation should be responsible for about 63% of these strokes (for a rate of about 23%), and anterior circulation for the remainder for a rate of 13%.

PREMARKET DECISION

FDA determined that the collective evidence of the prospective IDE study data and the retrospective European data, as compared to the available literature data, demonstrated a reasonable assurance of safety and probable benefit for the indicated patient population. The decision to approve use in pediatric subjects aged 13 and over was based on the pediatric data provided by the sponsor and because the main limiting factor in device use is the recipient vessel size rather than patient age and by age 13 subjects should have approximately adult sized intracranial vessels. The device received FDA HDE approval on March 10, 2011.

COMPARABLE DEVICES

There are limited treatment options for a patient with an aneurysm or a skull base tumor affecting a large, intracranial artery that failed balloon test occlusion, cannot be sacrificed, or cannot be treated with conventional means due to local anatomy or complexity. Traditionally, aneurysms and/or tumors that cannot be treated via endovascular means are treated surgically by cutting off blood flow through the affected area while a bypass graft is placed. Although FDA has recently approved flow diversion devices for the endovascular treatment of aneurysms, no device has been cleared/approved for assisting in bypass grafting of aneurysms comparable to the Elana device. Furthermore, Elana is a tool which can be used to assist in the bypass treatment of skull based tumors, whereas flow diversion devices are only used in the treatment of aneurysms.

ANNUAL DISTRIBUTION NUMBER

The Pediatric Medical Device Safety and Improvement Act of 2007 allowed HDEs indicated for pediatric use and approved on or after September 27, 2007, to be sold for profit as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). The ADN is the number of individuals affected by the disease or condition per year multiplied by the number of devices reasonably necessary to treat an individual. The ADN for the Elana device was 1000 when it was approved by CDRH.

DEVICE DISTRIBUTION WITHIN THE UNITED STATES

Per the sponsor's Annual HDE Report dated March 6, 2013, and discussion through mid-April 2013, since HDE approval:

- A total of 15 devices were distributed to 4 medical facilities within the United States
- A total of 2 devices have been used (both in adults, and both enrolled in the post-approval study), 1 has been returned, and 12 remain at the sites in inventory
- No devices have been used in, or shipped for use in pediatric subjects

According to the sponsor, the availability of newer flow diversion devices and others since the time of HDE approval has reduced the number of bypass surgeries done for the treatment of aneurysms. The company notes that their device "is/will mainly be used as a last-resort option."

POSTMARKET DATA: MEDICAL DEVICE REPORTS RECEIVED BY FDA

The Manufacturer and User Facility Device Experience (MAUDE) database was searched to identify any Medical Device Reports (MDRs) associated with the Excimer Laser Assisted Non-occlusive Anastomosis device which had been reported to FDA since the time of approval. As of July 2013, *no* MDRs associated with the device have been received.

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 2012 PAC

As of July 30, 2012, the sponsor stated that all eight sites had IRB approval, and that 12 devices had been shipped to sites. No subjects had been enrolled, nor had any devices been used.

Updated PAS Status and Results as of April 2013

The database closing date for the most recent report was March 6, 2013. At that time, 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.

POSTMARKET DATA: LITERATURE REVIEW

Literature Review Presented at the 2012 PAC

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 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 last year.

SUMMARY

A total of 15 devices have been distributed in the U.S since HDE approval although only 2 have been used at the time of this Executive Summary. Both uses were in adult subject and these two subjects were enrolled in the post-approval study. No MDRs associated with ELANA have been received by FDA and no new articles have been published since last year's literature review. In large part due to the limited use of the device since approval, no new safety issues have been identified.

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