Food and Drug Administration
Center for Devices and Radiological Health

Summary Minutes of the Circulatory System Devices Panel of the Medical Devices Advisory Committee Meeting

JUNE 12, 2018

Location: Hilton Washington, DC/North, Salons A, B, C and D, 620 Perry Pkwy., Gaithersburg, MD 20877

Topic: The committee discussed the Premarket Approval Application for the INCRAFT AAA Stent Graft System, which is intended for the endovascular treatment of infrarenal abdominal aortic aneurysms in patients with appropriate anatomy.

The following is the final report of the Circulatory System Devices Panel of the Medical Devices Advisory Committee meeting held on June 12, 2018. A verbatim transcript will be available in approximately six weeks, sent to the Division of Cardiovascular Devices and posted on the FDA website at: MEDICAL DEVICES ADVISORY COMMITTEE PANEL MATERIALS

All external requests for the meeting transcript should be submitted to the CDRH Freedom of Information Office.

The Circulatory System Devices Panel of the Medical Devices Advisory Committee of the Food and Drug Administration, Center for Devices and Radiological Health met on June 12, 2018, at the Hilton Washington, DC/North, Salons A, B, C and D, 620 Perry Pkwy., Gaithersburg, MD 20877. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Cordis. The meeting was called to order by Richard Page, MD (Chairperson). The conflict of interest statement was read into the record by Evella Washington (Designated Federal Officer). There were approximately 125 people in attendance. There were seven Open Public Hearing (OPH) speaker presentations.

Introduction:

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on June 12, 2018 to discuss, make recommendations, and vote on information related to the premarket approval application for the Cordis INCRAFT AAA Stent Graft System. The INCRAFT AAA Stent Graft System is a modular system with endovascular grafts consisting of nitinol stent rings attached to woven polyester grafts, and delivery systems in which the implants are pre-loaded. The device is designed to exclude an infrarenal aortic aneurysm from blood flow.

The sponsor has proposed the following Indications for Use:

The INCRAFT AAA Stent Graft System is intended for the endovascular treatment of patients with infrarenal abdominal aortic aneurysms with the following characteristics:

- Adequate Iliac or femoral vessel morphology that is compatible with vascular access techniques, devices and accessories
- Proximal neck length ≥ 10mm
- Aortic neck diameters ≥ 17mm and ≤ 31mm
- Aortic neck suitable for suprarenal fixation
- Infrarenal and suprarenal neck angulation ≤ 60°
- Iliac fixation length ≥ 15mm
- Iliac diameters ≥ 7mm and ≤ 22mm
- Minimum overall AAA treatment length (proximal landing location to distal landing location) ≥ 128mm

Attendance:

MDAC Members Present (Voting): David Kanzari, MD; Kristen Patton, MD

MDAC Member Not Present (Voting): N/A

MDAC Member Present (Non-Voting): *Elijah N. Wreh* (Industry Representative); Rachel Brummert (Consumer Representative); Patricia Lupole (Patient Representative).

Temporary Members (Voting): Richard Lange, MD, MBA; Eugene H. Blackstone, MD; David L. Cull, MD, FACS; Edwin C. Gravereaux, MD; Jeffrey Brinker, MD; Albert G. Hakaim, MD; Todd E. Rassmussen, MD; Paul D. Stein, MD; Charles J. Shanley, MD, FACS, RPVI; Brian D. Choules, PhD; Lt. COL. Brandon W. Propper, MD, FACS, RPVI

Designated Federal Officer (Non-Voting): Evella F. Washington

FDA Participants (Non-Voting): Valerie M. Merkle, PhD; Robert E. Lee, MD

Open Public Hearing Speakers: Alvin Drapkin, Delray Beach FL.; Takao Ohki, MD, Kikei University School of Medicine, Tokyo, Japan;Peter A. Schneider, MD, Kaiser Permanente Medical Center-Honolulu, HI; William Ward; Gail Waagen, Sandford Clinic Broadway-Fargo, ND;Megan Polanin, PhD, National Center for Health Research-Washington, DC;Nelson Lim Bernardo, MD, MedStar Heart Institute.

The agenda was as follows:

Call to Order and Introduction of Committee	**Richard Page, MD** Chairperson, MDAC
Conflict of Interest Statement	**Evella Washington** Designated Federal Officer, MDAC
APPLICANT PRESENTATIONS	**Cordis, Incorporated**
Introduction	**Shaden Marzouk, MD, MBA** Chief Medical Officer Cardinal Health
Background on EVAR	**Robert Bersin, MD, FSCAI, FACC** Medical Director Emeritus Endovascular Services and Structural Heart Srvcs Swedish Medical Center, Seattle
Study Design and Primary Study Results	**Michel Makaroun, MD** Professor and Chair, Div. of Vascular Surgery Co-Director UPMC Heart and Vascular Institute University of Pittsburgh Medical Center Co-Principal Investigator, INSPIRATION Trial
Identified Events of interest	**Kenneth Ouriel, MD** President and CEO, Syntactx Medical Monitor for INSPIRATION Trial
Stent Strut Fractures	**Alan Pelton, PhD** Chief Technical Officer G. RAU Inc.
Proposed Post-Approval Plan	**Shaden Marzouk, MD, MBA** Chief Medical Officer Cardinal Health
Clinical Perspective	**Robert Bersin, MD, FSCAI, FACC** Medical Director Emeritus Endovascular Services and Structural Heart Srvcs Swedish Medical Center, Seattle
BREAK	
FDA PRESENTATION	
Introduction & Regulatory History	**Valerie M. Merkle, PhD** Lead Reviewer/Biomedical Engineer Division of Cardiovascular Devices Office of Device Evaluation (ODE)/CDRH

Clinical Background, INSPIRATION Study Design and Results	**Robert E. Lee, MD** Medical Officer/Vascular Surgeon Division of Cardiovascular Devices Office of Device Evaluation (ODE)/CDRH
Event Discussion & Synopsis	**Valerie M. Merkle, PhD** Lead Reviewer/Biomedical Engineer Division of Cardiovascular Devices Office of Device Evaluation (ODE)/CDRH

Clarifying Questions to FDA

LUNCH

Open Public Hearing

Panel Deliberations

BREAK

FDA Questions to the Panel

FDA and Sponsor Summations

Questions to the Committee:

1. DISCUSSION: **Transrenal Stent Fractures**

   Please comment on whether the lack of known clinical sequelae reported to-date (e.g., implant migration, Type I endoleaks, perforation) and migration resistance bench testing are sufficient to mitigate the concerns for long-term clinical sequelae associated with the observed fracture rate.

   Standard imaging evaluation by physicians is unlikely to detect fractures. Please comment on whether fracture detection would be needed for appropriate follow-up of patients treated with the INCRAFT device, given the high rate of fractures that were identified during the clinical study. Alternatively, would standard follow-up to evaluate aneurysm exclusion, device position, and aneurysm size be sufficient, particularly as the fractures have yet to be associated with clinical sequelae.

   Committee Discussion: The panel acknowledged that the fracture rate observed in the INSPIRATION study appeared high; however, the committee felt that the lack of clinical sequelae with 4 to 5 year follow-up and the tissue incorporation associated with bare stents suggested that the fractures were not clinically meaningful. The panel also recommended that standard follow-up to assess adequate seal, maintenance of implant location, and stability of aneurysm size is adequate for patients with an INCRAFT device; that is, the panel indicated that detection of fractures was not needed in routine clinical practice in the absence of other clinical events.

2. DISCUSSION: **Aneurysm Expansion**
   Please comment on the possible reasons for the observed rate of Type II endoleaks observed in the INSPIRATION study, for example, could the permeability of the graft material or the amount of wall motion contribute to the development of Type II endoleaks.

   Aneurysm expansion indicates that the treatment is failing to halt disease progression and leaves the patient at increased risk of rupture and death. Please comment on how subjects who experience aneurysm expansion in the presence of a Type II endoleak should be considered when evaluating the effectiveness of the device.

   Committee Discussion: In regards to the rate of Type II endoleaks observed in the INSPIRATION study, the panel indicated that the rate may be higher than reported in previous studies due to improvements in imaging. They also indicated that although there may be factors contributing to Type II endoleaks, these factors have not been identified. Most panelists did not believe Type II endoleaks were device-related.

   The panel was in agreement that aneurysm expansion in general indicates that the treatment is failing to halt disease progress and leaves the patient at an increased risk of rupture and death. In regards to the rate of aneurysm expansion that was attributed to Type II endoleaks in the INSPIRATION study, the panel indicated that although the rates are high, in absence of a device-related cause for the expansion, these expansions should not count against the device.

3. DISCUSSION: **Benefit-Risk Analysis**
   Based on the clinical data presented from the INSPIRATION study including the effectiveness-related observations noted in both the acute and long-term follow-up, please discuss the probable benefits and the probable risks of the INCRAFT device.

   Please comment on whether the proposed labeling is acceptable or whether modifications to sections such as the warnings/precautions or follow-up recommendations are recommended to minimize the risks that have been identified during the study.

   Committee Discussion: Taking into consideration all of the safety and effectiveness-related events reported in the INSPIRATION study, several panel members indicated that they would not recommend use of the INCRAFT device in a standard patient population that may be treated by commercially available devices; however, it may be suitable for patients with small access vessels and/or complicated iliac anatomies. When discussing the proposed indications for use statement, the panel did not have a specific recommendation for revised indications, or warnings and precautions to include in the labeling, and the majority believed the broad indication as proposed was adequate.

4. DISCUSSION: **Proposed Post-Approval Study (PAS)**
   Please comment on whether any additional study objectives, design features, or surveillance are recommended.

Committee Discussion: The panel recommended that a post approval study be conducted to collect data on additional patients. The panel recommended that the study include follow-up consistent with the follow-up schedule and imaging used in the INSPIRATION pivotal study, including Core Lab review of annual CT imaging, in particular. They recommended that the study endpoints be modified to capture additional effectiveness-related events and also suggested that the study enroll a higher percentage of women. The need for longer-term follow-up was proposed.

5. **VOTE:** Based on data in the briefing materials and presentations at today's meeting, do you believe that there is reasonable assurance that the *INCRAFT® AAA Stent Graft System* is safe for use in patients who meet the criteria specified in the proposed indication, while considering the additional procedures needed to maintain effectiveness?

   Vote Result: Yes: **11** No: **4** Abstain: **0**

6. V**OTE:** Based on data in the briefing materials and presentations at today's meeting, do you believe that there is reasonable assurance that the INCRAFT® AAA Stent Graft System is effective for use in patients who meet the criteria specified in the proposed indication?

   Vote Result: Yes: **14** No: **0** Abstain: **1**

7. V**OTE:** Based on data in the briefing materials and presentations at today's meeting, do you believe that the benefits of the INCRAFT® AAA Stent Graft System outweigh the risks for use in patients who meet the criteria specified in the proposed indication?

   Vote Result: Yes: **11** No: **4** Abstain: **0**

Committee Discussion: The panelists who voted "no" to Voting Question 1 and/or Voting Question 3 stated that their vote was related to the indication statement; specifically, that the indication should be narrowed to only treat small access vessels and/or complicated iliac anatomies; or, was related to the need for additional clinical data to better understand the reasons for the events observed in the study. There were several panelists who voted "yes" to Voting Question 3 that noted the importance of collecting additional clinical data through a post approval study to better inform the benefits and risks of the device in the future.

The meeting was adjourned at approximately 6:00 p.m.

I certify that I attended the *INCRAFT® AAA Stent Graft System* meeting of the Circulatory System Devices Panel of the Medical Devices Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

Evella F. Washington

Evella Washington
Designated Federal Officer