Panel Questions

INCRAFT AAA Stent Graft System

June 12, 2018

Transrenal Stent Fractures

- 19/190 with at least 1 transrenal stent fracture
- 7 subjects with multiple fractures identified
  - 5 of which have fracture propagation

	1-month	6-month	1-year	2-year	3-year	4-year	5-year
# of subjects w/imaging adequate to assess fracture	183	172	163	144	132	108	38
# of subjects newly identified with at least 1 fracture[&]	-	3	5	2	3	4	2
Cumulative # of subjects with a fracture[$$]	-	3	8	10	13	17	19
Cumulative # of fractures[&&]	-	7	14	22	26	31	38

Visit windows are defined based on imaging windows: Procedure (day 0), 1 Month (1 - 90 days), 6 Months (91 - 270 days), 1 Year (271 – 540 days), 2 Years (541 - 900 days), 3 Years (901 - 1260 days), 4 Years (1261 - 1620 days), and 5 Years (1621 - 1980 days).

$$ - Subjects with fractures identified will continue to be included in the numerator and denominator for later time points.

& - Number of subjects newly identified with at least 1 fracture indicates those subjects that were not previously reported as having at least 1 transrenal stent fracture

&& - Cumulative number of total fractures observed – once a fracture is reported, it will continue to be reported for later time points

Question #1: 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.

Question #1: Transrenal Stent Fractures

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.

Aneurysm Expansion

- **29 subjects (29/189, 15.3%)** have had **aneurysm expansion**
  - **25 likely attributable to Type II endoleaks**
  - 3 likely attributable to Type I endoleak
  - 1 likely attributable to endotension
- **25% (25/101) of subjects with a Type II endoleak** had **aneurysm expansion** attributed to that endoleak

Question #2: 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.

Question #2: Aneurysm Expansion

- 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.

Benefit/Risk Analysis

- Composite safety and effectiveness endpoints were met

Observation		Clinical Event	
Description	**Subjects**	**Subjects**	**Event**
Transrenal stent fracture(s)	19	0	No known clinical sequelae
Type I endoleak (after 30 days)	10	3 8	Aneurysm expansion Secondary interventions
Type II endoleaks	101	25 16	Aneurysm expansion Secondary interventions
Type V endoleak	1	1	Aneurysm expansion
Stent graft stenoses	16	7 *(1)*	Secondary intervention *(conversion to open repair)*
Occlusion	10	10 *(1)* *(1)*	Secondary intervention *(conversion to open repair)* *(axillo-bifemoral bypass)*

Question #3: 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.

Question #3: Benefit-Risk Analysis

- 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.

Question #4: Post Approval Study

- **Objective:** To confirm the safety & effectiveness of the INCRAFT device
- **Design:** Multi-center, prospective, open-label observational study
- **PAS Enrollment**
  - 150 subjects from INSIGHT European registry
  - 150 de novo U.S. subjects
- **Follow-up**
  - **Standard of care** out to 5-years

Question #4: Post Approval Study

- Please comment on whether any additional study objectives, design features, or surveillance are recommended.


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