FDA PANEL QUESTIONS

Note: Please refer to the FDA Executive Summary, including the "Rationale for the Agency's Non-Voting and Voting Questions for the Panel" section for background information related to the question.

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Panel Non - Voting Question 1

- Please comment on a 15% non-inferiority margin used for the Cartiva clinical study in terms of effectiveness, safety, and overall success. If a 15% margin for overall success is an appropriate margin for this study, please explain your rationale. If the Panel does not believe this margin to be appropriate or clinically meaningful, please recommend a non-inferiority margin that you believe to be appropriate and clinically meaningful for this study.

Panel Non - Voting Question 2

- Both groups experienced pain reduction. However, the reduction from baseline pain scores was substantially lower for Cartiva subjects compared to Arthrodesis subjects at the pre-specified primary time point of 1 year. Similar results for comparisons of pain reduction occurred at every time point from 6 weeks to 2 years. Please discuss the clinical interpretation of these findings for the Cartiva device group and the Arthrodesis control group.

Panel Non - Voting Question 3

- Arthrodesis was substantially better for the pre-specified primary functional assessment, FAAM Sports at Month 12. In examining change from baseline FAAM ADL (FDA requested post-hoc) scores, Arthrodesis subjects performed better than Cartiva subjects at every time point from Month 3 to Month 24. A responder analysis showed non-inferiority, but to be a responder, the only requirement is to not worsen by 8 or 9 points in terms of function. In consideration of these assessment criteria, please discuss the clinical interpretation of these findings for the Cartiva device group, in which the device is intended to maintain motion over time, and the Arthrodesis control group.

Panel Non - Voting Question 4

- The rate of Subsequent Secondary Surgical Intervention (SSSI) events among randomized Cartiva subjects through 24 months was 10%. This does not include the 18% of roll-in subjects and does not include 4 SSSI events that occurred after 24 months. There is an element of subjectivity for determining the threshold for surgical intervention in either the Cartiva or Arthrodesis groups. Please comment on whether or not SSSI patients in the Cartiva and the reported procedures for device removal following successful Arthrodesis should be successes or failures. Please discuss the long term clinical interpretation of these findings for the Cartiva device group and the Arthrodesis control group.

Panel Non - Voting Question 5

- The two devices have different criteria for determining radiographic success or failure. Please discuss the clinical interpretation of these findings for the Cartiva device group, in which the device is intended to maintain motion over time, and the Arthrodesis control group which is intended to eliminate motion.

Panel Non - Voting Question 6

- Prospective subjects will likely have the impression that increased mobility will allow for greater function in Cartiva as compared to Arthrodesis. However, the level of function for Cartiva appears to be the same or worse than Arthrodesis from 3 months to 2 years. Does the Panel have any suggestions regarding the education of prospective subjects so they are able to make informed decisions with regards to realistic expectations and goals regarding function following Cartiva or Arthrodesis procedures? Can the Panel provide a discussion on how best to objectively capture patient preferences with regards to either procedure?

Reminder

- The discussion of a PAS prior to FDA determination of product approvability should not be interpreted to mean that FDA is suggesting that the product is safe and effective.

- The plan to conduct a PAS does not decrease the threshold of evidence required by FDA for product approval.

- The premarket data submitted to the Agency and discussed today must stand on its own in demonstrating a reasonable assurance of safety and effectiveness and an appropriate risk/benefit balance.

Panel Non - Voting Question 7

- Please comment on the need for PAS (Post Approval Study(ies)) and what questions should be addressed by such study(ies), should FDA determine that this PMA application is approvable.

Panel Voting Questions

- The following Indications for Use are proposed by the sponsor in the PMA application:
- "The Cartiva® Synthetic Cartilage Implant is intended for use in the treatment of patients with degenerative or post-traumatic arthritis in the first metatarsophalangeal joint in the presence of good bone stock along with the following clinical conditions: hallux valgus or hallux limitus, hallux rigidus, and an unstable or painful metatarsophalangeal joint."

Panel Voting Question 1

Is there a reasonable assurance that the Cartiva Synthetic Cartilage Implant is safe for use in patients who meet the criteria specified in the proposed indications for use described above?

Panel Voting Question 2

Is there a reasonable assurance that the Cartiva Synthetic Cartilage Implant is effective for use in patients who meet the criteria specified in the proposed indications for use described above?

Panel Voting Question 3

Do the benefits of the Cartiva Synthetic Cartilage Implant outweigh the risks when used in patients who meet the criteria specified in the proposed indications for use described above?

THANK YOU