FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH

Brief Summary
of the
Gastroenterology and Urology Devices Panel Meeting
TransMedics Organ Care System (OCS) Liver
July 14, 2021

Introduction:

The Gastroenterology and Urology Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on July 14, 2021, to discuss, make recommendations, and vote on information regarding the premarket approval application (PMA) for the Organ Care System (OCS) Liver System, by TransMedics, Inc.

The proposed Indication for Use for the OCS Liver System, as stated in the PMA, is as follows:

The TransMedics® Organ Care System (OCS™) Liver is a portable extracorporeal liver perfusion and monitoring system indicated for the resuscitation, preservation, and assessment of liver allografts from donors after brain death (DBD) or liver allografts from donors after circulatory death (DCD) ≤55 years old in a near-physiologic, normothermic and functioning state intended for a potential transplant recipient.

Panel Deliberations/FDA Questions:

1. Question 1a asked if the early allograft dysfunction (EAD) results for the primary effectiveness endpoint support a reasonable assurance of the safety and effectiveness of the OCS Liver System. Some of the panelists were uncertain of EAD as a surrogate endpoint and indicated a preference for a stronger clinical outcome. The preponderance of the panel agreed that the EAD results from the study provide reasonable assurance of safety and effectiveness.

   Question 1b stated that in the PROTECT trial, 63% of EAD cases in the OCS arm were only because of transaminase (AST)>2000, as were 77% in the Control arm. The panel discussed the impact of EAD being mostly driven by AST on the interpretation of study results. The preponderance of the panel accepted EAD, despite the dominance of AST.

2. Question 2 asked the panel about the secondary effectiveness endpoints, including recipient survival at 30 days post-transplant and recipient survival at initial hospital discharge post-transplant. Question 2 also referenced Kaplan-Meier curves of recipient and graft survival at 6, 12, and 24 months. The panel agreed that the secondary

effectiveness endpoints and the survival results support a reasonable assurance of the safety and effectiveness of the OCS Liver System.

3. Question 3 asked the panel to discuss whether EAD was an appropriate surrogate for survival in the OCS and Control arms considering the similarity of observed survival in the OCS and Control arms. Most panel members indicated that EAD is an acceptable, but not ideal, surrogate endpoint for survival.

4. Question 4 asked the panelists to discuss the safety assessment, which included liver-graft related serious adverse events (LGRSAE) through 30 days. LGRSAEs were also tracked at 6 months, and non-ischemic biliary complications were reported at 30 days. The panel agreed that these results demonstrate device safety for the intended population.

5. Question 5 asked the panel to discuss the uncertainty of the trial results given the trial randomization strategy and dry run/screen failures.

    a. Among the 476 donor livers in the PROTECT trial, 176 (37%) were screen failures and were excluded from the study. Some panel members expressed concern about the high number of screen failures and the resulting uncertainty, but did not see a systematic bias. The panel concluded that this was generally acceptable, given the difficulties of conducting clinical trials in transplantation.

    b. Among the 429 consented recipients, 129 (30%) were excluded from the PROTECT trial and had no primary and limited secondary endpoint data collected. Of these excluded subjects, 49 (11%) were randomized and transplanted outside of the trial and not followed. The panel concluded that this does not materially impact how the study results should be interpreted, but for future studies, there should be follow up on these patients.

6. Question 6 asked the panelists to comment on the significance of the three device malfunctions, which were reported in the OCS arm, one of which resulted in the organ transfer to cold static storage for transplantation. Panel members spoke about the significance of device malfunctions and the need for device labeling to be clear on what to do in the event of a device malfunction. The panel concluded that the sponsor has adequately addressed backup, including reverting to cold storage in the case of a malfunction.

7. Question 7 asked the panelists to discuss the three livers turned down for transplant that were initially assessed as “transplantable” following donor organ retrieval surgery but were deemed “non-transplantable” following OCS preservation. The panel concluded

that it was a low number of liver turndowns; turndowns should be tracked going forward, and could help inform design of a post approval study if the device is approved.

8. Question 8 was related to indications for use and labeling claims.

    a. Question 8a asked the panel if the OCS Liver System *ex vivo* measurement of liver enzymes, lactate, and bile production is sufficient to determine that certain donor livers are not appropriate for transplantation. Panel members discussed the need for consideration of other information (e.g., biopsies and donor history), and the need for more data are needed to understand how this device would be used in clinical practice. The panel concluded that measurements made by the OCS device are not adequate to make the complex clinical decision of turning down a liver.

    b. Question 8b asked the panel if the data provided for DCD donor livers support an indication for use that includes DCD livers. Most of the panel agreed with the indication including DCD livers, and that more data should be collected on DCD livers.

    c. Question 8c asked the panel if the study demonstrated improved utilization for DCD livers. The majority of the panel stated that the labeling should not include claims of increased utilization of DCD livers.

    d. Question 8d asked the panel if the labeling should support a claim of a reduction in ischemic biliary complications. The majority of the panel said that the data do not support a labeling claim of reduction of ischemic biliary complications.

9. Question 9 asked if a new enrollment post approval study (PAS) was needed and, if so, what would be the key design elements of the study, and is it appropriate to leverage the TOP Registry for the new study. The majority of the panel agreed that the sponsor should conduct a new enrollment study that examines the following: higher risk donor livers (particularly DCD livers but also DBD livers, steatotic livers, and livers from older donors); device malfunctions; ischemic biliary complications; non-biliary complications; higher risk transplant recipients; and patient reported outcomes. The panel indicated that a single-arm study design with 2 years of follow-up post-transplant would be adequate. The panel also recommended a survey of surgeons to better understand their decision-making process, such as reasons for graft turndowns and whether presence of the OCS device impacts their decision to procure/transplant a marginal liver. Some panelists recommended leveraging the TOP registry for this new enrollment PAS.

Vote:

Voting Question 1, regarding whether there is reasonable assurance that the TransMedics OCS Liver is safe for use in patients who meet the criteria specified in the proposed indication, the panel voted:

Yes: 14

No: 0

Abstain: 0

Voting Question 2, regarding whether there is reasonable assurance that the TransMedics OCS Liver is effective for use in patients who meet the criteria specified in the proposed indication, the panel voted:

Yes: 14

No: 0

Abstain: 0

Voting Question 3, regarding whether the benefits outweigh the risks of the TransMedics OCS Liver for the proposed indication, the panel voted:

Yes: 12

No: 1

Abstain: 1

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