

OPTN Liver & Intestinal Organ Transplantation Committee

Meeting Summary

October 16, 2023

Detroit, Michigan

Scott Biggins, MD, Chair

Shimul Shah, MD, MHCM, Vice Chair

Introduction

The OPTN Liver and Intestinal Organ Transplantation Committee met in Detroit, MI, and via Citrix Webex teleconference on 10/16/2023 to discuss the following agenda items:

1. Review: Continuous Distribution Public Comment Feedback
2. Recap: Liver Continuous Distribution Decisions
3. Preview: Optimization Analysis Dashboard
4. Discussion: Continuous Distribution, Travel Efficiency Attribute
5. Update: OPTN Taskforce on Efficiency
6. Discussion: Continuous Distribution, Utilization Efficiency Attribute
7. Data Request: Geographic Equity Attribute
8. Review: Median MELD at Transplant (MMAT) Around the Donor Hospital, Six-month Monitoring Report
9. Discuss: National Liver Review Board (NLRB) Subcommittee Project, Transplant Oncology Guidance
10. Discuss: Impact of Terlipressin on MELD Score

The following is a summary of the Committee's discussions.

1. Review: Continuous Distribution Public Comment Feedback

The Committee reviewed the public comment received on *Update on Continuous Distribution of Livers and Intestines, 2023*.

Summary of discussion:

A member commented that they were impressed by how quickly the transplant field is evolving, especially with the increased prevalence of machine perfusion. They encouraged the Committee to design a flexible system to accommodate future changes that may arise and noted that as an advantage of continuous distribution.

Another member noted that they thought it was interesting how pediatrics was a common theme amongst feedback, and the community feels that there should be a focus to prioritize pediatric candidates.

A member questioned the relevance of patient access versus transplant program access which was seen in the feedback. The Vice-Chair reminded the Committee that larger transplant programs may notice benefit in a new system, which has already been seen with machine perfusion. They cautioned that as distribution becomes more complex and requires more logistics regarding placement efficiency, the smaller transplant programs may not benefit in the same way as the large transplant programs.

A member suggested that the Committee revisit the post-transplant outcome attribute due to some public comment feedback. The Chair reminded the Committee that the post-transplant survival outcome was not able to be successfully modeled.

Next steps:

The Committee will consider public comment feedback when designing the continuous distribution system.

2. Recap: Liver Continuous Distribution Decisions

The Committee reviewed decisions to date on attributes within liver continuous distribution.

Summary of discussion:

A member commented that few split liver transplants are being performed and questioned the reasoning for that. They suggested the Committee should not add complexity to the split liver attribute, especially since split livers are great opportunities for pediatric candidates. The Chair said it is worthwhile to continue considering split liver transplants and agreed that it is complicated for a variety of reasons. They agreed that split livers are beneficial for pediatric candidates and added that small-statured adults would also benefit from split livers.

The Vice Chair commented that the data surrounding split liver transplants is complex, specifically the definition and what constitutes a split liver transplant.

A member noted that the Committee should spend more time on the medical urgency attribute, specifically the exceptions, as they comprise about 20% of the match run. Another member indicated their desire to determine what kind of priority exception candidates will receive and attempt to model that upfront.

Next steps:

The Committee will continue to develop the continuous distribution system.

3. Preview: Optimization Analysis Dashboard

The Committee reviewed the optimization analysis dashboard developed for the OPTN Kidney Transplantation Committee and how it was utilized to develop kidney continuous distribution.

Summary of discussion:

A member noted that this dashboard has the same constraints as other models since historical data is being used.

Another member asked if it was possible to compare attributes within the dashboard, specifically geographic distances versus population density. The Chair asked how model for end-stage liver disease (MELD) exceptions would be incorporated into the dashboard, or if the Committee was tasked with that prior to inputting information into the dashboard. Staff commented that thinking about the purpose of the exceptions is going to drive how they are incorporated into continuous distribution.

Next steps:

The Committee will continue to make decisions regarding attributes that will aid in the creation of the liver continuous distribution dashboard.

4. Discussion: Continuous Distribution, Travel Efficiency Attribute

The Committee reviewed the travel efficiency attribute within liver continuous distribution.

Summary of discussion:

The Committee reviewed the rating scales that the OPTN Lung Transplantation and Kidney Transplantation Committees developed for their respective continuous distribution frameworks.

A member voiced their concern about having hard cutoffs with nautical mileage (NM) when addressing the travel efficiency attribute, because a five NM difference could impact the availability of offers a transplant program may receive. Another member reminded the Committee that there are multiple attributes that contribute to a composite allocation score, so the specific NM may not have an impactful difference.

A member noted that flights begin to be considered when their drive time is longer than two hours. Another member stated that their transplant program uses a three-hour drive cut off. A member questioned whether there should be differences in drive time within the rating scale, or if driving should receive the same number of points.

A member noted that livers are more similar to lungs in terms of cold ischemic time than kidneys, thus the Committee should consider the OPTN Lung Transplantation Committee's decisions regarding the travel efficiency attribute. Another member pointed out that lungs will start flying at a shorter distance compared to livers. A member commented that livers have more biological necessity than kidneys in terms of cold ischemic time.

When reviewing the travel efficiency rating scale that the OPTN Kidney Transplantation Committee developed, a member stated that the inner plateau should be longer than 50 NM, if adapted for liver. A member suggested that the part of the rating scale that accounts for driving remain high with a low slope, and then the part for flying have a steeper slope.

A member stated that the Committee should ensure that these decisions do not disadvantage smaller transplant programs and recommended that be considered when determining inflection points for when transplant programs begin to fly rather than drive.

The Vice-Chair indicated that it is difficult from a clinical perspective to travel any further than 500 NM. A member pointed out that machine perfusion could alter that. A member commented that creating the slope to be steeper for liver than kidney makes more biological sense, especially if the organ is not being mechanically perfused, since it will not fly long distances.

A member asked how this will impact pediatric candidates. The Chair commented that if pediatric access needs to be adjusted, then the Committee should consider the pediatric attribute rather than the travel efficiency attribute.

Next steps:

The Committee will continue to develop the travel efficiency rating scale with the help of data to determine specific inflection points.

5. Update: OPTN Taskforce on Efficiency

The Committee received an update on the development of an OPTN taskforce on efficiency and brainstormed ideas for committee or taskforce work regarding efficiency in organ allocation and utilization.

Summary of discussion:

A member suggested that organs are not being utilized out of transplant program's fear of being flagged in performance metrics. They elaborated, detailing that expectations of the system must be inclusive of transplant programs willing to take risks and feel that the expectations are too high. They also criticized

the 5-tiered system, which impacts candidates' willingness to list at transplant programs that are below tier 4. They continued, saying that the 5-tiered system is more hurtful than helpful and innovation at transplant programs is stifled by regulation. They emphasized that it is undesirable to have every transplant program as a tier 5 because that is indicative of the transplant program not taking enough chances.

A member questioned if organ non-use is the correct metric for this information and noted that transplant program aggressiveness may have more impact on organ non-use. They commented that medically complex organs may complicate a non-use metric since medically complex organs are not able to be used sometimes, thus impacting a transplant program's rating. They mentioned that knowing the quality of graft will help the community understand what the problem is. Another member noted that the way transplant programs are scored is well-intentioned, however, agreed that transplant programs that take more risks are being flagged, and thus being punished.

The Vice-Chair noted that medically complex and out-of-sequence grafts are conflicting metrics because they believe both metrics cannot be perfect at the same time. A member pointed out that the main concern that is trying to be eliminated is an out-of-sequence allocation where there is another transplant program, that was prepared to procure the organ and would have accepted the offer but did not receive the organ offer.

The Chair mentioned that a challenge with out-of-sequence allocation is optics, because, to someone who is not active in the transplant realm, it sounds unfair. They elaborated, saying that sometimes it is necessary to avoid non-use. The Chair acknowledged that the liver is different in terms of out-of-sequence allocation because the allocation of livers occurs later in the procurement process and can be more complicated.

A member commented that the Taskforce should include perspectives from machine perfusion companies and suggested including them in efficiency efforts. The Chair voiced their agreement about the importance of having them as expert opinions on informing the machine perfusion process but noted their worry about having them on the task force from a conflict-of-interest perspective.

Next steps:

The Committee will continue to develop ideas to bring to the OPTN Taskforce on Efficiency.

6. Discussion: Continuous Distribution, Utilization Efficiency Attribute

The Committee discussed the utilization efficiency attribute within liver continuous distribution.

Summary of discussion:

A member commented that it would be difficult to develop a patient-centered rating scale for the utilization efficiency rating scale. The member explained that especially when considering medically complex liver offers, a candidate may be willing to accept a medically complex graft, but the transplant program may not. Another member suggested asking candidates a "yes/no" question to identify which candidates would be willing to accept a medically complex donor. A member commented that candidate characteristics may change, thus transplant programs should be able to easily change whether specific candidates are willing to accept a medically complex graft. The Chair suggested the attribute's rating scale could be transplant program-based with the consideration of candidate characteristics.

A member stated that the goal for a medically complex liver offer is to create the shortest match run possible in order to allocate that offer to the candidate that is willing to accept it as fast as possible. The Chair suggested the potential to create a model that could predict which transplant program will accept

a medically complex liver offer for a specific type of candidate. The Chair asked the Committee to consider which candidate characteristics should be adjusted for at a transplant program level.

An SRTR representative recommended that the Committee consider how to develop a rating scale that will allow transplant programs to become more aggressive if they choose and give them the ability to do so and vice versa.

The Vice-Chair voiced their confidence in how the current allocation system functions, being that medically complex donor grafts that are donated after circulatory death (DCD) or age over 70 should be prioritized for candidates less than 150 NM. They believe how the system functions to place medically complex livers is working well and it should remain as is.

The Chair emphasized the interactions between the travel efficiency and utilization efficiency attributes are important considerations but encouraged the Committee to think about utilization efficiency as a standalone attribute first. They asked what candidate characteristics they would want to include. A member commented that highly medically urgent candidates should receive negative points in a utilization efficiency attribute to ensure they receive access to all organ offers.

The Chair indicated that as candidates get sicker, they are less likely to be offered medically complex organs, regardless of the transplant program's behavior. They asked the Committee if there are other candidate characteristics besides medical urgency that would determine whether a transplant program would accept a medically complex liver offer. A member said a lot of the medically complex liver offers are accepted for candidates with exception scores. Another member stated that a transplant candidate's proximity to the transplant program is important when considering whether to accept a medically complex liver offer because time is a factor.

The Chair suggested asking for data that analyzes which transplant programs are more likely to accept a DCD liver offer or an age over 70 liver offer. The Chair also suggested requesting data to analyze which candidates that transplant programs are accepting medically complex liver offers for such as age, MELD score, cancer diagnosis, and distance from transplant program.

A member stated it may be beneficial to review both transplant program data and candidate data because both aspects are continually changing. Members emphasized that the OPTN data will result in analyses based on required data collection and some information may remain unknowable due to it not being currently collected.

The Chair emphasized that the Committee is interested in transplant program behavior, with the caveat being, how candidate characteristics adjust the transplant program's behavior. They mentioned that for some transplant programs, the distance may not matter, but for others, it is extremely significant. They reminded the Committee about the public comment feedback which emphasized the importance of having patient-centric attributes.

A member noted that medical staff change at transplant programs, which can alter a transplant program's behavior pattern, as well as their performance metrics. Another member voiced their concern for transplant program acceptance characteristics, as they feel that this creates a closed feedback loop where only certain transplant programs would receive certain offers. An SRTR representative explained that a rating scale could be based on a transplant program's offer acceptance ratio. The SRTR representative explained that if a transplant program's offer acceptance ratio is high, then the transplant program would receive a higher number of points in this rating scale, and thus receive more offers. They continued that by virtue of receiving more offers, it will increase the number of offers that a transplant program is expected to accept and therefore will create negative pressure on the offer acceptance ratio. The SRTR representative explained that the opposite situation can also occur, where a

transplant program has a lower offer acceptance ratio, so they receive fewer points within a utilization efficiency rating scale, thus receiving fewer offers. However, by receiving fewer offers, the expected offer acceptance will be lower, which may increase the offer acceptance ratio through positive pressure. The SRTR representative added that the weight of the utilization efficiency can remain low in order to mitigate some of the concerns about a negative feedback loop.

The Chair mentioned that the increase utilization of machine perfusion could impact any potential utilization efficiency attribute and suggested that the Committee consider ways to adjust for the changing landscape. A member agreed, emphasizing an earlier point made that the Committee should be cautious about how much time is spent on this since machine perfusion is rapidly advancing.

The Vice-Chair asked whether the Committee should consider addressing non-utilization and allocation out of sequence for donation after brain death (DBD) donors that meet standard criteria. A member noted that this may be due to operational considerations rather than allocation sequencing.

Next steps:

The Committee will continue to develop a rating scale for the utilization efficiency attribute.

7. Data Request: Geographic Equity Attribute

The Committee reviewed a data request for Census American Community Survey (ACS) data to calculate population density circles around each transplant hospital in order to develop a rating scale for the geographic equity attribute.

Summary of discussion:

Decision: The Committee has elected to submit the data request.

There was no further discussion on this item.

Next steps:

The Committee will submit the data request to the Health Resources and Services Administration (HRSA).

8. Review: Median MELD at Transplant (MMaT) Around the Donor Hospital, Six-month Monitoring Report

The Committee reviewed the six-month monitoring report for *Calculate MMaT around the Donor Hospital and Update Sorting within Liver Allocation*.

Data summary:

Waiting list removal and transplant rates remained similar for exception candidates across eras. There rates can no longer be stratified by allocation score for adult exception candidates because adult exception candidates' allocation scores are not known until match and vary with each match run.

Distribution of score adjustment, allocation score at transplant, and MMaT at transplant for exception candidates and recipients were similar. Interquartile ranges remained the same or became tighter post-policy compared to pre-policy.

Summary of discussion:

The Chair noted that not being able to analyze metrics based on allocation MELD results in a level of opacity. The Chair added that implementation of MMaT around the donor hospital has provided candidates with more equitable access to transplant.

The Vice Chair noticed that waitlist deaths or removals have increased with candidates who have non-HCC exceptions. Staff noted that this increase was not statistically significant, and there were small sample sizes in some regions resulting in wide confidence intervals.

An SRTR representative requested the standard deviation of MMaT by donor service area (DSA) pre- and post-policy. Staff noted that the monitoring report provides information stratified by region. The SRTR representative stated that it is important to ensure that equity is not worsening by centering MMaT around the donor hospital.

The Vice Chair asked if HCC candidates receive too high of an exception score because they are getting transplanted frequently. A member suggested the Committee consider how often HCC exception candidates are transplanted in sequence because they felt it rarely occurred. The member noted that HCC candidates are receiving organ offers that are not utilized by highly medically urgent candidates, which they believed is appropriate. They questioned if the actual point value would change their access very much. A member commented that when looking at the waitlist mortality and transplant rate data for non-HCC candidates, it is equivalent to HCC candidates, so access is equivalent. Another member noted the current exception score for HCC candidates seems to be correct, however there may be opportunity to better stratify HCC candidates.

Next steps:

The Committee will continue to monitoring the impact of *Calculate MMaT around the Donor Hospital and Update Sorting within Liver Allocation*.

9. Discuss: National Liver Review Board (NLRB) Subcommittee Project, Transplant Oncology Guidance

The Committee reviewed and discussed the drafted NLRB guidance for two diagnoses: colorectal liver metastases and intrahepatic cholangiocarcinoma ≤ 3 cm.

Summary of discussion:

Colorectal Liver Metastases

A member suggested that more specificity should be added to “prior extra-hepatic disease” exclusion criterion.

The Vice Chair noted that it is important for some of the criteria to remain on the more conservative side in order to monitor outcomes. The Vice Chair stated there is not enough data to support including KRAS as a criterion for primary diagnosis. Some members suggested mandating data collection in order to help inform future decisions. The Chair reminded the Committee that they previously decided this project should be the development of guidance which means that all information would be entered via a justification narrative for the NLRB to review and there would be no granular data collection. The Chair suggested that the guidance could include a footnote indicating that there is insufficient data to support inclusion, but KRAS could be considered and encourage transplant programs to submit the data in the justification narrative. Another member agreed it may be important to note that candidates should be tested, and that information reported if available.

The member questioned the evidence to support including BRAF wild type as a criterion for primary diagnosis. Another member responded that data may be limited related to transplant, but that there is data to support it in the surgical oncology literature.

A member asked whether right-sided lesions should be considered exclusionary criteria. The Vice Chair stated that with more data, that may be added into the guidance in the future.

The Committee discussed the score recommendation of MMaT minus 20. The Vice Chair noted that MMaT minus 20 will have most candidates at a MELD score around 15 which would allow access to medically complex liver offers. A member stated that there are some areas where MMaT is 37, so candidates in those areas could end up with a MELD score of 17. The Committee considered whether the score recommendation should be adjusted to MMaT minus 25 to ensure all candidates with these exceptions receive a MELD score of 15.

The Committee discussed whether the guidance should specify a twelve-month period of stability or a twenty-four-month period of stability. A member noted that the Oslo protocol stated that less than two years of stability was a bad prognostic indicator. Another member stated that twelve months is a starting point, and the guidance document could note that longer periods of stability may have better outcomes. A member stated that the Committee can update the guidance document based on new data and evidence. The Committee agreed to utilize a twelve-month time period for stability.

Intrahepatic Cholangiocarcinoma ≤ 3 cm

The Chair stated that guidance should be clear that six-months of tumor stability is necessary before the application of initial exception request.

Another member suggested that the criterion related to no evidence of extrahepatic disease should clarify that it includes prior or historic evidence. The Committee agreed that specifying this criterion to use chest CT as modality is an important clarification.

A member suggested clarifying that the guidance is not applicable for tumors that are downstaged into a solitary tumor less than three centimeters. Members agreed.

The Committee discussed whether the guidance should address poor differentiation.

Another member asked if the guidance includes any criteria related to mixed HCC. The Vice Chair stated the guidance as currently drafted is specific to intrahepatic cholangiocarcinoma. The Committee agreed that small mixed intrahepatic cholangiocarcinoma/HCC should be included in the guidance.

The Chair asked whether these exceptions should be reviewed by the HCC review board. Members agreed that both diagnoses should be added to the HCC guidance document, and that the HCC guidance document and review board should become an oncology guidance document and review board.

Next steps:

The Committee will continue to finalize the project with the aim of submitting a proposal for winter 2024 public comment period.

10. Discuss: Impact of Terlipressin on MELD Score

The Committee reviewed the impact of Terlipressin on MELD scores and discussed potential solutions.

Summary of discussion:

Members presented current evidence and literature on the impact of Terlipressin on MELD scores.^{1,2}

¹ Wong F, Pappas SC, Curry MP, Reddy KR, Rubin RA, Porayko MK, Gonzalez SA, Mumtaz K, Lim N, Simonetto DA, Sharma P, Sanyal AJ, Mayo MJ, Frederick RT, Escalante S, Jamil K; CONFIRM Study Investigators. Terlipressin plus Albumin for the Treatment of Type 1 Hepatorenal Syndrome. *N Engl J Med.* 2021 Mar 4;384(9):818-828. doi: 10.1056/NEJMoa2008290. PMID: 33657294.

² Sanyal AJ, Boyer TD, Frederick RT, Wong F, Rossaro L, Araya V, Vargas HE, Reddy KR, Pappas SC, Teuber P, Escalante S, Jamil K. Reversal of hepatorenal syndrome type 1 with terlipressin plus albumin vs. placebo plus albumin in a pooled analysis of the OT-0401 and REVERSE randomised clinical studies. *Aliment Pharmacol Ther.* 2017 Jun;45(11):1390-1402. doi: 10.1111/apt.14052. Epub 2017 Mar 29. PMID: 28370090; PMCID: PMC5434950.

The Chair summarized that there may be reluctance to give Terlipressin to liver candidates in order to help them avoid dialysis or avoid a simultaneous liver-kidney transplant because the Terlipressin impacts the MELD score.

A member stated that anecdotal feedback noted that due to the recent FDA-approval of Terlipressin, the impact on liver candidates may not yet be palpable but that it can likely be anticipated since Europe has already developed a solution for their transplant system.

The Chair asked if the Committee proposed a policy change that would freeze MELD scores of candidates on Terlipressin, would transplant programs give Terlipressin to candidates with ATN in order to lock in a MELD score. A member stated that is a possibility, although they hope that would not happen. The member suggested that the MELD score could freeze after a couple of days on Terlipressin to ensure that the treatment pathway is committed to help alleviate any potential manipulation.

The Chair stated that if a solution is developed that does not discourage the use of Terlipressin, then there is the potential to avoid SLK transplants.

Another member stated that the Committee should understand whether this is a problem for transplant programs before developing a solution. The member stated that from their conversations with transplant programs in the southeast, there was sentiment that this drug has not been in use for a long time and even then, it is being used sparingly. Another member asked whether transplant programs are using Terlipressin sparingly because of the impact on MELD scores. A member responded that they believe the lack of use is due to the impact on patient outcomes rather than MELD scores. Another member agreed. A member responded that the longer the Committee waits to develop a solution means that the usage of Terlipressin could remain low because of the fear of impacting the MELD score.

A member stated that if the Committee develops a solution, they need to ensure that it works for all areas of the country since there remains variations in MMaTs.

Another member stated that the Committee should understand the population that is being disadvantaged prior to developing a solution.

A member noted that there are other drugs that impact MELD scores. The member suggested that an overarching solution could be to change the time interval for high MELD score lab value updates. Another member suggested locking the creatinine values within the MELD equation for candidates on Terlipressin. Another member suggested that the INR value within the MELD equation could be capped.

The Committee asked for more information on the rationale for the current lab update schedule. Members agreed that the Committee should continue to explore the problem and develop any solutions if warranted.

Next steps:

The Committee will continue to explore this as a project idea.

Upcoming Meetings

- November 3, 2023 (teleconference)
- November 17, 2023 (teleconference)

Attendance

- **Committee Members**
 - Aaron Ahearn
 - Allison Kwong
 - Chris Sonnenday
 - James Pomposelli
 - Joseph DiNorcia
 - Kymberly Watt
 - Neil Shah
 - Scott Biggins
 - Shimul Shah
 - Shunji Nagai
 - Tovah Dorsey-Pollard
 - Vanessa Cowan
 - Vanessa Pucciarelli
 - Christine Radolovic (virtual)
 - Colleen Reed (virtual)
 - Jenn Muriett (virtual)
 - Lloyd Brown (virtual)
 - Sophoclis Alexopoulos (virtual)
- **HRSA Representatives**
 - Jim Bowman
 - Marilyn Levi
- **SRTR Staff**
 - Katie Audette
 - Nick Wood
 - Ryo Hirose
 - Simon Horslen
 - Tim Weaver
- **UNOS Staff**
 - Betsy Gans
 - Delaney Nilles
 - Erin Schnellinger
 - Houlder Hudgins
 - James Alcorn
 - Joel Newman
 - Katrina Gauntt
 - Kayla Balfour
 - Laura Schmitt
 - Meghan McDermott
 - Niyati Upadhyay
 - Susan Tlusty
- **Other Attendees**
 - David Weimer
 - S. DeLair
 - Samantha Taylor
 - Ted Papalexopoulos