

## **OPTN Liver and Intestinal Organ Transplantation Committee**

### **Meeting Summary**

**September 16, 2022**

**Conference Call**

**James Pomposelli, MD, PhD, Chair**

**Scott Biggins, MD, Vice Chair**

### **Introduction**

The OPTN Liver and Intestinal Organ Transplantation Committee (the Committee) met via Citrix GoToMeeting teleconference on 09/16/2022 to discuss the following agenda items:

1. Public Comment Presentation: Redefining Provisional Yes and the Approach to Organ Offer and Acceptance
2. Continuous Distribution Attribute: Hepatocellular Carcinoma (HCC) Stratification
3. Simultaneous Liver-Kidney (SLK) Project Update

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

#### **1. Public Comment Presentation: Redefining Provisional Yes and the Approach to Organ Offer and Acceptance**

The Committee received a presentation on the OPTN Operations & Safety Committee's concept paper, *Redefining Provisional Yes and the Approach to Organ Offer and Acceptance*.

#### Summary of discussion:

The Chair stated that the concept of a tiered system may work better for kidney offers compared to liver offers. The Chair explained that transplant programs who utilize donation after circulatory death (DCD) livers often have to wait for the organ offer and acceptance processes to progress to be able to accept the offer for a transplant candidate with a lower model for end stage liver disease (MELD) score. A member agreed and added that being able to indicate which transplant candidates the transplant program would consider the offer for would be helpful. The member stated that responding for one transplant candidate is limiting. The member stated that it may be beneficial for the organ procurement organization (OPO) to see which transplant candidates the transplant programs would consider the offer for. The presenter responded that the OPTN Operations & Safety Committee has discussed various criteria and kidney donor profile index (KDPI) thresholds to aid in a more efficient placement of hard to place kidneys.

The Chair suggested the system allow for a pre-offer. The Chair explained that the OPO could notify transplant programs that an organ offer may be impending, which would then allow the transplant program more time to evaluate their transplant candidates. The Chair recognized this is similar to the concept of tier three. The presenter agreed and added that additional feedback from the transplant community has highlighted that the use of offer filters may address this issue.

A member noted that call teams change during the process of an organ offer and acceptance which sometimes hinders the ability to accept an organ offer because there are different acceptance practices among various staff within a transplant program.

Another member suggested that OPOs should standardize how they evaluate a deceased donor and available information. The member explained that some inefficiencies result from the various OPO practices of donor evaluation.

The Chair asked what the concept of a tiered system is trying to fix. The presenter stated that the problem is predominately with kidney organ offers. The presenter explained that transplant programs will enter a provisional yes without fully evaluating the organ offer or checking in with the transplant candidate. The presenter stated that the concept of the tiered system is aiming to make the organ offer and acceptance processes more efficient and reduce late declines.

SRTR staff stated that the inefficiencies in the organ offer and acceptance processes have been amplified by the implementation of acuity circles due to the larger number of transplant programs within the first unit of distribution. SRTR staff emphasized that these inefficiencies are most relevant with hard to place organs. A member added that the increase in organ offers is also due to the recent Centers for Medicare & Medicare Services (CMS) metric that pressures OPOs to recover every organ.

## **2. Continuous Distribution Attribute: Hepatocellular Carcinoma (HCC) Stratification**

The Committee discussed hepatocellular carcinoma (HCC) stratification as a potential attribute to incorporate into continuous distribution of livers and intestines.

### Summary of discussion:

Research and input compiled from Committee members prior to this meeting included:

- HCC transplant urgency and benefit is heterogeneous
- The size of the impacted population is about 10-20% of the adult liver transplant waitlist
- The problem does not impact a disadvantaged group
- Focus on group of transplant candidates with HCC that receive median MELD at transplant (MMaT) minus three
- Prior to implementation of the National Liver Review Board (NLRB), about 19.4% of transplants were HCC exceptions, compared to about 13.8% of transplants after implementation on the NLRB<sup>1</sup>
- There are similar pre-transplant mortality rates, similar transplant rates, and similar five year graft survival for the non-HCC population compared to the HCC population
- Within the HCC population, there are low risk and high risk groups which result in different waitlist dropouts or urgency of transplant
  - Low risk HCC group may be categorized as the following:
    - Alpha fetoprotein (AFP) <20
    - Small solitary tumor 2-3 centimeters
    - Child-Turcotte-Pugh (CTP) A, MELD lower than 15
    - Well-differentiates
    - Response to locoregional therapy
  - High risk HCC group may be categorized as the following:
    - AFP >500-1000
    - Larger/multifocal tumor
    - Outside Milan criteria (DS/AC)
    - CTP B/C, higher MELD
    - Poorly differentiated

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<sup>1</sup> National Liver Review Board Two Year Post-Acuity Implementation Report, available at [optn.transplant.hrsa.gov/](https://optn.transplant.hrsa.gov/)

- HCC prioritization within liver allocation focuses on balancing waitlist dropout and post-transplant survival
- HCC transplant recipients with a natural MELD score of 6-13 have a negative survival benefit<sup>2</sup>
- HCC transplant candidates are less likely to be able to undergo locoregional therapy, have few locoregional therapy options, and have a higher likelihood of decompensation after locoregional therapy
- MELD score, Milan criteria, response to locoregional therapy, and AFP are four factors that can determine the benefit of liver transplant<sup>3</sup>
- MELD, CTP, number of lesions, AFP are factors that can determine risk of waitlist dropout<sup>4</sup>
- The population of low risk HCC transplant candidates have been growing over time and currently account for about 20% of the liver waitlist<sup>5</sup>
- A proposed solution for HCC stratification into liver allocation may be to prioritize based of low, medium, and high risk HCC transplant candidates while still allowing for the NLRB to allow exceptions
- Models reviewed:
  - Stratification by risk or transplant benefit using a MELD-HCC score that includes MELD and AFP as factors<sup>6</sup>
  - Waitlist dropout score includes MELD-Na score, CTP score, AFP at listing, and listing tumor burdens to stratify dropout risk score<sup>7</sup>
  - HALT-HCC score focuses on a continuous scale that reflects HCC dropout risk and is balanced with post-transplant survival. The score includes MELD-Na, tumor burden score, and AFP.<sup>8</sup>

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<sup>2</sup> Berry K, Ioannou GN. Comparison of Liver Transplant-Related Survival Benefit in Patients With Versus Without Hepatocellular Carcinoma in the United States. *Gastroenterology*. 2015 Sep;149(3):669-80; quiz e15-6. doi: 10.1053/j.gastro.2015.05.025.

<sup>3</sup> Lai, Q., Vitale, A., Iesari, S., Finkenstedt, A., Mennini, G., Spoleтини, G., Hoppe-Lotichius, M., Vennarecci, G., Manzia, T. M., Nicolini, D., Avolio, A. W., Frigo, A. C., Graziadei, I., Rossi, M., Tsochatzis, E., Otto, G., Ettorre, G. M., Tisone, G., Vivarelli, M., Agnes, S., ... European Hepatocellular Cancer Liver Transplant Study Group (2017). Intention-to-treat survival benefit of liver transplantation in patients with hepatocellular cancer. *Hepatology (Baltimore, Md.)*, 66(6), 1910–1919. <https://doi.org/10.1002/hep.29342>.

<sup>4</sup> Mehta N, Dodge JL, Hirose R, Roberts JP, Yao FY. Predictors of low risk for dropout from the liver transplant waiting list for hepatocellular carcinoma in long wait time regions: Implications for organ allocation. *Am J Transplant*. 2019 Aug;19(8):2210-2218. doi: 10.1111/ajt.15353.

<sup>5</sup> Kwong AJ, Ghaziani TT, Mehta N. Decreased Urgency Among Liver Transplantation Candidates With Hepatocellular Carcinoma in the United States. *Liver Transpl*. 2022 Apr;28(4):725-727. doi: 10.1002/lt.26373. Epub 2021 Dec 13. PMID: 34806834.

<sup>6</sup> Vitale A, Volk ML, De Feo TM, Burra P, Frigo AC, Ramirez Morales R, De Carlis L, Belli L, Colledan M, Faggioli S, Rossi G, Andorno E, Baccarani U, Regalia E, Vivarelli M, Donataggio M, Cillo U; Liver Transplantation North Italy Transplant program (NITp) working group. A method for establishing allocation equity among patients with and without hepatocellular carcinoma on a common liver transplant waiting list. *J Hepatol*. 2014 Feb;60(2):290-7. doi: 10.1016/j.jhep.2013.10.010.

<sup>7</sup> Mehta, N., Dodge, J. L., Roberts, J. P., & Yao, F. Y. (2021). A novel waitlist dropout score for hepatocellular carcinoma - identifying a threshold that predicts worse post-transplant survival. *Journal of hepatology*, 74(4), 829–837. <https://doi.org/10.1016/j.jhep.2020.10.033>

<sup>8</sup> Firl DJ, Sasaki K, Agopian VG, Gorgen A, Kimura S, Dumronggittigule W, McVey JC, Iesari S, Mennini G, Vitale A, Finkenstedt A, Onali S, Hoppe-Lotichius M, Vennarecci G, Manzia TM, Nicolini D, Avolio AW, Agnes S, Vivarelli M, Tisone G, Ettorre GM, Otto G, Tsochatzis E, Rossi M, Viveiros A, Cillo U, Markmann JF, Ikegami T, Kaido T, Lai Q,

- Additional continuous scales include MELD-Eq<sup>9</sup>, deMELD<sup>10</sup>, and HCC-MELD<sup>11</sup>. These scales show that very few transplant candidates would be in a transplantable range if prioritization is based on HCC matching the MELD score.
- OPOM includes 28 total variables.<sup>12</sup> OPOM will be discussed further during the October 11, 2022 Committee meeting.
- Increasing prioritization for this population has implications on post-transplant survival which needs to be considered
- There needs to be consideration on what an unacceptable post-transplant survival may be for an HCC transplant candidate
- For HCC transplant candidates, it is not only about waitlist dropout concerns, but also the access/window for transplant
- The Committee should discuss whether to consider variables at registration, dynamic changes such as score changes while waiting, response to locoregional therapy, or new tumor developments
- HCC stratification as an attribute in continuous distribution optimizes for urgency and utility, therefore aligning with the final rule requirement to seek the best use of donated organs
- The OPTN currently collects the necessary data to address HCC stratification in liver allocation policy. However, biomarkers NLR DCP L3 may be beneficial to add in the future.
- Concluded that there is enough evidence to prioritize HCC T2 transplant candidates based on urgency/benefit rather than one common score

The Chair stated that it is important to stratify HCC transplant candidates.

SRTR representative reminded the Committee that they will present on OPOM in an upcoming Committee meeting. The SRTR representative stated the Committee needs to determine whether they are going to incorporate pre-transplant mortality or post-transplant outcomes as a main attribute. The Chair added that there is literature under review regarding a post-transplant survival score for liver transplant candidates that the Committee should review once it is published. The SRTR representative encouraged the use of machine learning, artificial intelligence, and neural networks.

#### Next steps:

The Committee will continue discussing HCC stratification as a potential attribute in the continuous distribution of livers and intestines.

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Sapisochin G, Lerut J; European Hepatocellular Cancer Liver Transplant Study Group, Aucejo FN. Charting the Path Forward for Risk Prediction in Liver Transplant for Hepatocellular Carcinoma: International Validation of HALTHCC Among 4,089 Patients. *Hepatology*. 2020 Feb;71(2):569-582. doi: 10.1002/hep.30838.

<sup>9</sup> Marvin MR, Ferguson N, Cannon RM, Jones CM, Brock GN. MELDEQ : An alternative Model for End-Stage Liver Disease score for patients with hepatocellular carcinoma. *Liver Transpl*. 2015 May;21(5):612-22. doi: 10.1002/lt.24098.

<sup>10</sup> Alver SK, Lorenz DJ, Marvin MR, Brock GN. Projected outcomes of 6-month delay in exception points versus an equivalent Model for End-Stage Liver Disease score for hepatocellular carcinoma liver transplant candidates. *Liver Transpl*. 2016 Oct;22(10):1343-55. doi: 10.1002/lt.24503.

<sup>11</sup> Toso C, Dupuis-Lozeron E, Majno P, Berney T, Kneteman NM, Perneger T, Morel P, Mentha G, Combescure C. A model for dropout assessment of candidates with or without hepatocellular carcinoma on a common liver transplant waiting list. *Hepatology*. 2012 Jul;56(1):149-56. doi: 10.1002/hep.25603.

<sup>12</sup> Bertsimas D, Kung J, Trichakis N, Wang Y, Hirose R, Vagefi PA. Development and validation of an optimized prediction of mortality for candidates awaiting liver transplantation. *Am J Transplant*. 2019 Apr;19(4):1109-1118. doi: 10.1111/ajt.15172.

### **3. Simultaneous Liver-Kidney (SLK) Project Update**

The Committee has proposed a project to expand geographic area for simultaneous liver-kidney (SLK) allocation to align with heart-liver/kidney allocation and ensure more equitable access to transplant for SLK transplant candidates. The OPTN Policy Oversight Committee approved the Committee's SLK project but recommended that the OPTN Ad Hoc Multi-Organ Transplantation Committee sponsor the project.

#### Summary of discussion:

Feedback from the OPTN Kidney Transplantation, Multi-Organ Transplantation, and Policy Oversight Committees is as follows:

- Provide evidence that a problem exists
- How will the proposed change impact kidney-alone/kidney-pancreas candidates?
- Is the 500 nautical mile (NM) too large in population centers such as the east coast?

The Chair stated that they have experienced not receiving an SLK offer for an SLK transplant candidate in the 250 – 500 NM range. A member shared that they have also experienced that but noted that more recently it has not appeared to be a problem. Another member agreed and noted the same experience.

The Chair stated that they do not expect this policy alignment to have a huge impact on the kidney community. The Chair added that they do not support organ procurement organizations (OPOs) having the discretion to turn down a transplant candidates who qualifies for an SLK. A member agreed if OPOs are not practicing uniformly across the country, then there should be alignment of the policy.

An SRTR representative noted that they have experienced variable OPO practice in SLK offers. The SRTR representative noted that this is a regional problem, mostly effecting the west coast and larger geography areas.

A member stated they support the proposal. The member added that even if it is not a current problem for every area, it could always change with a shift in personnel.

Another member asked what data is collected to analyze this situation. The Chair responded that the Committee will need to determine what data to request in order to perform an analysis. The Chair emphasized that the proposal is to align multi-organ policy.

The Vice Chair stated that another pathway is that the Committee could create a guidance document for the OPOs to reference. The Vice Chair stated that a guidance document may help standardize OPO practice, and then a policy solution could be implemented with the continuous distribution of livers and intestines.

#### **Upcoming Meeting**

- September 30, 2022 @ 3:00 PM ET (teleconference)
- October 7, 2022 @ 3:00 PM ET (teleconference)
- October 11, 2022 @ 9:00 AM CT (Chicago, IL)
- November 4, 2022 @ 3:00 PM ET (teleconference)

## Attendance

- **Committee Members**
  - Allison Kwong
  - Bailey Heiting
  - Colleen Reed
  - Diane Alonso
  - Erin Maynard
  - James Eason
  - James Pomposelli
  - James Trotter
  - Joseph Dinorcia
  - Neil Shah
  - Scott Biggins
  - Sophoclis Alexopoulos
  - Sumeet Asrani
  - Vanessa Pucciarelli
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **SRTR Staff**
  - John Lake
  - Katie Audette
  - Nick Wood
  - Tim Weaver
  - Ryo Hirose
- **UNOS Staff**
  - Betsy Gans
  - Erin Schnellinger
  - Jennifer Musick
  - Joann White
  - Joel Newman
  - Krissy Laurie
  - Matt Cafarella
  - Megan Oley
  - Meghan McDermott
  - Niyati Upadhyay
  - Rob McTier
  - Sarah Scott
  - Susan Tlusty
- **Other Attendees**
  - Dave Weimer
  - Jesse Schold
  - Kimberly Koontz
  - Neil Mehta
  - Pratima Sharma
  - S DeLair
  - S Taylor

- Sanjay Mehrotra