OPTN Liver and Intestinal Organ Transplantation Committee
National Liver Review Board (NLRB) Subcommittee
October 10, 2023
Conference Call

James Pomposelli, MD, PhD, Chair

Introduction

The OPTN National Liver Review Board Subcommittee (the Subcommittee) met via WebEx teleconference on 10/10/2023 to discuss the following agenda items:

1. National Liver Review Board (NLRB) Transplant Oncology
2. Monitoring Report: NLRB Enhancements

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

1. National Liver Review Board (NLRB) Transplant Oncology

The Subcommittee reviewed literature and discussed changing the guidance for intrahepatic cholangiocarcinoma from ≤ 2 cm to ≤ 3 cm.[1,2,3]

Summary of discussion:

> Decision #1: The Subcommittee agreed that the size criteria for intrahepatic cholangiocarcinoma should be less than or equal to 3 centimeters.

The Chair supported using ≤ 3 cm as the criteria in guidance because it aligns with the thresholds used for hepatocellular carcinoma (HCC). Members agreed with changing the guidance to ≤ 3 cm. A member agreed with the cutoff but questioned if protocols should be reviewed by the NLRB. They continued, voicing their concern about the stringency with which this diagnosis could be documented, as well as the multi-disciplinary management. Another member responded that transplant programs will submit information in their justification narrative and that this diagnosis may not require as much stringency as hilar cholangiocarcinoma (CCA). The Chair agreed, noting that this is simpler and more straightforward.

A member suggested specifying what bridging therapy entails. A member voiced their concern, as they believe listing all the bridging therapies could be complex, as there are several modalities of bridging

[1] Sapisochin, G., et al. (2014). "Very early" intrahepatic cholangiocarcinoma in cirrhotic patients: should liver transplantation be reconsidered in these patients?. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons, 14(3), 660–667. https://doi.org/10.1111/ajt.12591

[2] 3 Sapisochin, G., et al. (2016). Liver transplantation for "very early" intrahepatic cholangiocarcinoma: International retrospective study supporting a prospective assessment. Hepatology (Baltimore, Md.), 64(4), 1178–1188. https://doi.org/10.1002/hep.28744

[3] De Martin E, Rayar M, Golse N, et al. Analysis of Liver Resection Versus Liver Transplantation on Outcome of Small Intrahepatic Cholangiocarcinoma and Combined Hepatocellular-Cholangiocarcinoma in the Setting of Cirrhosis. *Liver Transpl*. 2020;26(6):785-798. doi:10.1002/lt.25737

therapy. Another member noted that HCC can be observed, thus it does not have to be treated. A member recommended inserting language to specify the type of chemotherapy or type of intervention. Another member suggested including "6 months tumor stability, with or without therapy". A member recommended that a solution may be including "either locoregional or systemic treatment".

Another member suggested that the language clarifies that extrahepatic lesions are not included. A member agreed, saying that this change would make the wording more precise, which is necessary. The Chair commented that inserting a criterion regarding the rule out of extrahepatic disease would be beneficial. The Subcommittee discussed including that the extrahepatic disease must be ruled out by a chest CT. Some members did not believe it to be necessary to be as prescriptive, others advocated that the language should align with HCC criteria.

A member voiced their support for adding the word "solitary" to specify that this guidance is specific to a solitary intrahepatic cholangiocarcinoma lesion.

Another member asked whether "stability" should be defined in the guidance. The member asked whether "stability" means that the lesions stays < 3 cm or that there is no growth. A member stated that they interpret stability as the lesion would stay within 3 cm. Another member suggested that if growth is acceptable, then the language should remove the word "stability" and state "less than 3 cm".

A member asked whether KRAS should be included within the primary diagnosis category along with BRAF and MSI.

A member noted some initial community feedback that the criteria for tumor stability should be longer than 90 days. The member stated that extending the timeframe may make it safer in terms of outcomes. The member noted that there is literature soon to be released on updated post-transplant survival outcomes for this population. The Subcommittee discussed the potential to collect data to ensure that there is an ability to monitor the outcomes for this population. A member pointed out that the less restrictive the language is, the worse outcomes could be. The member explained that this should be to be a highly curated population. The Chair voiced their support for stability or regression of diseases with systemic and/or locoregional therapy for at least 180 days rather than 90 days.

Next steps:

The Subcommittee will present this to the OPTN Liver and Intestinal Organ Transplantation Committee on Monday, October 16.

2. Monitoring Report: National Liver Review Board (NLRB) Enhancements

The Subcommittee reviewed the monitoring report for enhancements related to the NLRB.

Data summary:

The number of exception cases for portopulmonary hypertension decreased for both initial and extension forms, however the proportion of approvals increased. There were no changes in transplant volumes for candidates with portopulmonary hypertension exceptions in the post-policy era.

The number of exception cases for polycystic liver disease decreased for both initial and extension forms, however the proportion of approvals increased. The proportion of transplants for candidates with polycystic liver disease did decrease in the post-policy era.

In regard to the changes to the Pediatric MELD/PELD Exception Review guidance document, the number of forms submitted has increased since the updates were implemented. The distribution of outcomes for these forms has remained relatively similar when compared to the pre-implementation era.

The number of forms submitted for hilar CCA decreased in the post-policy era. The proportion of cases reviewed by the NLRB also decreased.

The number of forms submitted for neuroendocrine tumors (NET) decreased in the post-policy era. The proportion of cases approved remained similar.

The number of forms submitted for primary and secondary sclerosing cholangitis increased post-implementation of updates to guidance. The number of forms approved also increased.

Summary of discussion:

Decision #1: The Subcommittee requested additional data to help understand the trends reflected.

A member requested data to explain the reasoning for the declines for polycystic liver disease forms. Another member agreed, emphasizing that the data would be worthwhile to have.

A member noted that one of the reasons that the Pediatric MELD/PELD Exception Review guidance document was updates was to try to reduce the number of pediatric exceptions, and they felt like that did not occur, therefore having the denominator number would be helpful to see. Another member commented that if every candidate is applying for and receiving a transplant on an exception, it is demonstrative of the ineffectual way in which pediatric prioritization is being allocated. A member flagged that this is where creatinine would be helpful to consider, and that data will not be available for at least another year. They continued, noting that it would be useful to see the graph of the overall proportion of transplants, with or without exceptions.

Another member asked to have data detailing the large number of declines for primary and secondary sclerosing cholangitis exceptions and the reasoning behind the large number. The member also requested if the data could be stratified by primary and secondary if possible.

Next steps:

The Committee will review additional data at an upcoming meeting.

Upcoming Meetings

- November 14, 2023 (teleconference)

Attendance

- **Committee Members**
  - Allison Kwong
  - Chris Sonnenday
  - James Pomposelli
  - Joseph DiNorcia
  - Kym Watt
  - Neil Shah
  - Scott Biggins
  - Shimul Shah
  - Sophoclis Alexopoulos
- **HRSA Representatives**
  - Marilyn Levi
- **SRTR Staff**
  - Jack Lake
  - Katie Audette
  - Simon Horslen
- **UNOS Staff**
  - Erin Schnellinger
  - Katrina Gauntt
  - Kayla Balfour
  - Meghan McDermott
  - Niyati Upadhyay
- **Other**
  - Kathryn Fowler