OPTN Histocompatibility Committee
Meeting Summary
February 9, 2021
Conference Call

Peter Lalli, Ph.D., D(ABHI), Chair
John Lunz, Ph.D., D(ABHI), Vice Chair

Introduction

The Histocompatibility Committee met via Citrix GoToMeeting teleconference on 03/19/2021 to discuss the following agenda items:

1. Public Comment Presentation: OPTN Strategic Plan 2021-2024
2. Discussion: Role of HLA Matching in Kidney Allocation

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

1. Public Comment Presentation: OPTN Strategic Plan 2021-2024

UNOS Policy and Community Relations liaison presented on the OPTN Executive Committee's proposal out for public comment.

Summary of discussion:

The committee chair provided the feedback that the initiatives are broad and encompassing, and help committees guide their focus. They help drive the allocation of resources, and the histocompatibility committee proposals all fall well within the current and proposed plan. The plan seems appropriate, and seems to encompass the major focuses of the committee and community.

2. Discussion: Role of HLA Matching in Kidney Allocation

Committee chair presented on the historic role of HLA matching in kidney and pancreas allocation and asked for committee feedback on its role in the upcoming policy changes to a points-based allocation system.

Data summary:

In 1989, the HLA matching priority for kidney was as follows:

- No A, B, DR mismatch = 10 points
- No B, DR mismatch = 7 points
- No A, B mismatch = 6 points
- 1 B, DR mismatch = 3 points
- 2 B, DR mismatches = 2 points
- 3 B, Dr mismatches = 1 point

Current OPTN policy gives additional points and priority for 0-ABDR mismatches, and 0- or 1-HLA-DR mismatches.

Summary of discussion:

Questions posed to the group were as follows:

- Is there a risk of introducing disparities in access to transplant by prioritizing HLA matching? Can we quantify it?
- What matches should continuous distribution prioritize? Are there certain patients where matching matters more than others?
- Are there additional data the Kidney/Pancreas Committees need to make an informed decision as to how to incorporate HLA matching into continuous distribution?

Committee members unanimously agreed that HLA matching benefits solid organ transplant recipients in the longevity of the transplant and the amount of rejection and sensitization if a transplant fails. A fair amount of the literature recently has focused on epitope/eplet matching, but emphasizes the point that there are benefits to the matching process. The concern of the committee is introducing disparity as a result of implementing some sort of matching.

The committee agreed that matching is more important for pediatric patients than adult patients, as there is a need for longer graft survival and the recipients are more likely to need re-transplant. The committee agreed that pediatrics ought to be prioritized more than adult recipients, and that the effects of prioritizing pediatrics would not affect the donor pool as much due to their small numbers. Prioritizing pediatrics would have a much larger outcomes benefit, and a much smaller potential to cause inequality. One committee member proposed that a conservative matching proposal would be simply to start with a pediatric population, or even a recipient population under 30. One member brought up that recipients transplanted over 65 are likely to maintain graft function throughout their lifetime and so prioritizing matching for them wouldn't provide the same benefit.

Committee members unanimously agreed that Class II HLA (DR, DQ) are more beneficial for matching. Committee members were split on whether the matching should be limited to DR, DQ, or both loci. Committee members pointed out that DQ has become more of interest recently for de novo donor-specific antibodies (DSA), and that there is a linkage disequilibrium between DR and DQ that could allow for less racial bias in matching. However, one member brought up that a significant portion of the data on this is based on more homogenous populations than that in the United States.

One potential issue brought up by a member is that DQ data is not required within UNet currently, and that the data may be incomplete. Most members reported that they type at all loci, but one member reported that their programs only type at HLA-A, B, and DR. An ASHI representative brought up that they tried to change the regulations to typing at all loci, and that the member's specific hospital provided the most significant pushback, and that most hospitals seem to already be typing at all loci.

One member brought up that about 90% of candidates currently have DQ typing submitted, based on SRTR SAF data, up from about 80% reported ten years ago.

The committee discussed whether the matching would be at the antigen level or eplet level, and brought up that the committee would need to require higher-resolution typing. The committee chair brought up that most likely in the future the committee would be discussing eplet-level matching, but that based on the capabilities across the US that isn't feasible at this point.

One member brought up that she has started a study on 0-ABDR mismatch patients for the past five years at her hospital, and that there wasn't a statistically significant difference on outcomes for DR vs. DQ matching. One committee member asked what percent of the 0-ABDR mismatch patients have a DQ mismatch, and the first member said that she would pull the data and share it, but only one patient developed de novo DSA and antibody-mediated rejection (AMR) to DQ. She also pointed out that both her recipient and donor populations are fairly homogenous in her region.

One committee member recommended simulation modeling through the SRTR to ensure that certain racial/ethnic groups aren't being unfairly prioritized, to see how match runs would be affected with prioritization with DR and/or DQ.

Another committee member brought up that long-term immunosuppression can be an issue when evaluating long-term outcomes. One member brought up that the comprehensive immunosuppressive drug coverage act could affect this moving forward.

One member brought up that there's a study based out of Northwestern for a multi-center retrospective analysis going on with 3-5 years of outcomes data for DQ matching, but it likely wouldn't be available until late 2021.

One member recommended continuous re-evaluation of any matching system implemented, due to concerns about potential inequities. One recommended a pilot system to collect more data before a national launch, or a temporary national launch so any potential disparities could be addressed at an early stage.

One committee member recommended increased priority matching for high CPRA candidates for all organs, not just kidney, and maybe on a sliding scale instead of a linear one. Another pointed out that CPRA is already being discussed for lung candidates for continuous distribution, and this may be a discussion to have with the lung committee moving forward.

One member recommended adding back priority for patients based on the likelihood of getting a specific match, so that there may be less inherent bias in matching for groups less represented in the donor population. Two members agreed with this approach, that they recommend weighting matches based on the frequency of a haplotype or genotype within a population. Committee members agreed that this would be more difficult to implement, but likely more equitable.

Committee members discussed how to quantify the benefit of HLA matching and how it influences different patient populations, as the waitlist population and donor population have different demographics. Committee members want to make sure that we aren't prioritizing one race or ethnicity over another by introducing bias into the matching algorithm through biased HLA matching. One committee member brought up that donor and recipient pools also vary across the country, so any analysis of potential matching affects would require stratification by region.

Next steps:

Research is working to develop a data request for review by the Kidney/Pancreas continuous distribution workgroup and Histocompatibility Committee.

Upcoming Meetings

- March 9, 2021, 12 PM EST, Teleconference
- April 13, 2021, 11 AM EST, Teleconference
- May 11, 2021, 12 PM EST, Teleconference

Attendance

- **Committee Members**
  - Bill Goggins
  - Cathi Murphey
  - Evan Kransdorf
  - Idoia Gimferrer
  - Jerry Morris
  - John Lunz
  - Karl Schillinger
  - Marcelo Pando Rigal
  - Peter Lalli
  - Phyllis Weech
  - Reut Hod Dvorai
  - Taba Kheradmand
  - Tracy McRacken
  - Valia Bravo-Egana
  - Vikram Pattanayak
  - Yvette Chapman
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **SRTR Staff**
  - Katie Audette
- **UNOS Staff**
  - Abby Fox
  - Adel Husayni
  - Amanda Robinson
  - Betsy Gans
  - Courtney Jett
  - Joann White
  - Kelsi Lindblad
  - Lindsay Larkin
- **Other Attendees**
  - Loren Gragert
  - Medhat Askar