OPTN Histocompatibility Committee
Meeting Summary
July 13, 2021
Conference Call

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Introduction

The Histocompatibility Committee met via Citrix GoToMeeting teleconference on 07/13/2021 to discuss the following agenda items:

1. Assessing the Impact of the Proposed New CPRA Calculations: Part 2
2. Antigen Recognition Domains and Allelic Unacceptable Antigens

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

1. Assessing the Impact of the Proposed New CPRA Calculations: Part 2

UNOS Research staff presented the second part of an analysis on the impact of the proposed new CPRA calculation. This included comparisons of the predictive rate of transplant and candidate CPRA versus actual compatible deceased kidney donors during the study cohort. These analyses compared current CPRA calculation to the proposed genotype calculation using frequencies derived from stem cell donors and a four group or seven group ethnic weighting system. These comparisons were also stratified by candidates who have unacceptable antigens the current CPRA does not include vs. all candidates.

Analyses found that the proposed CPRA is slightly more predictive of transplant rates than the current CPRA is, and that the current CPRA substantially underestimates sensitization when compared to the number of actual compatible candidates. The analyses also found that the proposed CPRA substantially overestimates sensitization when compared to actual compatible candidates, with the caveat that deceased donor HLA typings at the time of match run are almost exclusively at the serologic antigen level. This would mean that any CPRA calculation that includes allele-level typing would be expected to show some level of overestimation of sensitization due to the limitations in donor HLA data reported in DonorNet at the time of match run.

Summary of discussion:

Committee members asked why there would be incompatible donors for candidates with a CPRA of zero. UNOS Research staff explained that this analysis uses a rounded CPRA, and that candidates can have unacceptable antigens listed and their CPRA can still round to zero or be indistinguishable from zero on the scatterplot.

2. Antigen Recognition Domains and Allelic Unacceptable Antigens

UNOS Policy and Community Relations staff presented on a concern discovered in the analysis earlier in the meeting, that the NMDP data used by the CPRA project's contractor combines all alleles that share an antigen recognition domain (ARD). This is primarily an issue in the DQA1 alleles, where it's causing up to a 34% discrepancy between expected CPRA based on allele frequency and the output within the calculator, as all two-field alleles within the ARD share the same weight.

Summary of discussion:

Committee members expressed concerns that for certain rarer DQA1 alleles, a candidate may receive a large boost in CPRA points and allocation priority even if they won't be screened off of match runs or have many incompatible donors. The CPRA contractor posed that the immune system may not be able to recognize differences between two-field alleles within the same ARD, but multiple committee members posed that different assays differentiate these and they may be clinically relevant in some cases. One member expressed concerns that ARDs aren't consistent with what is currently within the HLA equivalency tables in OPTN policy. Members discussed whether or not discrepant alleles should be included or excluded, with concerns expressed that including them could artificially inflate CPRA for certain candidates, and that excluding them could de-prioritize candidates who are highly sensitized. Members agreed that they would need to see data on the extent of the impact of these discrepancies prior to making a decision on next steps.

Next steps:

UNOS staff will evaluate the extent of the impact on CPRA, including the number of candidates on the waiting list who have allele-level unacceptable antigens to DQA1 currently entered.

Upcoming Meetings

- August 10, 2021, 12 PM ET, Teleconference

Attendance

- **Committee Members**
  - Bill Goggins
  - Caroline Alquist
  - Evan Kransdorf
  - Gerald Morris
  - Jennifer Schiller
  - John Lunz
  - Karl Schillinger
  - Marcelo Pando
  - Omar Moussa
  - Pete Lalli
  - Phyllis Weech
  - Reut Hod Dvorai
  - Valia Bravo-Egana
  - Vikram Pattanayak
  - Yvette Chapman
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
  - Raelene Skerda
- **SRTR Staff**
  - Katie Audette
  - Nick Salkowski
- **UNOS Staff**
  - Abby Fox
  - Betsy Gans
  - Courtney Jett
  - Emily Kniepp
  - Kelsi Lindblad
  - Leah Slife
  - Nicole Benjamin
  - Samantha Weiss
- **Other Attendees**
  - Annette Jackson
  - Loren Gragert
  - William Hildebrand