OPTN Histocompatibility Committee
Meeting Summary
January 12, 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 01/12/2021 to discuss the following agenda items:

1. OPTN Final Rule Training
2. CPRA Project Update
3. CPRA Modeling Request

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

1. OPTN Final Rule Training

UNOS Policy and Community Relations staff presented on the OPTN governance structure.

Data summary:

Slides attached.

Summary of discussion:

Committee members had no questions or concerns.

2. CPRA Project Update

Histocompatibility Committee Chair presented on the current progress of the CPRA calculator revision project.

Data summary:

The proposed CPRA calculation incorporates sensitization at DQA, DPB, and DPA loci and uses a frequency cohort that contains >6,000,000 more high-resolution HLA typings than the OPTN cohort. The current OPTN data cohort is >13 years old and only includes low-resolution specificities.

The current CPRA calculation is haplotype-based and using low-resolution specificities for HLA A, B, DR, DQB1, and C. The proposed CPRA calculation is genotype-based and uses high-resolution specificities for HLA A, B, DR, DQB1, C, DQA1, DPB1, DPA1, and DR51/52/53. The haplotype-based calculation with all loci incorporated and high-resolution specificities would be over 511 separate calculations, and is far more difficult and assumes Hardy-Weinberg equilibrium across broadly-defined population groups.

Summary of discussion:

One committee member mentioned that just because the UNOS frequency data is old doesn't mean that it's invalid, but that it's lower resolution and that there have been noted inaccuracies in the current data set used to calculate CPRA.

Next steps:

The Committee will work with UNOS Research to develop a modeling request to evaluate the current vs. the proposed CPRA calculation.

3. CPRA Modeling Request

UNOS Research staff presented on potential analyses to perform prior to public comment in order to evaluate the proposed CPRA revision.

Data summary:

Proposed analysis goals:

- Demonstrate NMDP data is an appropriate substitute for solid organ donor data
- Estimate size of proposed CPRA's impact
- Demonstrate degree of improvement with proposed CPRA

Summary of discussion:

One committee member pointed out that not all programs enter unacceptable antigens for DPB1 or DQA1 loci as they don't currently receive CPRA points for it, and that there will be some amount of missing data. He suggested that we stratify the analysis for candidates who have antibodies to values included in the current CPRA calculation vs. those who don't.

Another member suggested comparing the current vs. the proposed CPRA calculator and potential compatible donors for those with CPRA 99.95 and above, as well as stratifying the analyses by race/ethnicity, pediatrics, and highly sensitized candidates.

One member pointed out that the current calculation only uses Caucasian, African American, Hispanic, and Asian/Pacific Islander for race/ethnicity categories, and so the current calculator isn't calibrated for smaller racial or ethnic groups and won't be correct. American Indian isn't included in the current calculation.

The CPRA contractor mentioned that the current version of the calculator algorithm will output a list of compatible genotypes for highly sensitized patients, and transplanted vs. waitlisted patients can be compared in that way. He also mentioned that SRTR would be able to do minority and pediatric equity modeling, but multiple other people mentioned that it was a nice to have instead of a need to have, especially since the scope of work it would take to remodel KPSAM for the different CPRA calculations.

One member mentioned that the analyses should be stratified by region. Multiple people mentioned the potential research project to have differing regional CPRAs, but agreed that it's far outside of the scope of this project.

Members agreed that the rate of a highly sensitized candidate appearing on match runs is not a necessary analysis, but that the proportion of compatible donors for highly sensitized candidates is preferable. One concern brought up is that many donors only have antigen-level typing available in UNet, and the calculator will be using allele-specific unacceptable antigens.

Next steps:

UNOS Research analyst will draft a committee data request and submit to committee leadership for approval.

Upcoming Meetings

- February 12, 2021, 12 PM EST Teleconference
- March 9, 2021, 12 PM EST Teleconference
- April 13, 2021, 10 AM CST, Chicago, IL

Attendance

- **Committee Members**
  - Bill Goggins
  - Cathi Murphey
  - Evan Kransdorf
  - Idoia Gimferrer
  - Jennifer Schiller
  - Jerry Morris
  - John Lunz
  - Karl Schillinger
  - Marcelo Pando-Rigal
  - Pete Lalli
  - Phyllis Weech
  - Reut Hod Dvorai
  - Taba Kheradmand
  - Valia Bravo-Egana
  - Vikram Pattanayak
  - Yvette Chapman
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **SRTR Staff**
  - Katie Audette
- **UNOS Staff**
  - Adel Husayni
  - Betsy Gans
  - Courtney Jett
  - James Alcorn
  - Kelsi Lindblad
  - Leah Slife
  - Rebecca Murdock
  - Susan Tlusty
- **Other Attendees**
  - Giovanni Biagini
  - Loren Gragert
  - Marian Dribus
  - Medhat Askar