OPTN Histocompatibility Committee
CPRA Calculation Sub Committee Meeting Summary
December 5, 2019
Conference Call

Cathi Murphey, Ph D, Chair

Introduction

The CPRA Calculation Sub Committee met via teleconference on 12/05/19 to discuss the following agenda items:

1. Project Description
2. Project Timeline
3. Next Steps
4. Frequency of Meetings

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

1.   Project Description

Cathi Murphey will chair the subcommittee.

The Histocompatibility Committee is working on a project to build a new calculator to support a larger cohort of data, adding loci that reflect the OPTN donor pool. UNOS will issue a Request for Proposal to have that work accomplished.

The CPRA or Calculated Panel Reactive Antibodies system calculates the CPRA using the unacceptable values that have been entered for a transplant candidate. To determine a value, the UNet system uses an established formula and HLA frequencies derived from the HLA types found in more than 12, 000 donors. The NMDP donor pool is significantly greater than that of the OPTN. Adding more antigens will improve the accuracy of the CPRA and provide equity for those patients who possess such antibodies. More candidates may experience increased graft survival and better outcomes.

- **What data is required?**

  Donor typing at A, B, C, DR1, DR3, DR4, DR5, DQA1, DQB1, DPA1, and DPB1 for all donors since the NMDP began collecting data on these loci at the high resolution level.

- **Frequency of genotypes?**

  Genotypes

- **Is this a one-time request or would it be done on an annual basis w/ subsequent refreshes?**

  Will likely call this a one-time request. Will need to refresh the data eventually, but more along the lines of once every ten years vs. once a year.

- **How would this data be processed?**

  The parties responding to the RFP to build a new CPRA Calculator will need to present a plan indicating how they will process the data. Broadly, the NMDP data needs to be converted into frequencies of genotypes by ethnicity for the donor pool.

- **What is the pipeline?**

  The parties responding to the RFP will propose their own pipelines and UNOS/OPTN will negotiate that accordingly.

CPRA is being used for more than was originally intended. Important for kidney allocation. Expanding donor pool to use the NMDP database. Trying to enter into data use agreement to expand available data beyond what we are using currently. Working on the formal agreement now. UNOS is in process of putting RFP together to identify who would be interested in partnering to develop and build new calculator.

There is a lack of understanding of how current CPRA calculator works. Need to educate the community.

Per the Chair-1st based on haplotype frequencies and Evan K. has a good handle on this.

Per Evan Kransdorf: did use UNOS data-problems had A, B, DR. C and DQ added later. In one of those additions were not done the right way. He believes current calculator broken. Worked with Darren Stewart, UNOS Research, but it is 10 years old and hard to go back and find errors. Went back to recalculate. Somewhat complex and hard to explain. Want to go to allele level and do excludes for epitopes-this gets complicated.

Adding other loci that are now denying DPB (DPA-maybe start collecting)

Hoping to have manuscript submitted by the end of the year. Current calculation is wrong in more than one place. Rounding errors. Lower CPRA should not happen. Calculator is wrong and not getting allocation points they should be getting.

Current CPRA does not reflect what we should be putting out there-correct calculator as is-that should be non-controversial. Then build on alleles-DP-some may not think these people deserve extra points.

Biology and policy start overlapping can have rejection to DPB antibodies.

Antigens first and alleles later. Many that we do not yet have frequencies for. Makes sense to add alleles and antigens at the same time due to magnitude of work.

C differential-can either assign unacceptable or not. It is available for people to use now.

DPB and DQA assigned as UAs-now about 25% .

Even though not getting CPRA points it is still valuable to assign UA for safety purposes.

Vendor kits don't allow typing to be performed at certain level so matching should not be used at that level yet.

Restructure how we do tables and have one centralized table-how often is frequency for 6 million people-this is likely to be robust and not need frequent changes.

Subcommittee needs to make sure RFP has all deliverables, identify unintended consequences. Need to work on this to keep with timeline. Need to identify any other potential bidders interested in working on RFP.

UNOS does not do this very often-usually use IT in-house so has not moved along quicker.

Any discussions with Histo Trac or Matilda for those with best ability to respond? Histo Trac takes UNOS calculator and import it into their database. The Chair does not have Matilda. Matilda used to have their own calculator although it was bad. Now they use API but these companies would be worth notifying.

Sometimes pre-bid conference is performed to help those interested in applying.

Main objective: improve the calculator; explain number of loci and make sure that we are covering more of donor population (e.g. make sure all minority pops are represented in database). IT needs to decide on back end code.

Are we optimistic about NMDP-very willing to work with us-just a matter of putting agreement in place.

One member (Taba K.) may also be aware of another possible responder to the RFP.

2. Project Timeline

Aiming for Fall Public Comment (August-October 2020); POC/Executive Committee consideration, Feb.2020

3. Next Steps

Enter into data use agreement with NMDP; develop Request for Proposal to have new CPRA Calculator built.

4. Frequency of Meetings

Monthly

Upcoming Meeting(s)

- Monthly, TBD, 2020