OPTN/UNOS Histocompatibility Committee
Meeting Minutes
February 15, 2019
Conference Call

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Introduction

The Histocompatibility Committee met via Citrix GoTo teleconference on 02/15/2019 to discuss the following agenda items:

1. Future Project Discussions
2. CPRA Calculator update
3. Project Implementation Update- Addressing HLA Typing Errors
4. Project Portfolio Review

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

1. Future Project Discussion

The Committee discussed two future projects.

Data summary:

The first project discussed was the Modify Appointment Process for the Histocompatibility Vice Chair.

- The Histocompatibility Vice Chair is elected through a national election. The Vice Chairs for all other OPTN committees are appointed by the OPTN Vice President.
- Committee members would like the appointment process for the Histocompatibility Vice Chair to be consistent with other OPTN committees.

The second project discussed was the Histocompatibility Table Update (2019).

- OPTN Policy 4.9 *HLA Antigen Values and Split Equivalences* requires periodic review of equivalence tables. Previous discussions with the Committee, the community, and leadership alluded to the need for an update. Some problems to be addressed are:
    - Need for greater clarity in the community in regards to DP Beta one. (DPB1)
    - Potentially added Bw4/Bw6 in the equivalency tables.
    - What additions/deletions are needed based on capabilities of current human leukocyte antigen (HLA) test kits.
- During recent project discussions UNOS staff supporting the Committee shared the following:
    - The data requested by the committee on the DPB1 allele use in DonorNet℠ and Waitlist®. More specifically what does the current usage look like to help the committee decided which DPB1 values should be available to select in Waitlist.

During the implementation of the most recent equivalency tables in December 2018 it altered what DPB1 alleles can be selected for donors and Waitlist candidates. Although OPTN database includes 662 different possible DPB1 values, not all are used or even available to select. For donor typing in DonorNet any value for DPB1 is possible however only 26 are available as unacceptable antigens for Waitlist and KPD candidates.

UNOS staff fulfilled an earlier OPTN data request on the frequency of DPB1 alleles reported in DonorNet[SM] and Waitlist®.

1. Top 10 DPB1 alleles selected in DonorNet[SM].
2. Frequency of DPB1 alleles across ethnicities.
3. Top 10 DPB1 unacceptable antigens selected in Waitlist®.

Summary of discussion:

Modify Appointment Process for the Histocompatibility Vice Chair project discussion.

- The Vice Chair started off the discussion explained the scope of the project, and highlighted its importance to simplify the process and help the continuity of the committee.
- Members verbalized concerns that there could be no guarantee that a Vice Chair candidate had expertise in histocompatibility. There was also discussion on how regional representatives where chosen and UNOS staff helped clarify any confusion. At the conclusion of the discussion, the Committee unanimously recommended this project be considered by the OPTN/UNOS Policy Oversight Committee (POC) at their next meeting.

Histocompatibility Table Update (2019) project discussion.

- The Vice Chair reminded the Committee the last review of the tables included the addition of several equivalences to help streamline the data entry process. However, there are concerns that from the most recent update surrounding the DPB1 options to available for data entry. He then continued on to remind the Committee of the scope of the issue; the last table update the Committee decided to list only DPB1 alleles available on antibody testing kits, however some laboratories have been using common epitope matching to select additional (not represented) alleles in their unacceptable's for candidates.
- After this discussion UNOS staff presented the data requested by the committee on the DPB1 allele usage in DonorNet and Waitlist.

DPB1 Allele Usage in DonorNet and Waitlist data discussion.

- After the data was presented several members expressed concerns over the following:
    - The Waitlist frequencies presented don't include the common alleles listed in DonorNet.
    - Several frequencies in Waitlist unacceptable's are beads that give false positives and could possibly be resulting in transplant program's listing antigens that may not be true.
        - However one member did note that not all transplant programs are listing DPB1 unacceptable's or are doing so, but at a higher threshold.
    - Not seeing common ones such as 0401, 0402, and 0201, on the Waitlist frequencies top 10 list.
    - This data illustrates that transplant programs are choosing to avoid antigens that are not represented on the current list provided.
- Some comments made by members included that the practice of listing unacceptable's to DP varies from center to center and that a lot of the Waitlist frequencies seen in the presentation are a part of a specific epitope group (DEAV epitopes).
- The Vice Chair thanked UNOS staff and presented the committee with the following options:
    - 1. Only include DPB1 unacceptable's that are listed in the bead testing kits **or**
    - 2. List all DPB1 unacceptable's in Waitlist which would consist of around 700 choices.

- One member commented that the committee is not limited in terms of scope to just the choices listed above. Shortly after the Vice Chair encouraged the need for a solution that should be “usable, functional but not overwhelming”. He then reminded the committee that the purpose of the data presented was to help the Subcommittee identify a solution on how to move forward during the next table update. It was also stated that this problem would be discussed further at the in-person meeting in March 2019.
- A member then asked if the committee has received the National Marrow Donor Program (NMDP) data on the most frequent alleles for DP from the subject matter experts (SME) responsible for that data. The Vice Chair stated that these data are not available. The member then continued and stated that the subcommittee responsible for the next table update should use the National Marrow Donor Program (NMDP) data to cross reference with what the testing kits have, due to the advanced typing used to capture NMDP data. In order to prevent the committee from back tracking when the testing kits evolve.
    - The SME on the call stated that the summary of DQA1 and DPB1 antigens frequencies of NMDP data was given to the current Chair and immediate past Chair and if any other members are interested in the summary it is available to share.
        - Members stressed that the Subcommittee should have both data sets (NMDP data and the OPTN data) to evaluate what is appropriate to include for DPB1 for the next table update.
        - The SME then explained to the committee that the NMDP data has some limitations.
            - The data does not distinguish alleles with differences outside the antigen recognition domain. Consequently some OPTN listed antigens only differ outside this domain therefore when computing NMDP Calculated Panel Reactive Antibodies (CPRA) these antigens will have to be considered equivalent unless more information about their relative frequencies is known. He went on to further explain that in the NMDP data the G groups are combined due to typing practices on exon 2 of the chromosome in the class 2 category. Only more recently typing has moved to exons 2, 3 and 4 however some of OPTN listed alleles only differ in exon 1 which makes it a challenge to compare that to NMDP data.
                - A member commented that this typing method may not be relevant for solid organ transplant at this point.

<u>Next steps:</u>

Modify Appointment Process for the Histocompatibility Vice Chair next steps:

- UNOS staff will research the history of this policy.
- Development timeline in order to apply to the next Vice Chair appointment process as of February 15th, 2019:
    - POC consideration in March 2019
    - Committee vote in June 2019
    - Public Comment August 2019
    - Board consideration December 2019

Histocompatibility Table Update (2019) next steps:

- A subcommittee will have members review current test kits and compare against tables in OPTN Policy 4.10 *Reference Tables of HLA Antigen Values and Split Equivalences*.

- Development timeline as of February 15th, 2019:
    - POC consideration in May 2019
    - Committee vote in November 2019
    - Public Comment January 2020
    - Board consideration June 2020

2. CPRA Calculator update

The Committee will receive a status update on obtaining NMDP data for use in project development, as well as what steps to take to move the project forward.

Summary of discussion:

- The Vice Chair commended the SMEs working on this project for all their hard work.
- This conversation was a primer for the further discussion of this topic at the in person meeting in March 2019. The Vice Chair presented questions to think about in regards to this project to keep this project moving forward on the Committee side. The questions are as follows:
    - How do we use the NMDP data to improve current organ allocation?
    - How the new CPRA calculator would be constructed?
    - Would haplotype or count data be used?
    - How should the skeleton for the calculator be built?
    - How would NMDP data be considered in the calculator?
- The Committee had no comments or questions.
- The SME gave a brief update; their group is currently attempting to replicate the OPTN CPRA panel using the same data and technical methods but are have some complications.

Next steps:

At the March 2019 in person meeting the committee would like to discuss this further and would be interested in an updated report from the SMEs.

3. Project Implementation Update- Addressing HLA Typing errors

UNOS staff will update the Committee on implementation plans for the Board-approved proposal.

Data summary:

UNOS staff reminded the committee of the two components of implementation of this project.

- 1. Updating DonorNet and Agreements effective March 1st, 2019
    - OPOs and the labs they work with will need to have a process in place to ensure that the raw HLA data for deceased donors is uploaded in DonorNet.
    - Histocompatibility laboratories must have written agreements with every OPO member the laboratory serves that must include a process for **verifying and reporting HLA** typing results to the OPTN Contractor.
- 2. IT Programming
    - The service level agreement (SLA) for this project is within twelve months of Board approval.
    - UNOS staff prompted that several committee members wanted to be more involved with beta testing and this was a situation to “kick the tires” prior to its implementation.

4. Project Portfolio Review

The Histocompatibility Vice Chair presented older project ideas to the committee as a primer for the committee's in person meeting in March 2019.

Data summary:

Project Portfolio Review

- Active Committee Projects
    - Addressing HLA Typing Errors
    - Change CPRA Calculation
- Future projects
    - CPRA for Thoracic Organs
    - Updating Bylaw Language for Key Personnel Requirements, etc.
    - DR Priority Points
    - Updating Data Flagged As Discrepant on Discrepant Typing Reports
    - Add DPA Equivalences

Summary of discussion:

The Vice Chair expressed to the Committee the need to refocus on their projects and get back on track. He also reminded the Committee that at the in-person meeting there will be a brief discussion on old project ideas and to bring any new ideas to the in person meeting.

Next steps:

Committee members were asked to bring new project ideas to the in person meeting.

Several members brought up an issue about an email sent out by the UNOS staff about CPRA calculator changes. UNOS staff will get more information about these changes and respond back to the member and the Committee.

Upcoming Meeting(s)

- March 26th, 2019 In-person committee meeting Chicago, IL
- Second Tuesday of each month 12-1 PM (Eastern) – conference calls