OPTN ORGAN PROCUREMENT AND TRANSPLANTATION NETWORK

OPTN/UNOS Histocompatibility Committee
Meeting Minutes
March 26, 2019
Chicago, IL

Cathi Murphey, Ph.D, HCLD/CC, Chair
Peter Lalli, Ph.D, Diplomat (ABHI), Vice Chair

Introduction

The OPTN Histocompatibility Committee met in Chicago, IL on 03/26/2019 to discuss the following agenda items:

1. OPTN/UNOS Policy Oversight Committee (POC) Update
2. Addressing Differences between OPTN Policy and programming for DP Beta 1(DPB1)
3. Project Discussion: Updating OPTN *Policy 4.10 Reference Tables of HLA Antigen Values and Split Equivalences*
4. Request from OPTN/UNOS Data Advisory Committee
5. Histocompatibility Discrepancy Review
6. Obtaining Recipient HLA typing from Other Transplant Hospitals
7. User Enhancements to the Current Calculated Panel Reactive Antibody (CPRA) Calculator
8. Project Discussion- Change in Calculated Panel Reactive Antibody (CPRA) Calculation
9. Kidney Transplantation & Cross Match Results

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

1. OPTN/UNOS Policy Oversight Committee (POC) Update

The Vice Chair provided an update from the recent POC discussions.

Data summary:

- The Vice Chair presented an update from the POC, reminding members about POC role, OPTN Strategic Plan, recent work and new approved projects.

Summary of discussion:

- The Vice Chair reminded members that the committee currently has a project to modify the Vice Chair appointment process going to POC.
- There was discussion about the over allocation of the second OPTN strategic goal; provide equity in access to transplants.
- Members has some questions on how regional representative are selected across various region for the OPTN Histocompatibility Committee. There was also concern on the lack of uniformity across the regions. UNOS staff clarified the process and will circle back with members.

2. Addressing Differences between OPTN Policy and programming for DP Beta 1(DPB1)

Members of histocompatibility Community have shared feedback re: recent programming changes to DPB1 entry, and this indicates a programming update may be required. The committee's input is needed to identify a solution.

Data summary:

- The problem currently is that there are 27 DPB1 (short list) unacceptable antigens choices for candidates to select in Waitlist®. However in OPTN *Policy 4.10. Reference*

Tables of HLA Antigen values and Split Equivalence, Table 4-14: HLA DPB1 Unacceptable Antigen Equivalences there are around 641 unacceptable antigens available to select from. This created a difference between what is in listed in policy and what is programmed into Waitlist.

- There has been several emails and phone calls from the transplant community about this discrepancy and the inability to select DPB1 antigens.
- UNOS staff reminded the committee about the report presented to the members in February as a resource to help make their decision. The following are the list included in the report:
    - Top 10 DPB1 Alleles selected in DonorNet℠.
    - Frequency of DPB1 alleles across ethnicities.
    - To 10 DPB1 unacceptable antigens selected in Waitlist®.

Summary of discussion:

- Members had several questions and concerns about a solution to this discrepancy:
    - A suggestion to add the common and well documented alleles to the short list was presented.
    - Questioned what percentage of the population is covered on the short list versus another list.
    - Mapping epitopes as a future project was discussed.
    - Members agreed that nothing on the current short list should be removed.
    - How should we list unacceptable antigens if we cannot define them on antibody testing kits?
    - Members asked to possibly reference what DPB1 unacceptable antigens (UAs) are listed in Canada.
    - The inclusion of NMDP (National Marrow Donor Program) DPB1 data as a resource.
- The final decision was to create a short list. To include the 27 currently listed in waitlist and to add the top 25 DPB1 donor antigens from the UNOS staff report as UAs to cover 99% of donors.

Next steps:

- UNOS staff with take the committee decision, have a discussion with IT and present the committee a plan to implement this.

3. Project Discussion: Updating OPTN *Policy 4.10 Reference Tables of HLA Antigen Values and Split Equivalences*

The Committee will discuss:

- What table updates are required
- If/what new tables may be required

At the conclusion of the discussion, the Equivalency Table Review Subcommittee will be charged with determining what additional updates may be required based on cross reference with current testing kits.

Summary of discussion:

- Members expressed that in the new table update discussions that a new mechanism of table updates should be discussed.
    - UNOS staff presented the idea of an expedited pathway. Explaining that using this process, table updates would proceed through the policy development

process faster. Staff continued to explain that to insure, that this could apply to future updates the policy language for this pathway would be added to the proposal for the next table update.

- Members suggested putting into policy a list of alleles referencing an outside source such as World Health Organization (WHO) or International Immunogenetics Information System (IMGT). However there were concerns on the reputability of these sources and the process of inclusion in future updates to the tables.
- Member raised some concerns on how new alleles would be captured both in documentation in UNet®, OPTN policy, and for the transplant community. The committee stressed a future need for policy or guidance to help with this.
- The alleles that need to be added are DP Alpha (DPA) and possibly other DP's.

Next steps:

- UNOS staff will put out a survey for a subcommittee call date.
- Staff will also identify the specific mechanism for the expedited pathway and how to add that policy to the upcoming table update.

4. Request from OPTN/UNOS Data Advisory Committee

The Data Advisory Committee (DAC) working on a project to amend data submission requirements outlined in OPTN Policy 18. They would like input from the Histocompatibility Committee on the Donor and Recipient Histocompatibility Form requirements, review the submission timeline for individual forms, and the policy requirement for Timely Data Submission in Policy 18.4.

Data summary:

- UNOS staff supporting the DAC presented the future changes in data submission and asked the committee for their input on the following question:
    - 1. What impact, if any, would eliminating Policy 18.4 have on Histocompatibility Labs ability to meet the 30 day timeframes?
    - 2. What factors, if any, may be present challenges for Histocompatibility Labs when submitting data by the timeframes?
    - 3. What is a reasonable amount of time for Histocompatibility labs to ensure submitted data is accurate?
    - 4. What circumstances or factors require labs to revise previously submitted data?

Summary of discussion:

- For the first two questions above the members had the following question and concerns:
    - Concerned about the 30 day deadline. For example if a discrepancy in data occurs at the end of the 30 days and NGS (next generation sequencing) has to be done it may take another 30 days. Several other member agreed that 30 days is too short.
    - Members asked why 30 days was chosen to be put into policy why not 60 days.
    - Certain situations where re-typing has occurred (due to a re-transplant or inactivity for example) and the data needs to be changed and updated past the date of submission.
    - There is variation on the granularity of alleles entered. In some cases when a candidate is listed, initially only A, B and DR alleles are reported while other transplant hospitals will do more granular typing 5 years later when the candidate is closer to receiving a kidney transplant.

    - Would this limit the entry of HLA data after transplant has occurred or on new candidate registration forms?
    - Takes a large amount of staff time to fill out the form in Tiedi®, this contributes to the need for a longer than 30 day deadline. Members suggested automating it.
- In conclusion the committee was not able to answer all questions and would like more time to think about these questions and possibly form a discrepancy subcommittee to look into this DAC project

Next steps:

- UNOS staff will take this feedback back to DAC committee. Staff will follow back with the committee on this project and ask for additional feedback.

5. Histocompatibility Discrepancy Review

Members of the Discrepant HLA Typing Subcommittee will provide an update on 2018 data review.

Data summary:

- The Vice Chair presented the discrepant typing reports from Quarter 1, 2, and 3 of 2018.
- Overall there was a decrease in discrepant typing.

Summary of discussion:

- There was no discussion on this topic however this presentation led into further detailed discussion of the next topic below.

6. Obtaining Recipient HLA Typing from Other Transplant Hospitals

The Committee will discuss the practical benefits of being able to obtain HLA typing information on a transplant recipient who is being referred to another transplant hospital for follow-up care.

Summary of discussion:

- Majority of the discussion stemmed from the previous topic of discrepant typing reports.
- Members had several questions and concerns:
    - Asked when the API (application programming interface) for unacceptable antigens import into waitlist project would be implemented. Staff followed up and presented the date as quarter three of 2019.
    - The following is an issue several members are currently facing:
        - When a recipient gets transplant at one transplant hospital (TX hospital) and moves to another TX hospital to get treatment, the second TX hospital cannot access that recipients HLA information.
        - Members would like access to the recipient typing as well and the donor and recipient's blood type.
    - A checklist or guidance of how to upload data for each histocompatibility lab (labs).
    - Clearer communication between the OPTN and labs. Labs send histocompatibility reports to organ procurement organizations (OPOs) and OPO staff are unsure how to input data correctly.
    - A need for there to be a standard process for uploading both HLA typing and unacceptable antigens (UAs) information.
    - Need a standard contact person if there are issues that appear.
    - The formation of a subcommittee was suggested and several member volunteer.

Next steps:

- UNOS staff will follow up with IT, legal, and communication about the information transfer from one TX hospital to another.
- Staff will contact members who volunteered to participate for the subcommittee.

7. User Enhancements to the Current Calculated Panel Reactive Antibody (CPRA) Calculator

UNOS staff will provide an overview of user enhancements to the CPRA calculator and be available for questions.

Summary of discussion:

- The current CPRA calculator on the OPTN site has a check box feature and has a very busy look. UNOS research and communications worked together to try and create a better version. The new calculator was demo-ed for the committee.
- Members showed overall support and liked the new look.
- There was suggestion in the future to take this new look and apply this to UNet® applications.
- Members also stressed the need to test this before final implementation.
- The timeline for final implementation is unknown.

8. Project Discussion- Change in Calculated Panel Reactive Antibody (CPRA) Calculation

The Committee will have the opportunity to discuss several key elements to this project including:

- The pros/cons of the count vs haplotype methods.
- Short review on the current CPRA calculator, and discuss the pros/cons of a 8 locus model vs a 11 locus model.
- Discuss what loci are considered in the future calculator and articulate why.
- Data report from project SME

At the conclusion of the discussions, the Committee will identify what items are at the decision stage and what items need further discussion/data to reach the decision stage.

Data summary:

Brief Background:

- Past discussions supported transition from haplotype frequency to counts.
- Current CPRA calculation uses haplotype frequency data from 2007/2008.
- Switching to counts would allow system updates with reduced resource burden.
- Easier model for the transplant community and public to understand.
- Excellent collaboration with subject matter experts (SMEs) as well as the NMDP data set.

Summary of discussion:

- Members discussed the validity of the count method in depth:
    - Pro
        - NMDP SME have this data available.
        - No need to update as often as is currently done with the tables in OPTN policy.
        - Possibly useful for the inclusion of DP and DR alleles in CPRA.

- Con
    - The United States diverse ethnic population would be difficult to account for using this method.
- Members and SMEs had a discussion on if the count method would result in drastically different results for the user however there was no consensus on the final answer.
    - SME believe that this method will not be different due to the algorithm they have created will fill in any missing data. While member had a differing opinion.
- Members asked the SMEs to see the count data set with the DP alleles and to send that to all committee members
- SME gave an updated on the following items:
    - They have the NMDP count data and haplotype data however they cannot release it due to the unpublished paper (that SME are creating). However they will follow up on the status.
    - Is still in the process of completing a comparison between the count data from NMDP CPRA and OPTN CPRA calculation.

- Next there was discussion on the loci that should be included in the future calculator.
    - Currently only A, B,C, DR, DQB is used the two options presented were the following:
        - 8 loci – A, B, C, DR, DPA, DQA, DQB, DPB
        - 11 loci – A, B, C, DR, DQA, DQB, DPA, DPB, DR 3/4/5
    - Overall members supported the 11 loci model going forward. There was stress on including DR 3/4/5 alleles due to their prevalence and its presence in NMDP data set.
    - Other comments included a possible autofill for allele equivalences during the process. In addition the removal of current CPRA table in OPTN policy once this project is implemented.
    - In conclusion members stated the need to see the NMDP counts data set in comparison with OPTN data before any further decisions are made.

Next steps:

- UNOS staff will work internally about the data transfer process and will work together with SME to develop a plan.
- On the next call once the committee has seen the appropriate data and make a decision on haplotypes or counts.

9. Kidney Transplantation & Cross Match Results

A member will share recent concerns identified in Region 9 re: having the results of a cross match available prior to a kidney transplanted.

Summary of discussion:

- A member shared with the committee an issue that he went through about the current definition of a cross match with the government of New York.
- Member shared their concerns about virtual and physical cross matching in the climate of broader sharing.

Upcoming Meeting

- May 14th, 2019 Full Committee Call