OPTN Histocompatibility Committee
Meeting Summary
January 10, 2023
Conference Call

John Lunz, Ph.D., F(ACHI), Chair
Gerald Morris, MD, Ph.D., Vice Chair

Introduction

The Histocompatibility Committee met via Citrix GoToMeeting teleconference on 01/10/2023 to discuss the following agenda items:

1. CPRA >98% Form
2. ASHI ARB Memo: Overreporting of HLA Typing Discrepancies
3. Revising the Donor and Recipient Histocompatibility Forms

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

1. CPRA >98% Form

OPTN Contractor Member Quality staff presented on site survey findings for OPTN *Policy 8.5.F: Highly Sensitized Candidates* since 2016, the beginning of monitoring for this policy implementation.

Data summary:

OPTN Contractor staff presented the site survey process and policy being monitored for background for members.

Site survey began monitoring this policy in 2016. Since then, 353 surveys have been conducted, 1149 records reviewed, and 147 found noncompliant. The overall compliance rate is 87.3%. For the first site survey cycle from 2016-2019, the compliance rate was 86.3%. For the second site survey cycle from 2019-2022, the compliance rate was 89.1%.

Of the 147 noncompliant records, the most common findings which made up 77.4% of the noncompliance were:

- MD signed written approval after candidate was made eligible to receive offers – 47 records = 31.9%
- Both MD and HLA lab director signed written approval after candidate was made eligible to receive offers – 25 records = 17%
- Signed written approval not documented in medical record – 22 records = 14.9%
- MD written approval not documented in medical record – 20 records = 13.6%
- Written approval in medical record not dated, therefore unable to determine the unacceptable antigens listed were reviewed prior to date candidate was made eligible to receive offers – 15 records = 10.2%
- HLA lab director written approval not documented in medical record – 4 records = 2.7%
- HLA lab director signed written approval after candidate was made eligible to receive offers – 2 records = 1.3%
- "Data entry errors"

- HLA lab director entered in WL as having reviewed and approved the unacceptable antigens listed did not match the signed written approval in medical record – 7 records = 4.7%
- MD entered in WL as having reviewed and approved the unacceptable antigens listed did not match the signed written approval in medical record – 5 records = 3.4%

Summary of discussion:

One member commented that it seemed like the policy violations were all documentation-related and didn't seem to be improper assignment of unacceptable antigens and asked the OPTN Contractor staff if they had ever had that issue. The OPTN Contractor staff responded that they have not seen inappropriate listing of unacceptable antigens, and that most of the member confusion seems to be around the timing of the documentation requirement.

One member asked if the candidate was able to receive national share kidney offers before the approval was documented in the chart. OPTN Contractor Staff clarified that once the unacceptable antigens are listed in the OPTN Computer System and once the approving transplant surgeon or physician and HLA lab director's names are listed, the patient is eligible to receive the national shares. Staff clarified that the documentation being discussed doesn't exist in the OPTN Computer System, and is in the member's chart. Staff clarified that the documentation in the member's chart must be dated on or prior to the date of entry into the OPTN Computer System to be compliant with policy. The Committee member then asked why the form was for CPRA >98% because he thought that national allocation was only for CPRA 100% candidates, and CPRA 99% candidates were shared at 250 nautical miles (NM). Staff and committee leadership clarified that CPRA 99% candidates also receive national shares under the current allocation system.

One member stated that she couldn't imagine surgeons are verifying unacceptable antigen listing on the forms, and that her audits have never seemed to evaluate the appropriateness of listing unacceptable antigens. She stated that she doesn't think the audits really evaluate whether or not unacceptable antigens are listed correctly. The Committee chair stated that the intent of the forms was to prevent inappropriate listing of unacceptable antigens, and agreed that the audits really don't examine that. He stated that it was a good intention when implemented, but that it has become an administrative burden with only a potential negative impact for the program or candidate. One member stated that it's an undue burden for clinicians, directors, and patients, and that it should be removed. Multiple other members agreed.

Next steps:

The Committee will pursue this as a project. The next step is to present the project to the Kidney Transplantation Committee for their feedback.

2. ASHI ARB Memo: Overreporting of HLA Typing Discrepancies

The Committee Chair presented on a memo from the American Society of Histocompatibility and Immunogenetics (ASHI) Accreditation Review Board (ARB) Committee and the response.

Data summary:

The Committee Chair presented on the content of the letter from the ASHI ARB. The letter raised the concern of deceased donor HLA typings reported in TIEDI as "discrepant" due to high-resolution confirmatory donor typing. He then responded with the Committee's current efforts related to these concerns.

The Chair then presented on the Committee's current efforts that were outlined in the response. The efforts fell into the following categories:

- Updated Data Services Portal discrepancy report
    - Unblinded, lab-specific version of the quarterly committee discrepancy report
    - Updated mid-2022
    - Added HLA equivalency tables as logic to reduce number of discrepancies displayed due to increases in typing resolution
- Revise logic behind TIEDI HLA discrepancy report
    - Planned for Q1 2023
    - Will use HLA equivalency tables as logic to reduce the number of discrepancies displayed due to increases in typing resolution
- Increased screening of OPTN Patient Safety Portal Reports prior to investigation
    - Developing a protocol for patient safety/Histocompatibility Staff to use to close cases of increased typing resolution without action
    - Requires review and approval by Committee

The Committee Liaison then presented the goal of the increased screening of the Patient Safety Portal Reports as developing a set of protocols to close cases of non-critical HLA discrepancies without MPSC action in order to reduce the stress/effort of labs and other members related to an unnecessary investigation. The process has historically required full investigation into every case, even if case details indicate a non-critical HLA discrepancy. The proposed protocols will be reviewed by the HLA Discrepant Typings Subcommittee. These involve a Member Quality protocol for patient safety staff who are less familiar with HLA, for cases that involve all HLA reportable through the OPTN Computer System, and a Histocompatibility staff protocol for HLA not available in the OPTN Computer System using IMGT/HLA equivalences. If staff are unable to resolve, cases are referred to Histocompatibility Committee leadership or the Membership and Professional Standards Committee (MPSC) Histocompatibility Subcommittee for review.

Summary of discussion:

One member stated that the majority of discrepancies the committee evaluated in the past two quarters weren't discrepancies in typing resolution, and another stated that the initiatives in the past year for improving the analysis may have helped that.

The Chair stated that this discrepancy work will need to be proactive with more labs moving to higher resolution typing. Multiple members agreed with implementing protocols for which cases are reviewed by the MPSC, to remove discrepancies due to typing resolution only.

One member suggested a recommendation on reporting for labs for ambiguous HLA typings, including using p-groups for DP alleles.

3. Revising the Donor and Recipient Histocompatibility Forms

The OPTN Contractor's Committee Liaison provided an overview of the OPTN data review process and facilitated a discussion on the reasons for collecting virtual crossmatching data.

Data summary:

The Committee Liaison presented on check-in process with the Data Advisory Committee (DAC), DAC requirements for sponsoring committees, OPTN Data Collection Principles, and the Data Standardization Checklist.

The discussion questions for virtual crossmatching data were on the goals of this data collection and what the use of this data collection would be.

Summary of discussion:

One member stated that it would be helpful to have more data on the use of crossmatches by type, especially for final crossmatch used. He stated that this data can be collected through surveys or registries, but that it should ultimately be collected where members are registering crossmatches for transplants on the donor or recipient histocompatibility forms. He also clarified that the form shouldn't be overwhelming for members, so there shouldn't be too many added questions, and any added questions should be meaningful and ultimately add to the understanding of crossmatching and how it's being used.

Another member added that the criteria centers are including in their virtual crossmatching is important, like mean fluorescence intensity (MFI) cutoffs for antibodies. Another member countered that the MFI cutoff would be difficult to use, because MFI is different everywhere, and you would need to ask questions like if the serum was treated with Ethylenediaminetetraacetic acid (EDTA). He mentioned there are so many variable parameters, including aggressive versus conservative centers choosing their MFI cutoffs and peri-transplant desensitization protocols. He mentioned that age of the serum used may be a useful data point to include. Another member agreed that age of the serum would be an important data point which could vary significantly by place and by organ.

Another member agreed with age of the serum and added that physical crossmatching isn't standardized so asking for standardization of MFIs is unrealistic. The member added that the physical crossmatching section of the form should also have "indeterminate" as an option, not just positive or negative. The member recommended re-examining the physical crossmatch section in addition to adding a virtual crossmatch section.

One member stated there needs to be a difference between virtual crossmatch for final acceptance and virtual crossmatch or donor specific antibody (DSA) analysis prior to physical crossmatch for final acceptance. Another member agreed that there needs to be a way to determine whether the virtual crossmatch was the final crossmatch for organ offer acceptance.

The Scientific Registry of Transplant Recipients (SRTR) representative on the committee recommended collecting data on what DSA exist and what their MFI is. He also recommended separating out T and B cell crossmatch data.

One member stated that she thinks the details of what exactly the data collection will be will be sorted out by the subcommittee, but felt that the goals of the data collection were really to inform the community on the utility, success rate, and prevalence of using virtual crossmatch. The Chair agreed and added that virtual crossmatching also has a potential impact on efficiency of allocation that would be important to have data on.

Another member stated that MFIs aren't comparable across different platforms, which would be something to consider if the committee wanted to collect MFI. Another member agreed, and said that maybe presence or absence of DSA would be a better data point to collect. Another member pointed out that with each vendor the levels for MFIs and DSA are slightly different.

A member stated that this form needed to be simple for labs to fill out, and the addition of new data needed to be meaningful and weighted against the burden of filling the forms out.

Another member stated that MFIs are only semi-quantitative, not quantitative, and there's too much variability to be useful to collect data on.

Next steps:

The Committee will submit the project to the Data Advisory Committee (DAC) for consideration of endorsement of potential data collection changes. Multiple members volunteered for a subcommittee to review the DHF and RHF.

Upcoming Meetings

- February 14, 2023, 12 PM ET, Teleconference
- March 14, 2023, 12 PM ET, Teleconference
- April 11, 2023, 8:30 AM CT, Chicago, IL

Attendance

- **Committee Members**
  - Andres Jaramillo
  - Bill Goggins
  - Caroline Alquist
  - Gerald Morris
  - Hua Zhu
  - John Lunz
  - Kelley Hitchman
  - Laurine Bow
  - Lenore Hicks
  - Manu Varma
  - Omar Moussa
  - Peter Lalli
  - Qingyong Xu
  - Reut Hod Dvorai
  - Valia Bravo-Egana
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **SRTR Staff**
  - Katherine Audette
  - Rajalingam Raja
- **UNOS Staff**
  - Amelia Devereaux
  - Courtney Jett
  - Isaac Hager
  - Karen Wooten
  - Liz Fridell
  - Rob Patterson
  - Susan Tlusty
  - Thomas Nolan