OPTN

Board Report to the OPTN Board of Directors

Require Human Leukocyte Antigen (HLA) Confirmatory Typing for Deceased Donors

OPTN Histocompatibility Committee

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Require Human Leukocyte Antigen (HLA) Confirmatory Typing for Deceased Donors

Affected Policies: *4.3.A: Deceased Donor HLA Typing*
Sponsoring Committee: *Histocompatibility*
Public Comment Period: *January 19, 2023 – March 15, 2023*

Executive Summary

Human Leukocyte Antigen (HLA) typing is a vital step for successful organ transplantation. An incorrect HLA typing can lead to hyperacute rejection, graft failure, and death. These errors can place the life of the recipient at risk, and can cause unnecessary organ non-utilization and prolonged waiting time for multiple candidates. Furthermore, any incorrect typing results have the potential to significantly delay the allocation process. The OPTN implemented a requirement for dual manual entry of HLA typings to reduce clerical discrepancies in 2020.

The OPTN Histocompatibility Committee, the Committee, proposed in public comment to create additional safety protocols for other causes of HLA discrepancies by requiring two HLA typings be performed on all deceased donors with samples drawn at two separate times. Requiring confirmatory HLA typing for deceased donors could help ensure a recipient is receiving a compatible organ that will function to improve their health and increase post-transplant survival. Highly sensitized candidates, female candidates, and black candidates are particularly vulnerable in cases of incorrect HLA typings, as these groups are more likely to have pre-formed antibodies that could cause an adverse immunologic reaction.

After reviewing public comment feedback, the Committee is not asking the Board to consider the proposal at this time. The Committee is evaluating additional data and alternative options to both reducing and better understanding critical discrepancies at this time. These options include revising the OPTN Computer System discrepancy reporting data collection and a possible guidance document. This report is being provided to the Board as an update, and there is no action the Committee is requesting the Board to take at this time.

Overview of Proposal

Purpose

The purpose of this proposal was to ensure the accuracy of immunologic testing results used in allocation and reduce the chance of unintended HLA incompatibility within the transplant system. The Committee proposed requiring two HLA typings be performed from specimens drawn at two separate times for all deceased donors, similar to the existing requirement for blood group typing. Incorrect typings in either category have the same immunologic potential, and the Committee proposed they should receive the same safeguards. In addition, an increased confidence in HLA typing result accuracy could increase utilization of virtual crossmatching, in turn leading to a decreases in cold ischemic time and late organ declines due to positive crossmatch, and an increase equity for highly sensitized candidates.

Questions asked of the Community

- Would laboratories be able to run tests in parallel or would they anticipate an increase in the required time for HLA typing?
- Would a potential increase in turnaround time for initial HLA typing be worth the increased confidence in the results, and the ability to confidently use virtual crossmatching?
- Would potential increased costs for confirmatory typing of the deceased donor's HLA be prohibitive for labs or OPOs?
- Should the use of two different testing modalities be a requirement that is included in the new policy?

Summary of Public Comment Feedback

Sentiment is collected on public comment proposals and is measured on a 5-point Likert scale from strongly oppose to strongly support (1-5). These reports are helpful to spot high-level trends, but they are not meant as public opinion polls or to replace the substantive analysis below. Generally, public comment sentiment has been unsupportive of this proposal as written, as indicated by the average sentiment score of 2.4. **Figure 1** shows sentiment received from all respondents (regional meeting, online, and email) by their stated member type. Organ Procurement Organizations (OPOs) were the least supportive of the proposal, with an average score of 1.8, and patients were more supportive of the proposal, with a sentiment score of 3.2.

Figure 1: Sentiment by Member Type

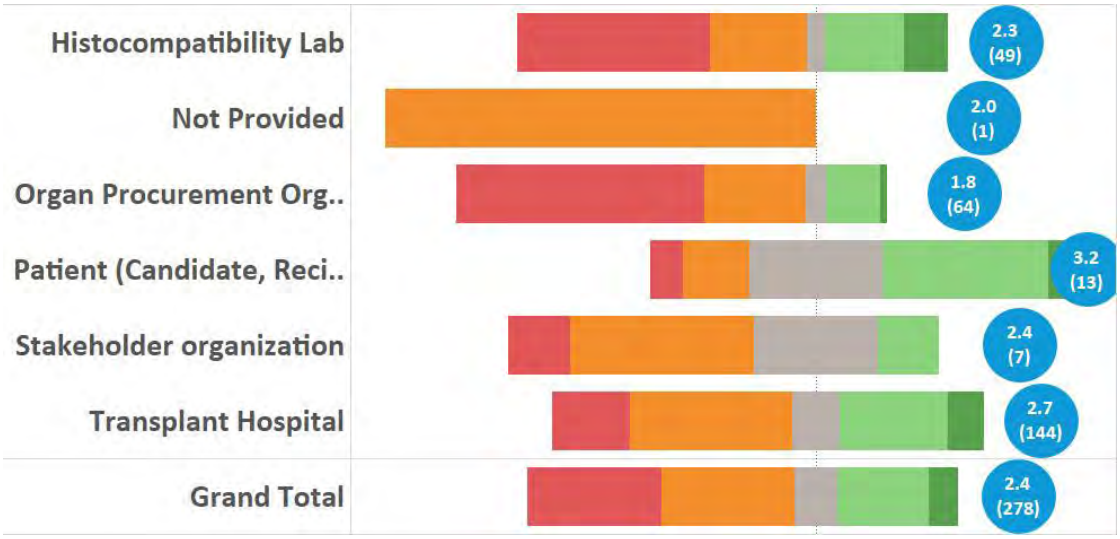
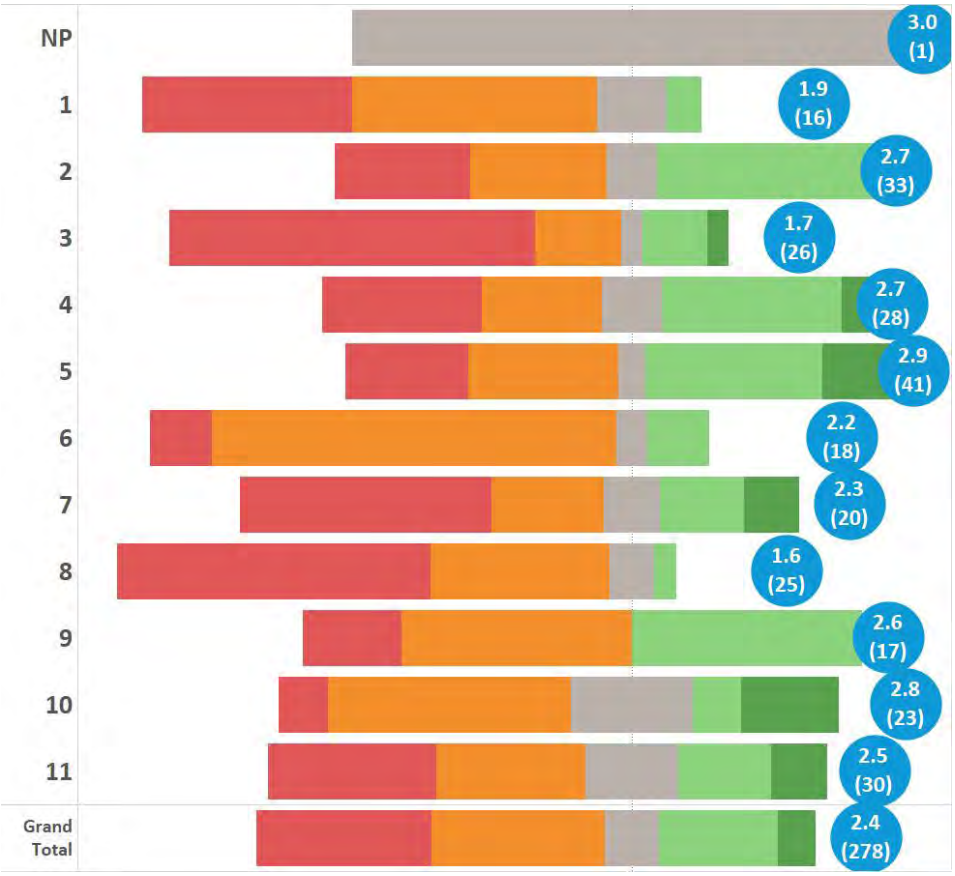


Figure 2 shows sentiment received by region, with "NP" representing sentiment for commenters whose location was not provided. Opposition was raised in all regions, mostly under the theme of concerns about burden. Commenters in Region 8 expressed the most concern of any region, and had the lowest average sentiment of 1.6.

Figure 2: Sentiment by Region



Concerns about burden

The primary concerns raised about this proposal were related to member burden. Many commenters expressed concerns about the fiscal impact of this proposal, and cost estimates from the community ranged from a national fiscal impact of five to 26 million dollars. Many commenters expressed concerns about a low cost to benefit ratio based on the number of events. Multiple commenters also expressed concerns about laboratory staffing, although the Committee felt that most laboratories would be able to run tests in parallel, causing minimal impact on staffing needs. Multiple members commented that the Committee did not propose a process to resolve discrepancies in this proposal, and that the process to resolve any discrepancies that do arise could add additional time to allocation.

Recommendations for supporting data needed

Many commenters proposed that the committee gather additional supporting data. Multiple commenters noted that the data presented did not warrant the substantive change proposed by the Committee. Additional data proposed in public comment included:

- Granular fiscal analyses
- Root causes of reported discrepancies
- Post-discrepancy outcomes data when an organ was transplanted
- Whether an organ was unable to be utilized due to a critical discrepancy
- Comparative rates of discrepancies at labs performing confirmatory typings
- How discrepancies were identified, whether they are self-reported, discovered by OPTN Computer System reports, or discovered by repeat testing at recipient centers
- Location at which sample switch occurs, whether it be the OPO or laboratory

The Committee carefully considered the feedback received and remains committed to the goal of reducing critical discrepancies. They plan to gather and review additional data such as a report on aggregate root causes for critical discrepancies submitted through the OPTN Improving Patient Safety Portal, after which they will request any additional available data required to determine next steps for the proposal.

Alternative safety measures to consider

Numerous commenters proposed additional or alternative safety measures for the Committee to consider. These included:

- Require multiple testing methods or assays, which may reduce likelihood of errors due to technical limitations or assay failures
- Require automatic upload for donor HLA typing
- Duplicate typing or additional safety measures for living donor typing
- Increase training/quality assurance/quality improvement initiatives
- Informatics tools to analyze typing data and identify potential mistypings
- Develop guidance on reducing and resolving HLA typing discrepancies
- Implement robust check in systems for samples at laboratories
- Work with histocompatibility laboratory accrediting organizations on standards to address common root causes
- Chain of custody/processes for OPOs and laboratories when handling more than one HLA sample/typing at a time
- Requirements for the labeling process
- Pilot study for confirmatory typings with a small number of OPOs
- Revise OPTN Computer System discrepancy reports and collect additional data on discrepancies

The Committee evaluated these recommendations in their April meeting. They felt it would be premature to make a final decision on the potential method, or methods, used for reducing HLA critical discrepancies prior to evaluating additional data related to root causes. In addition, they received a presentation on an Application Programming Interface (API) under development for automated upload of deceased donor HLA typing, which will be released by the end of the year and will likely address many clerical errors, or data entry errors. This will not address switched samples or other types of errors, but may reduce the total volume of discrepancies observed.

Next Steps

The Committee is not recommending the proposal to require confirmatory HLA typing for deceased donors from consideration for the OPTN Board of Directors at this time. The Committee will review root cause data submitted to the OPTN Improving Patient Safety Portal. The Committee is evaluating alternative options related to both reducing and better understanding critical discrepancies, including revising the OPTN Computer System discrepancy reporting data collection and a possible guidance document. This report is being provided to the Board as an update, and there is no action the Committee is requesting the Board to take at this time.