

**OPTN Kidney & Pancreas Transplantation Committee  
Continuous Distribution Workgroup  
Meeting Summary  
February 26, 2021  
Conference Call**

**Silke Niederhaus, MD, Chair  
Rachel Forbes, MD, Vice Chair  
Vince Casingal, MD, Chair  
Martha Pavlakis, MD, Vice Chair**

## **Introduction**

The Kidney & Pancreas Transplantation Committee Continuous Distribution Workgroup (the Workgroup) met via Citrix GoToMeeting teleconference on 02/26/2021 to discuss the following agenda items:

1. Welcome & Review of Project Goals
2. Recap of February 12<sup>th</sup> Meeting
3. Overview of Human Leukocyte Antigen (HLA) Matching: Final Rule Review
4. Overview of HLA Matching: Current Literature Review
5. Discussion: HLA Data Request
6. Next Steps

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

### **1. Welcome & Review of Project Goals**

The Workgroup reviewed the goals of the Continuous Distribution project as well as the Workgroup's next steps, including the second phase of the project (assigning values to attributes) and the development of a concept paper summarizing the identification and categorization of attributes.

#### Summary of discussion:

The Workgroup had no comments or questions.

### **2. Recap of February 12<sup>th</sup> Meeting**

The Workgroup reviewed highlights from their February 12<sup>th</sup> meeting. During that meeting, the Workgroup began discussions on HLA matching priority and the impact of HLA matching on O-ABDR mismatches, DQ locus matching, graft life and pediatric priority, and race and equity in access. The Workgroup introduced a concept to more critically scale HLA matching priority based on calculated panel reactive antibodies (CPRA), or the rarity of certain HLA matches.

#### Summary of discussion:

The Workgroup had no comments or questions.

### **3. Overview of HLA Matching: Final Rule Review**

The Workgroup reviewed the requirements of the Final Rule as they relate to allocation policy development to further define the project scope, highlighting specific sections of the Final Rule to use as guiding principles for discussion.

#### Summary of discussion:

The Workgroup had no comments or questions.

#### **4. Overview of HLA Matching: Review of Current Literature**

The Workgroup reviewed examples of HLA rating scales based on data and findings in the current literature.

#### Data Summary:

The practical end goal is a formula to calculate a composite allocation score, in order to rank potential recipients on a match run based on donor characteristics, candidate characteristics, and the interaction between them.

HLA matching will factor into two parts of the composite allocation score.

1. Weight of the post-transplant survival, to be determined by the Workgroup at a later date through values discussion and data
2. Rating scales, to compare one HLA match to another and determine which HLA matches should hold priority over others

An example rating scale for HLA matching based loosely on Kidney allocation, on a 100 points scale would assign priority in a decreasing fashion based on age. Age 0-10 candidates with 0-ABDR mismatch would receive 100 points, while candidates age 11-17 would receive 75 points, 75 percent of the priority assigned to younger candidates. Adult 0-ABDR candidates would receive 25 points, 33 percent of the priority of similar adolescent patients and 25 percent of the priority of similar young pediatric candidates. This model could also incorporate level of HLA matching in a decreasing linear fashion. Any candidate with a 0-DR mismatch and 1-AB mismatch would earn 8 points, as that match is 50 percent of 0-ABDR mismatch and earns 33 percent of a 0-ABDR mismatch priority. A candidate any age with 1-DR mismatch and 1-ABDR mismatch would earn 4 points, and so on.

An example rating scale for HLA matching in current pancreas allocation on a similar 100-point scale would assign 100 points to any 0-ABDR mismatch candidate, and no points for 1 or more ABDR mismatches.

These examples model how HLA matching priority *could* look. Once the Workgroup has determined the appropriate HLA matching priority from data and clinical judgement, a statistical model can be built from relative survival benefits to inform the shape and slope of the rating scale.

The Workgroup reviewed proposals for other HLA matching models in current literature.

#### Summary of discussion:

A Workgroup Chair noted that pancreas alone candidates benefit from a well-matched organ, particularly if the graft fails or that recipient later needs a kidney. Increased matching priority could prevent sensitization and improve utilization, though there may be unintended consequences of equity and access.

#### **5. Discussion: HLA Data Request**

The Workgroup continued discussions to develop a rating scale and data request for HLA matching.

#### Summary of discussion:

The Histocompatibility Committee Chair remarked that the HLA matching rating scale doesn't necessarily need to change from its current state, and that assigning points would require a more

complicated sliding scale and a calculation based system. The Chair continued that considering equity and the improvement of immunosuppressant protocols over time, HLA matching may be a less important consideration, noting that data on adverse graft events related to HLA matching may change with many recipients now on life-long immunosuppression.

A member agreed HLA matching should prioritize the pediatric population, particularly as these patients often return to the kidney waitlist later in life, making organ longevity a critical consideration. The member continued that sliding scales will be important, and that the system should prioritize harder to match patients utilizing frequency data of antigens and alleles in the donor population. The member added that homozygous patients, with one antigen at each loci, are particularly disadvantaged, and that a sliding scale can further balance equity in access. The member noted that further information is needed to evaluate what kinds of patients receive 0-ABDR mismatch offers and transplants. A Workgroup Chair agreed that frequency data would be critical to building a scale that prioritizes hard to match patients.

Staff noted that a distinction between the transplant characteristic of a 0-ABDR mismatch, which is an interaction between donor and candidate HLA typing that impacts post-transplant survival, and candidate biology, or the characteristics of a patient that impacts their chance of finding a well-matched donor. Staff noted that understanding which HLA matches need prioritization will help target which patients may benefit from HLA matching, and asked what questions the group would like answered by the data request.

A Workgroup Chair asked the group to determine what measurable goals should be achieved through the HLA matching rating scales, noting that equity in matching for difficult to match patients and longevity of transplanted organs were previously mentioned. These goals can allow HLA matching to be compared to other attributes – an additional 2 life years, for example, from a 0-ABDR mismatch transplant can be tangibly measured and compared. The Workgroup Chair continued, noting that HLA matching may not be the attribute where the greatest push for equity can be accomplished, but that shouldn't prevent HLA matching from being appropriately considered for the benefits it can provide for patients, particularly in long term outcomes. The group will need to determine what a 0-ABDR mismatch transplant is worth for those who can get it, and build another system for those who will never receive a good match to have access to transplant.

One member contributed that DQ matching should be evaluated against post-transplant survival, noting that a previous study found a greater survival benefit for DQ matching over DR matching. A Workgroup Chair agreed, and added that a study conducted at their center had found certain DQ mismatches were associated with graft failure, while others were not. The Workgroup Chair continued that identifying adverse DQ mismatches will allow for more specificity in the use of frequency data for DQ matching.

A Workgroup Chair suggested that candidate estimated post-transplant survival (EPTS) could be used to determine how much weight is given to HLA matching, so the post-transplant survival benefits are utilized for candidates who will best realize them. In terms of graft life years and sensitization, candidates who are not expected to live for 35 more years or otherwise be relisted after initial transplant will not likely reap the benefits of a strong HLA match, particularly not as low EPTS or pediatric patients would. Two other Workgroup Chairs agreed, and one shared that pancreas-alone candidates have higher life expectancy than simultaneous kidney-pancreas (SPK) candidates, and thus it could be argued that pancreas-alone candidates need a better HLA match. The Workgroup Chair also asked how this practice would impact pancreas after kidney (PAK) patients, and noted that many pancreas and kidney-pancreas (KP) patients need re-transplant. Stronger emphasis on HLA matching for pancreas and KP patients could prevent the need for re-transplant and improve patient access. The Histocompatibility Committee Chair agreed that the argument for EPTS driving HLA matching priority is

easier for pancreas alone candidates, particularly as kidney candidates face a significantly more limited organ supply. Staff asked if a rating scale utilizing this concept could use pre-existing EPTS structures to assign patients priority, and then incorporate levels of HLA matching, such as level of ABDR mismatch or mismatches at DR and DQ.

A Scientific Registry of Transplant Recipients (SRTR) representative mentioned a publication from 2004 that found removing locus B matching from allocation led, to a 25 percent change in the transplant rate between African American and White patients, and increased the transplant rate for other ethnic minorities. Another member agreed, noting that frequency data could be critical to closing racial disparities in HLA matching by giving more points to a less frequent match in an appropriate group, such as pediatric or low EPTS.

An SRTR representative expressed concern that this level of complexity being proposed could make it harder to complete a data study that will give the correct answer, particularly with the number of judgement calls necessary in balancing pediatric and low EPTS, match frequency, and level of mismatch. A Workgroup Chair agreed, and challenged the group to determine how much a 0-ABDR mismatch is worth prioritizing. If it's worth a little, then it may be smarter to keep it simple, but if it's worth a lot, then it will be worth doing the hard work to build an appropriate data-driven study and system. Another member agreed, noting that 0-ABDR mismatch transplants made up only 4 percent of all kidney transplants last year.

The Histocompatibility Chair expressed a need for more data on the benefits of 0-ABDR mismatch transplants and DR and DQ matching to verify the argument that people who need re-transplants will be better off with 0-ABDR or DQ and DR matches. In particular, having data on CPRAs of relisted candidates with respect to their previous transplants 0-ABDR mismatch status and level of DR or DQ matching could provide explicit evidence of reduced sensitization.

## **6. Next Steps**

Staff will digest discussions and provide more information on what data is available, and the kinds of questions that can be answered by that data.

The Workgroup will continue discussions to develop the data request on HLA matching.

### **Upcoming Meetings**

- Friday, March 12, 2021 (Teleconference)
- Friday, March 26, 2021 (Teleconference)

## Attendance

- **Committee Members**
  - Silke Niederhaus
  - Martha Pavlakis
  - Vincent Casingal
  - Jim Kim
  - Arpita Basu
  - Caitlin Shearer
  - Cathi Murphey
  - Deirdre Sawinski
  - Elliot Grodstein
  - Loren Gragert
  - Abigail Martin
  - Oyedolamu Olaitan
  - Parul Patel
  - Peter Kennealey
- **HRSA Representatives**
  - Adriana Martinez
  - Marilyn Levi
- **SRTR Staff**
  - Ajay Israni
  - Bryn Thompson
  - Nick Salkowski
- **UNOS Staff**
  - Lindsay Larkin
  - Joann White
  - Rebecca Brookman
  - Tina Rhoades
  - Kayla Temple
  - Alesha Henderson
  - Alison Wilhelm
  - Amanda Robinson
  - Ben Wolford
  - Courtney Jett
  - James Alcorn
  - Kaitlin Swanner
  - Kelley Poff
  - Kelsi Lindblad
  - Kerrie Masten
  - Lauren Motley
  - Leah Slife
  - Matt Prentice
  - Melissa Lane
  - Nang Thu Thu Kyaw
- **Other Attendees**
  - John Lunz
  - Peter Lalli