OPTN Pancreas Transplantation Committee
Meeting Summary
February 28, 2022
Conference Call

Rachel Forbes, MD, Chair
Oyedolamu Olaitan, MD, Vice Chair

Introduction

The Pancreas Transplantation Committee (the Committee) met via Citrix GoToMeeting teleconference on 2/28/2022 to discuss the following agenda items:

1. Public Comment Presentation: Change Calculated Panel Reactive Antibody (CPRA) Calculation (OPTN Histocompatibility Committee)
2. Research Update: Two Year Monitoring of Changes to Kidney-Pancreas (KP) Waiting Time Criteria Data Analysis

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

1. Public Comment Presentation: Change Calculated Panel Reactive Antibody (CPRA) Calculation (OPTN Histocompatibility Committee)

The Committee received a presentation on the OPTN Histocompatibility Committee's *Change Calculated Panel Reactive Antibody (CPRA) Calculation* proposal. It was explained that the revised CPRA calculation will better reflect actual sensitization and improve access to transplant for the highly sensitized and minority OPTN candidates.

The OPTN Histocompatibility Committee includes the following in their proposal:

- Add human leukocyte antigen (HLA)-DQA1, DPB1, DPA1 and allele-level antibodies to CPRA calculation
- National Marrow Donor Program (NMDP) expands data cohort
  - Includes much higher typing resolution than most OPTN deceased donors
- Use genotype instead of haplotype calculation to better approximate rate of incompatible donors
- Expand from four to seven groups for deceased donor ethnicity
  - Expand from kidney-specific donor ethnicities to all organs

This proposal will not change required testing or data collection and there will be a transition period to obtain documentation for candidates with 99-100% CPRA prior to implementation.

Summary of discussion:

A member voiced support in the calculation including other loci; however, one week is a very short time to certify all highly sensitized patients for the new calculation. The presenter explained that a lot of patients already have unacceptable antigens for HLA-DPB1 included in their forms but they're not currently getting any points for it. As the new calculator is implemented, even with the same

information in the system, there are patients that will move up on the match. The presenter mentioned that this proposal does not require additional testing – there will just be a notification sent to centers identifying patients who will need a CPRA verification form that will need to be signed by the lab director and transplant program within one week. The presenter stated that the OPTN Histocompatibility Committee found that about 1,000 patients between kidney, kidney-pancreas (KP) and pancreas will change categories across the country, so the burden is likely on the lower side for centers. The presenter recommended that if members know that their patient has a lot of unacceptable antigens for loci that are not currently included in the calculation, then they may want to anticipate the patient moving up on the match sooner than they thought and prepare for them to need to be worked up a bit more than they currently are in their status.

A member inquired about what was mentioned in regards to adding these additional loci to the perfect match allocation, especially since the zero antigen mismatch may not be incorporated into kidney and pancreas continuous distribution. The presenter explained that there needs to be more discussion on this topic. The presenter mentioned that one of the concerns is that HLA types follow different ethnicities so, by adding matching points for either complete ABDR matching or individual loci matching, it may prioritize certain ethnic groups above others.

A member mentioned that highly sensitized patients received a lot of priority when the kidney allocation system (KAS) went into effect in 2014 and inquired about how that is impacting overall longevity post-transplant. The presenter stated that part of this ends up being an ethical decision – should utility or fairness be prioritized overall within the allocation system. The presenter also mentioned that there is not good enough data to see if the hard to match patients are being prioritized and transplanted appropriately, but, even if there were the ethical question has not been answered.

A member inquired whether it's possible the Kidney and Pancreas Continuous Distribution Workgroup can put forward a proposal that decreases the priority for sensitization. The presenter explained that it is still possible with the kidney and pancreas continuous distribution project and encouraged members to participate in the analytic hierarchy process (AHP) exercise to capture how they feel about the importance of prioritizing sensitization in the continuous distribution framework.

A member emphasized that determining outcomes is extremely important and inquired about who should be analyzing this data to make a determination regarding the weighting of these various factors. The presenter stated that the OPTN Histocompatibility Committee can work with the OPTN Kidney Transplantation Committee to see if they can understand the outcomes data better.

A member highlighted that the proposal mentions looking at various ethnic groups and stated that the use of race needs to be consistent, especially since race is being removed from the estimated glomerular filtration rate (eGFR) calculation. The presenter explained that eGFR is probably less ethnic driven than HLA. Often, less frequent HLA typings are seen in minority populations and, as a result, the minority populations will often have antibodies against HLA types that are not included in their own typing. This means the minority populations may be more apt to develop antibodies against more common HLA types. The presenter stated that this could lead to the majority population being prioritized over the minority population.

A member inquired how the proposal is planning to identify biracial patients. The presenter explained that self-reporting will be used to identify biracial patients.

A member inquired if there has been thought about awarding points to highly sensitized patients in a gradated fashion. The presenter stated that 99.5% calculated panel reactive antibody (CPRA) is one out of every 200 donors, so those patients are certainly prioritized over others. It was mentioned that the

proposal to change the slope of the line that is used to determine CPRA calculation points is something that will be discussed in the future.

2. Research Update: Two Year Monitoring of Changes to Kidney-Pancreas Waiting Time Criteria Data Analysis

The Committee reviewed results from the two year monitoring report of Changes to Kidney-Pancreas Waiting Time Criteria, which removed body mass index (BMI) and C-peptide thresholds for kidney-pancreas (KP) waiting time accrual from OPTN policy. With this policy change, candidates still need to be registered for a KP, meet kidney waiting time criteria, and be on insulin to accrue waiting time.

Data Summary:

- Waiting list: volume and proportion of KP registrations added to the waiting list increased for candidates with type 2 diabetes, C-peptide >2 ng/mL, and BMI 30+
- Transplants: volume and proportion of KP transplants for recipients with type 2 diabetes, C-peptide >2 ng/mL and BMI 30+ also increased
- Post-transplant outcomes: decreases in unadjusted one year post-transplant patient, kidney graft, and pancreas graft survival were more pronounced among recipients with type 2 diabetes and BMI 30+
- Kidney-alone: no signs of negative impact on pediatric or adult kidney-alone candidates

Summary of discussion:

A member stated that they were surprised to see a decrease in patient and graft survival and was wondering if deaths related to the Coronavirus disease 2019 (COVID-19) pandemic were included because that may explain the differences between pre- and post-policy eras. Staff explained that there wasn't a way to exclude COVID-19 deaths, so that could be playing a factor.

A member inquired about the dates of the pre- and post-policy eras. Staff stated that the pre-policy cohort was from mid-March 2017 through July, 10, 2019 and the post-policy cohort was from July 11, 2019 through October 2021.

A member noted that they keep hearing that pancreas transplant volumes have decreased due to COVID-19; however, this data shows that the volumes have stayed the same. The Chair explained that the last time the Committee had reviewed data, pancreas transplants had actually increased last year, although that might have been a bolus effect post-lockdown.

The Chair stated that they don't find it surprising that the Type II diabetics and high BMI patients have worse outcomes. The Chair noted that this begs the question of whether these patients have worse outcomes with kidney-pancreas (KP) transplants or waiting on the list. Additionally, has this policy change increased access to KP transplants?

Staff explained that in 2020 there were 827 KP transplants and in 2021 there were 820 KP transplants. It was also noted that these transplant numbers have decreased a little since 2019, when there were 872 KP transplants.

Members agreed that it seems pancreas and KP transplants are staying fairly steady, but there needs to be a steadier dataset before the Committee can make assumptions.

A member inquired if there was an increase in the number of listings for KP transplants. Staff explained that there were a little over 3,000 listings in the pre-policy era and about 3,300 in the post-policy era. The member noted that that doesn't translate to an increase in transplants, which could also be due to COVID-19.

The Chair stated that if the number of KP transplants is staying steady, then an increase in transplants for Type II diabetic patients means fewer Type I diabetics may receive KP transplants and inquired if that's appropriate since outcomes for Type II diabetic KP recipients are not as good.

A member inquired how the Committee would know if the Type II diabetics received more transplants. The Chair stated that the Committee could tell by the breakdown of C-peptide greater than two or less than two. The Chair emphasized that that's a gross definition for Type I and Type II diabetes and mentioned that they aren't sure any determination can be made from the data due to all the confounding factors.

A member suggested that the Committee may want to look at another six months of data, since they strongly suspect that COVID-19 had a large impact on whether centers were willing to accept a kidney but not a pancreas when it was suspected the donor was positive for COVID-19.

A member agreed and mentioned that it would be important to compare pre-policy to a cohort where COVID-19 has become steady or decreased. Staff mentioned that the two-year monitoring report was the final report that was planned for this policy, but these concerns could be incorporated into the policy monitoring for circle-based allocation and continuous distribution.

Staff also mentioned that the six month monitoring report for this policy used a cohort from around the time the Committee was wanting to look at – July 2019 through mid-January 2020. Staff stated that the overall trends for waiting list additions and transplants in the two year monitoring report were similar to the six month monitoring report, but they will still circulate the six month report to the Committee.

There were no further comments. The meeting was adjourned.

Upcoming Meetings

- March 21, 2022 (teleconference)

Attendance

- **Committee Members**
  - Rachel Forbes
  - Oyedolamu Olaitan
  - Silke Niederhaus
  - Antonio Di Carlo
  - Megan Adams
  - Nikole Neidlinger
  - Parul Patel
  - Todd Pesavento
- **HRSA Representatives**
  - Marilyn Levi
  - Raelene Skerda
- **SRTR Staff**
  - Bryn Thompson
  - Jonathan Miller
  - Raja Kandaswamy
- **UNOS Staff**
  - Joann White
  - Rebecca Brookman
  - Lauren Mauk
  - Lauren Motley
  - Leah Slife
  - Sarah Booker
- **Other Attendees**
  - Peter Lalli