OPTN/UNOS HISTOCOMPATABILITY COMMITTTEE
Teleconference
March 23, 2012
1:00-4:00 (EDT)
Interim Report

Lori Gore, UNOS liaison to the Histocompatibility Committee, opened the meeting by telling the regional representatives that they will not have to make any updates at the upcoming regional meetings.

Kidney Allocation Proposal

Ciara Samana, UNOS liaison to the Kidney Committee Transplantation Committee, gave a review of the proposed kidney allocation system to the Committee which included:

- Longevity matching (Top 20% of donors (KDPI) to top 20% of candidates (EPTS)
- The CPRA sliding scale
- National priority for CPRA ≥ 98% group, regional sharing for KDPI > 0.85 donors, "Share 0.35"
- A definition of KPDI

Ms. Samana closed by saying the reality of this new proposal is that the majority of kidneys will be placed very similarly to the current rules.

A member of the Committee asked why in the case where a donor has a KDPI of less than 20% , the ranking order of the proposed system put the regional top 20% below the local bottom 80%. Ms. Samana said it was a kind of compromise as to what would be palpable to the majority of stakeholders for the new system. She said with paybacks going away there remains a concern with the transplant community centered about shipping out large numbers of kidneys. Dr. Bowman, from HRSA, added that the intent of this new system was not to make a radical change in the local, regional, national order of allocation but to improve donor/recipient matching. Ms. Samana again emphasized that this new allocation system strongly resembles the current system and does not represent a radical change.

There was concern about the possibility of sensitized candidates (especially retransplant candidates) not falling within the top 20% EPTS kidney candidates, and that the proposed system was limiting their access to the entire donor pool. Ms. Samana said that was an excellent point and said the Kidney Committee should take a look to see if a relativity young person who had received a transplant with no diabetes or other comorbidities could be able to be included within the top 20% EPTS kidney candidates. Anna Kucheryavaya, research liaison to the Committee, reminded members of data she presented to the Committee at the July 2011 meeting which showed that more than 40% of retransplant patients have CPRA of greater than 95%. Ms. Samana said the Kidney Committee would be very interested in these data.

Dr. Reinsmoen, chair of the Committee, said that members of the Kidney Committee are also discussing the possibility of making it possible for centers to have two separate pools of unacceptables for a given candidate, one for local placement, that may not be stringent and one for imports that would be more robust. A Committee member asked why this would be desirable. Members of the committee answered because a center may want to be very conservative when listing unacceptables for an import offer to preclude, as much as possible, the unexpected positive crossmatch. One may decide not to list

those antibodies or not include antibodies with a lower intensity for a local share because a center may be able to transplant across a weak positive cross match for a local offer.

Ms. Samana encouraged the Committee to provide this feedback to the Kidney Committee in a formal memo. She said this is exactly the expertise they are asking for.

The Committee continued the discussion with the SRTR, and asked when the next phase of simulation modeling would be released. Adrianne Chung, from the SRTR, answered simulation modeling should be available in the spring of 2012 (possibly May). Ms. Samana added that the earliest that the new kidney allocation proposal could go out for public comment would be in the fall of 2012 with it going to the BOD in the summer of 2013.

Members of the Committee wanted to make sure that the SRTR staff took into account while doing their simulations that when an indidividual with a high CPRA is listed, it is really an under estimate because current CPRA does not take into account the antigens C, DP, and DQA. Many individuals who are listed with a CPRA of 80% or lower may actually have a higher chance of an incompatible donor than their CPRA value represents.

Members also wanted to make sure that the simulation was using the unacceptables listed and not just using the percent incompatible donors represented by the CPRA when doing their simulation. They asked if Appendix 3A was being used. They also asked if they were also taking into account that when a candidate has C marked as an unacceptable, their CPRA value will not change but they will be screened from donor match runs. SRTR staff assured the Committee that all of these factors are a part of the simulation model.

A member of the Committee asked how many candidates with high CPRA's would in reality never get a compatible donor unless it were a 0MM. Ms. Kucheryavaya said she had this data and she could supply it to the Committee at its next face to face meeting in August.

Members of the Committee asked if the simulation would indicate how often a kidney was not put into the intended recipient due to a positive crossmatch. Dr. Israni, from the SRTR staff, said there was no way to do this. The simulation could only represent kidney offers not individual center behavior. He did say that the next simulation would evaluate the number of transplants by CPRA for local/non local offers.

The Committee again expressed concern that all data they have reviewed so far with the sensitized candidates was done in a manner that they had having access to the entire donor pool not just 80% of it. They asked how to make sure we are not working against these patients by this 20/80 split? How many sensitized candidates are being screened from what may be their only chance for a compatible donor because they fall in the wrong bucket?

The discussion closed with Dr. Reinsmoen stating she would write a formal memo to the Kidney Committee that will be circulated back to the full Committee to express these concerns.

Data Request

Next, Ms. Kucheryavaya presented data from a request made in July 2011 on the CPRA analyses for large adult kidney programs stratified by the percentage of broadly sensitized candidates (80% + CPRA). At the time of

the request, the Committee reviewed an analysis of waiting list during the 18 month period before and after CPRA implementation. At that time, it was found that at least some larger kidney transplant programs (defined here as programs with >100 adult kidney alone registrations) had relatively small percentages of broadly sensitized registrations. To further investigate this finding, the Committee asked for a comparison of candidate/recipient demographics, transplant, and offer data for larger transplant programs. Additionally, the Committee planned to compare these findings to what is presently observed throughout the kidney allocation system.

First, Ms. Kucheryavaya provided the distribution of the percentage of 80%+ candidates for large centers included in this report. She said there were 5 big centers with <5% broadly sensitized candidates, 135 with 5-25% broadly sensitized candidates and 17 with >25% broadly sensitized candidates. Next she compared the percentages of re-transplant, female and minority candidates between the different groups of centers:

- The percentages of re-transplant and female candidates were similar in <5% and 5-25% centers. But they were significantly lower than in the >25% centers.
- The centers with 5-25% broadly sensitized candidates had the lowest percentage of African Americans (34%). The percentage was significantly higher for <5% broadly sensitized candidates centers (40%). Centers with >25% of broadly sensitized registrations had the highest percentage of African Americans (43%).

The Committee commented that the demographics for the centers with <5% broadly sensitized candidates was not significantly different from the other groups. Therefore, those centers should have approximately the same number of sensitized candidates as the other groups.

Then the Committee looked at the transplant rates for the different groups of centers by transplant type (0ABDR vs. non 0ABDR mismatch).

- Small number of transplants for centers with <5% broadly sensitized candidates resulted in wide confidence intervals for the group. None of the transplant rates for this center group was significantly different from rates for centers with 5-25% broadly sensitized candidates.
- With exception of 80%+ CPRA group, overall transplant rates for centers with >25% broadly sensitized candidates were significantly higher than for centers with 5-25% broadly sensitized candidates. These differences were driven by non 0ABDR mismatch transplants. Transplant rates for 0ABDR mismatch transplants were similar for two groups of centers (5-25% and >25%).

Committee members said this data verified that the overall transplant rates between the three groups did not differ significantly. The Committee was pleased to see that those centers that did list unacceptables (with >25 broadly sensitized candidates) had the highest rate of transplant for their highly sensitized candidates.

Next the Committee compared the percentage of kidney offers refused due to the positive crossmatch by offer type (0ABDR vs. non 0ABDR mismatch), sensitization level and center group:

- Not surprisingly the centers <5% broadly sensitized candidates had the highest percentage of offers refused due to positive crossmatches (1.5%). It was significantly higher than the percentages for the centers with 5-25% broadly sensitized candidates (0.5%) and centers with >25% broadly sensitized candidates (0.6%).
- Due to the small number of zero ABDR mismatch offers, all of the differences in the percentage of positive crossmatches reported as a reason for organ refusals were not statistically significant.

The Committee examined the number and percentage of kidney offers refused due to the positive crossmatch by offer type (local vs. non local), sensitization level and center group:

- For each group of centers the percentage of local offers refused due to positive crossmatches was significantly higher than for non local offers.
- For local offers, there was no significant difference in percentages for centers with <5% broadly sensitized candidates and centers with >25% groups broadly sensitized candidates (1.9% vs. 2.4%). Both percentages were significantly higher than the percentage for centers with 5-25% broadly sensitized candidates (1.0%).
- For non local offers, there was no significant difference in percentages for centers with 5-25% broadly sensitized candidates and centers with >25% groups broadly sensitized candidates (0.1% vs. 0.1%). Both percentages were significantly lower than the percentage for centers with <5% broadly sensitized candidates (1.3%).

The Committee stated that the data confirmed their hypothesis that the centers not listing unacceptable antigens are using the crossmatch as their screening mechanism. They asked if such a practice would not only disadvantaging the patient but also slow down the entire allocation system. The next set of data confirmed this by showing the number and percentage of kidney offers accepted for transplant but not transplanted into intended recipient.

It showed the centers with <5% broadly sensitized candidates had the highest percentage of such offers (42.4%). It was significantly much higher than the percentages for centers with 5-25% broadly sensitized candidates (9.6%) and centers with >25% (2.7%) broadly sensitized candidates.

Ms. Kucheryavaya also shared data which showed the median positions of transplanted patients on the match run by sensitization level and center group. For all sensitization groups, recipients in the centers that had <5% broadly sensitized candidates had by far the highest median position on the match run (for non sensitized recipients 83.5 vs. 3-7 all other large centers).

The members of the Committee were highly dismayed when they saw the results of this data request. They believe the practice of these centers not only disadvantages the individual patient but also the entire allocation system by causing delays for candidates in other centers. When similar analyses are presented in the future, they asked to show the number of patients affected by offers refused due to positive crossmatches and offers accepted but organs not transplanted.

The Committee recognizes that currently there is no policy that requires the listing of unacceptable antigens or one that dictates an acceptable number or percentage of offers that can be declined due to positive crossmatches for shipped organs. The majority of the Committee said it is now time for such policies.

Several Committee members thought the place to begin the process was to decide what a reasonable rate of organs not being used within the intended recipient because of a positive cross match should be. This could be done by first establishing a national average.

Ms. Gore reminded the Committee that there must be a written formal problem statement that could be presented to the BOD to begin the process of formulating these policies. Dr. Reinsmoen agreed to help.

Questions

Ms. Kucheryavaya needed some clarification on a research request that was put to her from the Committee at the last July meeting. She said that as part of the request the Committee asked her to compare the CPRA of candidates who were multiply listed or had transferred to another center. While doing this request, it had come to her attention that when a candidate moved to another center, the unacceptable antigens were not always entered right away. She asked the Committee what would be a reasonable amount of time to wait so she could make a fair comparison between the two centers. Members of the Committee said she should wait at least 4-6 weeks from time of listing. Ms. Kucheryavaya asked if there would be a danger of a kidney candidate having a sensitizing event during that time frame; members of the Committee felt that was highly unlikely.

Ms. Kucheryavaya then asked the Committee to compare the DPB drop down on various forms found within the UNet system, namely Teidi (Donor and Recipient Histocompatibility forms), and KPD. She pointed out to the Committee that they varied and asked which the Committee preferred for Donor and Recipient Histocompatibility forms. The Committee felt that this issue needed additional discussion. It was decided Ms. Kucheryavaya will send an email around to the Committee asking how the DPB drop down on Histocompatibility forms should look.

Letter from ASHI

Ms. Gore shared a memo from ASHI with the Committee asking to consider making the typing of DPB mandatory for all donors. The Committee agrees with this request in theory and is currently taking steps to get there. The first of these steps would be to have the field available on UNet which is within the Committee's current scope of work. A few members volunteered to write a formal reply to ASHI that will be reviewed by the full Committee.

Update from Bylaw Rewrite Subcommittee

Ms. Gore reported to the Committee that the bylaw rewrite project continues. She reported that the subcommittee met (by teleconference) with members of UNOS and HRSA to ask if the UNOS/OPTN could require "accreditation from an outside entity as condition of membership into the OPTN". Members of the subcommittee wanted to require accreditation to ensure a level of proficiency. Most of the UNOS staff did not support this idea because the OPTN would lose control of the applied standards. After a lengthy discussion a middle ground was found. The following language is in the process of being approved:

Each OPTN Histocompatibility Laboratory Member must:

- Comply with all applicable provisions of the National Organ Transplant Act (NOTA), as amended, …
- Comply with all applicable provisions of the OPTN Final Rule, *42 CFR Part 121*
- Comply with the OPTN Charter, Bylaws and Policies
- *Maintain the standards (as of June xx, 2012 or other date) of any accrediting agency that has current deemed status with the OPTN Contractor. This may be verified by the OPTN or through current accreditation.*

Deemed Status – The OPTN Board of Directors may grant deemed status to a histocompatibility laboratory accrediting agency in formal recognition that the agency's review, ongoing review, and

evaluation programs meet quality criteria related to transplantation and organ procurement and other requirements established by the OPTN Board of Directors.

Update on proposals that went out for public comment.

The proposals are on track to go to the BOD in June.

NAME	COMMITTEE POSITION	03/23/2012
Nancy Reinsmoen, PhD	Chair	x
Lee Ann Baxter-Lowe, PhD	Vice chair	x
Massimo Mangiola, PhD	Region 1 Rep.	x
Dimitri Monos, PhD	Region 2 Rep.	x
Robert Bray, PhD	Region 3 Rep.	x
Cathi Murphy, PhD	Region 4 Rep.	x
Dolly Tyan, PhD	Region 5 Rep.	x
Paul Warner, PhD	Region 6 Rep.	x
David Maurer, PhD	Region 7 Rep.	x
Sara Dionne, PhD	Region 8 Rep.	x
Rex Friedlander	Region 9 Rep.	
A. Bradley Eisenbrey MD, PhD	Region 10 Rep.	x
David Kiger	Region 11 Rep.	x
Laine Krisiunas, BS,MBA	At Large	x
Luis Campos, MD	At Large	
James Selby	At Large	
Howard Gebel	SRTR Liaison	x
Bryn Thompson	SRTR Liaison	
Lori Gore	Committee Liaison	x
Anna Kucheryavaya	Support Staff	x
Jory Parker	Support Staff	x
James Bowman	Ex officio (HRSA)	x
Raelene Skerda	Ex officio (HRSA)	