Innovation in Transplantation:
Accountability, Collaboration, and the Value of the Patient Voice
By Kevin Fowler

On September 27 and 28, 2018, the Food and Drug Administration (FDA) convened and facilitated the workshop “Science Based Treatment Decisions: The Right Dose and Regimen—the Right Patient/Individualized Treatment.” The focus of the workshop was on the patient, specifically on utilizing biomarkers during the drug development process to determine the right treatment regimen to prevent long-term rejection of the patient’s transplanted organ. I participated in the meeting on behalf of the Kidney Health Initiative (KHI) as Vice-Chair of the Patient Family Partnership Council (PFPC).

The workshop was the byproduct of two factors. The first was the creation of the Transplant Therapeutic Consortium (TTC) in March 2017. The TTC was launched to identify and develop mechanisms to accelerate drug discovery for transplant through the collaborative involvement of key stakeholders in the field, first focusing on kidney transplant. The TTC is part of the Critical Path Institute (CPI), founded in Tucson, Arizona, in 2005 as an independent nonprofit dedicated to bringing together experts from regulatory agencies, industry, and academia to collaborate and improve the medical product development process.

The second element contributing to the workshop was the FDAs commitment to help facilitate innovation in the transplant community. The FDA has conducted transplant workshops for the past four years:

- 2015: “Surrogate Endpoints for Clinical Trials in Kidney Transplantation”
- 2016: “Patient Focused Drug Development in Patients Who Have Received an Organ Transplant”

With the exception of the 2017 FDA Transplant Workshop, I have attended every meeting. Unlike the previous FDA meetings, the 2018 workshop left me with a clearer sense of the path to drug development, and to delivering unmet patient and medical needs. My vision was formed based upon the following three meeting observations:

Accountability of American Society of Transplantation/American Society of Transplant Surgeons

Ulf-Meier-Kriesche, MD, Chief Scientific Officer of Veloxis and a transplant nephrologist, acknowledged during his presentation that the current transplant clinical endpoint, one year acute rejection rates, has been diminished significantly in utility and value. He acknowledged that it is very difficult to exceed the one year acute rejection rates established by cyclosporine and tacrolimus. Acute rejection is a high bar for pharma companies to exceed thereby influencing their reluctance to invest in transplant therapeutics. Moreover, Dr. Ulf-Meier-Kriesche made clear that it is the responsibility of the transplant community to establish clinical endpoints relevant to today’s clinical practice, and to pharma innovators.

Collaborative Approach

The TTC and, by extension, the CPI, developed a 2-day workshop notable in its collaborative agenda. Unlike previous meetings where the agenda was conducted by the familiar transplant professionals, at the TTC these familiar voices were complemented by professionals from oncology and CKD, and by transplant professionals from Europe. The infusion of different voices and disciplines brought a much-needed breath of fresh air to the meeting, and a different way of approaching innovation. I would like to recognize the efforts of Kenneth Newell, MD, PhD, Professor of Surgery, Division of Transplantation, Department of Surgery, Emory University; Peter Nickerson, MD, Flynn Family Chair in Renal Transplantation at the University of Manitoba; and Rita Alloway, PharmD, Research of Nephrology, University of Cincinnati, who had the wisdom to look outside the transplant community for answers.

There was one new voice that stood out at the meeting: Alexandre Loupy, MD, a transplant nephrologist from Paris and a member of the Paris Transplant Group. The Paris Transplant Group is developing a personalized transplant medicine approach that integrates multiple sources of information including classical histology and biology, as well as novel information from molecular biology, immunology, and genetics and biomarkers. In essence, the Paris Transplant Group is providing leadership not only in precision medicine but in an integrated approach to transplant patient care and improvement in patient care guidelines. Like most of medicine, transplant medicine has been practiced reactively. This collaborative approach is a welcome shift in the future practice of transplant medicine.

At the FDA meeting, Dr. Loupy presented the final product proposed by the Paris Transplant Group, the “Ibox.” Rather than estimating prognostic allograft survival based upon serum creatinine function and proteinuria, the Ibox expands the sources of information, thereby developing a comprehensive picture of the patient’s transplanted organ. Based upon the varied sources of information, the Ibox has the ability to develop a prognostic score and accurately predict individual long-term graft survival. Dr. Loupy presented how the Ibox had potential applications in the development of clinical trial endpoints in transplantation. The prognostic ability of the Ibox has the potential to examine investigative transplant medications that may impact on long-term kidney transplant outcomes, thus serving as a cost-effective alternative to long-term kidney transplant trials. I considered Dr. Loupy’s presentation the brightest light at the meeting.

Value of the patient voice

One tangible outcome of the 2016 FDA Transplant Workshop was “The Patient Voice Report: Patient-Focused Drug Development in Patients Who Have Received an Organ Transplant.” The report serves as a source of information on the treatment burdens that the handful of FDA-approved transplant medications impose upon people living with a transplanted organ. This document was referenced several times by the presenters.

A conversation I had with Mark Stegall, MD, Professor, Transplant Surgery, Mayo Clinic, reinforced my belief that the transplant community has enhanced its understanding of people living with a transplant. Dr. Stegall understands the significance of cognitive impairment that occurs with kidney disease and that is further accentuated by the cognitive impact of one of the approved transplant medications. The limitation of current medications could provide a path to approval for new medications, Dr. Stegall noted.

While I left the meeting optimistic that there is a path to bring innovative medications to the transplant community, I would like the TTC to consider one thing. While people living with a transplant were represented at the meeting, a patient voice strategy was not apparent. The TTC can learn valuable lessons on developing a patient voice strategy from KHI and the PFPC. We are happy to share our lessons.

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