CRITICAL PATH INSTITUTE

Impact For Patients: TTC's iBox Scoring System

Impact For Patients: Transplant Therapeutics Consortium

These stories highlight the value and impact that C-Path's Transplant Therapeutics Consortium's (TTC) work brings to patients, patient organizations, the bio-pharmaceutical industry, diagnostic companies, the academic community, nonprofits, regulators and more. TTC is working to qualify the iBox Scoring System with FDA as a reasonably likely surrogate endpoint (RLSE) for kidney transplant clinical trials. The availability of an RLSE is vital to stimulate innovation in immunosuppressive drug development that will serve transplant recipients by improving short and long-term outcomes.

The American Society of Transplantation's Transplant Community Advisory Council provides patient voice and perspective to the Society and is the first patient led committee at ***AST***. This group of transplant community members, including organ transplant candidates and recipients, living donors, caregivers, and family members of deceased donors, engages primarily in advocacy, education and raising awareness of the patient experience regarding organ donation and transplantation-related topics. These are some of their stories…

Ben, Heart Transplant Recipient

Medicine is a big part of our life. Our 10-year-old son, Benjamin, was not aways immunocompromised. For the first month of his life, he seemed normal, but by his second month, he was in heart failure, during which time inotropes (drugs that make the heart muscles to beat or contract with more or less power) were an important bridge to transplant. After the transplant, Ben was on a large number of suspension medicines. The photo only reflects about half of what Ben needed for three days, and only two of his medicines were immunosuppressants directly related to transplant. The rest were to counteract the side effects of the immunosuppressants. The regimen was so much that, as a baby, he sometimes had difficulty keeping them all

down.

Ben is still on his immunosuppressants — they have protected his lifesaving transplant. He doesn't take as many supporting medicines, but they are still there, along with the side effects. For example, Ben must take care to avoid sunburn as medication increases skin cancer risk. He has had three COVID vaccinations, with zero measurable immune response due to suppression. He takes growth hormone injections as his other medications have affected his growth rate. Ben also takes prescribed mineral supplements as the immunosuppressants leach valuable iron and magnesium from his system. All of this is to say nothing of the act of balancing the right level of suppression of the immune system. Over suppression can lead to infections such as post-transplant lymphoproliferative disease (PTLD – a form of cancer) or cardiac allograft vasculopathy (CAV), while under suppression leads to graft rejection.

We wouldn't have it any other way, given the choices, because Ben is able to be a kid. He is able to have fun with neighborhood friends, he went to Transplant Camp, he takes archery and tae kwon do, and he is able to do most "kid" activities. But the side effects take a toll, and the fewer of them he has to deal with, the better prepared his body will be for the decades ahead. This can primarily be accomplished with newer transplant medicines that will allow young bodies to properly develop, making it less likely for some young patients to suffer from failure to thrive.

-Joseph Hillenberg, Ben's father

Dr. Alin Gragossian, Heart Transplant Recipient

I got my heart transplant three years ago and I am very appreciative of my second chance in life. Heart transplant surgery has given me a way to continue my career as an ICU fellow, as well as traveling and spending time with friends and family. It hasn’t been easy though. Many of the medications that I take have serious side effects, including prednisone. The drug caused necrosis of my joints and I had to get both of my hips replaced in 2021 at the age of 34.

Keeping up with steady-state medication levels, especially the first year after transplant, can be difficult. I do think that what will help transplant patients as far as therapeutics will be finding medications that do not need ongoing dose adjustment and monitoring. I understand that immunosuppressants will always have their drawbacks as their primary mechanism of action is to suppress the immune system, but I am grateful for how far we've come and excited to see the future of transplant medicine.

-Dr. Gragossian

Lisa, Liver and Kidney Transplant Recipient

My name is Lisa, and I received a liver transplant in January 2007 when I was 29-years-old. My liver failed due to complications of cystic fibrosis, which I was diagnosed with when I was one day old. The immunosuppressive drugs to protect my new lifesaving liver caused kidney damage within the first two months post-transplant. I switched to a immunosuppressive drug less toxic to the kidneys, but I continued on a very slow decline until eventually I was put on dialysis in February 2021. Fortunately, I was only on dialysis for seven months before I received a kidney transplant in August 2021 when I was 43.

Cindy and me pre-op 1/10/2007

Andrea and me pre-op 8/12/2021

I am so grateful for my medical teams for both transplants and to both of my living donors. Cindy, my liver donor, is my mom's best friend from childhood and Andrea is a friend from a town near where I grew up in rural Iowa.

I would not trade the world for being blessed to grow up on a farm in small town Iowa. Friends and family always supported me, especially when I had health problems due to cystic fibrosis. They supported my family when I was in and out of the hospital, bringing food out to the house for my dad, brother and sister, while my mom would stay at the hospital with me. Always calling to check in if we needed anything, and even volunteering to donate a kidney to me. For what small town Iowa may lack in big cities, professional sports teams, concerts or other hustle and bustle activities, it more than makes up for in compassionate, kind, self-giving and just downright good-hearted people.

While I am thankful my skin is no longer green, my belly no longer filled with fluid (ascites) or that I'm not "locked down" due to dialysis schedules and feeling overall unwell, life after transplant isn't perfect or back to normal.

After my liver transplant, I thought needing to take

Me, Andrea, my kidney donor, Andrea's daughter Sophia, Mom and Dad (July 2022)

immunosuppression medication for the rest of my life was no big deal since I had taken medication all my life. I didn't realize the problematic long-term effects the drugs would cause down the road.

Despite being vigilant about wearing sunscreen, immunosuppressive drugs have caused me many trips to the dermatologist to remove skin cancers. They have caused my bones to become more brittle and I fear broken bones in the future from even a simple misstep. I also fear the elevated risk of cancer in the future or contracting even a common infection that could put me in the hospital or worse.

When it was time for my kidney transplant, I was hoping for a kidney plus pancreas transplant so I could get rid of my diabetes as well. This was not an option because immunosuppressive drugs cause my blood labs to have so low counts that the doctors would not consider it.

Still, I thank God for the invention of immunosuppressive drugs which allow me to live with my new organs. My plea is that researchers invent "smart" immunosuppressants, so that I don't need to worry about being out in the sun, giving friends hugs, getting a secondary cancer, breaking a bone or catching an infection my body can't fight off. Science and the human body are fascinating and I know there are smart scientists, researchers and doctors that can make "smart" immunosuppressants to better the health of transplant recipients.

-Lisa

Molly, 3x Kidney Transplant Recipient

On June 22, 2012, I was beginning to wake up from anesthesia after kidney transplant surgery, my third and God-willing, the last I will need in my lifetime. Like anyone getting an organ transplant, I had every hope and prayer that I would be lucky enough to have a good outcome that would allow me to return to a normal life and enjoy the activities I did before getting sick.

Fortunately, I had a better than good outcome. Despite this being my third transplant, I am thrilled to say that I have never felt so good, so strong and so healthy in my life. I owe that to the transplant team at the UW Hospital in Seattle for their incredible care, and of course to my husband, family, friends and colleagues, for taking such loving care of me then and every day since.

For anyone who has gone through an organ transplant or watched a loved one go through the experience, you, too, are part of the club that deeply understands that transplant is not a cure. While we may leave behind the complexities of end stage organ failure, we don't sail out of the hospital with our new transplants and a

clean bill of health never to think about it again.

Instead, we become part of the club who takes powerful immunosuppressants on a rigorous schedule every single day for the rest of our lives with the hope that we don't reject our organ. We accept the dramatically increased risk of cancer. And we learn to live with the ticking clock inside us wondering whether that new ache is because of the heavy planter we moved yesterday, or if it may be a sign our organ is rejecting.

Despite the challenges, I have been so incredibly blessed. Blessed beyond words and not a day goes by that I don't think about it. When the first and second times came, both of my parents were generous enough to donate their kidneys to me, and after a six year wait, I received a kidney from a 32-year-old woman who passed away from a heart episode. I have been fortunate to have supportive bosses and coworkers, to have fantastic insurance, and to know how to navigate our healthcare system that can be complicated, confusing and at times, a bit elitist.

Molly, on her wedding day, which would not be possible without transplant

I worry about patients and caregivers who may not have the blessings I have. How do they cope with the demands and challenges of life with a transplant? It boggles my mind and reminds me that I need to do more than count my blessings. Engaging with transplant-related groups involved in innovation, advocacy and lobbying has been educational and satisfying, and I find myself eager to learn where else patients, as lucky as me, can offer our time, skills and experiences in service of the transplant community.

With that in mind, I also try to demonstrate my gratitude by sharing my story with the hope that it may help someone who's struggling, by partnering with some of the country's best transplant centers to help them

consider the patient impact of their practices and cultures, and by taking every opportunity possible to inspire innovation in the field of drug development with the aspiration that the next generation of recipients who come behind me will have the opportunity to skip out of the hospital after their transplants with a truly clean bill of health, never again to face another transplant.

A couple of weeks ago, some transplant friends and I had the privilege to speak about our experiences at the American Transplant Congress in Boston. An event typically devoted to the science and practical innovations in transplant; it was the first-time teams of recipients and living donors were invited to the ATC to speak about our experiences. While I won't tag the other speakers here to protect their identities, we were thrilled at the reception we got from some of the most influential scientists on the planet. While one may not think that living donors and recipients have much to offer such an esteemed group, we all took away from that a renewed commitment to the need to continue the discussion. Not to find fault or point fingers, but instead to offer our time and energy to help make it better for others.

Ten years out I can only hope and pray that the next 10 years will be filled with as much strength, good health and happiness as the first. And in case my future is different from my past, I will face the next set of challenges with gratitude for the good and fortitude to face the bad. The science of medicine is assumed, but the art of medicine is often not as widely appreciated. While most humans appreciate that our time here is short, I think anyone who has faced a major health crisis is even more aware of how fragile our health is. As I reflect on the last ten years of health, I remind myself that every day should be spent making a difference on behalf of others, and I underscore my commitment to continue to seek out ways to be the voice for transplant patients who have not been as fortunate as me.

And may I ask a favor? Next time you are renewing your driver's license and are asked if you want to be an organ donor, please consider saying yes. Because one woman did, I am still here.

-Molly

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