Islet Transplant Update & Biologics License Application (BLA)

Type 1 diabetes (T1D) is an autoimmune disease in which the body mistakenly destroys insulin-producing beta cells in genetically predisposed individuals resulting in poor glycemic control. This chronic condition, which manifests in early childhood, can lead to severe hypoglycemia (low blood sugar levels) and the inability to identify the physical signs. This can inadvertently lead to disorientation, loss of consciousness, accidents and even death. With islet replacement therapy, insulin producing beta cells are isolated from a cadaveric donor pancreas, infused through the recipient portal vein and engraft in the liver. The procedure is simple, less invasive and the patient recovers quicker than from a whole pancreas transplant.

As part of the National Institutes of Health’s multi-center Clinical Islet Transplantation (CIT) Consortium, Northwestern University has performed over 30 islet transplants in 18 type 1 diabetics. Interim data show strong efficacy with regards to hypoglycemia and glycemic control. Safety data also suggests no unexpected complications or adverse events.

Under Dr. Xunrong Luo’s investigator initiated protocol (A Phase 3 Single Center Study of Islet Transplantation in Non-uremic Diabetic Patients - NCT01897688, STU00059469) - the islet transplant program has performed three allogeneic human islet transplants and is actively enrolling. Recently, a study participant successfully underwent a second islet transplant under this protocol. One month post-transplant the subject is insulin free and has reported no hypoglycemic events. The triumphant accomplishment by Northwestern’s multidisciplinary team in performing and caring for the very first transplant in a med/surg unit (11 East) demonstrates our readiness for transitioning this exciting therapy into standard of care.

The Human Islet Transplant Program led by Xunrong Luo, MD, PhD is aggressively working towards securing a Biologics License Application (BLA) with the U.S Food and Drug Administration (FDA). Licensing allogeneic islets as a therapeutic treatment for T1D will permit insurance reimbursement through Medicare, Medicaid, and other third-party payers. Though the FDA does not regulate vascularized whole organ transplants, cellular products derived from donor human pancreas (allogeneic islet cells) are considered therapeutic biological products, thus subject to FDA regulations under Section 351 of the Public Health Service Act. Navigating the FDA’s Regulatory maze for the purpose of licensure is a tremendous undertaking. Prior to licensure, we, as manufacturers, must demonstrate consistency and reproducibility of high quality & high potency islet products. The manufacturing team led by Dr. Xiaomin Zhang continues to work tirelessly with the help of the Mathews Center for Cellular Therapy (MCCT) for the islet processing to validate and implement controls at every step of the manufacturing process, through written standardized procedures, qualification of source materials and components used throughout the manufacturing process. Furthermore, the end product must also be validated and meet release criteria which include sterility, potency, purity, viability and minimal islet mass requirement for each recipient (≥5,000 IEQ/kg). A second critical component of the licensure application is providing robust clinical data to demonstrate efficacy and safety of the biological product, i.e. allogeneic human islets. The clinical team is led by Ojoma Agbo and Patrice Al-Saden RN. The team not only manages all islet transplant clinical trials, but are also actively building a validated database from which statistical safety analyses and Clinical Study Reports (CSR) can be generated, essential components of the BLA submission.

For more information, please contact Xunrong Luo, MD, PhD at xunrongluo@northwestern.edu