M. Louise Markert, MD, PhD
Professor
Pediatrics and Immunology

Cultured Thymus Tissue Implantation: Bench to Bedside

M. Louise Markert, M.D., Ph.D. is Professor of Pediatrics and Immunology at Duke University in North Carolina. She trained in Pediatrics at Duke under Dr. Samuel Katz and then in Pediatric Allergy and Immunology under Dr. Rebecca Buckley. Dr. Markert joined the Duke faculty in 1987. Dr. Markert served on the American Board of Allergy and Immunology from 1996 – 2004 and was Chair of the Board in 2002. She served on the Institute of Medicine Committee to Review Adverse Effects of Vaccines from 2009 to 2011. Dr. Markert has pioneered the development of cultured thymus tissue implantation (CTTI) for infants born with the fatal primary immunodeficiency complete DiGeorge anomaly in which infants are born without a thymus. In 2013, she was awarded the Duke University Department of Pediatrics Michael M. Frank, M.D. Research Prize in recognition of her significant lifetime contributions to the field of Pediatric Immunology. In 2017, she was awarded a Duke University and Health System Presidential Award for Executive Leadership related to her research. Lastly, in 2017, Duke licensed Dr. Markert's CTTI technology to the company Enzyvant GmbH. They are working together to obtain a Biologic License from the Food and Drug Administration so that CTTI will become a standard approved procedure for infants with congenital athymia.

Abstract:

Disclosures:

- Cultured thymus tissue (CTT) is an investigational product implanted into patients under an Investigational New Drug (IND) application with the Food and Drug Administration (FDA). Dr. Markert is the "sponsor" of the investigations.
- Dr. Markert developed the technology for CTTI (cultured thymus tissue implantation).
- Duke has licensed the technology to Enzyvant Therapeutics GmbH.

- Dr. Markert and Duke have received royalties from Enzyvant.

- Portions of Dr. Markert's and her research team's salaries are being paid by funding from Enzyvant.

- Grants have been obtained from the National Institutes of Health (NIH), Food and Drug administration (FDA), and the Hartwell Foundation in the past to support the use of CTT in congenital athymia.

- If the technology is commercially successful in the future, Dr. Markert and Duke may benefit financially.

Abstract: Children with congenital athymia are born without a thymus, resulting in severe immunodeficiency, often accompanied by autologous graft versus host disease (aGVHD), and autoimmunity. Congenital athymia is rare, affecting approximately 20 infants per year. This condition is fatal because of the patient's inability to produce functioning T cells, which defend against infection. Congenital athymia is associated with Complete DiGeorge Anomaly (cDGA), 22q11.2 deletion syndrome, CHARGE (coloboma, heart defect, choanal atresia, growth or mental retardation, genital anomaly, and ear anomalies and or deafness), infants of diabetic mothers, and FOXN1 deficiency.

Treatment of congenital athymia is by implantation of cultured thymus tissue (CTT) into the quadriceps muscle. CTT is an investigational product that has been approved by the Institutional Review Board (IRB) for clinical research studies. It is implanted under an Investigational New Drug Application with the Food and Drug Administration (FDA, IND 9836). Naïve T cells typically appear between 6 and 12 months. The Kaplan-Meier estimated survival rates at Year 1 and Year 2 post-implantation in the EAS (efficacy analysis set) N=95, were 77% (95% confidence interval [CI; 0.670, 0.844]) and 76% (95% CI [0.657, 0.834]), respectively.

The FDA has granted Orphan Drug Designation, Breakthrough Therapy Designation, Regenerative Medicine Advanced Therapy Designation, and Rare Pediatric Disease Designation for CTT. Work supporting FDA review and approval of a Biologics License Application is ongoing.