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High response rates, long-term remissions in Penn trials of personalized cell therapy

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Ninety-three percent of pediatric patients (55 of 59) with relapsed/refractory acute lymphoblastic leukemia (ALL) went into remission after receiving an investigational therapy made from their own immune cells, with continuous remissions of over one year in 18 patients and over two years in nine patients. In an emerging new use of the same therapy, known as CTL019, more than half of patients (15 of 28) with non-Hodgkin lymphoma (NHL) also responded to infusions of the personalized cellular therapy.

Findings from these two clinical trials, conducted by researchers from the Perelman School of Medicine at the University of Pennsylvania and The Children's Hospital of Philadelphia, will be presented during the 57th Annual Meeting of the American Society of Hematology (ASH). The results expand Penn's work with chimeric antigen receptor (CAR) therapies, building on initial findings in patients with chronic lymphocytic leukemia dating back to the start of the first Penn clinical trial of CTL019 in 2010.

"With each child we treat as part of this trial, we learn more about the potential of CTL019 to help patients whose cancers cannot be controlled with conventional therapies," said Stephan Grupp, MD, PhD, the Yetta Deitch Novotny Professor of Pediatrics in Penn's Perelman School of Medicine and director of the Cancer Immunotherapy Frontier Program at The Children's Hospital of Philadelphia. "The response rate and durability we are seeing are unprecedented, and gives us hope that personalized cellular therapies will be a powerful key to long-term

control of this difficult cancer."

Grupp will present results from a trial of 59 children with relapsed /refractory ALL infused with CTL019 cells, in which 55 (93 percent) experienced complete remissions, with an overall one-year survival of 79 percent. Relapse-free survival at six months was 76 percent, and 55 percent at one year. With a median follow-up of 12 months, 34 patients remain in complete remission, with six undergoing additional treatments such as stem cell transplant. Among 20 patients who relapsed, three saw their disease come back after additional therapies and 13 patients' cancers returned with CD19-negative cells, which are not amenable to targeting with CTL019. (Abstract #681)

Fifty-seven percent of patients (15 of 28 evaluable patients) in the non-Hodgkin lymphoma trial had responded to the therapy by three months after receiving their cellular infusion. Response rates were 72 percent (8 of 11 patients) among patients with follicular lymphoma, 47 percent (7 out of 15 patients) in diffuse large B cell lymphoma (DBCL) and 50 percent in mantle cell lymphoma (1 of 2 patients). Overall, 14 patients experienced complete remissions of their disease. All patients had stopped responding to conventional therapies before receiving the investigational cellular therapy, including stem cell transplants in many cases. Median progression-free survival among the responding FL and DBCL patients has not yet been reached after a median follow-up of 14+ months. (Abstract #183)

"The field of immunotherapy has provided an array of promising new investigational treatments for blood cancers in the past few years, and our early results in this trial provides increasing evidence for the role of personalized cellular therapies in patients with NHL," said Stephen Schuster, MD, the Robert and Margarita Louis-Dreyfus Associate Professor in Chronic Lymphocytic Leukemia and Lymphoma Clinical Care and Research in Penn's Abramson Cancer Center and Perelman

School of Medicine.

The investigational therapy, CTL019, begins with each patient's own T cells, collected through a procedure similar to dialysis. The cells are then reprogramed in a laboratory to hunt and potentially kill cancer cells in the patient's body. After the patient undergoes lymphodepleting chemotherapy, they receive an infusion of their newly engineered cells. The modified T cells contain an antibody-like protein known as a chimeric antigen receptor (CAR), which is designed to target the CD19 protein found on the surface of B cells, including the cancerous B cells that characterize both ALL and NHL. The modified "hunter" cells are then infused back into the patient's body, where they multiply and are believed to attack the cancer cells. A signaling domain built into the CAR promotes rapid multiplication of the modified cells that tests reveal can grow to more than 10,000 new cells for each single engineered cell patients receive.

Some patients who received the investigational T cell therapy developed cytokine release syndrome (CRS) within several weeks after their infusions, typically during the time when the modified cells expanded to their greatest number in the body. This condition includes varying degrees of flu-like symptoms, with high fevers, nausea, and muscle pain, and neurologic symptoms including hallucinations and delirium and in more severe cases, low blood pressure and breathing difficulties which may require intensive care. Eighteen of the lymphoma patients experienced CRS. In the pediatric ALL trial, 88 percent of patients developed CRS. The CHOP/Penn team has developed a management strategy to treat these side effects, including the IL-6 blocking drug tocilizumab. All patients in these two trials recovered from their CRS. One lymphoma patient suffered from severe encephalitis several months after receiving their cells.

Other clinical trials utilizing CAR technology are currently underway at

Penn for the treatment of chronic lymphocytic leukemia, multiple myeloma, mesothelioma and ovarian, pancreatic and brain cancer.

Because CTL019 is an investigational therapy, the safety and efficacy profile has not yet been established. Access to investigational therapies is available only through carefully controlled and monitored clinical trials. These trials are designed to better understand the potential benefits and risks of the therapy.

Editor's note: The University of Pennsylvania has licensed technologies involved in this trial to Novartis. Some of the scientists involved in these trials are inventors of these technologies. As a result of the licensing relationship with Novartis, the University of Pennsylvania receives significant financial benefit, and these inventers have benefitted financially and/or may benefit financially in the future. Additional disclosure information is available in the meeting abstracts.

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