TPS10074 Poster Session

A phase 1/2, open-label study evaluating the efficacy, safety, and pharmacokinetics of luveltamab tazevibulin in infants and children < 12 years of age with *CBFA2T3::GLIS2* acute myeloid leukemia.

Sarah K Tasian, Himalee Sabnis, Todd Michael Cooper, Francisco José Bautista Sirvent, Arnaud Petit, Matthew Kutny, Elizabeth Krieger, Laura Graves Schuettpelz, AeRang Kim, Anne E. Borgman, Stan Frankel, Anna Butturini, Lin Lu, Kate Murray, C. Michel Zwaan; Children's Hospital of Philadelphia, Philadelphia, PA; Department of Pediatrics, Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta and Emory University, Atlanta, GA; Seattle Children's Hospital, Cancer and Blood Disorders Center, Seattle, WA; Princess Máxima Center for Pediatric Oncology and Department of Pediatric Oncology and Hematology, Hospital Niño Jesús, Utrecht, Spain; Gustave Hospital Armand Trousseau, APHP, Sorbonne Université,, Villejuif, France; University of Alabama at Birmingham, Pediatric Hematology/Oncology, Birmingham, AL; VCU Medical Center North Hospital, Richmond, VA; Saint Louis Children's Hospital, Webster Grvs, MO; Center for Cancer and Blood Disorders, Washington, DC; Sutro Biopharma, Inc., South San Francisco, CA; Sutro Biopharma, South San Francisco, CA; Prinses Máxima Centrum, Utrecht, the Netherlands and Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands

Background: *CBFA2T3::GLIS2*-rearranged acute myeloid leukemia (AML) is a rare subtype of AML occurring exclusively in very young children and is associated with poor prognosis ($<15\%$ 5-year event-free survival [EFS]) with best-available multi-agent chemotherapy. Luveltamab tazevibulin (luvelta) is an anti–FRα-targeting antibody-drug conjugate with a stable cleavable linker and a 3-aminophenyl hemiasterlin warhead (DAR = 4), which induces cytotoxic and immunologic cell death. *CBFA2T3::GLIS2* AML uniquely expresses high cell surface levels of the FRα, suggesting that FRα-targeted therapies may be effective. Preclinical studies have demonstrated that treatment with luvelta can result in leukemia clearance. Preliminary safety and efficacy data from 25 children with relapsed/refractory *CBFA2T3::GLIS2* AML treated with luvelta via compassionate use are promising [Williams, et al, BLOOD 2023, 142 (1): 4295]. **Methods:** This registration-enabling phase 1/2 study (clinicaltrials.gov NCT06679582) will investigate the pharmacokinetics, safety and preliminary efficacy of Luvelta in relapsed or refractory children with *CBFA2T3::GLIS2* AML and $\geq 5\%$ bone marrow (BM) involvement by morphology. The *CBFA2T3::GLIS2* fusion will be confirmed at Foundation Medicine by next generation sequencing (NGS). The trial will open in up to 35 centers across US, Europe, Canada and Australia and is actively enrolling. The initial part of the trial will test luvelta monotherapy at 3.5 mg/kg or 4.3 mg/kg administered IV every 2 weeks in a 28-day cycle. Bayesian sequential monitoring is used for safety monitoring. The study committees will review the data to identify the recommended phase 2 dose of luvelta which will then be tested in the second part of the trial. Children who achieve BM morphological complete response (CR) may proceed to allogeneic hematopoietic stem cell transplantation (HSCT) or continue single-agent luvelta for up to 2 years at the investigators' discretion. Patients without CR after 2 cycles of luvelta monotherapy may add chemotherapy (cytarabine +/- fludarabine or azacytidine) in cycle 3 and beyond. Post-HSCT maintenance therapy with luvelta monotherapy is also allowed for up to 2 years. The primary endpoint is morphologic CR defined as $<5\%$ AML blasts in BM with absolute neutrophil recovery to >1000 and platelets $>100{,}000$ and absence of extramedullary disease. Secondary endpoints include PK levels and assessment of anti-drug antibody formation, safety, EFS and overall survival. Rates of measurable residual disease-negative CR and FRα antigen levels pre- and post-luvelta will also be explored. Clinical trial information: NCT06679582. Research Sponsor: None.