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POSTER ABSTRACTS

616.ACUTE MYELOID LEUKEMIAS: INVESTIGATIONAL THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Anti-Leukemic Activity of Luveltamab Tazevibulin (LT, STRO-002), a Novel Folate Receptor-α (FR-α)-Targeting Antibody Drug Conjugate (ADC) in Relapsed/Refractory CBF2AT3::GLIS2 AML

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Introduction: CBFA2T3::GLIS2 (CBF-GLIS) is an oncogenic fusion associated with a lethal and highly refractory childhood myeloid leukemia manifested by the RAM phenotype, uniquely expressed in infants and young children. Conventional chemotherapy and stem cell transplant (SCT) result in extraordinarily high rates of induction failure (>80%) and near uniform fatality with 2-year survival <15%. When conventional therapy fails, this leukemia is refractory to all reinduction therapies with post-relapse survival of nearly 0%. We have previously reported that FR-α is expressed on the surface of CBF-GLIS AML cells and that LT, an investigational ADC, demonstrated potent *in vitro* and *in vivo* anti-leukemia activity in CBF-GLIS AML cell lines and xenograft models (PMID: 36149945). LT has been provided under single patient IND to pts with CBF-GLIS AML. Herein, we update the clinical experience.

Methods: All pts were required to demonstrate CBF-GLIS fusion by PCR or sequencing. Each investigator in consultation with Sutro Biopharma Inc. defined the treatment plan as to dose, schedule, and combination therapy administered.
Results: Between August 2021 and March 2023, 25 pts with relapsed/refractory CBF-GLIS AML were treated with LT at doses of 4.3 or 5.2 mg/kg every 2-4 weeks (4 received smaller fractionated doses (FD) on days 1, 3, 5 per cycle). Median age at treatment was 2 years (range 0.7-8) with median number of prior therapies of 2 (range 1-7). 10 pts had relapsed after SCT. The remaining 15 had primary refractory, relapsed or MRD+ AML. Median time from initial diagnosis was 7.9 months (range 1.5-82.5).
Of the 25 pts who received LT, 18 had ≥5% blasts (morphologic disease, MD) and 7 had <5% blasts (sub-morphologic disease, SMD). 21 pts initially received LT monotherapy (mono) (15 with MD and 6 with SMD), 9 of which went on to receive combination (combo) with additional therapies. The remaining 4 received LT in combo upfront.
Morphologic or molecular/MRD- response was observed in 12/25 pts (48%). Among those with MD, 7/18 (39%) reached a CR/CRh (5 MRD-) and among those with SMD, 5/7 (71%) reached MRD- CR. Median number of doses received before response was 2.
Responses were observed among patients receiving both mono and combo. Among the 11 MD pts treated with mono (excluding FD), 3 reached CR (27%). Among 10 pts with MD who received combo either initially or following mono, 4 reached CR/CRh (40%). Among the SMD pts, 4 reached MRD- with monotherapy and 1 with combo.
Of the 10 pts with post-SCT MD relapse, 7 patients received non-fractionated LT either as mono or combo therapy. Of these, the CR rate was 71% (5/7).
LT therapy enabled these children to receive potentially definitive therapy. Of the 7 pts with MD in CR, 4 proceeded to SCT, 2 received donor lymphocyte infusions and 1 received consolidation therapy. Of the 5 pts with SMD in MRD- CR, 1 proceeded to SCT, 2 received consolidation therapy in preparation for SCT, and 2 received LT maintenance therapy.
In total, 12 pts remain on treatment. Of the 25 pts who received LT, 17 (63%) are alive, 7 died of progressive disease (5 with relapse post-SCT) and 1 died from SCT-related complications. Of the 10 pts who received LT (non-fractionated) post-transplant, 7 are alive (78%). Pt status and treatment are shown in Figure 1.
LT was generally well tolerated. TEAEs reported at an incidence of ≥ 25% included decreased neutrophil, platelet, WBC, or lymphocyte count, anemia, increased AST or ALT, diarrhea, and pyrexia. Grade 3+ TEAEs (≥ 10%) included decreased neutrophil, platelet, WBC, or lymphocyte count, anemia, febrile neutropenia, ALT increased, vomiting and hypoxia. Observed cytopenias were often reported in pts with baseline cytopenia. Grade 5 SAEs were limited to fractionated dosing pts: apnea (n=1) and cardiopulmonary failure (n=1). Neither event was considered related to LT.
The median duration of LT treatment was 9.1 weeks (2.1-60) and 60% of pts received ≥5 doses. While the initial dose was typically delivered inpatient, approximately 80% of subsequent doses were delivered outpatient.
Conclusion: LT based therapy in CBF-GLIS AML provides clinical and laboratory responses that are highly unusual in this refractory patient population. LT has an acceptable safety profile and does not require inpatient delivery. Importantly, LT appears to be enabling these children to receive potential definitive therapy. These data support further characterization of this drug in pediatric CBF/GLIS AML.

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OffLabel Disclosure: STRO-002 (Luvelta) is being used off label to treat relapsed/refractory CBFT2A::GLIS2 pediatric AML. The purpose of this treatment is to induce/reinduce remission and bridge patients to a definitive treatment. Each patient is treated through compassionate use / single patient IND.

Swimmer's Plot

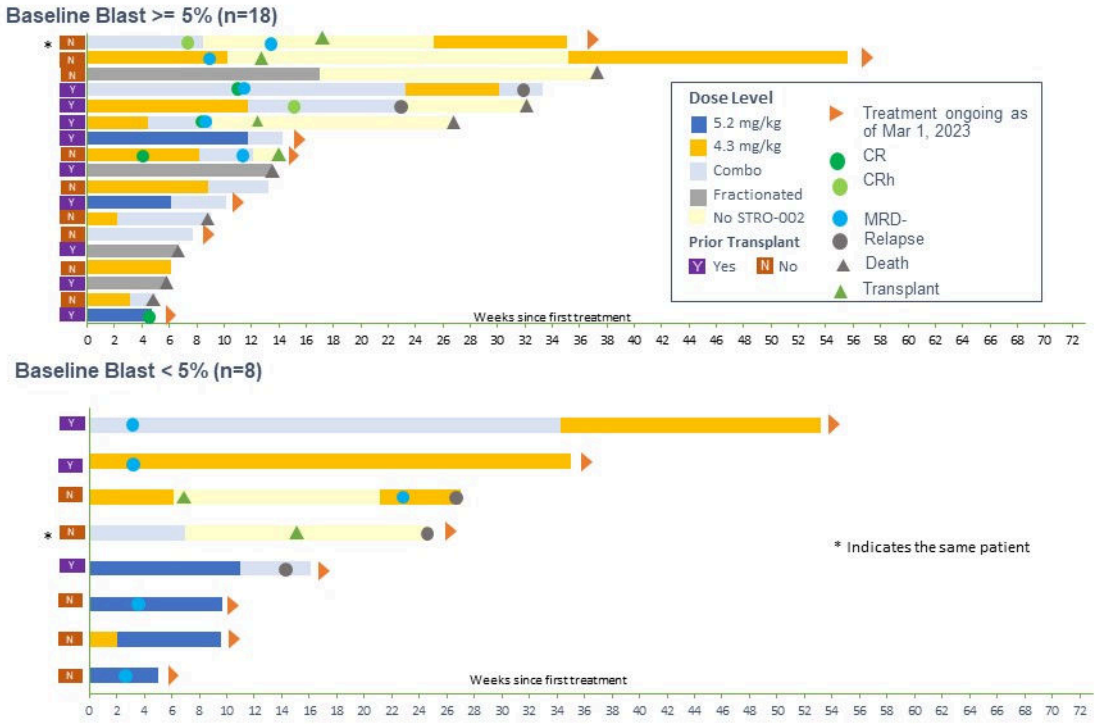

Figure 1

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