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POSTER ABSTRACTS

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

Single Agent Tagraxofusp in Relapsed/Refractory CD123-Positive Acute Myeloid Leukemia: A Preliminary Analysis of Italian Gimema AML2020 Trial

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Background and Aims:
Tagraxofusp (SL-401; TAG) is a recombinant protein drug consisting of IL3 fused to a truncated diphtheria toxin payload that targets CD123, a subunit of the IL3 receptor, expressed on the surface of Acute Myeloid Leukemia (AML) blasts. TAG is currently approved for the treatment of blastic plasmacytoid dendritic cell neoplasm by the FDA and EMA. Here, we report the results of a preliminary analysis of the GIMEMA AML2020 trial which is the first study in Europe investigating the activity and safety of single agent TAG in patients with relapsed/refractory (R/R) CD123-positive AML.
Patients and Methods: In this open-label, multi-center phase 2 study (NCT04342962) adult patients with R/R CD123-positive AML patients who received no more than 2 previous lines of therapy were eligible for enrollment. Tagraxofusp was administered at a dose of 12ug/kg from days 1 to 3 in the first cycle and then given for 5 days. Written informed consent for treatment, data collection and biobanking of biological samples was obtained for each patient enrolled.
Results: As of July 2023, 23 patients have been enrolled. Median age was 65 years (41-75). Ten patients had refractory disease; 13 patients had relapsed disease. Nine patients were classified high risk at diagnosis according to ELN2017 classification. First-line treatment consisted of fludarabine-based induction, CPX-351, conventional anthracycline/Ara-C (3+7) induction for 22 patients and 1 patient received reduced intensity induction with hypomethylating agents + venetoclax. Second line treatments included azacytidine, azacytidine + venetoclax, gilteritinib; six patients received TAG as second line treatment. Two patients, who received allogeneic stem cell transplantation (allo-BMT) while in complete remission (CR), were enrolled at first relapse post-transplant.

The median number of TAG cycles was 2 (range 1-10). Overall response rate (ORR) was 34.8% with 2 patients achieving MRD negative CR and 6 patients achieving partial remission (PR). As for treatment duration, 1 patient receiving 4 courses achieved PR and died due to CNS bleeding; 1 patient received 7 courses of TAG for early relapse after allo-BMT and achieved PR; 1 patient received 10 courses achieving PR. Early treatment discontinuation in the other cases was due to disease progression or adverse events (AEs).
Emergent AEs are summarized in Figure 1. In addition, 3 patients developed leucocytosis immediately following TAG administration on the first course; in one case it was also associated with lung infiltrates.
Capillary leak syndrome (CLS), a disorder characterized by leakage of intravascular fluids into the extravascular space, was reported in 5 patients: 2 patient experienced grade 2 (symptomatic) CLS which resolved with mild supportive treatment; 1 patient experienced grade 3 (severe), 1 grade 4 (life-threatening) and in one case the onset of CLS triggered by infectious event resulted fatal.
One patient experienced the onset of acute renal failure and severe hypertension after C1 day 1 which resulted fatal, possibly being consistent with CLS.
Conclusions: These results show that single agent TAG can exert anti-leukemic activity in R/R CD123-positive AML, even in cases with very unfavourable prognosis. However, further studies are necessary to disclose predictors of response and of the risk of adverse events. The safety profile observed here is similar to that previously observed for TAG requiring close monitoring of patients and timely supportive measures. However, overlapping of TAG-induced systemic inflammatory responses with refractory disease led to complex clinical management in some cases. Investigation of combinations strategies with TAG is warranted in order to optimize treatment efficacy, especially in the context of R/R AML.

Disclosures Cattaneo: *pfizer, jazz:* Other: travel grants. **Bocchia:** *Novartis:* Honoraria; *Incyte:* Honoraria; *BMS:* Honoraria. **Fracchiolla:** *Abbvie, Jazz, Pfizer, Amgen:* Speakers Bureau; *Abbvie, Jazz, Pfizer, Amgen:* Other: travel grants. **Martelli:** *Abbvie:* Consultancy, Honoraria; *Amgen:* Consultancy, Honoraria; *BMS:* Consultancy, Honoraria; *Jazz Pharmaceuticals:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria; *Laboratoires Delbert:* Consultancy, Honoraria. **Curti:** *Pfizer:* Membership on an entity's Board of Directors or advisory committees; *Novartis:* Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Membership on an entity's Board of Directors or advisory committees. **Pagano:** *Jazz:* Honoraria; *Janseen:* Honoraria; *Gilead:* Honoraria; *Pfizer:* Honoraria; *Novartis:* Honoraria; *Menarini:* Honoraria; *Moderna:* Honoraria; *AstraZeneca:* Honoraria. **Venditti:** *Medac:* Consultancy; *Janssen:* Consultancy, Honoraria, Other: travel support ; *AbbVie:* Consultancy, Honoraria, Other: travel support ; *Jazz:* Consultancy, Honoraria, Other: travel support ; *Amgen:* Consultancy, Honoraria, Other: travel support ; *Pfizer:* Consultancy, Honoraria, Other: travel support , Speakers Bureau; *Novartis:* Consultancy, Honoraria, Other: travel support .

OffLabel Disclosure: Tagraxofusp is administered for relapsed/refractory acute myeloid leukemia

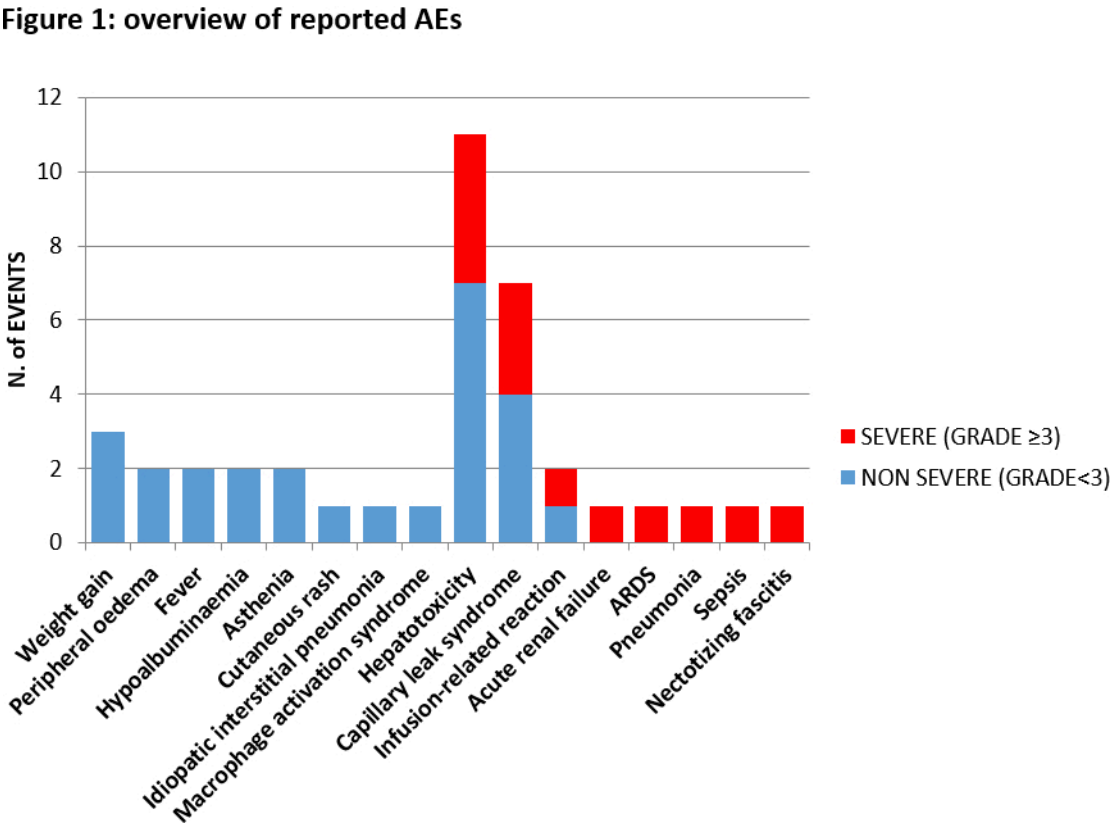

Figure 1

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