**Background**

- Flotetuzumab (MGO006/SB088D): Novel T-cell redirecting CD123 x CD3 bispecific DART protein
- Cytokine secretion with ensuing potential for cytokine release syndrome (CRS) is inherent in T-cell activation and is observed with T-cell redirecting therapies
- Two flotetuzumab lead-in dose (LID) strategies, in conjunction with T-cell redirecting therapies
- Determinants of IRR/CRS

**Methods**

- Phase 1 study of patients with relapsed/refractory acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS)
- LID-1 schema: Flotetuzumab administered at 100 ng/kg/day (d) for 3d, 100 ng/kg/d for 4d and 300 or 500 ng/kg/d on Day 8 (two-step LID)
- LID-2 schema: Flotetuzumab administered at 30 ng/kg/d for 3d, 100 ng/kg/day (d) for 4d followed by 3d pause and resumption at 300 or 500 ng/kg/d starting on Day 8 (one-step LID)

**Results**

- IL-2, IL-6, IL-8, IL-10, TNF-α, INF-γ, and GM-CSF were measured and CRS severity graded according to Lee DW, et al. Blood, 2014
- Peak cytokine values during first reported CRS events, occurring within 10 days of start of first dose, were evaluated
- Median peak cytokine levels were compared between patients with and without 2-step LID
- Other potential CRS determinants evaluated

**Correlation Between CRS Grade and Cytokine Levels**

- CRS severity and incidence decreased upon repeated dosing of flotetuzumab during Cycle 1
- Among 36 patients with complete cytokine data, 27 reported at least one IRR/CRS event; 56% (15/27) experienced CRS within 2 days of start of flotetuzumab; and 44% (12/27) within 3–10 days (22% Gr 1, 44% Gr 2, and 8% Gr 3)

**Conclusions**

- Preliminary flotetuzumab data suggest that a patient’s baseline circulating T-cell number may be a potential predictor of CRS
- Cytokine levels correlate with T-cell activity and CRS severity; CRS severity did not correlate with anti-leukemic activity
- Two-step LID showed effectiveness in limiting IRR/CRS events and cytokining over one-step LID

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**Lead-in Dose Optimization to Mitigate Cytokine Release Syndrome in AML and MDS Patients Treated with Flotetuzumab, a CD123 x CD3 Bispecific DART® Molecule for T-cell Redirected Therapy**

Kenneth Jacobs, MD1, John Godwin, MD2, Matthew C. Foster, MD3, Norbert Vey, MD4

1-3 – 10 days (22% Gr 1, 44% Gr 2, and 8% Gr 3)