INTRODUCTION

- MCLA-117 Bidorica® binds with high affinity to CLEC12A, expressed onAML blasts and leukemic stem cells, and with lower affinity to CD3 expressed on T cells.
- Targeting CLEC12A-expressing cells by MCLA-117 is designed to preferentially eradicate AML blasts and leukemic stem cells, while sparing normal hematopoietic stem cells.
- In preclinical studies, MCLA-117 activated resting T cells resulting in killing of CLEC12A+ AML blasts and T cell cytokine release.
- The PK profile associated with the full-length IgG format permits short (2-4 h) intravenous administration and the silenced Fc region effector function permits specificity for CLEC12A, to avoid side effects caused by non-specific Fcy receptor-mediated T cell activation.

OBJECTIVES & METHODS

- The study aims were to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, preliminary efficacy of MCLA-117, and to determine the MTD/RPOD.
- MCLA-117 is given as a single agent including a ramp-up phase, currently at 5/15/25 mg flat dose on Days 1, 4, and 8, followed by weekly infusion at the target dose starting on Day 15. Mandatory premedication included H1/H2 blockers, no steroids.

BASELINE CHARACTERISTICS

As of 31 March 2020, 58 patients have been treated across 11 dose levels and received a median of 5 infusions (target dose range 0.65–240 mg).

RESULTS

- **BM blast reduction across several dose levels**
- **% change from baseline in BM blast count by CLEC12A expression**

CONCLUSIONS

- MCLA-117 is safe and well tolerated with manageable CRS events, following a ramp-up dosing scheme. No MTD reached up to dose of 240 mg.
- Clinical activity is observed with ≥ 50% blast reduction in BM, including 1 patient achieving morphologically leukemia-free state.
- Pharmacokinetics is dose proportional with a half-life of about 5–6 days across all dose levels.
- Pharmacodynamic activity is evident by activation and margination of peripheral T cells.
- Given the observed clinical activity, enrollment into the planned dose expansion cohorts will not be initiated. Further evaluation of the clinical trial data and characteristics of responses is ongoing.
- Potential ways to further improve clinical activity:
  - Pharmacometric modelling to understand optimal dose window
  - Optimize T cell activation (e.g. dosing regimen, drug combinations)
  - Patient selection based on CLEC12A expression levels

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References

2. Lee et al. (2019), Blood Cancer Journal, 9:460-469. DOI: 10.1038/s41375-019-0211-9