BL-M11D1, A NOVEL CD33 ANTIBODY-DRUG CONJUGATE (ADC), IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA: INITIAL RESULTS FROM A FIRST-IN-HUMAN PHASE 1 STUDY

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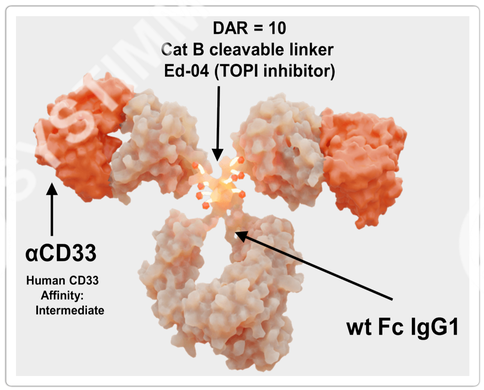
INTRODUCTION

BL-M11D1 is a novel ADC consisted of a CD33 monoclonal antibody bound to a novel TOP1 inhibitor payload via a cleavable linker. Due to its CD33 binding, BL-M11D1 specifically targets CD33 expressing hematopoietic malignancies including AML.

Fig 1. Structure of BL-M11D1



AIM

This is a first-in-human phase I clinical trial with i3+3 design for dose escalation.

Primary outcome:

The safety and tolerability of BL-M11D1 in patients with R/R AML.

- DLT and MTD
- Recommended Phase II Dose

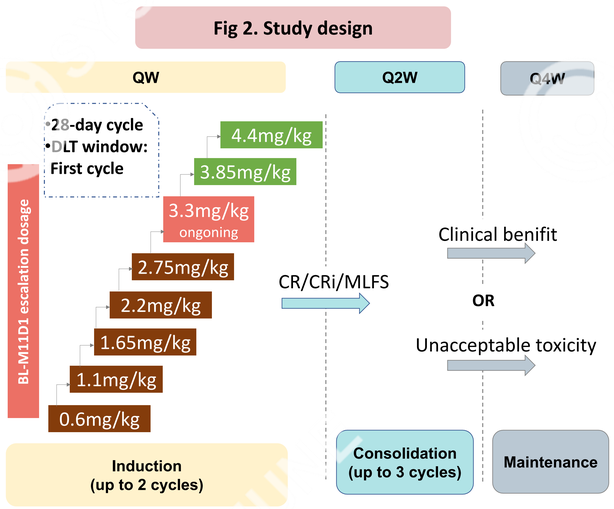
Secondary outcome:

- TEAE
- PK and PD data
- Efficacy

METHODS

- Key inclusion criteria:
  - Male or Female aged 18-75 years;
  - ECOG≤2;
  - Relapsed/refractory acute myeloid leukemia (AML) confirmed by histopathology and/or cytology;
  - Patients with essentially normal function of liver, renal, coagulation, kidney, lung and heart.
- Dose escalation: accelerated titration combined with i3+3
- Dosing: IV, QW for induction; IV Q2W for consolidation
- Efficacy is assessed based on ELN2017.

Fig 2. Study design



RESULTS

Baseline Characteristics

As of July 25, 2024, 40 patients were enrolled at doses ranging from 0.6 mg/kg to 2.75 mg/kg.

Median, range	Total (N=40)
Age, years	54.0, 19-75
Male, Sex, n(%)	21 (52.5)
ECOG, PS, n(%)	
0-1	37 (92.5)
2	3 (7.5)
Percent of BM blast (%, median, range)	35.93 (5.6-90)
WBC count (×10⁹, median, range)	8.85 (0.3-118.5)
Median number of line	4, 1-9
Primary refractory AML, n	10
Refractory AML, n	24
Relapsed AML, n	6

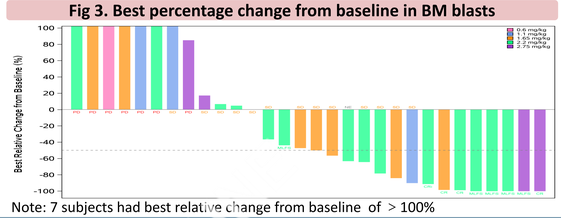
Efficacy

30 patients had at least 1 post-treatment assessment. Responses were observed starting at the 1.65 mg/kg dose, with a complete response (CR) of 6+ months duration.

(mg/kg)	0.6 N=1	1.1 N=3	1.65 N=7	2.2 N=15	2.75 N=4
ORR*	0 (0)	0 (0)	1 (14.3%)	6 (40.0%)	2 (50%)
CR	0	0	1	1	1
CRi	0	0	0	1	0
MLFS	0	0	0	4	1

* The objective response was CR/CRi/MLFS;

Fig 3. Best percentage change from baseline in BM blasts



Note: 7 subjects had best relative change from baseline of > 100%

Safety

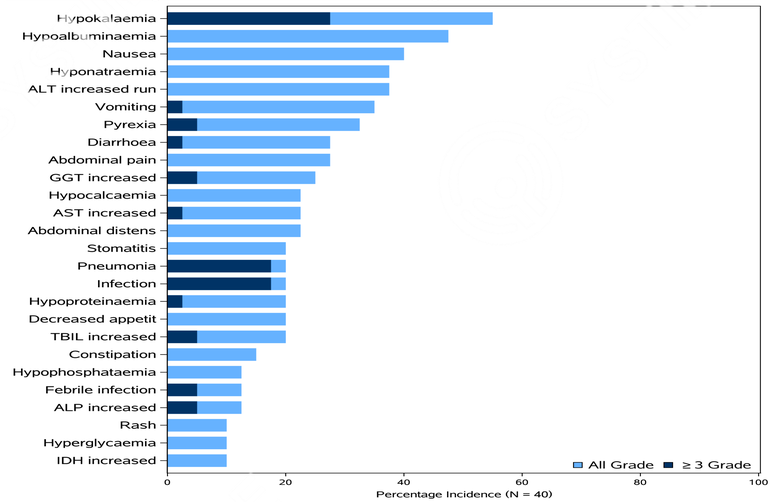
The most common non-hematological treatment-related adverse events (TRAEs) in ≥20% of pts were hypokalemia (55.0%), hypoalbuminemia (47.5%), nausea (40.0%), ALT increased (37.5%), hyponatremia (37.5%), vomiting (35.0%), pyrexia (32.5%), etc.

The most common grade ≥3 non-hematological TRAEs were hypokalemia (27.5%), pneumonia (17.5%), infection (17.5%), etc.

Two pts died due to infection, which might be associated with BL-M11D1 by investigators' evaluation.

No grade 3 or higher organ injury has been seen to date, and no veno-occlusive disease (VOD) observed in any patient.

Fig 4. Treatment-related non-hematologic AEs (Frequency ≥20%)



IDH: lactate dehydrogenase; ALP: alkaline phosphatase; TBIL: total bilirubin; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase; ALT: alanine aminotransferase.

CONCLUSIONS

Based on preliminary results of this phase I study, BL-M11D1 has demonstrated an acceptable safety profile and encouraging anti-cancer activity, including in refractory patients who had not previously achieved remission from prior therapy. The dose escalation of BL-M11D1 is ongoing to better define the safety profile, anti-cancer activity and the RP2D for future development.

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