A Phase 1b Study Evaluating the Safety and Efficacy of AK117 (anti-CD47 monoclonal antibody) in Combination with Azacitidine in Patients with Treatment-naïve Acute Myeloid Leukemia

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#4280

BACKGROUND

- AK117 is a humanized IgG4 monoclonal antibody that specifically targets CD47, a "don't eat me" signal excessively expressed on tumor cells.
- AK117 has emerged as a potential best-in-class therapy without inducing hemagglutination effects (**Figure 1**).[1] Additionally, AK117 does not require a lower 'priming' dose to prevent anemia.
- Here, we present preliminary safety and efficacy data in patients with treatment-naïve acute myeloid leukemia who were deemed unfit for intensive chemotherapy (1L unfit AML).

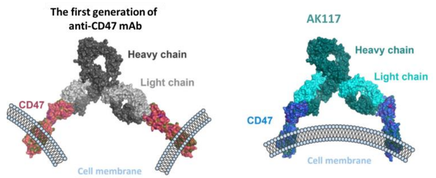
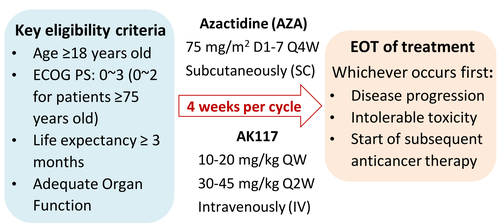


Figure 1. Binding conformation of AK117 in complex with CD47

METHODS

- This multi-center, open label, phase Ib study (NCT04980885) is summarized in **Figure 2**.

Figure 2. Study design



Primary endpoint:
- Safety (graded according to NCI-CTCAE v5.0)
- Composite complete remission rate (CCR=complete remission (CR) + CR with incomplete hematologic recovery (CRi)) per ELN 2017 criteria

Secondary endpoint
- CR rate, time to response (TTR), event-free survival (EFS) and overall survival (OS)
- Pharmacokinetic characteristics, anti-drug antibody (ADA) assessment

RESULTS

Baseline Characteristics

- As of August 25, 2023, 43 patients were enrolled, with 22 patients assigned to the recommended phase 2 dose (RP2D, 30mg/kg Q2W) group. Most patients had abnormal hematologic conditions at baseline (**Table 1**).

Table 1. Baseline characteristics

Characteristics	All (N=43)	RP2D (N=22)
Age (years), median (range)	61 (25-81)	63 (37-80)
Gender (Male/Female), n (%)	18 (41.9)/25 (58.1)	7 (31.8)/15 (68.2)
ECOG PS, n (%)		
0	12 (27.9)	6 (27.3)
1	10 (23.3)	2 (9.1)
2	20 (46.5)	13 (59.1)
3	1 (2.3)	1 (4.5)
WHO Classification, n (%)		
AML wih recurrent genetic abnormalities	14 (32.6)	6 (27.3)
AML with myelodysplasia-related changes	4 (9.3)	1 (4.5)
AML, NOS	22 (51.2)	13 (59.1)
Unknown	3 (7.0)	2 (9.1)
Gene mutations, n (%)		
TP53	4 (9.3)	3 (13.6)
RUNX1	1 (2.3)	1 (4.5)
IDH1/IDH2	10 (23.3)	5 (22.7)
ASXL1	4 (9.3)	3 (13.6)
FLT3-ITD/TKD	12 (27.9)	5 (22.7)
NPM1	5 (11.6)	0 (0.0)
Hematologic conditions (grade ≥ 3), n (%)		
Anemia	35 (81.4)	21 (95.5)
Neutrophil count decreased	27 (62.8)	14 (63.6)
Platelet count decreased	22 (51.2)	12 (54.5)

Safety

- Among the 43 treated patients, 42 patients (97.7%) experienced at least one treatment-emergent adverse events (TEAEs). 1 patient (2.3%) discontinued treatment due to TEAE.
- Anemia (a primary adverse event associated with CD47 blocking antibodies) occurred in 30.2% of the patients. Hemoglobin changes from baseline over time on treatment is shown in **Figure 3**.
- Most of the TEAEs were hematological events, which are also commonly considered complications of AML, as indicated in the baseline characteristics table. Commonly observed TEAEs (≥20%) are presented in **Table 2**.

Figure 3. Hemoglobin changes from baseline over time (N=43. Data shown are median (Q1, Q3) change in blood samples drawn before each cycle)

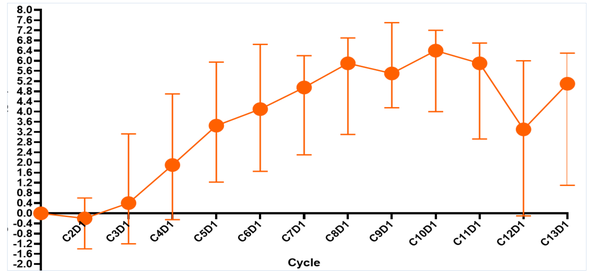


Table 2. Most frequent TEAEs

Preferred Term (PT)	All (N=43)	
	Any grade TEAEs, n (%)	Grade ≥ 3 TEAEs, n (%)
White blood cell count decreased	31 (72.1)	25 (58.1)
Lymphocyte cell count decreased	26 (60.5)	13 (30.2)
Platelet count decreased	25 (58.1)	21 (48.8)
Neutrophil count decreased	23 (53.5)	21 (48.8)
Pyrexia	23 (53.5)	2 (4.7)
Constipation	17 (39.5)	0 (0.0)
Vomiting	16 (37.2)	0 (0.0)
Pneumonia	13 (30.2)	9 (20.9)
Anemia	13 (30.2)	10 (23.3)
Diarrhoea	9 (20.9)	0 (0.0)
Hypokalemia	9 (20.9)	1 (2.3)

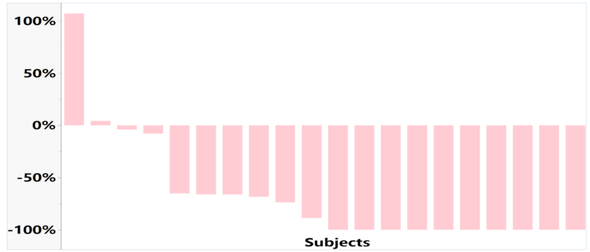
Efficacy

- As of August 25, 2023, among 20 evaluable patients in the RP2D group, the CR rate was 50.0% and CCR rate was 55.0% (**Table 3**).
- The median time to response (TTR) was 1.17 months, while the median time to CR (TTCR) was 1.84 months.
- The best percent change from baseline in bone marrow blasts of the RP2D group is shown in **Figure 4**.

Table 3. Efficacy outcomes of the RP2D group

Outcome	RP2D (N=20)
CCR, % (n)	55.0 (11)
CR, % (n)	50.0 (10)
CRi, % (n)	5.0 (1)
PR, % (n)	5.0 (1)
Time to response, median (range), month	1.17 (0.9, 2.7)
Time to CR, median (range), month	1.84 (1.0, 2.9)

Figure 4. Best percent change from baseline in bone marrow blasts of the RP2D group



CONCLUSIONS

- The combination of AK117 and AZA exhibited a manageable safety profile with a low incidence of anemia, and demonstrated promising efficacy as a first-line treatment in AML patients who were unable to undergo intensive chemotherapy.
- A randomized, open-label, phase 2 study is currently being planned to evaluate the safety and efficacy of AK117 in combination with venetoclax and AZA in 1L unfit AML patients.

ACKNOWLEDGEMENTS

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REFERENCES

1. Tailong Qu et al. J Immunother Cancer. 2022; 10: e005517.