A Phase 1 Study Investigating AFM11 in Patients with Relapsed/Refractory B-cell Precursor Acute Lymphoblastic Leukemia: Preliminary Results

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Introduction

• AFM11 is a bispecific, tetrameric T cell-engaging antibody construct binding to CD19 on tumor cells and to CD3 on T cells
• AFM11 elicits T cell-mediated killing of CD19-positive (CD19+) leukemia and lymphoma cells

Mechanism of action of AFM11

• In vivo anti-tumor activity of AFM11 was investigated in a Raji tumor xenograft model in NOD/scid mice reconstituted with human PBMCs
• Tumor growth in all AFM11-treated groups was significantly reduced
• The lowest dose group showed delayed (~60%) tumor growth

Safety

• No DLTs were observed in Cohorts 1 through 5; 2 DLTs were observed in cohort 6
• The lowest dose group showed delayed (~60%) tumor growth

Pharmacokinetics

• Serial serum PK samples were measured in all patients. In 11 patients, samples were below LOD (4.5 pg/mL) and PK parameters could not be derived
• In 5 patients from cohorts 3 to 6, PK samples were measured and a one-compartment PK model was fitted to the observed concentration profiles
• In 1 patient, the PK parameters (CL and Vss) were appreciably different from the other 4 patients (empty circle in figure)
• In 4 patients, average serum concentrations at steady state (Cav,ss) increased with dose but the increase was less than dose proportional; i.e. exponent of the power model (0.72) was <1 (see figure)
• The estimate of % cardiac output binding to CD19+ cells was 3.2 ± 1.2% (mean ± SD) of total cardiac output

Response

• 3 patients enrolled in Cohorts 4 through 6 achieved a complete response (2 CRs, 1 CR)
• In all 3 patients, the responses were seen after cycle 1
• In 2 of 3 patients (1 in Cohort 4 and 1 in Cohort 6 whose doses were reduced to Cohort 5 dose level due to toxicity), the responses were transient and the patients relapsed after cycle 2
• In 1 patient (Cohort 5), the CR deepened to MRD negativity after cycle 3 and the investigator reported continued CR for several months post-study

Enrollment status

• 17 patients were enrolled in 6 dose observation periods
• 14 patients completed the DLT observation period, 3 discontinued early due to disease progression
• No DLTs were observed in Cohorts 1 through 5
• Two DLTs were observed in Cohort 6, including one fatal event

Pharmacokinetics

- Characteristic
  - Total patient population (N=17)
  - No.
  - Age, years, median (range)
  - Male, female
  - Gender
  - Prior Therapies, No.
  - 1
  - 2
  - 3
  - 4
  - Prior stem cell transplant

  - Total dose over 2 weeks (µg)
  - y = 1.6773x

  - Cav,ss (pg/mL)

  - Total number of patients (N=17)
  - No. (%)

  - Neutropenia
  - Alt increase
  - AST increase
  - Bone pain
  - Febrile neutropenias
  - Myalgia
  - Neutropenia
troller
  - TRAEs all CTCAE grades
  - Safety profile (N=17)
  - No. (%)

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  - Most common TRAEs in 2 patients: CTCAE all grades and Gr3

Conclusions

• AFM11 was well tolerated in the first 5 dose cohorts of the Phase 1 dose-exposure study, with the MTD not yet defined
• Neurotoxicological observations studied in the appearance in frequency and severity compared to other CD19-targeting agents
• AFM11 treatment was able to elicit CRs in three patients treated at tolerable dose levels, with one CR reported as durable for several months post-study
• Additional clinical testing of AFM11 is needed to define the MTD and to establish clinical benefit of AFM11 in a larger group of R/R ALL patients

AFM11 completely suppresses tumor growth in Burkitt lymphoma xenograft model

Poster 3969

Response assessment

- Cohort 1
- Cohort 2
- Cohort 3
- Cohort 4
- Cohort 5
- Cohort 6

TRAEs, all CTCAE

- Safety profile

- TRAEs all CTCAE grades

- Safety profile (N=17)

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