ALX148, a CD47 Blocker, in Combination with Rituximab in Patients with Relapsed/Refractory (R/R) Non-Hodgkin Lymphoma

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Background

- CD47-SIRPα signaling is a nuanced checkpoint mechanism that regulates the inflammasome to initiate inflammation. Aberrant expression of CD47 on tumors and regulation of SIRPα by immune cells can contribute to a more tolerogenic tumor microenvironment.
- ALX148 is an engineered fusion protein composed of a high affinity CD47 blocker that enables increased recruitment of immune cells to tumors.

Methods

AT148001 Study Design

- Part 1 (single agent): 10 mg/kg QW, maximum administrable dose
- Part 2 (combination): ALX148 (administered 10 mg/kg QW) with standard regimen of rituximab (administered 375 mg/m² QW 4-6 weeks after first cycle of ALX148 administration)

Endpoints and Assessments

- Primary endpoints: First cycle of ALX148 dosing tangency (SLT) in combination with rituximab.
- Additional assessments: Serum cytokine levels, anti-ALX148 antibody titers, biomarkers of CD47 blockade.

Results

Patient Baseline Characteristics

- ALX148 in combination with rituximab has been administered to 32 patients with relapsed/refractory lymphoma.
- Enrollmen into the ALX148 10 mg/kg QW and ALX148 15 mg/kg QW combination expansion cohorts.
- Majority of patients entered were male (75%), Asian (62%) and had an ECOG PS score of 0 (70%).

Safety

- ALX148 in combination with rituximab was well tolerated, and no serious adverse events were observed across the ALX148 exposure range evaluated (10 mg/kg QW - 15 mg/kg QW).
- No patient required a dose reduction, and the most common reason for discontinuation was disease progression.

Study Population

- Key Inclusion Criteria:
  1. Patients ≥18 years with B-cell non-Hodgkin lymphoma for which no curative therapy is available, or who are refractory to standard approved therapy.
  2. Adequate organ function and transaminases ≤5 x upper limit of normal.
- Key Exclusion Criteria:
  1. Patients with history of ALL or other hematologic malignancies.

Conclusions

- ALX148 with standard regimen of rituximab was well tolerated in a Phase 1 study and demonstrated activity with durable responses in combination with rituximab.
- ALX148 in combination with rituximab was associated with improved median progression-free survival (mPFS) and response rates compared to standard approaches in the clinic.

References


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