(PS1485) COMBINATION THERAPY WITH BLINATUMOMAB AND ASCIMINIB FOR PHILADELPHIA CHROMOSOME-POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA: RESULTS FROM A PHASE I/II STUDY

Topic: 02. Acute lymphoblastic leukemia - Clinical

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Background

Despite improvements in frontline therapy for Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL), the outcomes of relapsed Ph+ ALL remain poor. We hypothesized that the combination of blinatumomab + asciminib, a potent allosteric inhibitor of BCR::ABL1, may lead to deep and durable remissions in patients (pts) with relapsed/refractory (R/R) Ph+ ALL after failure of standard therapies.

Aims

This is a phase I/II study evaluating the combination of blinatumomab + asciminib in pts ≥12 years of age with R/R Ph+ ALL or CML-LBP.

Methods

In the phase I portion, pts receive up to 5 cycles of asciminib at a dose of 80mg, 120mg or 200mg orally daily in combination with continuous infusion blinatumomab in a standard 4-week on/2-week off schedule (42-day cycles). CNS prophylaxis with 6-8 doses of IT chemotherapy is recommended. For pts not proceeding with allo-HSCT or CAR T-cell therapy, asciminib is continued indefinitely. The primary endpoint of the phase I study is the minimum safe and biologically effective dose of asciminib in combination with blinatumomab.

Results

As of February 2026, 10 pts have been treated in the phase I portion of the study (9 with Ph+ ALL and 1 with CML-LBP). The median age is 47.5 years (range, 15-65). Five pts had received ≥2 prior TKIs, 5 pts had received prior blinatumomab + ponatinib, and 1 pt had undergone prior allo-HSCT.
Three pts received asciminib 80mg, 3 received 120mg and 4 received 200mg. No DLTs nor any grade 3 or higher related adverse events were observed. Four pts experienced CRS (all grade 1) and 2 pts experienced neurotoxicity (grade 1 tremor in both). There was one on-study death (due to CNS relapse).

All 10 pts (100%) achieved CR, all after the first cycle. Eight pts had a trackable sequence for NGS IG/TR MRD (sensitivity: 10^{-6}): 5/8 (63%) achieved NGS MRD negativity after cycle 1 and 7/8 (88%) as best response; the other pt had NGS MRD below the level of detection as best response. The 2 pts without a trackable IG/TR achieved PCR negativity for *BCR::ABL1* after cycle 1.
The median follow-up is 10.7 months (range, 0.6-17.8 months). The median number of cycles received is 3.5 (range, 1-5). Among the 10 treated pts, 2 have relapsed (1 of whom was nonadherent to therapy) and 8 are in ongoing continuous remission. One relapse was bone marrow-only and 1 was CNS-only (5.1 and 6.5 months from start of therapy, respectively). The asciminib doses in the relapsed pts were 80mg and 120mg, respectively. Among the 8 pts in continuous remission at last follow-up, 1 received allo-HSCT (pt with CML-LBP), 4 received CD19 CAR T-cell consolidation (1 brexu-cel and 3 obe-cel), and the 3 have not received consolidation therapy (2 still receiving combination therapy and 1 receiving asciminib maintenance).
As of last follow-up, 1 pt has died (CNS relapse). The estimated 1-year RFS and OS rates are 75% and 88%, respectively.

Summary/Conclusion

In this ongoing phase I/II study, the combination of blinatumomab + asciminib is safe and highly effective in pts with R/R Ph+ ALL, including those with prior exposure to blinatumomab + ponatinib. No DLTs have been observed at doses of asciminib up to 200mg daily. Responses have been deep, with NGS MRD negativity in 88% of evaluable pts. The study continues to accrue R/R pts. Given the encouraging activity observed in the R/R population, the study has been expanded to also enroll frontline pts ≥18 years of age.