Abstract: P492

Title: SAFETY AND EFFICACY OF LP-108 AS MONOTHERAPY AND COMBINED WITH AZACITIDINE IN PATIENTS WITH RELAPSED/REFRACTORY MYELODYSPLASTIC SYNDROMES, CHRONIC MYELOMONOCYTIC LEUKEMIA, OR ACUTE MYELOID LEUKEMIA

Abstract Type: Poster Presentation

Session Title: Acute myeloid leukemia - Clinical

Background:

BCL-2 inhibition to target intrinsic apoptotic pathways that confer a survival advantage to leukemic blasts has become a key therapeutic strategy for patients (pts) with myeloid malignancies. LP-108 is an oral highly potent and selective inhibitor of BCL-2 with comparable or more potent in vitro inhibitory activity compared to the FDA approved oral BCL-2 inhibitor venetoclax.

Aims:

We present safety and preliminary efficacy data of pts treated in an ongoing phase 1 study (NCT04139434) evaluating LP-108 as monotherapy (Arm 1) and in combination with azacitidine (Arm 2) in pts with relapsed or refractory (r/r) MDS, CMML or AML.

Methods:

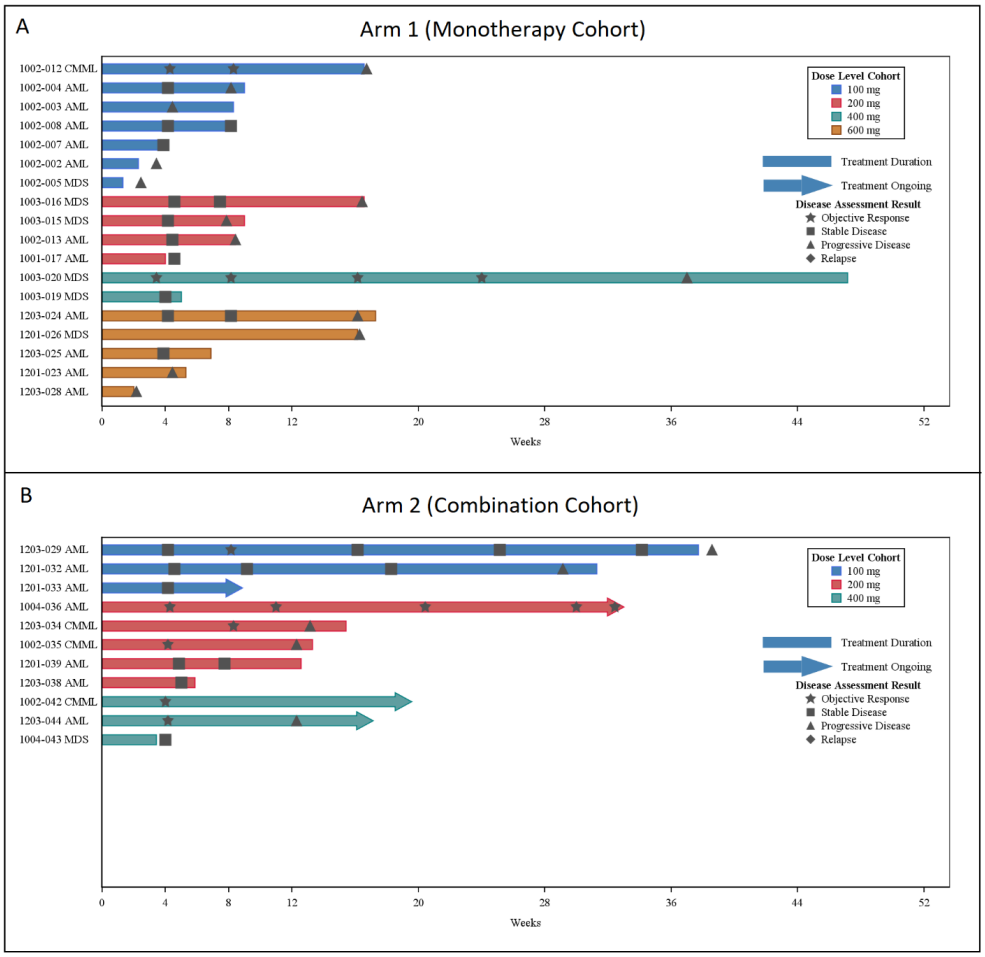
Pts age ≥18 with r/r MDS with excess blasts (MDS-EB) or high/very-high risk per IPSS-R (HR-MDS), r/r AML, or r/r CMML were enrolled in Arm 1, and pts with r/r MDS-EB/HR-MDS, r/r AML, or r/r CMML were enrolled in Arm 2. Pts with prior hypomethylating agents or venetoclax exposure were allowed to enroll in Arm 2. Blast count was required to be ≤ 30 × 109 cells/L at therapy initiation and ECOG performance status was ≤2. For Arm 1, LP-108 was given in several dose cohorts (100 mg, 200 mg, 400 mg, or 600 mg daily in 28-day (d) cycle). For Arm 2 azacitidine 75 mg/m2 was administered on d1-7 (or d1-5,8-9) of each 28-d cycle, and LP-108 was given in several dose cohorts (100 mg, 200 mg, or 400 mg daily in 28-d cycles). Primary objectives were to determine the safety/tolerability and the RP2D of LP-108 as a single agent and in combination with azacitidine. Key secondary objectives were to evaluate the objective response rate (ORR) of LP-108 (monotherapy and combination therapy) in r/r MDS/CMML/AML as well as progression free survival and overall survival.

Results:

At data cutoff February 20, 2023, 20 pts had received LP-108 monotherapy (Arm 1) and 12 pts in combination with azacitidine (Arm 2). 3 pts received LP-108 at the RP2D of 400 mg with azacitidine. In Arm 1, median age was 72 years (range 40-84), 55% male; 12 pts (60%) had r/r AML, 7 (35%) r/r MDS, and 1 (5%) r/r CMML. In Arm 2, median age was 61 years (range 46-83), 75% male; 8 pts (66.7%) had r/r AML, 1 (8.3%) r/r MDS, and 3 (25%) r/r CMML. 14 pts (70%) experienced any TRAE in Arm 1 (2 serious TRAEs) and 7 (58.3%) in Arm 2 (2 serious), the most common being neutropenia (4 pts, 20% Arm 1; 3pts, 25% Arm 2), nausea (3pts, 15% Arm 1; 1 pt, 8.3% Arm 2) and vomiting (3pts, 15% Arm 1; 2 pts,16.7% Arm 2). Grade 3/4 neutropenia was seen in 3 pts (15%) in Arm 1 and 3 pts (25%) in Arm 2; febrile neutropenia occurred in 1 pt in Arm 1 only. A grade 5 AE did occur in a pt receiving 200 mg LP-108 with azacitidine due to fusarium bacteremia that was not related to LP-108. Across all dosing cohorts in Arm 1, the ORR was 11.1% (2 pts) and 10 pts (55.5%) had SD as best response (18 evaluable pts). Across all dosing cohorts in Arm 2, the ORR was 54.5% (6 pts) and the remaining 5 pts (45.4%) experienced SD as best response (11 evaluable pts). In Arm 1 an outstanding responder with MDS was seen in the 200 mg LP-108 cohort, and in Arm 2 responses were seen in both CMML and AML pts. In Arm 1, the median PFS ranged from 7.0 to 37.0 weeks and the median OS ranged from 3.6 to 12.1 weeks across dosing cohorts. In Arm 2, the median PFS ranged from 12.3 to 29.1 weeks and the median OS ranged from 5.2 to not reached, across dosing cohorts. PFS/OS data are still maturing.

Summary/Conclusion:

LP-108 as monotherapy and in combination with azacitidine was overall well tolerated with an acceptable safety profile for r/r MDS, CMML, and AML pts. Notably, the combination was associated with encouraging efficacy including ORR and PFS.



Swimmers' plot of patients in Arm 1 (A) and Arm 2 (B). LP-108 dose level cohort indicated by different colors and disease assessment results are indicated.

Keywords: CMML, Targeted therapy, AML, MDS