Abstract: P536

Title: INTERIM SAFETY AND EFFICACY OF BP1001 IN A PHASE II ACUTE MYELOID LEUKEMIA STUDY

Abstract Type: Poster Presentation

Topic: Acute myeloid leukemia - Clinical

Background:

Oncogenic tyrosine kinases induce acute myeloid leukemia (AML) progression via the growth factor receptor bound protein-2 (Grb2). To inhibit Grb2 expression, BP1001, a liposome-incorporated Grb2 antisense oligonucleotide was developed. Preclinical studies indicated that BP1001 reduced leukemia proliferation and enhanced the inhibitory effects of chemotherapy, including decitabine (DAC) and venetoclax (VEN) against AML cells. A multi-center open-label Phase II study was initiated to assess whether the BP1001 + DEC + VEN combination provides higher response rates than historically reported responses of DEC + VEN in newly diagnosed AML (including secondary AML) (cohort 1) or refractory/relapsed (R/R; cohort 2) AML patients considered unsuitable for intensive chemotherapy [ClinicalTrials.gov Identifier: NCT02781883].

Aims:

Per protocol, when 19 evaluable patients are enrolled in each cohort, interim analysis will be performed to determine which cohort has ≥5 complete responses and will continue with enrollment.

Methods:

BP1001 was given, beginning on Day 4, at 60 mg/m2 IV, 2x weekly for a total of 8 doses over a 28-day cycle. DEC was given IV on days 1 to 5 at 20 mg/m2. VEN was given PO at 100 mg on day 1, 200 mg on day 2, and 400 mg from day 3 to day 14 or 21. Eligible patients were considered unsuitable for or refused intensive chemotherapy and had ECOG performance status of 0-2. Interim analysis was performed on Jan 24, 2024 on patients enrolled between July 28, 2020 and December 26, 2023. Evaluability for efficacy was defined as: completion of at least 4 cycles of combination therapy, documented Progressive Disease (PD) or any drug toxicity at any time, or CR/CRi/CRh prior to 4 cycles.

Results:

In Cohort 1, 31 newly diagnosed patients were enrolled; 20 evaluable patients (9 male: 45%) with a median age of 75 years (range, 69 - 84), treated with at least 1 cycle of BP1001 + DEC + VEN, had adverse-risk (n=12, ELN 2017 classification) or secondary AML (sAML; n=7) evolved from MDS (n=4), CMML (n=1) or treatment-related AML (n=2). Fifteen patients (75% of evaluable; 54% of enrolled) achieved CR/CRi/CRh; 2 patients achieved partial remission (PR) and 2 achieved stable disease (SD).

In Cohort 2, 38 R/R patients were enrolled; 23 evaluable patients (13 male: 57%) with a median age of 63 years (range, 24 - 89), treated with at least 1 cycle of BP1001 + DEC + VEN, had adverse-risk (n=13) or sAML (n=5). Twelve patients (55% of evaluable; 32% of enrolled) achieved CR/CRi/CRh; 1 pt achieved PR, 8 achieved SD and 1 had treatment failure.

Among the evaluable patients of both cohorts, AE's were consistent with those expected with DEC, VEN and/or AML, including fatigue (72%), anemia (60%) and neutropenia (49%), while the most frequent SAE's were febrile neutropenia (26%) and sepsis (5%).

Summary/Conclusion:

BP1001 + DEC + VEN has been safely administered to patients without drug-related toxicity. Since >5 responses are observed in both cohorts, the study will continue with enrollment up to 98 and 54 evaluable patients in cohorts 1 and 2, respectively. Efficacy data are encouraging in a challenging population of frontline

adverse-risk, sAML and R/R patients.

Table. Molecular abnormality of evaluable patients

	Cohort 1 (n=20)	Cohort 2 (n=23)
ELN Risk Groups	**n (%)**	**n (%)**
Intermediate	8 (40)	6 (26)
Adverse	12 (60)	13 (57)
Molecular Abnormality	**n (%)**	**n (%)**
TP53	4 (20)	4 (17)
RUNX1	2 (10)	5 (22)
BCOR	2 (10)	3 (13)
SRSF2	1 (5)	4 (17)
ASXL1	2 (10)	2 (9)
KMT2A	1 (5)	1 (4)
U2AF1	1 (5)	1 (4)
EZH2	0	2 (9)
SF3B1	0	2 (9)
GATA2	0	1 (4)
STAG2	0	1 (4)
TET2	3 (15)	5 (22)
FLT3	6 (30)	0
WT1	1 (5)	2 (9)
IDH1	2 (10)	1 (4)
IDH2	1 (5)	1 (4)
NRAS	1 (5)	1 (4)
JAK2	0	2 (9)
CUX1	0	2 (9)
DDX41	1 (5)	1 (4)
EGR1	0	2 (9)
CALR	1 (5)	0
DNMT3A	0	1 (4)
ETV6	0	1 (4)
FOXO1	0	1 (4)
HNRNPK	0	1 (4)
IKZF1	0	1 (4)
KRAS	0	1 (4)
MLL-PTD	0	1 (4)
NF1	0	1 (4)
MPL	0	1 (4)
PAX5	1 (5)	0
PTPN11	1 (5)	0
R-IPSS	1 (5)	0
SETBP1	0	1 (4)
SMC1A	0	1 (4)
SOCS1	0	1 (4)
CEBPA	0	1 (4)
None	4 (20)	4 (17)

Keywords: Tyrosine kinase, TP53, Venetoclax, Hypomethylating agents