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P561 REVUMENIB IN PATIENTS WITH ACUTE LEUKEMIAS: COMPASSIONATE USE PROGRAM EXPERIENCE

Topic: 4. Acute myeloid leukemia - Clinical

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Background:

Revumenib (REV; SNDX-5613), a menin inhibitor, is under investigation in patients (pts) with relapsed/refractory (R/R) acute leukemia harboring a *KMT2A* rearrangement (KMT2Ar) or *NPM1* mutation. A phase 1/2 study, AUGMENT-101 (NCT04065399), is ongoing; preliminary data were presented (Issa. *Blood.* 2022). Phase 2 initiated with a recommended dose of 163 mg q12h for pts receiving a strong cytochrome P450 3A4 inhibitor. A compassionate use program was available for pts ineligible or unable to enroll in AUGMENT-101 if slots were unavailable or sites were not yet open.

Aims:

To report REV compassionate use outcomes.

Methods:

Pts from the US, UK, France, Israel, Lithuania, Canada, and The Netherlands with R/R acute leukemia were treated with REV. Demographics, outcomes, and safety data were collected from single-pt protocols, physician communications, and source documents.

Results:

From Oct 2019 to Dec 2022, 36 pts (20 female) with R/R acute leukemia received REV. Ages ranged from 1.2 to 71 years (20 pediatric pts [<18 y]). Leukemia subtypes were acute myeloid leukemia (AML; n=30), acute lymphoblastic leukemia (n=4), and mixed phenotype acute leukemia (n=2). Most pts had KMT2Ar (n=34) and were heavily pretreated (≥3 prior regimens [n=26]; range, 1-6); 23/36 had prior hematopoietic stem cell transplant (HSCT). Thirty pts had active disease evaluable for response. Nine pts received prior REV on AUGMENT-101, achieved a response, and proceeded to HSCT but were ineligible to restart REV on trial. These pts received REV compassionate use as maintenance (n=6) or following relapse post-HSCT (n=3). The other reasons for trial ineligibility included age <18 y before AUGMENT-101 amendment reduced the minimum age to 30 d, concurrent malignancy, myeloid sarcoma, ongoing graft vs host disease, and prior menin inhibitor exposure. Of the 30 pts with active disease evaluable for response (19 pediatric), 4/19 pediatric pts reported a response, with 2 achieving minimal residual disease (MRD)–negative complete response (CR), 1 CR, and 1 CR-incomplete hematologic recovery (CRi); 3 of the 4 pts proceeded to transplant. One of 11 adults converted from MRD-positive to MRD-negative disease. Another adult had progressive disease (PD) as best response on 2 other prior menin inhibitors and best response of PD with REV. Of the 30 pts, 3 adults previously responded to REV on AUGMENT-101, proceeded to HSCT, and experienced relapse post-transplant; 2/3 were re-treated for 80 and 115 d before progressing and 1/3

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remained on treatment after 2 28-d cycles. An additional 6 pts (5 adults) received REV as maintenance therapy after achieving CR-partial hematologic recovery, CR-incomplete platelet recovery, or morphological leukemia-free state with REV on AUGMENT-101 and proceeding to HSCT or CD34+ boost. At data cutoff, 3/6 pts remained in remission and on treatment as of d 338, d 223, and d 158; 1/6 discontinued on d 30 and was reported well on d 285; and 2/6 progressed on d 160 and d 34. Given the nature of the compassionate use program, adverse events (AEs) were not consistently reported among all 36 pts. Reported AEs were consistent with common AEs in trials of pts with R/R acute leukemia, including thrombocytopenia (n=7), and with those of ongoing REV trials including differentiation syndrome and QTc prolongation (n=3 each).

Summary/Conclusion

In this compassionate use program, which included heavily pretreated pts, disease responses were observed. Several pts who started REV as maintenance post-HSCT experienced prolonged remissions. No new safety signals were reported.

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