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# POSTER ABSTRACTS

## 615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

### CPX-351 with Venetoclax in Patients with Relapsed/Refractory Acute Myeloid Leukemia: Results of a Phase Ib Study

*Alex Bataller, MDPhD[1], Alexandre Bazinet, MD[2], Gautam Borthakur, MD[1], Nicholas J. Short, MD[1], Elias Jabbour, MD[3], Koichi Takahashi, MD PhD[1], Naval Daver, MD[1], Ghayas C. Issa, MD[4], Courtney D. DiNardo, MD MSc[1], Naveen Pemmaraju, MD[1], Nitin Jain, MD[1], Guillermo Montalban-Bravo, MD[1], William G. Wierda, MD PhD[4], Farhad Ravandi, MD MBBS[1], Hagop M. Kantarjian, MD[1], Tapan M. Kadia, MD[1]*

[1] Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX
[2] Department of Leukemia, MD Anderson Cancer Center, Houston, TX
[3] University of Texas M.D. Anderson Cancer Ctr., Houston, TX
[4] The University of Texas MD Anderson Cancer Center, Houston, TX

**Introduction:** Relapsed/refractory acute myeloid leukemia (rAML) remains a significant challenge, with low response to therapy and poor long-term survival. Treatments focusing on achieving a response and, in eligible patients (pts), proceeding with an allogeneic stem cell transplantation (alloSCT) offer the best prospect for improved survival. CPX-351 is a liposomal fixed-ratio formulation of cytarabine and daunorubicin, which has demonstrated higher response rates and reduced early mortality in some subsets of AML and has also been shown to be active in rAML. The BCL2 inhibitor venetoclax (Ven) has demonstrated efficacy in AML in combination with other agents, such as hypomethylating agents, low dose cytarabine, and intensive chemotherapy. We conducted a Phase Ib/II dose-finding study to evaluate the combination of CPX-351 with Ven in AML. Herein we present the results of CPX-351 plus Ven in the cohort of rAML pts treated on study (NCT03629171).
**Methods:** The study was designed with a safety lead-in phase to establish the safe dose and schedule in R/R AML, followed by 2 expansion cohorts to explore efficacy in (1) R/R AML and (2) frontline AML. Prior Ven use was allowed for pts with R/R AML. The dose of CPX-351 was fixed : daunorubicin 44 mg/m2 and cytarabine 100 mg/m2 IV on days 1, 3 and 5 of induction, and daunorubicin 29 mg/m2 + cytarabine 65 mg/m IV on days 1 and 3 during consolidation. The starting effective dose of Ven was 300mg (at the -1 dose level) on D2-21 for the safety lead-in cohort with appropriate dose adjustment for concomitant CYP3A inhibitors. First, interruption of Ven after D14 was implemented if a D14 bone marrow was hypocellular and without evidence of leukemia. However, a second de-escalation was required (-2 dose level) with Ven given on day 2-8 of each cycle, and daunorubicin dose reduced to 22 mg/m2 during consolidation. This was found to be the recommended phase 2 dose.
**Results:** Between 11/2018 to 1/2022, 33 pts were enrolled. The median age was 53 yrs (range, 26-72) and 61% were female. Diploid karyotype was present in 7 pts (21%), core binding factor rearrangements in 2 (6%), *MECOM* rearrangement in 2 (6%) and 13 (39%) had a complex karyotype. The most frequent mutations were *DNMT3A* (37%), *TP53* (21%) and *NRAS* (21%). 8 (24%) pts had secondary AML including 4 (12%) with prior HMA exposure; the median number of prior lines of myeloid-directed therapies was 1 (1-7), including 58% of them with a previous exposure to Ven.
Pts received a median of 1 cycle (1-4), and the median number of cycles to first response was 1 (1-2). The ORR was 45% (15/33), with 5 patient (15%) achieving CR, 8 (24%) achieving CRi and 2 (6%) achieving MLFS. The ORR was higher in those pts with only one prior line of therapy (59%) compared to those with 2 or more previous therapies (31%). The ORR for pts with prior exposure to Ven was 37% (7/19) vs 57% (8/14) for those not previously exposed to Ven (p=0.4). The 4- and 8-week mortality was 9 and 21%. 9/15 pts (60%) underwent alloSCT including 14 with CR/CRi/MLFS and 1 pt with an aplastic bone marrow insufficient for response assessment.
The most frequent grade 3 or more adverse events were infections (45%, 30% of them pulmonary), febrile neutropenia (24%), and mucositis/stomatitis (6%). Three deaths occurred on study (2 due to sepsis and 1 due to cardiac arrest), all after one cycle of therapy. Other grade 3-4 events registered included rash (6%), cerebrovascular accident (6%), and intracranial hemorrhage (3%).
After a median follow-up time of 20.7 months, the OS at 12 and 24 months was 34% and 25%, respectively. The median OS was 6.4 months. The EFS at 12 and 24 months was 26% and 19%, respectively. The median EFS was 2.8 months. For those who

achieved response, the 2-year cumulative incidence of relapse and death without relapse were 41% and 28%, respectively. For those who underwent alloSCT, the median OS after alloSCT was 24 months, with 4 deaths after alloSCT, all following disease relapse.

**Conclusion:** In this phase Ib dose escalation study, standard dose CPX-351 combined with 7 days of Ven was found to safe and tolerable in pts with rAML. The combination produced encouraging response rates in a poor risk population, including those with prior Ven treatment, allowing a significant proportion to undergo allo-SCT and extended survival. The RP2D is being studied in pts with newly diagnosed and less heavily pretreated AML.

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Figure 1

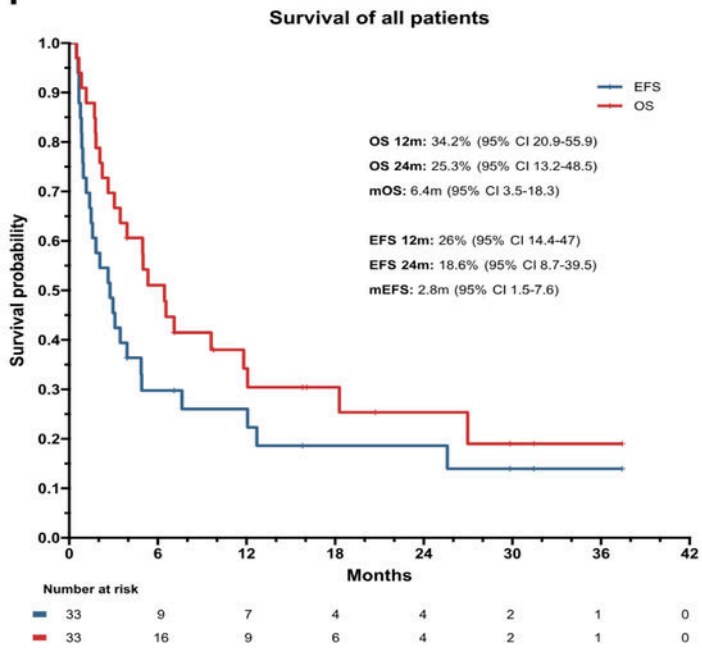


Figure 2

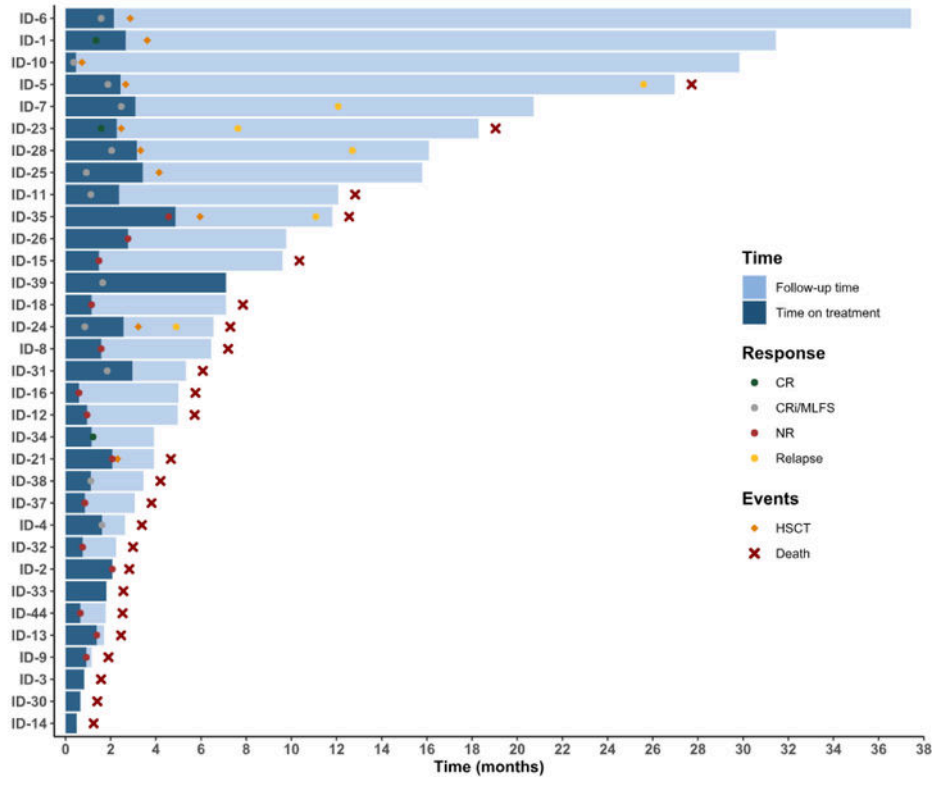


**Figure 1**

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