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POSTER ABSTRACTS

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

Phase 2 Study of CPX-351 in Combination with Venetoclax in Patients with Newly Diagnosed, High Risk Acute Myeloid Leukemia

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Background

CPX-351 is a nanoscale liposome of a fixed 5:1 molar ratio of cytarabine and daunorubicin which has improved survival of secondary acute myeloid leukemia (AML) [1]. Venetoclax (ven) is a BCL2 inhibitor which, in combination with azacitidine or cytarabine, has become the standard of care for elderly AML. Ven has shown synergism with chemotherapy, with high complete remission (CR) rates in newly diagnosed (ND) and relapsed / refractory (RR) AML [2]. In this study, we aim to assess the efficacy and safety of CPX-351 and ven (CPX-ven) in RR and ND AML.

Methods

This was a phase 2 study with a lead-in safety phase. Enrolment was allowed if the blasts were ≥10%. Patients (pts) age ≥18 with RR AML were eligible for the safety lead-in phase (LIP) or arm A. Arm B enrolled pts age 18 - 69 with ND AML. Other inclusion criteria included adequate liver, renal and cardiac function, and ECOG performance status ≤2. Pts with CNS involvement or prior CPX-351 were excluded. The recommend phase 2 dose was CPX-351 (daunorubicin 44 mg/m ^{2} and cytarabine 100 mg/m ^{2} IV on D1, 3 and 5 of induction, and daunorubicin 22 mg/m2 IV on D1 and 3 during consolidation) combined with ven on D2-8 of each cycle. Ven was dosed at 300mg daily and reduced to 150mg or 50mg daily for pts on a moderate or strong CYP3A inhibitors, respectively.

The primary outcome measure was complete remission (CR) or CR with incomplete count recovery (CRi). Here, we report the outcomes of arm B including pts with ND AML.

Results

14 pts were enrolled on arm B. One pt withdrew and one was too early in treatment, therefore 12 were evaluable. Baseline characteristics are shown in Table 1. The median age was 59.5 years (range, 44 - 69); Four (33.3%) were female. All 12 (100%) pts were classified as adverse risk per the 2017 European Leukemia Net Guidelines. Two (16.7%) pts had treatment for a prior non-myeloid malignancy (therapy-related AML). Eight (66.7%) had an antecedent haematological disorder (secondary AML), of whom seven had treatment (median 1 line, range 1 - 2). Four (33.3%) pts had a complex karyotype, of whom three harbored a *TP53* mutation.

Nine (75.0%) pts achieved a response, including four CR (33.3%), five CRi (41.6%), and one induction mortality (8.3%) prior to disease assessment. 3/4 (75.0%) pts with complex cytogenetics (including 2/3 (66.7%) with a *TP53* mutation) achieved a CR/CRi. Of the secondary AML pts with an evaluable response, 5/7 (71.4%) achieved a CR/CRi. Of the nine pts achieving CR/CRi, five (55.5%) were negative for minimal residual disease (MRD) by flow cytometry. The median number of cycles to CR/CRi was one (range 1 - 2). The median overall survival (OS) was 12.9 months (95% CI, 3.1 - not reached, NR, Figure 1). The median relapse-free survival (RFS) was 8.7 months (95% CI, 3.1 -NR). 7/9 (77.8%) of responding pts underwent an allogeneic stem cell transplant (SCT) after attaining CR/CRi.

There were 90 adverse events (AE) in 10 (83.3%) pts. 80 (88.9%) were grade 1 or 2, 10 (11.1%) were grade ≥3. The most common AE was gastrointestinal with seven (7.8%) occurrences. Four (33.3%) pts developed grade ≥3 infections; of these, one (8.3%) died. The cause of death was neutropenic septic shock due to pneumonia.

Conclusion

CPX-ven is a feasible option for remission induction in pts with high-risk, newly diagnosed AML. The combination produced high rates of response and MRD negativity in a cohort of pts with adverse risk features, including pts with adverse karyotype and AML following prior HMA-based treatment, allowing them to proceed with SCT. Toxicities are as expected for an intensive chemotherapy regimen. Further studies are needed to confirm the efficacy of this combination.

References

1. Lancet JE et al. *JCO* 2018; 36:2684
2. DiNardo CD et al. *JCO*2021; 39:2768

Disclosures DiNardo: *Notable Labs:* Honoraria; *ImmuniOnc:* Honoraria; *Fogham:* Honoraria; *Astellas:* Honoraria; *AbbVie/Genentech:* Honoraria; *Servier:* Honoraria; *Takeda:* Honoraria; *Novartis:* Honoraria; *BMS:* Honoraria; *Schrödinger:* Consultancy. **Chien:** *Rigel Pharmaceuticals:* Consultancy; *AbbVie:* Consultancy. **Masarova:** *MorphoSys US:* Membership on an entity's Board of Directors or advisory committees. **Daver:** *AbbVie:* Consultancy, Research Funding; *Glycomimetics:* Research Funding; *Trillium:* Consultancy, Research Funding; *Celgene:* Consultancy; *Trovagene:* Research Funding; *Hanmi:* Research Funding; *Gilead:* Consultancy, Research Funding; *Servier:* Consultancy, Research Funding; *Genentech:* Consultancy, Research Funding; *Shattuck Labs:* Consultancy; *Agios:* Consultancy; *Novartis:* Consultancy; *AROG:* Consultancy; *FATE:* Research Funding; *Syndax:* Consultancy; *Novimmune:* Research Funding; *Jazz:* Consultancy; *Astellas:* Consultancy, Research Funding; *Amgen:* Consultancy, Research Funding; *ImmunoGen:* Consultancy, Research Funding; *Pfizer:* Consultancy, Research Funding; *Kite, a Gilead company:* Consultancy, Research Funding; *Daiichi Sankyo:* Consultancy, Research Funding; *Bristol-Myers Squibb:* Consultancy, Research Funding; *Kronos Bio:* Research Funding. **Montalban-Bravo:** *Takeda:* Research Funding; *Rigel:* Research Funding. **Garcia-Manero:** *AbbVie:* Research Funding; *Bristol Myers Squibb:* Other: Medical writing support, Research Funding; *Genentech:* Research Funding. **Issa:** *Merck:* Research Funding; *Kura Oncology:* Consultancy, Research Funding; *Celgene:* Research Funding; *Syndax:* Research Funding; *NuProbe:* Consultancy; *Novartis:* Consultancy, Research Funding. **Short:** *Pfizer:* Consultancy; *Novartis:* Consultancy; *Astellas:* Research Funding; *Amgen:* Honoraria; *Takeda:* Consultancy, Research Funding; *Stemline therapeutics:* Research Funding; *AstraZeneca:* Consultancy. **Ravandi:** *Celgene/BMS:* Consultancy, Honoraria, Research Funding; *Astex/taiho:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Prelude:* Research Funding; *Abbvie:* Consultancy, Honoraria, Research Funding; *Amgen:* Honoraria, Research Funding; *Syros:* Consultancy, Honoraria, Research Funding; *Biomea fusion:* Honoraria, Research Funding; *Xencor:* Research Funding; *Astellas:* Consultancy, Honoraria, Research Funding. **Kadia:** *Genentech:* Consultancy, Research Funding; *Pfizer:* Consultancy, Research Funding; *Liberum:* Consultancy; *Novartis:* Consultancy; *SELLAS Life Sciences Group:* Research Funding; *Amgen, Inc.:* Research Funding; *Iterion:* Research Funding; *Cyclacel:* Research Funding; *Delta-Fly Pharma, Inc.:* Research Funding; *GenFleet Therapeutics:* Research Funding; *Hikma Pharmaceuticals:* Speakers Bureau; *Sanofi-Aventis:* Consultancy; *Ascentage Pharma Group:* Research Funding; *Regeneron Pharmaceuticals:* Research Funding; *Astellas Pharma Global Development:* Research Funding; *AbbVie, Amgen, Inc, Ascentage Pharma Group, Astellas Pharma Global Development, Astex, AstraZeneca, BMS, Celgene, Cellenkos Inc, Cyclacel, Delta-Fly Pharma, Inc, Genentech, Inc., Genfleet, Glycomimetics, Iterion, Janssen Research and Development:* Research Funding; *Janssen Research and Development:* Research Funding; *AstraZeneca:* Research Funding; *Pulmotect, Inc.:* Consultancy, Research Funding; *Cure:* Speakers Bureau; *Glycomimetics:* Research Funding; *Daiichi Sankyo, Genentech, Inc., Genzyme, Jazz Pharmaceuticals, Liberum, Novartis, Pfizer, PinotBio, Inc, Pulmotect, Inc, Sanofi-Aventis, Servier:* Consultancy; *Celgene:* Research Funding; *Cellenkos Inc.:* Research Funding; *Jazz Pharmaceuticals, Pfizer, Pulmotect, Inc, Regeneron Pharmaceuticals, SELLAS Life Sciences Group:* Research Funding; *Genzyme:* Honoraria; *Biologix, Cure, Hikma Pharmaceuticals:* Speakers Bureau; *Servier:* Consultancy; *Agios:* Consultancy; *Pinotb-Bio:* Consultancy; *BMS:* Consultancy, Research Funding; *Astex:* Honoraria.

Table 1

Age, median (range)	60 (44 – 69)	
Gender, n (%)	Male	8 (66.7%)
Ethnicity, n (%)	African	1 (8.3%)
	Other	1 (8.3%)
	White	10 (83.3%)
ECOG, n (%)	1	11 (91.7%)
	2	1 (8.3%)
Prior Non-Myeloid Malignancy, n (%)	4 (33.3%)	
Prior Chemo for Non-Myeloid Malignancy, n (%)	2 (16.7%)	
Prior Haematological Disease, n (%)	8 (66.7%)	
Number of Prior Treatment Lines for Haem Disease, n (%)	0	5 (41.7%)
	1	6 (50.0%)
	2	1 (8.3%)
ELN Category, n (%)	Adverse	12 (100.0%)
Complex Cytogenetics, n (%)	4 (33.3%)	
***TP53* Mutation**, n (%)	3 (25.0%)	
***ASXL1* Mutation**, n (%)	7 (58.3%)	
***RUNX1* Mutation**, n (%)	3 (25.0%)	
***DDX41* Mutation**, n (%)	2 (16.7%)	
Other MDS Mutations, n (%)	5 (41.7%)	

Figure 1: Overall Survival

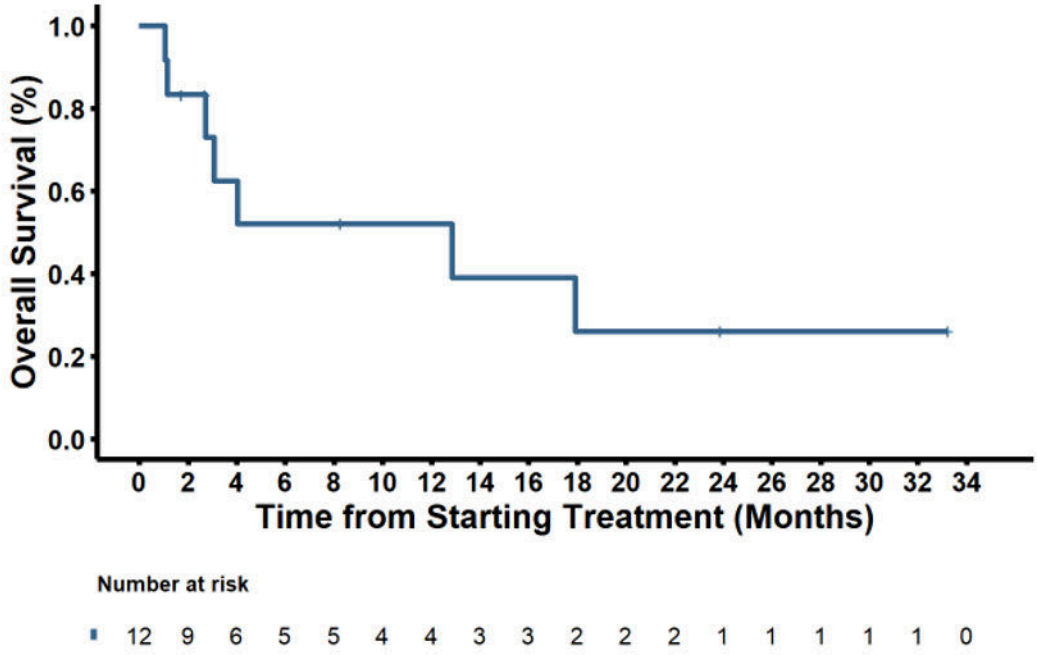

Figure 1

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