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

Real World Outcomes of CPX-351 Compared to Traditional Chemotherapy with Cytarabine Consolidation for Treatment of Secondary Acute Myeloid Leukemia

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Introduction: Outcomes in patients with secondary AML (sAML) are inferior to those with de novo AML which has led investigators to seek alternatives to traditional treatment. Liposomal daunorubicin and cytarabine, or CPX-351, for the treatment of sAML has shown superior complete remission/complete remission with incomplete count recovery (CR/CRi), event-free survival (EFS), and overall survival (OS) compared to the traditional non-liposomal formulations of daunorubicin and cytarabine ("7+3"). However, this agent was originally studied in combination with a suboptimal consolidation regimen which did not include standard of care high dose cytarabine (HiDAC). This is often cited as a limitation of the study and may have contributed to the significantly lower response rates reported when compared to historical data. Here we present a real-world comparison of the efficacy and safety of patients with sAML receiving CPX-351 versus traditional 7+3 with HiDAC consolidation.
Methods: Patients were at least 18 years of age with sAML, defined as: t-AML, AML-with Myelodysplasia-Related Changes (MRC), or AML with a history of chronic myelomonocytic leukemia (CMML). Patients were included if they had received induction (and consolidation, if applicable) with CPX-351 or induction with 7+3 (daunorubicin 60 mg/m ^{2} for 3 days and cytarabine 100 mg/m ^{2} for 7 days), followed by consolidation with cytarabine (≥1000 mg/m ^{2} x 6 doses). Nominal data were analyzed using chi squared tests or Fisher's exact tests. Continuous data were analyzed using the Mann-Whitney U test. A Kaplan Meier estimator was used for survival outcomes.
Results: Overall, 58 patients with sAML were included, with 36 (62%) receiving CPX-351 and 22 (38%) receiving 7+3 followed by cytarabine-based consolidation between April 2013 and June 2022. Patients in the CPX-351 were older (67.5 vs 62 years, p=0.04) and had a higher prevalence of poor-risk cytogenetics (p=0.22). Other baseline characteristics were similar (Table 1). The rate of CR/CRi following induction was significantly higher in patients who received 7+3-based induction vs patients who received CPX-351 (81.8% vs 44.4%, p=0.01). Twenty-five percent of patients achieved CR/CRi in the CPX-351 arm with one induction cycle, compared to 95.5% in the 7+3 group. Median progression-free survival (PFS) was 3 vs 6.1 months (p=0.67) and median OS was 18.3 vs 9.3 months (p=0.73) in the CPX-351 and 7+3 cohorts, respectively (Figure 1). Thirty-nine percent of patients in the 7+3 cohort proceeded to allogeneic stem cell transplant compared to 81% in the CPX-351 cohort, however median OS in patients who underwent transplant was similar between the two cohorts (16.8 vs 15.8 months). Median OS was longer in the CPX-351 cohort however this was not statistically significant (Figure 1).
Rates of both febrile neutropenia (94.3% vs 95.5%; P>0.99) and confirmed infections (54.3% vs 50%) were similar amongst those treated with CPX-351 and 7+3. Bacteremia and pneumonia were the most common infections in both cohorts. Median duration of neutropenia was significantly longer in the CPX-351 cohort (43 days vs. 27 days, p=0.002) with no major difference in duration of thrombocytopenia. In the 7+3 cohort, 11 deaths were directly attributed to progression, while 5 were associated with infection. In the CPX-351 cohort, 6 deaths were directly attributed to progression, while 8 were attributed to infection. At day 60, two deaths were observed in the CPX-351 cohort and there were no deaths in the 7+3 cohort.
Conclusion: These findings suggest use of traditional 7+3 induction followed by HiDAC consolidation may be an alternative to CPX-351 for patients with sAML. Although median PFS was longer in the 7+3 cohort, this did not translate into longer median OS, likely due to the low rate of patients proceeding to transplant. Similar rates of overall survival in patients undergoing allogeneic stem cell transplantation support the hypothesis that transplant should be the goal for most patients with sAML. The retrospective nature of the study may limit broader application of this data.

Disclosures Baratam: *Rigel:* Consultancy; *Protagnoist Pharma:* Consultancy; *ONO Pharma:* Consultancy; *KITE:* Consultancy.

Table 1. Patient/Treatment characteristics and Efficacy Outcomes

	CPX-351 n=36	7+3 n=22	P-value
Characteristics	**Median (range) or n, (%)**		
Age	67.5 (31-77)	62 (20-74)	0.04
Male sex	28 (78)	15 (68)	0.42
Race, non-Hispanic Black vs not	5 (13.9)	5 (22.7)	0.52
ECOG PS 0 or 1	31 (86)	20 (91)	0.86
Poor risk cytogenetics	22 (61.1)	10 (45.5)	0.22
FLT3 mutation positive	5 (13.8)	3 (13.6)	0.98
TP53 mutation positive	8 (22.2)	5 (22.7)	0.96
Consolidation regimen			
CPX-351	7/16 (44.8)	0	
HiDAC	1/16 (6.3)	16/18 (88.9)	0.03
HMA	3/16 (18.8)	0	
None	5/16 (31.3)	2/18 (11.1)	
Efficacy Outcomes	**Median (range) or n, (%)**		
CR/CRi	16 (44.4)	18 (81.8)	0.01
HSCT following CR/CRi	13/16 (81.3)	7/18 (38.9)	0.26
Median OS (months), in patients who proceeded to HSCT	15.8 (3.4-60)	16.8 (4.3-85)	
Median OS, months	18.3 (11.4-25.3)	9.3 (2.3-83.7)	0.73
Median PFS, months	3.0 (0.52-59.3)	6.1 (0.5-75.6)	0.67

Figure 1. Overall Survival Between Groups

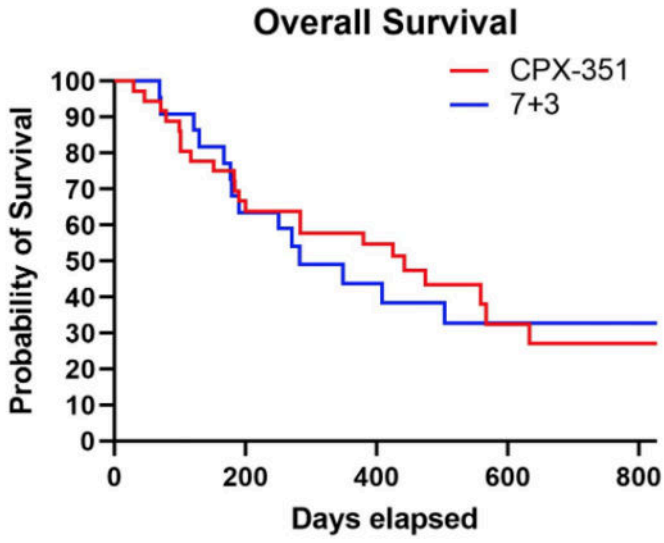

Figure 1

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