CPX-351 in Patients with Newly Diagnosed post myeloproliferative neoplasms acute myeloid leukemia

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INTRODUCTION

- Progression of myeloproliferative neoplasms (MPNs) including polycythemia Vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF) to acute myeloid leukemia (post MPN AML) is associated with a poor prognosis.
- Studies evaluating intensive chemotherapy showed response rates ranging between 40% and 50% and a median event-free survival (EFS) of 3-4 months.
- CPX-351 is a new formulation of cytarabine and daunorubicin encapsulated at a fixed 5:1 molar-ratio in liposomes that exploits molar ratio–dependent drug-drug synergy to enhance antileukemic efficacy.
- Induction therapy with CPX-351 is associated with a 47.7% response rate and significantly improved overall survival (OS) when compared to standard ICT (“7+3”) in older patients with newly diagnosed secondary AML (1). However, patients with post MPN AML were not eligible in that trial.
- We report here the preliminary results of a prospective trial evaluating the effects of CPX351 in this difficult-to-treat patient population.

METHOD

- We designed an open label multicenter phase II non-randomized study to evaluate CPX-351 in post MPN AML.
- Patients received one to two induction cycles with CPX-351 100 U/m2 on days 1, 3, and 5. Patients in CR/CRi after induction cycle(s) received up to 2 courses of consolidation therapy with CPX-351 65 U/m2 on days 1 and 3 (or on day 1 only in case of unacceptable toxicity).
- The primary objective was to evaluate the complete remission rate (cCR, including CR and CR with incomplete hematological recovery, CRi) after one or two induction cycles with CPX-351.

RESULTS

Table 1. Patient and disease characteristics by treatment type.

		(N=40)
Sex (male)		19 (47.5)
Age (median, range)		63 (40 - 75)
Prior MPN		
	ET	17 (42.5)
	PV	3 (7.5)
	PMF	12 (30)
	secondary MF (post TE)	5 (12.5)
	secondary MF (post PV)	3 (7.5)
Time between MPN diagnosis and transformation (months)		61 (0-425)
Haemoglobin		8.7 (6.2-15)
Platelets count		96 (7-771)
Leukocytes count		10.2 (0.8-77)
Neutrophils count		2.2 (0-41.6)
Peripheral Blasts count (%)		1.6 (0-40)
Bone marrow blasts (%)		40 (8-96)
Karyotype (ELN 2017)		
	adverse	20 (51.3)
	intermediate	9 (23.1)
	favorable	3 (7.7)

Key Findings:

- **cCR (CR/CRi) was observed in 16 patients (40%, 12 CR and 4 CRi) and PR was achieved in 2 patients (7.5%).**
- 2 patients were not evaluable (1 died during induction 1 because of multiorgan failure and 1 because of short follow up).
- 10 patients (25%) received a consolidation.
- **8 patients of the 18 responders (47%) transitioned to an allogeneic stem cell transplantation**
- With a median FU of 5 months, **median OS was 8.5 months.**
- Time for neutrophil count recovery (>0.5G/L) was 26 days (0-41) after the first induction cycle and mean time for platelet recovery (>50G/L) was 27 days (14-54, data available for 29 patients).

Table 2. Main severe adverse events (grade 3-4)

	total	grade 3	grade 4	grade 5
Infections	15	11	1	3
White blood decreased	15	3	12	0
thrombopenia	13	3	10	0
anemia	9	9	0	0
febrile neutropenia	7	7	0	0
gastrointestinal disorder	3	3	0	0
hypokaliemia	4	4	0	0
cardiac	3	2	1	0

Table 3. Main adverse events related to CPX-351

	total	grade 1	grade 2	grade 3	grade 4	grade 5
aplasia/white blood decreased	17	0	2	6	9	0
thrombopenia	13	0	0	3	10	0
Anemia	8	0	2	6	0	0
infection	7	1	0	4	1	1
gastrointestinal disorder	7	1	3	3	0	0
Febrile neutropenia	7	0	2	5	0	0
Toxiderma/erythema	4	2	1	1	0	0
Liver enzyme increased	3	0	1	2	0	0
multiorgan failure	1	0	0	0	0	1

Figure 1: Overall survival

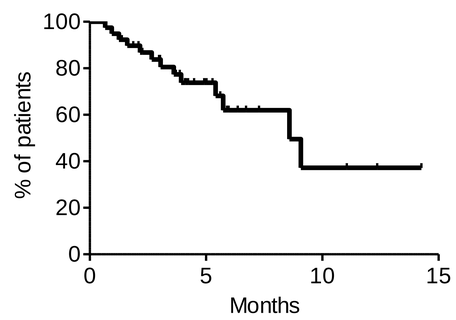
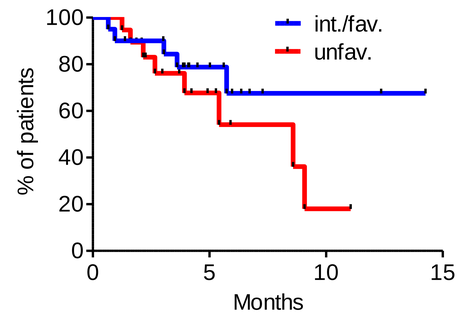


Figure 2: Overall survival by cytogenetics



CONCLUSIONS

- CPX-351 showed 40% response rates, which is comparable to 7+3 rates in this high-risk population with poor cytogenetics risk
- Toxicity profile is manageable in patients for whom increased heme toxicity is expected with conventional induction
- Allogeneic stem cell transplantation rate is almost 50% and seems better than with conventional chemotherapy

REFERENCES

1: Lancet JE, et al., CPX-351 (cytarabine and daunorubicin) Liposome for Injection Versus Conventional Cytarabine Plus Daunorubicin in Older Patients With Newly Diagnosed Secondary Acute Myeloid Leukemia. J Clin Oncol. 2018

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