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POSTER ABSTRACTS

616.ACUTE MYELOID LEUKEMIAS: INVESTIGATIONAL THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

CPX-351 in Patients with Newly Diagnosed Post Myeloproliferative Neoplasms Acute Myeloid Leukemia

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Background

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 (Vyxeos) 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 (sAML) (Lancet, JCO 2018). 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.

Methods

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 (including CR and CR with incomplete hematological recovery, CRi) after one or two induction cycles with CPX-351.

Results

In this interim analysis, we present the results for the first 29 patients (14 males and 15 females). The median age was 67 (50-78). Prior MPN before leukemic transformation was ET in 13 (44.8%), PV in 1 (3.4%), PMF in 9 (31%), post ET myelofibrosis in 4 (13.8%) and post PV myelofibrosis in 2 (6.9%) patients. Median hemoglobin, platelet count and white blood cell count were 8.7g/dL (6.2-14.7), 9G/L (7-771) and 6 G/L (1.5-77.3), respectively. BM involvement showed a median of 40% blasts (8-96%). Cytogenetics was favorable, intermediate, unfavorable, or missing in 1 (3.4%), 9 (31%), 17 (58.6%), 2 (6.9%) of cases. Twelve patients (41.3%) achieved a complete response (CR) or a complete response with incomplete hematologic recovery (CRi) after 1 or 2 induction cycles; two patients (6.9%) had a partial response, and 15 patients (51.7%) failed. Minimal residual disease analysis for responding patients is on-going. At the time of analysis, 5 patients transitioned to an allogenic stem cell transplantation. Time for neutrophil count recovery (>0.5G/L) was 26 days (0-41) after the first induction cycle. Mean time for platelet recovery (>50G/L) was 27 days (14-54). Main severe adverse events (grade 3-4) consisted in infections (8, 27.6%), cardiac toxicities (2 tamponades, 6.9%), and expected hematological toxicities. We registered 7 deaths (6 associated with treatment failure and 1 occurring on day-56 of induction-1 related to a fungal infection). With a median follow up of 3.5 months, estimated OS and EFS were 7.1 months.

Conclusion

CPX-351 showed encouraging response rates and survival with a manageable safety profile. The study continues to accrue patients and results of the entire planned study group (42 patients) will be presented.

Disclosures Mathilde: *Clinigen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Incyte:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Servier:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Research Funding; *Pfizer:* Other: Support for attending meetings. **Pigneux:** *Roche:* Research Funding; *Servier:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings, Research Funding; *Abbvie:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Support for attending meetings; *Gilead:* Honoraria; *Jazz Pharmaceuticals:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Honoraria; *BMS:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Astellas:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Pfizer:* Membership on an entity's Board of Directors or advisory committees. **Bertoli:** *Abbvie:* Honoraria, Other: Travel; *Servier:* Honoraria; *Jazz Pharmaceuticals:* Honoraria, Other: Travel; *BMS-Celgene:* Honoraria; *Astellas:* Honoraria; *Novartis:* Honoraria. **Meunier:** *Pfizer, Novartis, Alexion:* Honoraria. **Heiblig:** *Jazz Pharmaceuticals:* Honoraria; *AbbVie:* Honoraria; *Pfizer Inc.:* Honoraria; *Astellas:* Honoraria; *Servier:* Honoraria. **Cluzeau:** *Incyte:* Speakers Bureau; *Servier:* Consultancy, Speakers Bureau; *Keros:* Speakers Bureau; *Syros:* Speakers Bureau; *Jazz Pharma:* Consultancy, Speakers Bureau; *Abbvie:* Consultancy, Speakers Bureau; *Novartis:* Consultancy, Speakers Bureau; *BMS:* Consultancy, Speakers Bureau. **Jourdan:** *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Novartis:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Abbvie:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *GSK:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Recher:** *Jazz Pharmaceuticals:* Other: Personal fees, Research Funding; *Novartis:* Other: Personal fees; *Astellas:* Other: Personal fees; *BMS:* Other: Personal fees, Research Funding; *Amgen:* Research Funding; *Abbvie:* Honoraria; *Servier:* Other: Personal fees; *MaatPharma:* Research Funding; *IQVIA:* Research Funding; *Takeda:* Other: Personal fees.

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