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POSTER ABSTRACTS

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

Daunorubicin/Cytarabine Liposome +/- Gemtuzumab Ozogamicin for Adult Patients with Newly Diagnosed, Low-Intermediate Risk, FLT3-Wild Type, AML: A Pilot Study

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Introduction: Liposomal-encapsulated cytarabine and daunorubicin (CPX-351 or Vyxeos) has been approved by the Food and Drug Administration (FDA) for use in the treatment of newly diagnosed therapy-related AML (tAML) and AML with myelodysplasia-related changes (AML-MRCs). This was based on results of a phase III study conducted in patients with secondary AML (Lancet JE et al. JCO 2018). Despite data that highlighted the advantage of CPX-351 for sAML, it is intuitively likely that this powerful drug is also suitable for non-sAML. The mechanism of action is applicable for every AML. The aim of this study is to evaluate the role of CPX-351 for patients with *de novo* low/ intermediate risk, FLT3-negative AML. While a definitive phase III study is planned, herein is described the pilot forerunner study.
Methods: This pilot multi-center study is planned to recruit 20 patients, ages 18-70 years, with low-intermediate risk FLT3-negative AML. Induction therapy is with CPX-351 on days 1,3,5. One dose of gemtuzumab ozogamicin (GO) can be added on day 1, at the discretion of the treating physician. Re-induction with CPX-351 on day 1,3 is permitted based on the results of day 14 bone marrow examination and at the discretion of the treating physician. Post-induction therapy followed the practice of the participating institutions. The primary endpoint was response rate. A key secondary endpoint was MRD evaluation, after induction, by multi-parameter flow cytometry with a threshold of 0.1%. As the initial genetic evaluation at diagnosis takes time, it was assumed upfront that an adverse risk may only become apparent in some patients with AML after initiation of therapy. Such subjects would ultimately be excluded from the study analysis.
Results: Between August 2022 and June 2023, 20 patients were recruited and received the CPX-351 but 4 were finally diagnosed as high-risk and were excluded. The median age of the 15 patients that were included in the analysis was 56 years (range: 21-70), 53.3% were females. Eight of 15 patients (53.3%) were categorized as intermediate risk, according to the 2016 ELN guidelines, and 46.6% as favorable. Four patients (26.6%) received GO in addition to the CPX-351. None of the patients needed to receive re-induction. 100% of the patients achieved CR. Five of 13 evaluable patients (38.4%) achieved MRD-negativity post induction. No unfamiliar or severe adverse events were reported, even among patients who received GO. One patient died from sepsis after hematopoietic stem cell transplant. The median time from day 1 of treatment to neu-

trophil recovery (ANC≥500/μL) and platelet recovery (≥50,000/μL) was 29 and 24 days, respectively, for the entire cohort and 27 and 24 days, respectively, for those who also received GO.

Discussion: The hallmark of this study is reflected by the focus on patients with the low and intermediate-risk AML and not tAML and AML-MRCs, as was approved by the FDA. It includes also young patients (≥18 years), and not only those≥ 60 years. In addition, the CPX-351 was only given as induction therapy (with an option for re-induction) but not after achieving CR. The combination of CPX-351 with GO, although not previously reported, was based on current practice of adding GO to standard induction in some patients, allowing for a realistic future true comparator with standard 7+3 induction. In addition, MRD assessment post induction with CPX-351 has not been previously reported. The CR rate was 100% and the MRD results were a basis for subsequent studies. Finally, this is a pilot study that precedes a definitive planned phase III study that will compare standard induction with 7+3 versus CPX-351, with post-induction MRD monitoring and GO optional in both arms. Such a study may ultimately lead to a paradigm shift in the initial induction therapy of non-adverse risk patients with AML.

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OffLabel Disclosure: CPX-351 for adult patients with newly diagnosed, low-intermediate risk, FLT3-wild type, AML

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