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

Preliminary Results from a Phase 1/2 Study of Liposomal Annamycin (L-ANN) in Combination with Cytarabin for the Treatment of Patients with Acute Myeloid Leukemia (AML) That Is Refractory to or Relapsed (r/r) after Induction Therapy

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Background: Anthracylines still remain the backbone for the treatment of patients with acute myeloid leukemias (e.g., "7 + 3"), however, the dose escalation is impeded by a significant cardiotoxicity of these compounds. The design of the novel liposomal L-annamycin (L-ANN) was the replacement of a basic amine at the C-3' position with a hydroxy group, which was shown to significantly reduce cardiotoxicity when compared with doxorubicin. Moreover, this modification not only decreased cardiotoxicity, but also led to increased activity against mdr-1 tumors. In addition, L-ANN was found to be a TOPO-II poison, and it has been hypothesized that the drug may not alter TOPO-IIβ, an isoform which is known to be a key pathway involved in anthracycline-induced cardiotoxicity. However, this hypothesis has not yet been confirmed experimentally. L-ANN as a monotherapy has been evaluated in r/r AML patients and demonstrated an ORR of 80% (240 mg, administered on three consecutive days, MB-105, NCT03388749, Gil et al. 2023) with no sign of cardiotoxicity noted in any patient. L-ANN is currently being evaluated in a phase 1b/2 study in combination with cytarabine for the treatment of AML (MB-106; NCT05319587).
Study Design: MB-106 (NCT05319587) is aphase 1/2, multi-center, open-label, dose-escalation study to evaluate safety, tolerability, pharmacokinetics (PK) and efficacy of L-ANN in combination with cytarabine in adult r/r AML patients after induction therapy. Approximately 63 subjects will be enrolled, including up to 42 in the dose escalation phase, and up to 21 in the phase 2 expansion at the established recommended phase 2 dose (RP2D). The dose escalation phase of the study has explored 2 dose levels of L-ANN with a starting dose of 190 mg/m ^{2}/day and 230 mg/m ^{2}/day for 3 consecutive days. All patients will also receive cytarabine 2.0 g/m ^{2}/day for 5 consecutive days starting on the first day of L-ANN treatment. The primary objectives of the phase 1b portion of the study are to evaluate the safety and identify the RP2D of L-ANN in combination with a standard regimen of cytarabine. Routine safety monitoring including ECHOs, ECGs, GLS measurements, cardiac biomarkers, laboratory evaluations, and bone marrow assessments (BMA) will be performed. Secondary objectives include CR/CRi and mOS. Dose escalation was halted after the 230 mg/m ^{2}/day cohort due to the safety and efficacy data identifying this as the RP2D.
Results: To date, 6 patients have completed therapy cohort 1 (n=3) and cohort 2 (230 mg/m ^{2}/day, n=3) with no dose limiting toxicities (DLTs) noted. Prescheduled interim reviews of the data took place after completion of each dosing cohort. In the first cohort one patient achieved a CR following the first cycle of therapy which continued to exhibit durability at 5 months. In the second cohort one patient achieved a CRi and two patients showed progression. In light of the safety and efficacy data from this trial and the prior MB-105 trial, the current study has begun to expand enrollment of up to 21 additional patients at the 230 mg/m ^{2} L-ANN level to quantify efficacy.

Conclusion: Initial data suggested that L-ANN is safe and active in heavily pretreated r/r AML patients with no signs of cardiotoxicity. This study is currently being conducted in Europe across 5 sites in Poland and 3 in Italy. Results from the Phase 2 portion of this study will be presented at the meeting.

Disclosures No relevant conflicts of interest to declare.

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