



## The 65th ASH Annual Meeting Abstracts

## ONLINE PUBLICATION ONLY

**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 Cytarabine for the Treatment of Patients with Acute Myeloid Leukemia (AML) That Is Refractory to or Relapsed (r/r) after Induction Therapy**

Cristina Papayannidis, MD<sup>1</sup>, C Wadolowska<sup>2</sup>, Simona Sica<sup>3</sup>, Boguslaw Machlinski<sup>4</sup>, E Lech-Maranda<sup>5</sup>, Cindie Abbate<sup>6</sup>, Erikson Wasyl<sup>7</sup>, Paul Waymack<sup>8</sup>, Waldemar Priebe<sup>9</sup>, Wolfram Dempke, MDPhD<sup>10</sup>

<sup>1</sup>IRCCS Azienda Ospedaliero-Universitaria di Bologna Istituto di Ematologia "Seràgnoli", Bologna, Italy

<sup>2</sup>Uniwersytecki Centrum Kliniczne, Klinika Hematologii I Transplantologii, Gdansk, Poland, Gdansk, Poland

<sup>3</sup>Sezione di Ematologia, Dipartimento di Scienze Radiologiche ed Ematologiche, Università Cattolica del Sacro Cuore, Rome, Italy

<sup>4</sup>Pomeranian Medical University, Szczecin, POL

<sup>5</sup>Instytut Hematologii i Trasfuzjologii, Klinika Hematologii, Warszawa, Poland, Warsaw, Poland

<sup>6</sup>Moleculin Biotech, Inc, Houston, TX, USA, Moleculin Biotech, Houston

<sup>7</sup>Moleculin Inc, Houston

<sup>8</sup>Moleculin Biotech, Inc, Houston, TX, USA, Moleculin Inc, Houston

<sup>9</sup>MD Anderson Cancer Center, Houston

<sup>10</sup>Moleculin Biotech Inc, Unterageri, Switzerland

**Background:** Anthracyclines 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-II $\beta$ , 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 a phase 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<sup>2</sup>/day and 230 mg/m<sup>2</sup>/day for 3 consecutive days. All patients will also receive cytarabine 2.0 g/m<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup>/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<sup>2</sup> 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.

<https://doi.org/10.1182/blood-2023-184493>