**Background**

Treatment of elderly patients with acute myeloid leukemia (AML) remains a significant challenge. Poor outcomes result from morbidity and mortality due to intensive induction chemotherapy and short duration of remission when achieved. Although cytotoxic chemotherapy remains standard treatment for those who can tolerate such regimens, novel agents are needed to improve clinical outcomes.

**Methods**

A Phase 2 open-label trial evaluated GMI-1271 together with anthracycline-based induction and consolidation chemotherapy in this population of 25 elderly patients with newly diagnosed AML. Patient eligibility included: age ≥ 60 years, an ECOG score of 0-2, baseline WBC <40K/µL, adequate renal and hepatic function, and prior treatment of MDS was allowed. The first 3 patients were assessed for dose-limiting toxicity (DLT) and subsequently 4 additional patients were enrolled. DLT was defined as myelosuppression in the absence of disease or related Grade 3 non-hematologic toxicity beyond day 42. Induction chemotherapy consisted of infusional cytarabine and idarubicin (7+3); a second cycle of chemotherapy included granulocyte colony-stimulating factor (G-CSF) support. Consolidation chemotherapy was with IDAC (idarubicin, cytarabine, and cytosine arabinoside) and GMI-1271. Follow up was performed by data cutoff.

**Results**

**Demographics**

- **Overall**: N = 25
- **Patients with response**: N = 17
  - **CR + CRi + MLFS**: 20 (80)
  - **CR or CRi with first post induction or consolidation**: 25 (100)
  - **CR or CRi rate in this population (64%)**

**Toxicity**

- **Grade 3/4 safety summary**: Dose-limiting toxicity (DLT) was defined as myelosuppression in the absence of disease or related Grade 3 non-hematologic toxicity beyond day 42.
  - **Hematologic**: Neutropenia Grade 3-4: 11 (44) %; Neutropenia Grade 2: 3 (12) %; Neutropenic sepsis, at Day 3 and 23.
  - **Hematologic**: Anemia Grade 3-4: 11 (44) %; Anemia Grade 2: 3 (12) %; Pharyngeal mucositis 1 (6) %; Hypokalemia 3 (12) %; Hypocalcemia 2 (8) %.
  - **Non-hematologic**: Respiratory failure 2 (8) %; Cholecystitis 1 (4) %; Pancreatitis 2 (8) %; Hypoglycemia 1 (4) %; Thrombocytopenia 2 (8) %; Acute renal failure 3 (12) %; infections 2 (8) %.

**Biomarker Data**

- **Expression of E-selectin ligand on leukemic cell surface, as detected by flow cytometry**

**Subsequent Therapy and Interim Duration of Remission**

- **ALL-cause mortality is cumulative**
- **Deaths were from sepsis, at Day 3 and 23.**

**Conclusion**

E-selectin inhibition by GMI-1271 disrupts this interaction. The majority of patients had an E-selectin ligand on their leukemic blasts. In this study, we observed better CIR/CRI outcomes than expected for this population. This observation is likely contributed to selective E-selectin expression on leukemic blasts in patients with secondary disease.