**Repeted Dosing Of Anti-KIR (IPH2101) As Maintenance Therapy In Elderly Patients With Acute Myeloid Leukemia**

**Background**

- **Mechanism of Action:** anti-KIR mAbs block an inhibitory signal to NK cells

  **Without KIR expression**
  - NK cell activation is determined by the balance of activating (positive) and inhibitory (negative) receptor interactions
  - Target cells are able to evade immune surveillance through the interaction of KIR with self MHC class I and class I related molecules

  **With blocking this interaction, anti-KIR PH2101 facilitates the activation of NK cells in the presence of the target cell**

**Anti-KIR PH2101**

- IPH2101 is a 1st generation of anti-KIR antibody (now succeeded by PH2108)
  - Targets KIR2DL expressed by NK cells (but also targets 2DS-L)
  - Exhibits interactions with HLA-B and HLA-C5 antigens

**Preclinical in vivo Efficacy of Anti-KIR**

- Systemic blockade by IPH2101 in 1st generation of KIR antibodies resulted in long-term survival in SCD mice inoculated with tumor endogenous AML cells (7)

**Clinical Outcome**

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**Preclinical in vivo Efficacy of Anti-KIR**

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**Main Selection Criteria**

- **Age:** ≥ 60 years and ≥ 10 years
- **AML:** in CR or CRi after 1 or 2 cycles of induction chemotherapy & 1-6 cycles of consolidation
- **NPM1 mutation without FLT3-ITD:** Not identified molecular abnormality
- **HLA-C**
  - 71.0 ± 7.9 (64-75) months
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**Patient Characteristics**

- **Follow-up:**
  - 58 months
  - 60 months
  - 63 months

**Introduction**

- A previously reported phase 1 trial conducted in elderly patients with AML in CR indicated a survival benefit of 3 mg/kg PH2101. This study aimed to better define the tolerability and efficacy of PH2101 in elderly patients with AML in CR or CRi.

**Study Design**

- Open-label, multi-center extension to a phase 1 dose-escalation study in elderly patients with acute myeloid leukemia in complete remission (1). 2 cohorts of 6 patients enrolled sequentially at 1 mg/kg and 2 mg/kg every 4 weeks.

**Safety**

- **Related AEs:**
  - Grade 4 related AEs in 4 patients
  - Grade 3 related AEs in 5 (83%) patients
  - Grade 2 related AEs in 3 (50%) patients
  - Grade 1 related AEs in 5 (83%) patients

**Treatment**

- 2 patients received 6 cycles of PH2101 and the 5 others between 1 and 2 cycles
  - The 58-month-old patients received a dose of 1 mg/kg
  - 6 additional patients received 2 mg/kg

**Characteristics**

- **Number of consolidations:**
  - 1 mg/kg: 3 (60%), 3 (60%), 7 (53%)
  - 2 mg/kg: 6 (100%), 5 (83%), 11 (92%)
  - 3 (50%), 3 (50%), 8 (67%)
  - 5 (83%), 6 (100%), 11 (92%)

**KIR Occupancy by PH2101**

- **Safety**
  - **Related AEs:**
    - Grade 4 related AEs in 4 patients
    - Grade 3 related AEs in 5 (83%) patients
    - Grade 2 related AEs in 3 (50%) patients
    - Grade 1 related AEs in 5 (83%) patients

**Conclusion**

- **Clinical Outcome:**
  - Overall survival (OS) in 12 patients (1 patient in continuous CR for 16 months, 2 patients still alive after 60 and 63 months respectively)
  - In the cohort extension, 2 patients are still in continuous CR after 16 and 21 months, respectively, and 1 patient is still alive after 43 months. 11/12 patient was excluded from this analysis (relapse within 5 days).

**References**