Results from Ongoing Phase 2 Trial of SL-401 in Patients with Advanced, High-Risk Myeloproliferative Neoplasms Including Chronic Myelomonocytic Leukemia

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<th>ASH 2016 #4245</th>
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**Background and Highlights**

- SL-401 is a novel targeted therapy directed to the interleukin-12 receptor (IL-12Rβ1, CD210), a target overexpressed by many hematologic malignancies.
- SL-401 is currently being advanced through clinical trials in patients with a variety of MPN malignancies including dysplastic plasmacytoid dendritic cell neoplasms (DPDCN), acute myeloid leukemia (AML) in remission with high-risk features, myeloproliferative neoplasm (MPN), and multiple myeloma.
- Responses in patients treated with SL-401 have been observed in non-myeloid cell malignancies as well as in reflecting immune system cells, notably plasmacytoid dendritic cells (pDCs), in the bone marrow microenvironment of some patients with MPN including myeloproliferative neoplasms (CMML) and systemic mastocytosis.
- Microenvironmental (dC) have been implicated in promoting patient disease cell growth, including multiple myeloma, and preliminary data suggest that dC are also implicated in multiple myeloma. A therapy directed to both SL-401 and pDCs may be efficacious.

**MPN and response criteria**

- **Chronic Myelomonocytic Leukemia (CMML):** SL-401 is a novel targeted therapy directed to the interleukin-12 receptor (IL-12Rβ1, CD210). SL-401 has demonstrated clinical activity, including high overall response rates with multiple complete responses (CR), in patients with CMML.
- **Safety and MTD determination**
  - Dose escalation to next cohort.
  - Minimum of 2 patients per cohort.
  - Maximum tolerated dose (MTD) is defined as the dose level at which ≥1 patient out of 2 developed dose-limiting toxicity (SL-401).
- **Stage 1—dose escalation stage:**
  - Stage 1 has been completed; nine (9) patients were enrolled.
  - Preliminary Stage 1 results are reported here; Stage 2 expansion cohort currently enrolling.

**SL-401 Mechanism of Action**

- SL-401 has been designed to target the CD210 receptor and its ligand. It includes high-risk features, myeloproliferative neoplasm (MPN), and multiple myeloma.
- SL-401 has demonstrated clinical activity, including high overall response rates with multiple complete responses (CR), in patients with CMML.
- **Study Design**
  - Cohort 2: 9 patients.
  - Cohort 3: 9 patients.
  - Cohort 4: 9 patients.
  - Stage 1: Dose escalation to next cohort.
  - Stage 2: Expansion cohort.

**Best Response and Outcomes**

- **Clinical response:**
  - CR: Complete response.
  - PR: Partial response.
  - CRi: Complete response with incomplete blood count recovery.
  - MR: Minor response.
  - No change:
- **Safety and tolerability:**
  - Most common adverse events (AEs)
  - All Grades
  - All AEs
- **Phase 2, Stage 2 Expansion cohort currently enrolling patients with 4 types of advanced MPN: CMML, MF, SM, and PED (NCT02268210).”

**Study Design**

- **Two-stage design involving dose escalation (Stage 1) and expansion (Stage 2).”
- **Stage 1: Dose Escalation (3 cohorts)**
  - Cohort 1: 1 patient; 2×10⁹/kg/day for 3 days every 21 days.
  - Cohort 2: 2 patients; 2×10⁹/kg/day for 3 days every 21 days.
  - Cohort 3: 3 patients; 3×10⁹/kg/day for 3 days every 21 days.

**Response as defined in the International Working Group (IWG) for Myelodysplastic and Myeloproliferative Neuroplasms Research and Treatment and European LeukemiaNet (ELN) consensus report, requires complete blood cell count (CBC) with differential count 3 weeks after starting treatment response is explicitly defined.”

**Residual CD123+ Cells in CML-1 Patient After Chemo**

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**Conclusions and Next Steps**

- **Background and rationale:**
  - High-risk MPN encompasses a wide array of stem cell malignancies.
  - SL-401 targets CD210, a receptor present on MPN cells and containing an extracellular microenvironmental plasmacytoid dendritic cell (pDC) profile.
- **Phase 2, Stage 2 Expansion cohort currently enrolling patients with 4 types of advanced MPN: CMML, MF, SM, and PED (NCT02268210).”
- **Experimental results reported through 2017.”
- **Disclosures**
  - Financial Disclosures/Conflict of Interest: Authors are employed or working at various institutions or entities.

**Patient Demographics**

- **Study Design**
  - Cohort 2: 9 patients.
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**Patient Narratives and Treatment Course”

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