CLI24-001: First in Human Study of SEL24/MEN1703, an oral dual PIM/FLT3 kinase inhibitor, in Patients with Acute Myeloid Leukemia

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INTRODUCTION

- FLT3-ITD is one of the most common genetic lesions in acute myeloid leukemia (AML)
- PIM kinases are oncogenic FLT3-ITD targets expressed in AML.
- Increased PIM kinase expression is found in relapse samples from AML patients treated with FLT3 inhibitors
- Inhibition of PIM kinases restores sensitivity to FLT3 inhibitors
- Dual FLT3/PIM inhibition eradicates FLT3-ITD+ primary AML cells
- SEL24/MEN1703, a potent PIM/FLT3 dual inhibitor, demonstrates a significantly broader spectrum of activity in AML cell lines and primary AML blasts, irrespective of FLT3 status, compared to monotherapy with either FLT3 or PIM inhibitors (1,2)

OBJECTIVES

- Primary objective: Identification of the RP2D of SEL24/MEN1703 given as single agent in patients with AML
- Key secondary objectives include:
  - Pharmacokinetics
  - Pharmacodynamic activity
  - Single agent efficacy of SEL24/MEN1703
- Exploratory objectives include the assessment of relevant biomarkers (e.g. p56) in peripheral blood and bone marrow

METHODS

CLI24-001 (DIAMOND-01) is a First in Human, Phase I/II, open label, non randomized, multi-center, dose-escalation and cohort expansion study of SEL24/MEN1703 in AML patients (excluding Acute Promyelocytic Leukemia) not suitable for intensive chemotherapy.

Study design:
- The study is running the Dose Escalation Phase under a 3+3 design, with the exception of the starting dose
- Once the RD is determined, the Cohort Expansion Phase will start opening the recruitment in patients with or without FLT3 mutations and/or CD35 expression
- SEL24/MEN1703 dose levels range from 25 mg to 150 mg QD. Exploration of further dose levels escalation will be subjected to subsequent protocol amendment

Treatment outline:
- SEL24/MEN1703 is formulated as oral capsule to be given once daily, for 14 consecutive days over a 21-day treatment cycle, to be repeated until disease progression or unacceptable toxicity.

Main eligibility criteria:
- Patients ≥ 18 years old with (a) newly diagnosed AML, (b) relapsed AML or (c) primary refractory AML and that have no standard therapeutic options available.
- In both study parts, patients are eligible regardless of mutational status and/or prior exposure to FLT3 inhibitors
- Prior treatment with PIM inhibitors is not allowed
- A white blood count (WBC) ≤ 30 x 10^9/L is required prior to start study treatment (hydroxyurea/leukapheresis permitted to lower WBC)

Main exclusion criteria include hematopoietic stem cell transplant within 4 months of first dose of study drug and systemic immune-modulating therapy for the prophylaxis or treatment of graft versus host disease

RESULTS & CONCLUSION

- Recruitment start date: March 2017
- As of 31 May 2019, 22 patients were dosed
- New formulation introduced at dose level 100mg
- Dose level 125mg ongoing
- The study is enrolling at 5 US sites and will be extended both in US and EU

CLI24-001 is the first trial testing a dual PIM/FLT3 inhibitor with the potential to be active in AML regardless of FLT3 status and to overcome FLT3 inhibitor resistance.

REFERENCES


CONTACT INFORMATION

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