Here we aim to assess the activity and safety of olaptesed pegol in combination with bendamustine and rituximab (BR) in patients with relapsed / refractory CLL.

METHODS

28 relapsed or refractory CLL patients were enrolled and treated in this open-label, single-arm Phase IIa study: 28 relapsed or refractory CLL patients were enrolled and treated in this open-label, single-arm Phase IIa study.

Results from a Phase IIa Study of the Anti-CXCL12 Spiegelmer® Olaptesed Pegol (NOX-A12) in Combination with Bendamustine/Rituximab in Patients with Chronic Lymphocytic Leukemia

METHODS

Olaptesed pegol is a novel, L-stereoisomer RNA aptamer (Spiegelmer®) that binds and neutralizes CXCL12/SDF-1, a chemokine which attracts and activates immune and non-immune cells via interaction with the receptors, CXCR4 and CXCR7. Signaling of CXCL12 is pivotal to the interactions of leukemic cells with bone marrow microenvironment. The therapeutic concept of olaptesed is to inhibit such tumor-supporting pathways and thereby to mobilize and sensitize CLL cells to therapy.

RESULTS

• Rapid mobilization of CLL cells by a single dose of olaptesed, lasting throughout the observation time of 72h (Fig. 2, right panel).

• However in cycle 4, effective mobilization still observed for up to 24h (Fig. 2, right panel).

• Rapid mobilization of CLL cells by a single dose of olaptesed, lasting throughout the observation time of 72h (Fig. 2, right panel).

• Notably, RTX depletes CLL cells in cycle 1 at 3-24h so mobilization only observed at 1h (Fig. 2, middle panel).

• In the course of long-term mobilization.

• Rapid mobilization of CLL cells by a single dose of olaptesed pegol, lasting throughout the observation time of 72h (Fig. 2, right panel).

• Notably, RTX depletes CLL cells in cycle 1 at 3-24h so mobilization only observed at 1h (Fig. 2, middle panel).

• However in cycle 4, effective mobilization still observed for up to 24h (Fig. 2, right panel).

BACKGROUND

• For PK/PD investigation, administration of 1.2 or 4 mg/kg olaptesed alone to 3 pts/group (+ additional replacement pt) (pilot group only)

• Subsequently, dose titration with intravenous (IV) olaptesed at 1.2 and 4 mg/kg at cycles 1, 2 and 3, respectively, 1h before rituximab (RTX) treatment

• During cycles 4 to 6, olaptesed dosed at the highest individually titrated dose

• RTX administered IV at 375 mg/m² on day 1 of 1st 28-day cycle and 500 mg/m² on day 1 of subsequent cycles

• Bendamustine (70 - 100 mg/m²) given IV on days 1-2 (cycle 1) or days 1-2 (cycles 2-6) of each 28-day cycle following RTX

• Clinical response assessed according to NCI-WG Guidelines (Hallek et al. Blood 111; 2008: 5446-56).

• For PK/PD investigation, administration of 1.2 or 4 mg/kg olaptesed alone to 3 pts/group (+ additional replacement pt) (pilot group only)

• Subsequently, dose titration with intravenous (IV) olaptesed at 1.2 and 4 mg/kg at cycles 1, 2 and 3, respectively, 1h before rituximab (RTX) treatment

• During cycles 4 to 6, olaptesed dosed at the highest individually titrated dose

• RTX administered IV at 375 mg/m² on day 1 of 1st 28-day cycle and 500 mg/m² on day 1 of subsequent cycles

• Bendamustine (70 - 100 mg/m²) given IV on days 1-2 (cycle 1) or days 1-2 (cycles 2-6) of each 28-day cycle following RTX

• Clinical response assessed according to NCI-WG Guidelines (Hallek et al. Blood 111; 2008: 5446-56).

• Rapid mobilization of CLL cells by a single dose of olaptesed pegol, lasting throughout the observation time of 72h (Fig. 2, right panel).

• Notably, RTX depletes CLL cells in cycle 1 at 3-24h so mobilization only observed at 1h (Fig. 2, middle panel).

• However in cycle 4, effective mobilization still observed for up to 24h (Fig. 2, right panel).

• Rapid mobilization of CLL cells by a single dose of olaptesed, lasting throughout the observation time of 72h (Fig. 2, right panel).

• Notably, RTX depletes CLL cells in cycle 1 at 3-24h so mobilization only observed at 1h (Fig. 2, middle panel).

• However in cycle 4, effective mobilization still observed for up to 24h (Fig. 2, right panel).

CONCLUSION

Olaptesed pegol is a novel, L-stereoisomer RNA aptamer (Spiegelmer®) that binds and neutralizes CXCL12/SDF-1, a chemokine which attracts and activates immune and non-immune cells via interaction with the receptors, CXCR4 and CXCR7. Signaling of CXCL12 is pivotal to the interactions of leukemic cells with bone marrow microenvironment. The therapeutic concept of olaptesed is to inhibit such tumor-supporting pathways and thereby to mobilize and sensitize CLL cells to therapy.