Polatuzumab Vedotin plus Bendamustine and Rituximab in Relapsed/Refractory Diffuse Large B-cell Lymphoma (R/R DBLCL): Final Results of a Phase Ib/II Randomized Study and Single-Arm Extension Study

Background

- Polatuzumab vedotin is a CD79b-targeting antibody–drug conjugate approved for the treatment of relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) with ≥1 prior line of therapy
- Approval was based on findings from the GO29365 randomized Phase Ib/II study, which evaluated polatuzumab vedotin in combination with bendamustine and rituximab (Pola+BR) versus BR alone in patients with R/R DLBCL

- The main endpoint was an independent review committee (IRC)-assessed complete response (CR) rate of 40.0% with Pola+BR versus 17.5% with BR.

- A single-arm extension cohort including patients who received Pola+BR was later added, and efficacy was consistent with the randomized phase, with a CR rate of 38.7%.

- We report final results from the GO29365 study with extended follow-up of up to 5 years, including updated results from the Phase Ib safety run-in, Phase II randomization, and extended cohorts.

Methods

- GO29365 was a Phase Ib/II open-label, multicenter, randomized study, which included safety run-in, randomized, and extension cohorts (Figure 1).
- Patients received polatuzumab vedotin at a dose of 1.8mg/kg (Pola+BR arm only), bendamustine at a dose of 90mg/m², and rituximab at a dose of 375mg/m² every 21 days, for 6 cycles.

- The primary endpoint was IRC-assessed CR at primary response assessment (PPA; 6-8 weeks after completion of study treatment), measured by position emission tomography/computed tomography.

- Secondary endpoints included best overall response (BOR), best complete response (BCR), duration of response (DOR), progression-free survival (PFS), progression-free survival (PFS) post progression-free survival (PPFS), overall survival (OS), and safety.

Results

- All final data cut-off (October 21, 2021), median duration of follow-up for patients treated with Pola+BR was 77.4 months, 59.0 months, and 25.2 months, in the safety run-in, randomized, and extension cohorts, respectively.

- Baseline characteristics were similar between cohorts (Table 1).

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Baseline characteristic</th>
<th>Median age (years)</th>
<th>Median IPI score</th>
<th>Median number of prior therapies (n)</th>
<th>Median number of prior lines of therapy (n)</th>
<th>Median prior dose of therapy (mg/m²)</th>
<th>Primary refractoriness (%)</th>
<th>Median prior last line of therapy (n)</th>
<th>Median time of therapy (weeks)</th>
<th>Median number of cycles</th>
<th>Interim championing (yes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pola+BR</td>
<td>65 (12-90)</td>
<td>3 (0-5)</td>
<td>2 (1-3)</td>
<td>3 (1-3)</td>
<td>2 (1-6)</td>
<td>3 (0-100)</td>
<td>1 (0-3)</td>
<td>14 (6-24)</td>
<td>6 (5-7)</td>
<td>17 (12-32)</td>
</tr>
<tr>
<td>BR</td>
<td>65 (12-90)</td>
<td>3 (0-5)</td>
<td>2 (1-3)</td>
<td>3 (1-3)</td>
<td>2 (1-6)</td>
<td>3 (0-100)</td>
<td>1 (0-3)</td>
<td>14 (6-24)</td>
<td>6 (5-7)</td>
<td>17 (12-32)</td>
</tr>
</tbody>
</table>

- The study design figure is shown in Figure 1.

Efficacy

- A summary of efficacy results is presented in Table 2.

- In the randomized cohort, IRC-assessed CR at PPA was significantly higher for patients receiving Pola+BR compared with BR (42.5% versus 17.5%, p=0.0128)

- CR rate remained consistent in the extension cohort (39.8%).

- Median PFS, as assessed by IRC, was longer for patients receiving Pola+BR (9.2 months, 95% CI: 6.0-13.9) than BR (3.7 months, 95% CI: 2.1-4.5) in the randomized cohort (HR: 0.4, 95% CI: 0.2-0.7; Figure 2A)

- In the extension cohort, median IRC-assessed PFS was 7.0 months (95% CI: 5.1-9.8; Figure 2B).

- In the randomized cohort, median OS was longer for patients receiving Pola+BR (12.4 months, 95% CI: 9.3-32.0) compared with patients receiving BR (4.5 months, 95% CI: 0.3-13.4; Figure 3A)

- Treatment with Pola+BR reduced the risk of death by 60% compared with treatment with BR (HR: 0.4, 95% CI: 0.2-0.7).

- In the extension cohort, median OS was 12.3 months (95% CI: 8.3-17.0; Figure 3B).

Safety

- No new safety signals were reported in this final analysis (Table 3).
- In the randomized cohort, the incidence of G2/3 neuropathy (PNA) was higher in the Pola+BR arm than with BR (Table 3).
- Median time to PNA resolution (all grade) was 0.3 months in the Pola+BR arm of the randomized cohort, and 2.3 months in the extension cohort.

Table 3. Safety

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- In the randomized cohort, the incidence of G2/3 neuropathy (PNA) was higher in the Pola+BR arm than with BR.

- Median time to PNA resolution (all grade) was 0.3 months in the Pola+BR arm of the randomized cohort, and 2.3 months in the extension cohort.

Conclusions

- This planned final analysis reports 5 years of follow-up in the randomized cohort –compared efficacy post-first-line, with longer median PFS and OS in patients treated with Pola+BR compared with BR, consistent with previous results.
- In the extension cohort, median DOR was longer with increased follow-up, supporting a durable benefit of Pola+BR in patients who respond to treatment.
- Median PFS and OS were consistent with previous results.
- No new safety signals were reported.
- These long-term findings provide further evidence of the effectiveness of Pola+BR for the treatment of R/R DBLCL.