A Phase 2 Study of REGN1979, an Anti-CD20 x CD3 Bispecific Antibody (Ab), in Patients with Relapsed/Refractory (R/R) B-Cell Non-Hodgkin Lymphoma (B-NHL)

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Introduction

B-Cell Non-Hodgkin Lymphoma (B-NHL)

- Anti-CD20 Ab in combination with chemotherapy is the standard of care for the treatment of B-NHL; however, despite initial responses, many patients relapse, often with progressively shorter response durations in subsequent lines of therapy and poor outcomes.1,2
- Phosphatidylinositol 3-kinase inhibitors, including idelalisib, copanlisib and duvelisib, have been approved in the US as third-line treatment for follicular lymphoma (FL); however, they are associated with considerable toxicities, and their clinical activity and safety are being evaluated in confirmatory studies.1
- Patients with R/R diffuse large B-cell lymphoma (DLBCL) who have chemotherapy-resistant disease or are deemed to be ineligible for autologous stem cell transplant have a dismal prognosis, with a median overall survival (OS) of only 4 months.3
- High uric acid level also exists for treatment of R/R mantle cell lymphoma (MCL) after Bruton’s tyrosine kinase inhibitor (BTKi) failure. The median OS of patients after cessation of brutinib is brief at 2.9 months.3
- Patients with R/R marginal zone lymphoma (MZL) lack effective salvage therapies. Patients treated with brutinib have a median progression-free survival (PFS) of only 14.2 months and a complete response (CR) rate of 3.2%.1

REGN1979

- REGN1979 is a human IgG4-based bispecific Ab that binds to CD3+ T-cells and CD20+ B-cells, targeting CD20+ tumor cells via T-cell-mediated cytotoxicity.4
- Data from the ongoing Phase 1 study of REGN1979 (NCT0299051) in heavily pretreated R/R B-NHL patients, including some with progression after prior chimeric antigen receptor (CAR) T cell therapy, show broad antitumor activity and an acceptable safety profile at doses up to 320 mg weekly, with no dose-limiting toxicities (DLTs) observed during dose escalation.

Methods

Study Design

- This Phase 2, open-label, multi-cohort, multi-center study (NCT03888105) is designed to assess the antitumor activity and safety of REGN1979 in patients with B-NHL subtypes at approximately 130 sites across the US, Canada, Europe, and Asia Pacific regions.
- Five disease-specific cohorts are included, each with independent parallel enrollment (Figure 1: Table 1).
- The study opened with FL Grade 1–3a cohort.
- The other disease-specific cohorts have been included subsequently based on efficacy observations of the Phase 1 study.

REGN1979 monotherapy is administered as an intravenous infusion at an initial dose of 1 mg, an assigned weekly dose of 20 mg QW, and an assigned every 2 weeks (Q2W) nominal dose, and an assigned every 4 weeks (Q4W) nominal dose (Figure 1).

Patient flow diagram is shown in Figure 2.

Primary endpoint: Objective response rate (ORR) according to the Lugano Classification of response in malignant lymphoma (Cheson, 2014) by independent central review.

Secondary endpoints: ORR by investigator, CR rate, PFS, duration of response, disease control rate (DCR), duration of disease control, OS; incidence and severity of treatment-emergent adverse events; patient-reported outcomes; pharmacokinetics; and immunogenicity responses.

Statistical analysis

- ORR (primary endpoint), CR rate and DCR (secondary endpoints): summarized along with a 95% confidence interval (CI).
- Time to event outcomes: summarized, where appropriate, by median and the corresponding 95% CI using the Kaplan–Meier method.
- Cohort sizes: determined by analyses of the primary endpoint, ORR, of each cohort.

Figure 1. Study cohorts

Key exclusion criteria

Table 1. Patient eligibility

Key inclusion criteria

Table: Patient eligibility

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<table>
<thead>
<tr>
<th>B.NHL subtype</th>
<th>Study cohort</th>
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<tbody>
<tr>
<td>FL Grade 1–3a</td>
<td>FL Grade 1–3a, N=112</td>
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<tr>
<td>FL Grade 2–3a</td>
<td>FL Grade 2–3a, N=100</td>
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<tr>
<td>MZL</td>
<td>MZL, N=78</td>
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<tr>
<td>Other B-NHL</td>
<td>Other B-NHL (excluding FL Grade 1–3a, DLBCL, MCL, MZL, WM), n=47, 160 mg Q2W</td>
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Summary

- This Phase 2, open-label, multi-cohort, multi-center study (NCT03888105) will further assess the antitumor activity of REGN1979, a fully human, CD20 x CD3 bispecific IgG4 Ab, in five disease-specific cohorts of patients with B-NHL subtypes, each with independent parallel enrollment.
- This study will include approximately 130 sites across the US, Canada, Europe, and Asia Pacific regions. Recruitment is open for the FL Grade 1–3a cohort and planned for the other cohorts.

References


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