B-MIND: MOR208 + bendamustine (BEN) versus rituximab (RTX) + BEN in patients with relapsed or refractory (R-R) diffuse large B-cell lymphoma (DLBCL) – an open-label, randomized phase II/III trial

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Background

• Despite recent improvements in the management of DLBCL, approximately 30–40% of patients treated with RTX plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) relapse following initial immunochemotherapy.1

• As such RTX-based regimens have become standard first-line treatments in patients with DLBCL, the efficacy of RTX combined with chemotherapy in the second-line setting has decreased and there is a need for new therapies in patients progressing or relapsing after first- or second-line RTX-based treatment.2

• BEN has one of the highest anti-lymphoma activities of single agents used to treat R-R DLBCL and is generally well tolerated with a manageable, mainly hematological toxicity profile.2-4

• The CD19 antigen is an attractive target in DLBCL as CD19 is typically expressed in DLBCL cells, it has a signaling function that contributes to the malignant phenotype and it is not downregulated in patients pretreated with CD20-targeted agents.5,6

• MOR208 is an Fc-engineered, humanized, monoclonal antibody that targets CD19 on tumor cells leading to natural killer (NK) cell-mediated antibody-dependent cell-mediated cytotoxicity (ADCC), macrophage-mediated antibody-dependent cell-mediated phagocytosis and direct cytotoxicity (Figure 1).

Methods

• A randomized, two-arm, multicentre, open-label phase II/III efficacy and safety study of MOR208 in combination with BEN versus RTX in combination with BEN (NCT02763319; Figures 2 & 3).

• The study will be performed according to a group-sequential, adaptive design.

• In the initial phase II part of the study, a safety evaluation of the MOR208 + BEN combination will be performed by an independent data monitoring committee.

Figure 1. MOR208 mode of action

Figure 2. Study design

Figure 3. Participating countries

Outcome measures

Primary endpoint

• Progression-free survival.

Secondary endpoints

• Best overall response, duration of response, overall survival.

• Disease control rate, time to progression, time to next treatment.

• Incidence and severity of adverse events.

• Patient-reported quality of life outcomes.

• Anti-MOR208 antibody formation (immunogenicity).

• MOR208 pharmacokinetics.

Exploratory endpoints

• Exploratory biomarkers (e.g., CD19, CD20, BCL2, BCL6 expression, B-, T- and natural killer (NK) cell counts, CD16 expression on NK cells, ADCC capacity, and gene expression analysis for cell-of-origin subtyping).

Patients

Key inclusion criteria

• Histologically confirmed diagnosis of DLBCL according to the World Health Organization (WHO, 2008) classification.

• Not eligible for high-dose chemotherapy and autologous stem cell transplantation.

• R-R disease.

• At least one, but no more than three previous systemic therapy lines for the treatment of DLBCL.

• At least one previous therapy line must have included a CD20-targeted therapy.

• ECOG performance status of 0–2, adequate bone marrow, hepatic and renal function.

Key exclusion criteria

• NHL other than DLBCL.

• Primary refractory DLBCL.

• Treatment with a CD20-targeted therapy within 14 days prior to day 1 dosing.

• Prior treatment with CD19-targeted therapy or BEN.

Current status

• Recruitment start date: June 2016.

• Enrollment of 330 patients planned in Europe, US and the Asia-Pacific region (Figure 3).

• To date, 27 patients have been randomized, of which 25 received at least one study medication dose.

References


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Disclosures

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