premier research

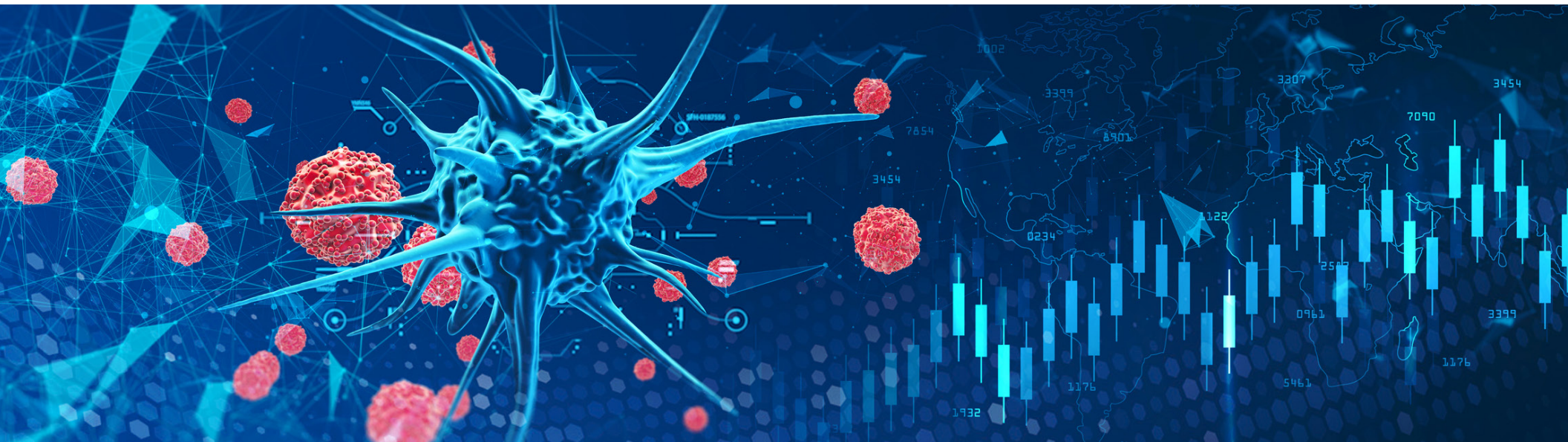
Built for Biotech℠

ONCOLOGY & HEMATOLOGY

Exceeding Expectations: Durable Remission in Diffuse Large B-Cell Lymphoma

Introduction

When a developer of a CD19-directed cytolytic antibody for B-cell Lymphoma engaged Premier Research to assist with screening and enrollment in a global Phase 2 study, the Premier project team devised an operational strategy with a goal to exceed expectations. Despite several challenges, the enrollment was completed three months ahead of schedule thanks to consistent communication and collaboration. Patients also demonstrated remarkable results to the treatment, with five showing complete response to the therapy and maintaining remission for at least eight years.

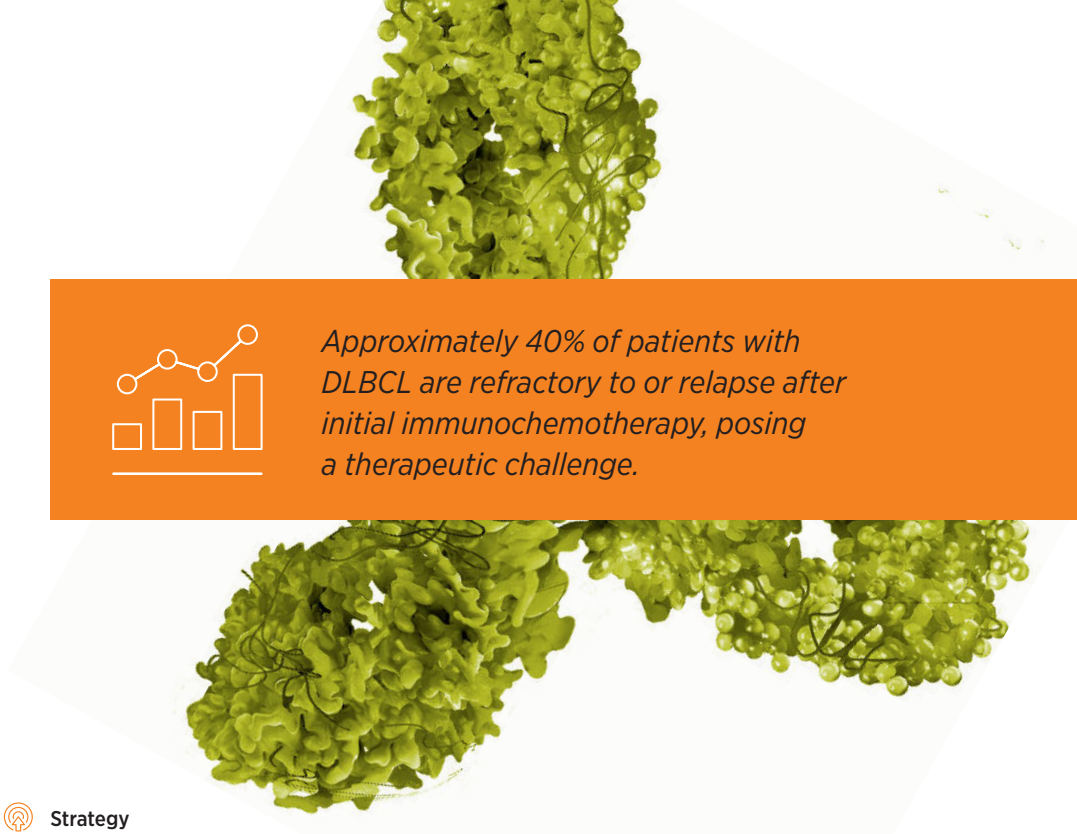


Background

Non-Hodgkin's lymphoma (NHL) is the most common hematological malignancy worldwide, accounting for nearly 3% of cancer deaths. A heterogeneous disease, NHL has over 40 major subtypes, each associated with unique driver genetic mutations and risk factors. In Western countries, the most common subtypes encountered in clinical practice are diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL). Approximately 40% of patients with DLBCL are refractory to or relapse after initial immunochemotherapy, posing a therapeutic challenge. Historically, management of relapsed or refractory DLBCL has relied on additional cytotoxic therapy with poor outcome, but novel non-chemotherapy-based approaches have been emerging.

Objective

The developer of a CD19-directed cytolytic antibody for B-cell NHL engaged Premier Research to assist with screening and enrollment in a global Phase 2 study to evaluate the compound's efficacy as a monotherapy in four NHL subtypes: DLBCL, FL, mantle cell lymphoma (MCL), and another indolent form of NHL.



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Challenges

This trans-Atlantic study was associated with several challenges:

- ***Recruitment.*** *MCL is relatively rare, and identifying eligible patients was difficult.*
- ***Study Duration.*** *The first patient was enrolled in March 2013 and the last patient was enrolled in November 2014. The protocol did not define any end, so the study continued as long as any patient continued to receive treatment. Inclusive of the follow-up and maintenance periods, the study closed in April 2022, requiring several study extensions outside of the initial plan. Ethically, this was beneficial to patients that continued to receive positive outcomes from the treatment, but it did pose challenges to ensure the study remained operationally stable. Of note, this period included the COVID-19 pandemic.*
- ***Resources.*** *The sponsor had four studies running in parallel, so their resources were constrained, and their time was limited.*

Strategy

Premier focused on:

- Identifying sites with access to the target patient population and supporting recruitment.
- Establishing and maintaining frequent, effective communication between the project team and study sites.
- Limiting staff turnover to minimize the need for onboarding and maximize consistency.
- Performing several ad hoc analyses and engagement in an FDA preparation meeting to support the application for marketing approval.

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Results

Premier engaged 26 sites—4 in the US and 22 in Europe. Based on early data, the sponsor narrowed the study scope to DLBCL and FL, the subtypes where the CD19-targeted antibody showed the most promise. Despite challenges with recruitment, Premier succeeded in enrolling 92 patients, with completion of enrollment achieved about three months ahead of schedule. Premier supported multiple ad hoc analyses and maintained the same expert biostatistician on the team for at least eight years of the study.

When the planned treatment rounds were completed and the study entered its follow-up period, results exceeded expectations, with five patients with DLBCL demonstrating complete response. At the height of the COVID-19 pandemic, when many hospitals were shut down and the supply chain was uncertain, Premier facilitated frequent communication between sites and patients such that no treatment visits were missed. We also ensured that supply of the investigational product, which was manufactured in Germany, was sufficient and timely for all treatment visits across all sites.

The five patients demonstrating complete response remained cancer-free throughout the follow-up and extended maintenance treatment periods for durable remissions that lasted until at least the close of the study in April 2022, which was up to eight years. These data contributed to accelerated approval of the compound as a second-line treatment for adults with relapsed or refractory DLBCL who are not eligible for autologous stem cell transplant.

Takeaway

Keeping project teams, sites, investigators, and patients motivated and engaged in the same study for over 10 years requires consistent communication and close collaboration. By establishing a strong relationship with all key study stakeholders, Premier supported the success of this lengthy study, helping the sponsor bring its CD19-targeted antibody to market in both the US and the EU.

[1] *Thandra KC, et al. Epidemiology of non-Hodgkin's lymphoma. Med Sci. 2021;9(1):5.*

[2] *Ngu H, et al. Revising the treatment pathways in lymphoma: new standards of care – how do we choose? American Society of Clinical Oncology Education Book;42:629-642.*

North America **+1 919 627 9100** | Europe **+44 118 936 4000** | **Info@premier-research.com**

Summary

Study Description

Phase 2 trial of a CD19-directed cytolytic antibody in B-cell non-Hodgkin's lymphoma

Therapeutic Area

Oncology

Geographic Scope

US and Europe

Number of Study Sites

26 (4 in the US and 22 in Europe)

Number of Patients Enrolled

92

Outcome

Enrollment completed three months ahead of schedule, with five patients demonstrating complete remission for more than eight years

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