

News Release

Title

Publication of long-term results of the world's first prospective clinical trial for intravascular large B-cell lymphoma

Key Points

- Intravascular large B-cell lymphoma (IVLBCL) is a rare type of malignant lymphoma. The disease normally lacks lymphadenopathy, making accurate diagnosis difficult. While the standard regimen, R-CHOP, has been applied to patients with IVLBCL in the same manner as for diffuse large B-cell lymphoma (DLBCL), which is the most common type of malignant lymphoma, high risk of secondary central nervous system (CNS) involvement has remained a clinical concern.

- A phase 2 prospective trial was conducted to assess the safety and efficacy of R-CHOP combined with high-dose methotrexate and intrathecal chemotherapy as CNS-directed therapy in untreated IVLBCL. In 2020, the primary analysis of the study showed good clinical outcomes, but long-term result on the safety and efficacy of the treatment had been desired.

- The long-term results of the study showed a durable response to the treatment, with a low cumulative incidence of secondary CNS involvement, underscoring the robustness of the safety and efficacy of the treatment for patients with IVLBCL.

Summary

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Malignant lymphoma is a heterogeneous hematological malignancy. IVLBCL is a rare type of malignant lymphoma characterized by the lack of lymphadenopathy, which makes accurate diagnosis difficult. Patients with IVLBCL has been treated with R-CHOP, the standard treatment for DLBCL, however the high risk of secondary CNS involvement (which can affect around 20% of patients) has been a significant concern. In addition, evidence based on prospective trials have been sparse, with the primary analysis of this study being the only available evidence.

The present study is a phase 2 trial of R-CHOP combined with high-dose methotrexate and

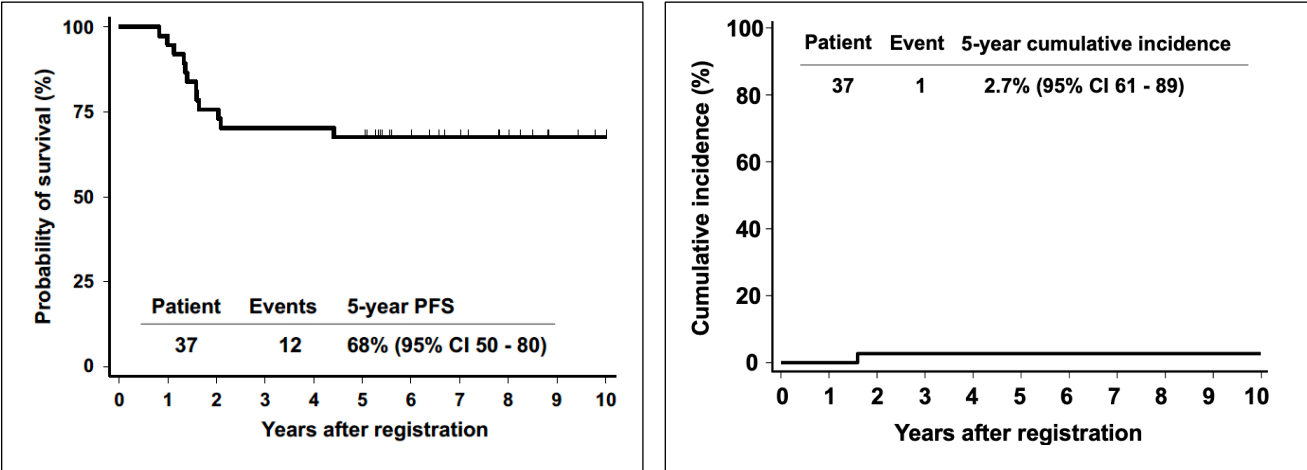
intrathecal chemotherapy as CNS-directed therapy. Thirty-eight patients with untreated IVLBCL without apparent CNS involvement at diagnosis were enrolled. In the primary analysis reported in 2020, 2-year progression-free survival (PFS) was 76% with overall survival (OS) at 2 years of 92% and a cumulative incidence of secondary CNS involvement at 2 years of 3%. The long-term result from the prespecified final analysis show 5-year PFS of 68%, 5-year OS of 78%, and a cumulative incidence of secondary CNS involvement at 5 years of 3%. There was no relapse and secondary CNS involvement after the primary analysis, indicating a durable response to the treatment. Adverse events after the primary analysis were acceptable. This trial remains the world's first prospective trial for IVLBCL, and the study treatment has been incorporated into clinical practice as a one of standard care for untreated IVLBCL. The long-term results underscore the sustained safety and efficacy of the treatment. The study was published in eClinicalMedicine on January 31, 2025.

Research Background

IVLBCL is a rare type of malignant lymphoma characterized by the selective growth of tumor cells in the lumina of small vessels. The disease normally lacks lymphadenopathy, making an accurate diagnosis difficult. Patients with untreated IVLBCL have been treated with R-CHOP, a standard regimen for DLBCL, however, the high incidence of secondary CNS involvement (approximately 20%) has remained a clinical issue. No prospective trial for the disease had been conducted due to its rarity of the disease, and no standard regimen was established.

Research Results

A multicenter phase 2 clinical trial was conducted to evaluate the safety and efficacy of R-CHOP combined with CNS-directed therapy including high-dose methotrexate and intrathecal chemotherapy in untreated IVLBCL patients without apparent CNS involvement at diagnosis. Thirty-eight patients (median age of 66 years, range 38-78 years) were enrolled. The primary analysis, published in 2020, showed a 2-year PFS of 76%, with OS at 2 years of 92% and a cumulative incidence of secondary CNS involvement at 2 years of 3%. In the long-term result, PFS, OS, and the cumulative incidence of secondary CNS involvement at 5 years were 68% (left), 78%, and 3% (right), respectively, confirming the durable response to the treatment. Adverse



events after the primary analysis were acceptable.

Research Summary and Future Perspective

The long-term results of the study provide evidence of a durable response to standard chemotherapy combined with CNS-directed therapy for untreated IVLBCL patients. Since the primary analysis, the study treatment has been adopted in clinical practice as a one of standard care for untreated IVLBCL. As treatments of malignant lymphoma continue to evolve, it is crucial to further improve clinical outcomes of IVLBCL. The outcomes of this study will serve as a benchmark for evaluating future therapies for IVLBCL.

Publication

Journal Name : eClinicalMedicine

Title : Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone combined with high-dose methotrexate plus intrathecal chemotherapy for newly diagnosed intravascular large B-cell lymphoma (PRIMEUR-IVL): long-term results of a multicentre, single-arm, phase 2 trial

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