Letter to the Editor

rare tumors

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Epcoritamab-bysp (Epkinly) – A phenomenal breakthrough in the treatment of diffuse large B-cell lymphoma

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Dear Editor,

The most prevalent non-Hodgkin lymphoma, Diffuse Large B-Cell Lymphoma (DLBCL), affects 25,000 people annually and accounts for roughly 30% of cases of Non-Hodgkin Lymphoma.[1] Rituximab and chemotherapy are commonly used in the treatment of diffuse large B-cell lymphoma (DLBCL) to cure the patient; however, a significant portion of patients, up to 40%, are bound to experience relapsed or refractory disease. In such cases, salvage chemotherapy followed by autologous stem cell transplantation is the standard approach, but less than half of the patients achieve long-term disease control.[2] Those who face refractory disease or experience relapse after transplantation have limited treatment options and generally have poor overall survival rates.[2,3] To address this unmet medical need, the Food and Drug Administration (FDA) has recently given Epcoritamab-bysp (Epkinly, Genmab US, Inc.) accelerated approval for the treatment of relapsed or refractory DLBCL, including cases where DLBCL arises from indolent lymphoma or high-grade B-cell lymphoma after two or more lines of systemic therapy. This approval signifies an important advancement, providing a potential therapeutic option for patients who have exhausted standard treatments.[4]

Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous group comprising intermediate- and high-grade B-cell lymphomas with diverse molecular backgrounds, clinical courses and responses to therapy. It can be classified on the basis of molecular diversity and gene expression profiling (GEP). The majority of DLBCL cases exhibit gene rearrangements in immunoglobulin heavy and light chains, with BCL2 protein expressed in about 80% and BCL6 protein in 70% of cases.[5] Abnormalities in the MYC gene may also be present. Flow cytometry analysis reveals the presence of CD19, CD20, CD22, CD45, and CD79a surface markers and rarely CD5 has also been seen.[6] DLBCL commonly affects extra nodal sites such as the brain, bones, kidneys, adrenal glands and soft tissues.[7] Epcoritamab-bysp (Epkinly), a humanized bispecific IgG1 antibody, is CD20-directed CD3 T-cell engager. Epcoritamab-bysp is produced utilizing recombinant DNA technology in Chinese Hamster Ovary (CHO) cells and has a molecular weight of approximately 149 kDa. Epkinly interacts with the CD3 receptor that is expressed on the surface of T cells as well as the CD20 receptor that is expressed on the surface of lymphoma cells and healthy B-lineage cells triggering lysis of B-cells, activated T-cells, and the release of proinflammatory cytokines in vitro.[8]

By Cycle 1 Day 15 (after the first full dose of 48 mg), in patients who had detectable B cells at treatment initiation, circulating B cells had decreased to undetectable levels (<10 cells/microliter) and the depletion had persisted throughout the patients' treatment. At dose levels of 0.04 mg and above, cytokine concentrations in the plasma (IL-2, IL-6, IL-10, TNF, and IFN) increased. Cytokine levels raised after EPKINLY administration within 24 h of the first dosage on Cycle 1 Day 1, peaked after 48 mg on Cycle 1 Day 15 and then fell back to baseline before the following 48 mg complete dose on Cycle 1 Day 22.[8] The open-label, multi-cohort, multicenter, single-arm EPCORE NHL-1 (Study GCT3013-01; NCT03625037) experiment

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examined the effectiveness of EPKINLY. 148 individuals with DLBCL, not otherwise specified (NOS), including DLBCL resulting from indolent lymphoma, and high-grade B-cell lymphoma following two or more lines of systemic therapy, including at least one therapy using an anti-CD20 monoclonal antibody, make up the efficacy population. With 38% of patients receiving complete responses, the ORR was 61% (95% CI: 53, 69). The estimated median duration of response (DOR) was 15.6 months (95%CI: 9.7, not reached) among respondents with a median follow-up of 9.8 months.[4]

Epcoritamab-bysp has demonstrated a manageable safety profile in clinical trials, with adverse events consistent with those expected for immunotherapies. The most common side effects reported, occurring in at least 20% of patients, were cytokine release syndrome (CRS), fatigue, musculoskeletal pain, injection site reactions, pyrexia, abdominal pain, nausea and diarrhea. Additionally, grade 3 to 4 laboratory abnormalities, observed in at least 10% of patients, included decreased lymphocyte count, decreased neutrophil count, decreased white blood cell count, decreased hemoglobin and decreased platelets.[5] These adverse outcomes are the main reason a boxed warning is required, alerting medical practitioners to the possibility of cytopenia, infections and embryo fetal toxicity.[6]

In conclusion, Epcoritamab-bysp represents a significant breakthrough in the treatment of relapsed or refractory Diffuse Large B-cell Lymphoma (DLBCL). Its FDA approval provides a crucial option for patients who have exhausted standard therapies. With its bispecific nature and the ability to engage both CD20 and CD3, epcoritamab-bysp offers a promising therapeutic approach that harnesses the patient's immune system to effectively combat the lymphoma. Ongoing research and clinical experience will continue to refine its optimal use and explore potential combinations with other therapies, aiming to further improve outcomes for DLBCL patients.

Author contributions

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