TPS7092 Poster Session

waveLINE-010: Zilovertamab vedotin plus R-CHP versus R-CHOP in untreated diffuse large B-cell lymphoma.

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Background: Despite recent advances in the treatment of diffuse large B-cell lymphoma (DLBCL), 5-year survival rates range between 60% and 80%. Modest improvements have been made over standard-of-care with rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) immunochemotherapy being used in the first-line setting. Zilovertamab vedotin, an ROR1-targeting antibody-drug conjugate with a monomethyl auristatin E payload, has demonstrated promising efficacy in patients with DLBCL. The randomized, open-label, phase III waveLINE-010 (NCT06717347) study will evaluate the efficacy and safety of zilovertamab vedotin in combination with rituximab plus cyclophosphamide, vincristine, and prednisone (R-CHP) versus R-CHOP in patients with untreated DLBCL. **Methods:** Eligible participants are aged ≥18 years and have histologically confirmed DLBCL per World Health Organization classification of neoplasms of the hematopoietic and lymphoid tissues (including but not limited to: DLBCL, not otherwise specified [NOS] germinal center B-cell type, or activated B-cell type; DLBCL leg-type; Epstein-Barr virus–positive DLBCL, NOS; and T-cell histiocytic-rich DLBCL), positron emission tomography–positive disease at screening (4-5 on the Lugano 5-point scale), no prior treatment for DLBCL, an International Prognostic Index (IPI) score of 2-5, and an ECOG performance status score of 0-2. Approximately 1046 patients will be randomly assigned (1:1) to receive zilovertamab vedotin 1.75 mg/kg plus R-CHP on day 1 of every 3-week cycle for 6 cycles, or R-CHOP on day 1 of every 3-week cycle for 6 cycles. Patients with high-risk DLBCL in both treatment arms will receive rituximab (or biosimilar) for an additional 2 cycles. Randomization will be stratified by 3 geographic regions (Western Europe, the United States, Canada, and Australia vs Asia vs rest of world), IPI score (2 vs 3-5), and bulk (<7.5 cm vs ≥7.5 cm). The primary end point is PFS per Lugano criteria by blinded independent central review (BICR). Secondary end points include complete response rate at end of treatment (EOT) per Lugano criteria by BICR, overall survival, event-free survival per Lugano criteria by BICR, duration of complete response, safety and tolerability, and changes from baseline in health-related quality-of-life assessments. Response assessments will be performed after day 1 of cycle 4 but before day 1 of cycle 5, and then at 12 weeks after cycle 4 scan (EOT assessment). Efficacy follow-up assessments will be completed every 24 weeks for 2 years from EOT assessment, then every year for 3 years (total of 5 years). Adverse events will be graded per NCI CTCAE v5.0. Recruitment is ongoing. Clinical trial information: NCT06717347. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.