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626.AGGRESSIVE LYMPHOMAS: PROSPECTIVE THERAPEUTIC TRIALS

Phase II Clinical Trial of R-CHOP Combined with Lenalidomide in the First-Line Treatment for Patients with High Risk Diffuse Large B Cell Lymphoma

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Introduction: Diffuse large B cell lymphoma (DLBCL) is the most common type of non-Hodgkin's lymphoma (NHL). Currently, R-CHOP (Rituximab-Cyclophosphamide, Epirubicin, Vincristine and Prednisone) is world-widely used in the first-line treatment for DLBCL, producing a long-term survival rate of approximately 60%. The unmet need is focused on high-risk DLBCL patients, having high International Prognostic Index (IPI) scores, non-germinal center-like B cell (non-GCB) origin, double expression of MYC and BCL2 protein, or TP53 aberrations. Lenalidomide is an active agent in the activated B cell-like (ABC) subtype of DLBCL by increasing interferon-stimulated gene transcription and activation of immunomodulatory mechanisms. At present, it has been approved for the treatment of multiple myeloma with good efficacy and safety. This is a prospective single arm, multi-center, phase II clinical trial and the goal of our trial is to assess the efficacy and safety of R-CHOP combined with lenalidomide in the first-line treatment for patients with high risk diffuse large B cell lymphoma.
Methods: We did an investigator-initiated, open-label, phase 2 trial at the Affiliated Cancer Hospital of Zhengzhou University in China. Patients were eligible if they were aged over 18 years, had histologically confirmed DLBCL. The key inclusion criteria included untreated and medium to high /high risk DLBCL (International Prognostic Index (IPI) score 3-5, aaIPI score 2-3 or NCCN-IPI score≥ 4/ Immunohistochemical staining of double expression (BCL2 ≥ 50% and C-MYC ≥ 40%) or P53 protein mutation positive ≥ 50%). Participants in RL-CHOP cohort were given Lenalidomide orally 25 mg per day on days 1 through 10 of each cycle and delivered concomitantly with standard dose R-CHOP-21 chemotherapy. We also set another group treated with conventional R-CHOP-21 used as a matched contemporary cohort. The primary clinical endpoint was 2-year progression-free survival (PFS). The secondary efficacy endpoints were objective response rate (ORR), 2-year overall survival (OS) and safety. This trial is registered with ClinicalTrials.gov, number NCT04214626.
Results: Between December 2019 and January 2023, 63 patients with untreated DLBCL enrolled and were evaluable in the investigator-initiated phase II study. The median age was 59 years (range: 25-76 years); 49.2% of patients were older than age 60 years. 46 of 63 patients (73.02%) had a ECOG score of 0-1; 43 of 63 patients (68.25%) had stage III-IV disease, and 33 of 63 patients (52.38%) had ≥2 extranodal localizations. The IPI score was high-intermediate and high in 73.02% (46/63) of patients. 51 of 63 patients (80.95%) were non-GCB subtype; 25 of 63 patients (39.68%) were double expressor. The TP53 protein was positive in 34.55% (19/55) of patients. In RL-CHOP cohort, the complete response rate was 80.95%, with overall response rate achieving 100%. The median follow-up time was 18.25 (3.73-42) months, median PFS and OS were not reached, and 2-year PFS and OS was 71.1% (+-6.7) and 87.4% (+-4.5), respectively. Comparing with historical matched contemporary cohort, the 2-year PFS and OS rates were improved for medium to high /high risk DLBCL. The most common adverse events of treatment were hematologic toxicities. Grade 3/4 AEs occurred in ≥20% patients were neutropenia, leukopenia, anemia, thrombocytopenia and decreased serum potassium, without bleeding complications. No grade 4 non-hematological adverse event was reported.
Conclusion: RL-CHOP is effective and safe in patients with newly diagnosed DLBCL with high risk. Relevance of molecular biomarkers on RL-CHOP response warrants further investigation in DLBCL.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: Lenalidomide is an active agent in the activated B cell-like (ABC) subtype of DLBCL by increasing interferon-stimulated gene transcription and activation of immunomodulatory mechanisms. At present, it has been approved for the treatment of multiple myeloma with good efficacy and safety. This study aimed to evaluate efficacy and safety of a combination of lenalidomide and R-CHOP (RL-CHOP) in the first-line treatment for patients with high-risk DLBCL.

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