LBA-1 The POLARIX Study: Polatuzumab Vedotin with Rituximab, Cyclophosphamide, Doxorubicin, and Prednisone (pola-R-CHP) Versus Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP) Therapy in Patients with Previously Untreated Diffuse Large B-Cell Lymphoma

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Program: General Sessions

Session: Late-Breaking Abstracts Session

Hematology Disease Topics & Pathways:

Clinical Trials, Biological, Lymphomas, Clinical Research, Diseases, Aggressive Lymphoma, Therapies, Immunotherapy, Lymphoid Malignancies

Background:

The current standard of care for patients with newly diagnosed diffuse large B-cell lymphoma (DLBCL) is R CHOP; however, approximately 40% of patients are not cured. The CD79b-targeting antibody–drug conjugate, polatuzumab vedotin, is approved in relapsed/refractory DLBCL in combination with bendamustine and rituximab, and has also demonstrated promising first line activity and safety when combined with rituximab, cyclophosphamide, doxorubicin, and prednisone (pola-R-CHP) in a Phase Ib/II study (Tilly, et al. Lancet Oncol 2019). Thus, in the Phase III POLARIX study (NCT03274492) we compared pola-R-CHP with R-CHOP in patients with previously untreated DLBCL.

Methods:

In this double-blind, placebo-controlled, international study, patients with previously untreated DLBCL and an International Prognostic Index (IPI) of 2–5 were randomized 1:1 to receive six cycles of pola-R-CHP (with a vincristine placebo) or R-CHOP (with a polatuzumab vedotin placebo); all patients also received two additional cycles of rituximab. Patients received polatuzumab vedotin 1.8mg/kg or vincristine 1.4mg/m² administered on Day 1, plus intravenous rituximab 375mg/m2, cyclophosphamide 750mg/m², doxorubicin 50mg/m², and placebo on Day 1, and oral prednisone 100mg once daily on Days 1–5. The primary endpoint was investigator-assessed progression-free survival (PFS). Secondary endpoints included investigator-assessed event-free survival (EFS), independent review committee-assessed

complete response (CR) rate at the end of treatment by positron emission tomography-computed tomography (PET-CT), disease-free survival (DFS), overall survival (OS), and safety.

Results:

Overall, 879 patients were randomized, 440 to pola-R-CHP and 439 to R-CHOP. Median age was 65 (range 19–80) years, and the majority of patients had IPI 3–5 (62.0%). At the data cut-off of June 28, 2021, and after a median follow-up of 28.2 months, PFS was superior with pola-R-CHP vs R CHOP (hazard ratio [HR] 0.73; 95% confidence interval [CI]: 0.57–0.95; P<0.02). The 2-year PFS rate was 76.7% (95% CI: 72.7–80.8) with pola-R-CHP vs 70.2% (95% CI: 65.8–74.6) with R-CHOP. EFS favored pola-R-CHP compared with R-CHOP (HR 0.75; 95% CI: 0.58–0.96; P=0.02). The end-of-treatment PET-CT CR rate was not significantly different with pola-R-CHP vs R-CHOP (78.0% vs 74.0%; P=0.16); however, DFS suggested responses were more durable with pola-R-CHP than with R-CHOP (HR 0.70; 95% CI: 0.50–0.98). There was no difference in OS between treatment arms (HR 0.94; 95% CI: 0.65–1.37; P=0.75). At the time of data cut-off, 99 (23%) and 133 (30%) patients in the pola-R-CHP and R-CHOP arms, respectively, had received at least one subsequent anti-lymphoma therapy. Fewer patients in the pola-R-CHP than the R-CHOP arm received subsequent anti-lymphoma treatments (radiotherapy, 9.3% vs 13.0%; stem cell transplantation, 3.9% vs 7.1%; chimeric antigen receptor T-cell therapy, 2.0% vs 3.6%). The safety profile was comparable for pola-R-CHP vs R-CHOP, including rates of grade 3–4 adverse events (AEs; 57.7% vs 57.5%), serious AEs (34.0% vs 30.6%), grade 5 AEs (3.0% vs 2.3%), and AEs leading to dose reduction (9.2% vs 13.0%), respectively. The frequency and severity of peripheral neuropathy were similar for pola-R-CHP vs R-CHOP (any grade, 52.9% vs 53.9%; grade 3–4, 1.6% vs 1.1%).

Conclusion:

The pola-R-CHP combination demonstrated a 27% reduction in the relative risk of disease progression, relapse, or death compared with R-CHOP, with a similar safety profile in the first-line treatment of patients with DLBCL.