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P1196 ORIENT STUDY: REGIMEN OF ORELABRUTINIB PLUS R-CHOP-LIKE FOR PATIENTS WITH NEWLY DIAGNOSED UNTREATED NON-GCB DLBCL

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

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Background:

The prognosis of patients (pts) with non-germinal center B-cell-like (non-GCB) diffuse large B-cell lymphoma (DLBCL) is poor. Bruton tyrosine kinase inhibitors (BTKi) have shown therapeutic activity in non-GCB DLBCL. Orelabrutinib (O), as a novel covalent BTKi with high target selection, was reported to preserve the NK-cell-mediated antibody-dependent cellular cytotoxicity (ADCC) induced by rituximab (R) and thus boosted the antitumor effect of R-based regimen.

Aims:

This study aimed to analyze the efficacy and safety of O plus R-CHOP-like (O+R-CHOP) for previously untreated non-GCB DLBCL pts who benefited from induction therapy of O plus R (OR).

Methods:

Pts with histopathologically confirmed newly diagnosed non-GCB DLBCL have enrolled in this ongoing, prospective, multicenter, open-label phase II study (NCT05498259). Pts received O (150 mg, once daily [qd]) and R (375 mg/m2, day 1) as induction therapy for 21 days. Then, pts with a reduction in a lesion of ≥25% received O (150 mg, qd) and R-CHOP as combination therapy on a 21-day cycle for 6 cycles. The primary endpoint was the complete remission rate (CRR) after 6 cycles of O+R-CHOP. Secondary endpoints were mini or better response rate (mRR, defined as the percentage of pts with complete remission [CR], partial remission [PR], and mini response [miniR, lesion reduction: 25.0%-50.0%]) after OR, Overall response rate (ORR) and progression-free survival (PFS) after O+R-CHOP, and safety profiles.

Results:

Ten pts were enrolled by the cutoff date (February 10, 2023). The median age was 61.5 (range 27-68) years. All had stage III-IV disease, extranodal involvement (70.0%), and MYC/BCL2 double expression lymphoma (DEL, 60.0%). Next-generation sequencing was performed in 9 (90.0%) pts to detect genetic mutations, including MYD88 (n=4, 44.4%), CD79A (n=2, 22.2%), and TP53 (n=1, 11.1%) mutations.

All 10 pts completed induction therapy, 9 pts attained a response, and the mRR was 90.0% (CR=40.0%, PR=40.0%, miniR=10.0%) and then 9 pts continued to receive O+R-CHOP. Six (66.7%) pts completed ≥3 cycles of O+R-CHOP and all achieved CR at the end of cycle 3; among whom 1 (11.1%) maintained CR at the end of cycle 6 (Figure 1). During the whole treatment, 8 (88.9%) of 9 pts had CR as their best response, with an ORR and CRR of 88.9%. No progressive disease or death was reported. By the subgroup analysis of 10 pts at the induction stage, pts with DEL had better mRR (100.0% vs. 66.7%) than that non-DEL. A similar result was observed in pts with extranodal involvement over those without (mRR, 100.0% vs. 66.7%). In 9 pts who received O+R-CHOP, pts with DEL and extranodal involvement achieved CRR of 100.0% and 85.7%, respectively. Pts with MYD88 (n=4) and CD79A (n=2) mutations obtained CR.

At the induction stage, 4 (40.0%) pts experienced adverse events (AEs), with grade 1-2 hematological AEs. During the whole treatment, AEs occurred in 8 (80.0%) pts, and the common AEs were lymphocyte count decreased (60.0%) and white blood cell decreased (50.0%). Grade ≥3 AEs occurred in 3 (30.0%) pts, including lymphocyte count decreased (10.0%), pulmonary infection (10.0%), and white blood cell decreased (10.0%). As data cutoff, 8 (88.9%) were still under treatment.

Summary/Conclusion:

Although preliminary, the responders to the OR induction therapy may attain a synergistic antitumor effect and thus achieve a high CRR when receiving subsequent O+R-CHOP. The safety was favorable. More updated data will be presented from this ongoing study.