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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Polatuzumab Vedotin, Zanubrutinib and Rituximab Achieved Rapid and Deep Response in Previously Untreated Frail and Elderly Diffuse Large B-Cell Lymphoma Patients

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Introduction: The incidence of diffuse large B-cell lymphoma (DLBCL) increases with age, while first-line treatment for frail and elderly DLBCL is a debating topic. R-miniCHOP, a reduced intensity regimen of R-CHOP, is currently the standard of care for this population, yet with limitation due to toxicities (Frédéric Peyrade *et al.*, Lancet Oncol, 2011). Chemo-free regimens combining Bruton kinase inhibitors, rituximab and lenalidomide showed fewer toxicities, but compromised on efficacy in elderly DLBCL in multiple previous reports (Pengpeng Xu *et al.*, Lancet Healthy Longev, 2022; Haiyan Yang *et al.*, ASH 2022). First-line treatment balancing efficacy with safety is urgently needed for frail and elderly DLBCL patients. Since polatuzumab vedotin was approved in China for first-line DLBCL this year and reportedly had synergistic effect with rituximab in cell line research (Natsumi Kawasaki *et al.*, Br J Haematol, 2022), we conducted a study of polatuzumab vedotin plus zanubrutinib and rituximab (ZPR) in previously untreated frail and elderly DLBCL to assess the efficacy and safety. Here we present the characteristics of 12 enrolled patients and preliminary results.
Methods: Previously untreated DLBCL patients aged over 70 years old, or aged between 60 to 69 with ECOG score 2 to 4 were enrolled in this study. All patients received a triplet regimen of ZPR. Twenty-one days was a cycle. Zanubrutinib was given 160mg twice a day orally from day 1 to day 21. Rituximab was given 375mg/m ^{2} intravenously on day 1. Polatuzumab vedotin was administered at a dosage of 1.8mg per kilogram intravenously on day 1. Patients would receive 6 cycles of ZPR regimen if assessed partial response (PR) or complete response (CR) after 3 cycles. If assessed CR after 6 cycles of ZPR, patients would receive zanubrutinib 160mg twice a day alone for another 6 cycles. Whole body 18F-FDG PET/CT scan or contrast-enhanced CT scan of cervical, thoracic, abdominal and pelvic parts was scheduled every 3 cycles. Treatment response was assessed by 2014 Lugano response criteria. Adverse events were graded by CTCAE 5.0. The primary endpoint is overall response rate (ORR) after 6 cycles of ZPR. The secondary endpoints are CR rate after 6 cycles of ZPR, and 2-year progression-free survival (PFS). Other endpoint is safety **(Figure 1)**.
Results: Twelve patients were enrolled in our study until Jul 24, 2023. Median age was 75 (range: 67-87). Six patients were female and six patients were male. Nine (75%) patients were classified non-GCB type according to cell of origin by Hans algorithm. Nine (75%) patients were assessed stage III to IV by Ann Arbor staging system. Nine (75%) patients had an international prognostic index (IPI) score of 2 or more. One (11%) patient had double-hit risk factor in 9 patients with gene rearrangement results. Six (75%) patients had *MYD88 L265P* mutation in 8 patients with sequencing results. After a median follow up of 2.1 months, four patients had PET/CT assessment results after 3 cycles of ZPR, and four (100%) of them achieved CR. The ORR after 3 cycles of ZPR regimen was 100% **(Figure 2)**.Grade 3 to 4 adverse events occurred in two patients, that one patient had grade 3 aspartate aminotransferase increase and alanine aminotransferase increase, and the other patient had grade 3 pneumonitis. Grade 1 to 2 adverse events included neutrophil count decrease (16%), dizziness (8%), and epistaxis (8%). All patients recovered from adverse events under best supportive care. There was no discontinuation of ZPR regimen due to severe adverse events.
Conclusion: Based on these results in our study, ZPR regimen showed rapid and deep response in previously untreated frail and elderly DLBCL patients with manageable safety profiles. We registered and initiated a phase 2b trial (NCT05940064) to further evaluate the efficacy and safety of ZPR regimen as first-line treatment for this population. Ongoing treatment and follow up of these twelve patients will also be further updated.

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: zanubrutinib in first-line treatment of diffuse large B-cell lymphoma

Figure 1. Scheme of ZPR regimen study

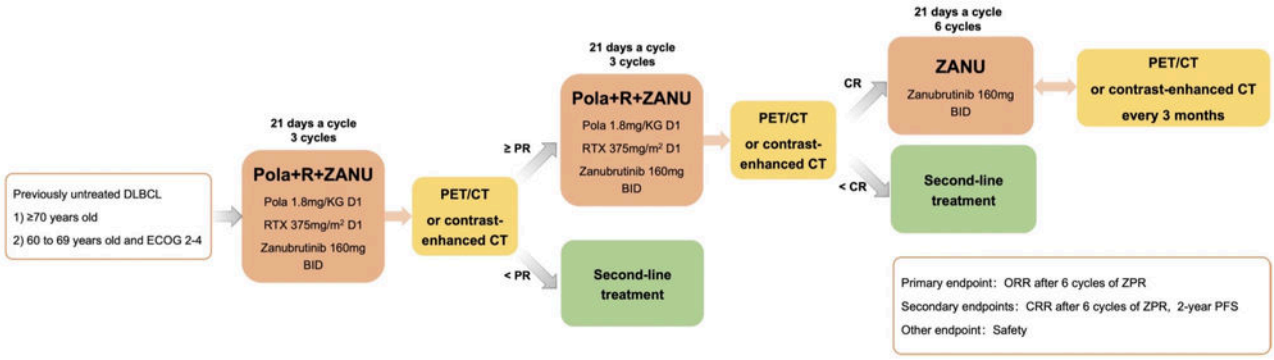

Figure 2. Duration of response and time of ZPR regimen study

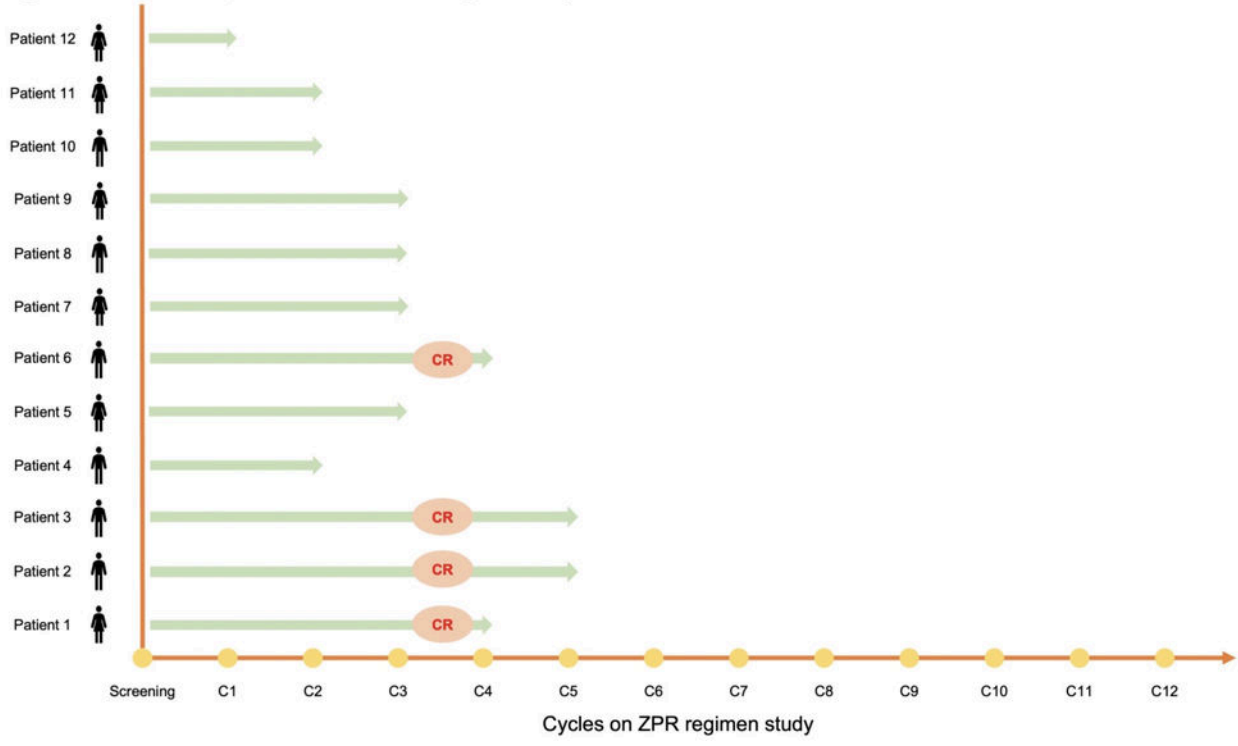

Figure 1

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