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P1242 ZANUBRUTINIB AND RITUXIMAB REGIMEN COMBINED WITH INTRAVITREAL METHOTREXATE FOLLOWED BY ZANUBRUTINIB MAINTENANCE FOR TREAT-NAIVE PRIMARY VITREORETINAL LYMPHOMA: A PROSPECTIVE PHASE II STUDY

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

Yan Zhang[1], Xiao Zhang[2], Wei Wang[1], Yan Zhang[3], Mei-fen Zhang[2], Wei Zhang[1], Daobin Zhou[1]

[1] Department of Hematology, Peking Union Medical College Hospital, Beijing, China;[2] Department of Ophthalmology, Peking Union Medical College Hospital, Beijing, China;[3] Department of Hematology, Beijing Longfu Hospital, Beijing, China

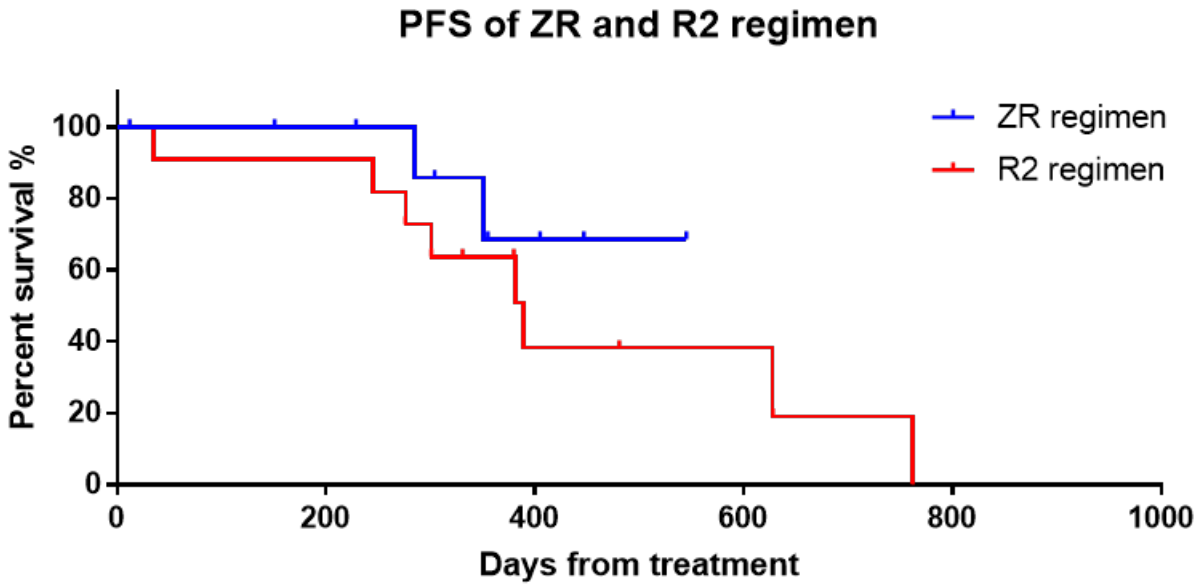
Background: Primary vitreoretinal lymphoma (PVRL) is a rare variant of extra-nodal lymphoma. The best therapeutic strategy for PVRL without CNS involvement remains undefined due to the paucity of high-quality trials in this rare disorder. Local treatments alone, including intravitreal or radiation, are related to a higher CNS relapsing rate, and systemic intensive regimens have demonstrated serious adverse effects. Many efforts have been made to balance toxicity and sustained disease control. However, rituximab and lenalidomide (R2) regimen was failed as front-line treatment in PVRL.

Aims: Zanubrutinib is a new-generation Bruton kinase inhibitor (BTKi) that had good blood-brain-barrier permeability and activities in CNS lymphoma. So we conducted a single-arm, phase II trial for newly diagnosed B-cell PVRL to evaluate the efficacy and safety of ZR (zanubrutinib plus rituximab) regimen with intravitreal MTX.

Methods: This is a prospective multi-center, open-label, phase II trial (NCT 04899453). Immunocompetent patients aged 18–75 years with newly diagnosed B-cell PVRL were eligible. Eligible patients received intravitreal MTX injection and the ZR regimen for 6 cycles as induction therapy, followed by zanubrutinib monotherapy for maintenance for 2 years, or until disease progression, intolerable toxicity, or death. The treatment schedule was: MTX (400 μg) intravitreally injection, weekly×4, biweekly×2, and monthly×10; ZR regimen: rituximab 375 mg/m2 d1, zanubrutinib 160mg bid, 21 days per cycle; Zanubrutinib maintenance: 160mg bid in patients who achieved CR/PR. The primary point was 1-year progression-free survival (PFS). The safety and toxicity were also investigated. Intraocular CR was defined as the intraocular lesion disappearance and undetectable IL-10 concentration in the aqueous humor.

Results: From August 2020 to January 2022, 10 patients were enrolled, and the cut-off date was February 25, 2022. The median age was 55 yr (range 39 to 70) and seven (70%) were female. Most patients (90%) had bilateral eyes involvement and increased baseline interleukin-10 in CSF (range 20.7~118ng/ml, normal range <5ng/ml). 9 patients have completed 6 cycles of ZR regimen and all achieved complete remission; 1 patient was under her first induction cycle. After a median follow-up of 12.4 (0.3-18.1)months, 2 patients suffered CNS relapsing at 9.5 and 11.7 months. The estimated 1 year PFS was 68.5%(95%CI 21.3% to 92.2%). Compared to the historical data (R2 regimen) in our institution, there was a trend that ZR regimen prolonged PFS (unreached vs 389 days, HR 0.47, 95%CI 0.13 to 1.75, p 0.289, see Fig. 1). The toxicities were quite mild. The most common adverse events were bleeding events, including bruising(grade 1, n=4), hypermenorrhea(grade 2, n=1); vitreous hemorrhage after intravitreal injection (grade 3, n=1). ≥10% Grade 1-2 AE included pruritus, fatigue, hypertension, and anemia. No other grade 3-4 AEs were observed.

Image:



Summary/Conclusion: Integration of ZR regimen and intravitreal MTX demonstrated excellent responses rate in newly diagnosed PVRL with very mild toxicity. To our knowledge, this is the first prospective trial to evaluate BTKi in PVRL. Although preliminary, these results provided evidence and support the use of ZR in PVRL. More clinical data will be updated from this ongoing study.