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P1120 THE EFFICACY AND SAFETY OF ZANUBRUTINIB AND DEXAMETHASONE IN SYMPTOMATIC WALDENSTROM MACROGLOBULINNEMIA

Topic: 18. Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

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Background: Bruton tyrosine kinase (BTK) inhibition is an effective treatment approach for patients with Waldenström macroglobulinemia (WM)but the efficacy of single drug is limited.

Aims: This single arm study (ChiCTR2000038140) evaluated the efficacy and safety of the combination of zanubrutinib, a novel, highly selective BTK inhibitor, and dexamethasone in patients with WM.

Methods: Symptomatic patients with WM were enrolled to the regimen of zanubrutinib and dexamethasone (ZD)*. The primary endpoint was objective response rate (ORR), progression-free survival (PFS). Key secondary endpoints included the proportion of patients achieving a complete or very good partial response (CR or VGPR), duration of response (DOR), Time to response (TOR), disease burden, and safety. The control group** were matched patients treated by chemotherapy or immunechemotherapy previously in Beijing Chaoyang Hospital.

Results: A total of 22 Patients with WM were enrolled in this study, median age 67(36-89); 68.2% males, 12 patients were untreated, others were treated patients. IPSS assessment grade1 23.8%; grade2 19.0%; grade3 57.2%. 90.9% (20/22) patients with MYD88L265P mutation, 27.3% (3/11) patients with CXCR4 mutation.

21 patients received ≥1 dose of study treatment. Median follow-up of 8.2 months, median DOR and PFS were not reached; 95% of patients were progression-free at 6 months. ORR was 95% in those (17/18) received ZD regimen more than 2 months. No patient achieved a CR. 33.3% of patients in ZD group achieved a VGPR, time to VGPR within 3 months in 57.1% of patientsa statistically significant difference with control group (0%, P = 0.001). Time to PR in ZD group was 2 months, much faster than control group (11 months) (P = 0.023) by K-M analysis.

The study-safety profile was consistent with previous BTK inhibitor clinical trial data. 45% of patients had any grade AEs. In which, the most frequent grade <=2 AEs were hemorrhage(18.2% all grade 1), rash(9.1%), hyperglycemia (13.6%), infection(9.1%), nausea and vomiting (9.1%), hypogammaglobulinemia(4.5%), neutropenia(9.1%). Grade 3/4 AEs were atrial fibrillation(4.5%), leading to treatment discontinuation. Other cause of treatment discontinuation is hyperglycemia, bowel obstruction by disease.

Comments

*The regimen of ZD : Zanubrutinib 240mg d1-28, dexamethasone 20mg D1-4,15-18. Patients more than 75 years old, Zanubrutinib 160mg d1-28, dexamethasone 10mg D1-4,15-18. After 8 cycle, Zanubrutinib use as maintenance.

** The control group: 22 treated patients with WM, median age 69.5(39-84); 68.2% males. IPSS Grade1 21.4%; Grade2 32.1%; Grade3 42.9%; Unknown 3.6%. 75%(9/12) patients with MYD88L265P mutation, 33%(1/3) patients with CXCR4 mutation. Treatment included chemotherapy(containing nitrogen mustard phenylbutyrate, fludarabine, cyclophosphamide), proteasome inhibitor regimens, rituximab regimens and immunomodulator regimens.

Summary/Conclusion: These results demonstrate that zanubrutinib and dexamethasone are quickly effective in the

treatment of WM, with more deeper response and less toxicity.