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652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

The Efficacy and Safety of Zanubrutinib, Dexamethasone and or Not Cyclophosphamide Regimen in Symptomatic Waldenstrom Macroglobulinnemia

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Background: Treatment of patients improved by Bruton tyrosine kinase (BTK) inhibitor in Waldenström macroglobulinemia (WM) , but the efficacy of BTK-based regimen is not clear.
A im: This single arm study evaluated the efficacy and safety of the com -bination of zanubrutinib, a novel, highly selective BTK inhibitor dexamethasone and or not cyclophosphamide in patients with WM.
Methods:Symptomatic patients with WM were enrolled to the regimen of zanubrutinib, dexamethasone (ZD); patients' whose willingness were limit-cycle treatment received zanubrutinib, dexamethasone and cyclophosphamide (ZCD) *. 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 30 matched patients treated by chemotherapy or immune-chemotherapy previously in Beijing Chaoyang Hospital.
Results: A total of 30 Patients with WM were enrolled in this study median age 67(36-89); 76.7% males, 15 patients were untreated, others were treated patients. IPSS assessment grade1 26.7%; grade2 16.7%; grade3 56.6%. 80.0% (24/30) patients with MYD88L265P mutation 17.6% (3/17) patients with CXCR4 mutation.
29 patients received ≥1 dose of study treatment. Median follow-up of 9.2 months, median DOR and PFS were not reached; 95%of patients were progression-free at 6 months in 25 evaluable patients. ORR was 95% in those (24/25) received ZD/ZCD regimen more than 2 months. No patient achieved a CR. 33.3% of patients in ZD/ZCD group achieved a VGPR, time to VGPR within 3 months who received treatment after 6 months,a statistically significant difference with control group (0%, P = 0.001). Time to PR in ZD/ZCD group was 2 months, much faster than control group (11 months) (P = 0.021) by K-M analysis. 2 patients stopped the treatment after VGPR in ZCD group, 8 patients change to zanubrutinib single drug as maintenance in ZD/ZCD group, 3 patients discontinued treatment by disease progression or patients' willingness, others were still in this study.
The study-safety profile was consistent with previous BTK inhibitor clinical trial data. 43.3% of patients had any grade AEs. In which, the most frequent grade <=2 AEs were hemorrhage(13.7% all grade 1), rash(6.7%), hyperglycemia (20%), infection(6.7%), nausea and vomiting (6.7%), hypogammaglobulinemia(3.3%), neutropenia(26.7%), thrombocytopenia (20.0%), Grade 3/4 AEs were neutropenia(3.3%), thrombocytopenia(6.7%), atrial fibrillation (3.3%), atrial fibrillation leading to treatment discontinuation. Other cause of treatment discontinuation is hyperglycemia, bowel obstruction by disease.
C onclusion: These results demonstrate that zanubrutinib, dexamethasone and or not cyclophosphamide are quickly effective in the treatment of WM, with more deeper response and less toxicity, maybe treatment discontinued by combining with cyclophosphamide after deep remission.

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 regimen of ZCD : Zanubrutinib 320mg d1-28, dexamethasone 20mg D1-4,15-18, cyclophosphamide 300mg, D1-4,15-18. Patients more than 75 years old, Zanubrutinib 160mg d1-28, dexamethasone 10mg D1-4,15-18, cyclophosphamide 200mg, D1-4,15-18. After 8 cycles, patients with VGPR remission receive Chlorambucil 6mg D1-4,15-18, dexamethasone 20mg D1-4,15-18, cyclophosphamide 300mg, D1-4,15-18 for 4cycles, others receive Zanubrutinib as maintenance.

** The control group: 30 treated patients with WM, median age 69.5(39-84); 60.0% males. IPSS Grade1 23.3%; Grade2 20.0%; Grade3 53.3%; Unknown 3.3%. 75% (9/12) patients with MYD88L265P mutation, 33.0% (1/3) patients with CXCR4 mutation. Treatment included chemotherapy (containing nitrogen mustard phenylbutyrate, fludarabine, cyclophosphamide), proteasome inhibitor regimens, rituximab regimens and immunomodulator regimens.

Disclosures Lu: *Jassen Pharmaceutical Ltd:* Consultancy, Speakers Bureau.

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