Abstract: P1108

Title: EFFICACY OF PIRTOBRUTINIB, A HIGHLY SELECTIVE, NON-COVALENT (REVERSIBLE) BTK INHIBITOR IN RELAPSED/REFRACTORY WALDENSTRÖM MACROGLOBULINEMIA: RESULTS FROM THE PHASE 1/2 BRUIN STUDY

Abstract Type: Poster Presentation

Session Title: Indolent and mantle-cell non-Hodgkin lymphoma - Clinical

Background:

Covalent Bruton tyrosine kinase inhibitors (BTKi) have been an important advancement of Waldenström macroglobulinemia (WM) treatment, but they are non-curative, and treatment effectiveness can be limited by intolerance and resistance. Pirtobrutinib is a highly selective, non-covalent (reversible) BTKi.

Aims:

We report the first sizeable cohort of WM patients from BRUIN.

Methods:

Patients with previously treated B-cell malignancies, including WM, were eligible for pirtobrutinib monotherapy in dose-escalation/expansion portions of BRUIN. Key endpoints: investigator-assessed ORR and DoR, per modified IWWM6 criteria, and safety. Major response was CR, very good partial response (VGPR)/PR. The response-evaluable cohort was relapsed/refractory (R/R) WM patients in phase 1/2 who had undergone first response assessment/discontinued therapy. The safety cohort was patients with B-cell malignancies receiving at least one pirtobrutinib monotherapy dose (n=725). Data cut: 31 January 2022.

Results:

Of 78 WM patients(median age: 68 [42-84] years), the median number of prior therapies was 3 (1-11). 66 (85%) patients had received chemotherapy+anti-CD20 antibody (CIT), 61 (78%) ≥1 prior BTKi (≥2: 13/61, 21%), and 50 (64%) CIT+BTKi. Of 61 patients who received ≥1 prior BTKi, 40 (66%) discontinued BTKi due to disease progression. 91% (71/78) received the recommended phase 2 dose (200 mg once daily) as starting dose. The major response rate for 72 response-evaluable patients was 68% (95%CI, 56-79); 17 VGPRs (24%), 32 PRs (44%). At a median response follow-up time of 7.7 months, median DoR among 49 responding patients was not reached (95%CI, 10-NE); 6-month estimated DoR rate: 86% (95%CI, 69-94). Of 55 response-evaluable patients who had received ≥1 prior BTKi, the major response rate was 64% (95%CI, 50-76); 13 VGPRs (24%), 22 PRs (40%) (median DoR also not reached [95%CI, 8-NE], 6-month estimated DoR rate: 83% [95%CI, 60-93]). Of 60 response-evaluable patients who had received CIT, the major response rate was 68% (95%CI, 55-80); 13 VGPRs (22%), 28 PRs (47%). Of 44 response-evaluable patients who had received CIT+BTKi, the major response rate was 64% (95%CI, 48-78); 9 VGPRs (21%), 19 PRs (43%). In the safety cohort of all pirtobrutinib-treated patients with B-cell malignancies (n=725), the most frequent TEAEs were fatigue (26%), diarrhea (22%), contusion (19%); most frequent Grade≥3 TEAE: neutropenia (20%). Low rates of Grade≥3 TEAEs hypertension (3%), hemorrhage (2%), atrial fibrillation/flutter (1%) were observed. Overall, 15 (2%) patients discontinued due to treatment-related AE.

Summary/Conclusion:

Pirtobrutinib was highly active in WM patients, regardless of prior therapy. Pirtobrutinib was well tolerated with low discontinuation rates.

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Keywords: Bruton’s tyrosine kinase inhibitor (BTKi), Clinical trial, Waldenstrom’s macroglobulinemia, Non-Hodgkin’s lymphoma