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Efficacy and safety of poziotinib in treatment-naïve NSCLC harboring HER2 exon 20 mutations: A multinational phase II study (ZENITH20-4)

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Background

Treatment of non-small cell lung cancer (NSCLC) with EGFR and HER2 exon 20 mutations is an unmet medical need. We evaluated the efficacy and safety of poziotinib, a potent tyrosine kinase inhibitor (TKI) able to overcome the restricted binding pocket of exon 20 mutations, in newly diagnosed patients with NSCLC and HER2 exon 20 insertion mutations in a multinational, multi-cohort Phase 2 study.

Methods

ZENITH20 study enrolled pts with advanced NSCLC with exon 20 insertion mutations: previously treated EGFR, previously treated HER2, naïve EGFR and naïve HER2 in Cohorts 1, 2, 3, and 4 respectively as identified by genetic profiling of tumor tissue. Poziotinib (16 mg) was administered orally daily either as once (QD) or twice (BID), allowing dose interruptions/reductions for toxicity. The primary endpoint was objective response rate (ORR) evaluated centrally by an independent image review committee using RECIST 1.1 criteria. Secondary endpoints included disease control rate (DCR), duration of response (DOR), progression-free survival (PFS) and safety. Data from Cohort 4 is presented.

Results

48 received 16 mg QD and 23 received 8 mg BID in Cohort 4. QD data is presented; BID dosing group is currently enrolling. In QD group, 48 patients with a median age of 61 years (34-87) were treated and 4 patients are ongoing in the study. Majority were White (75%), female (54%), non-smokers (69%) with ECOG PS of 1 (65%). 88% patients had dose interruptions and 76% had reductions from 16 mg starting dose. 12% had AE related discontinuations. The most common treatment-related Grade ≥3 AEs were rash (35%), diarrhea (14%), stomatitis (20%) and paronychia (8%). Primary endpoint ORR was 44% (95% CI: 29.5 – 58.8%) in the 48 treated patients. 2 additional patients had response not confirmed (uORR=48%). DCR was 75%. Median DoR was 5.4 months (range: 2.8-19.1+) with 3 patients continuing treatment. Median PFS was 5.6 months (range: 0-20.2+).

Conclusions

Poziotinib demonstrated clinically meaningful efficacy in newly diagnosed NSCLC patients with HER2 exon 20 mutations with 16 mg QD dosing. Safety profile was similar to other second generation TKIs with manageable AEs. Study is ongoing with BID dosing currently.

Clinical trial identification

NCT03318939.

Legal entity responsible for the study

Spectrum Pharmaceuticals, inc.

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Disclosure

L. Dreling: Financial Interests, Institutional, Full or part-time Employment: Spectrum Pharmaceuticals. G. Bhat: Financial Interests, Institutional, Full or part-time Employment: Spectrum Pharmaceuticals. F. Lebel: Financial Interests, Institutional, Full or part-time Employment: Spectrum Pharmaceuticals. All other authors have declared no conflicts of interest.