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Prospective observational study of brigatinib after alectinib in ALK-positive, non-small cell lung cancer: Efficacy and biomarker analyses from cohort A of the WJOG11919L/ABRAID trial

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Background

Brigatinib is a unique ALK-TKI that is effective against many resistance mutations. Although alectinib is widely used, there is no established strategy for subsequent treatment.

Methods

Cohort A of the WJOG11919L/ABRAID trial, a prospective multicenter observational study, enrolled patients who received brigatinib as the second ALK-TKI following alectinib. The primary endpoint was PFS. ctDNA obtained prior to brigatinib was analyzed using the PGDx Elio Plasma Resolve panel.

Results

Of 104 enrollments, 102 were evaluated for efficacy. Age [median (range)]; 63 (24–93), Adeno/others [n (%)]; 99 (97.1)/3 (2.9), PS 0/1/2/3; 42 (41.2)/49 (48.0)/6 (5.9)/2 (2.0), Stage III/IV/recurrence; 5 (4.9)/85 (83.3)/12 (11.8). The mPFS was 6.5m (95% CI: 4.83–8.84); PFS rates at 12m and 24m were 33.3% and 20.5%. The ORR and DCR were 31.4% (95% CI: 22.5–41.3), 70.6% (95% CI: 60.7–79.2), respectively. Among the 39 patients with CNS disease, mCNS-PFS was 10.8m (95% CI: 6.0–21.9). ALK mutations were detected in 16 of 87 ctDNA-analyzed cases: G1202R (n=2), V1180L (n=4), I1171X (n=4), L1196M (n=2), G1202R/I1171T, E1210K, F1174L, and N647Tfs*8 (n=1). Among three patients with G1202R, two achieved PR. In patients with ALK mutations including G1202R, the ORR was 43.8%, and mPFS was comparable with patients without [7.3m (2.5–23.8), 6.9m [4.7–11.0], HR 1.0 [95%CI: 0.54–1.88], p=0.99). TP53 mutations were detected in 19 patients (missense, n=10; nonsense/frameshift, n=9), who showed shorter PFS compared to patients without [5.8m (1.8–8.3) vs. 8.3m (4.9–12.1), HR 1.67 [95%CI: 0.96-2.92], p=0.068]. Common AEs included elevated CPK in 50 patients (48.1%), AST in 36 (34.6%), and ALT in 28 (26.9%). ≥Grade 3 was in 15.4%, 4.8%, and 4.8%, respectively. Pneumonitis/ILD occurred in 10.6% (≥Grade 3: 4.8%). One Grade 5 respiratory failure was reported.

Conclusions

In this large prospective study of post-alectinib cases, brigatinib appeared to be effective regardless of the presence of ALK resistance mutations, including G1202R. Together with the safety profile consistent with previous reports, these findings suggest that brigatinib may be an appropriate treatment option in this setting.

Clinical trial identification

UMIN000042439.

Legal entity responsible for the study

The West Japan Oncology Group (WJOG).

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Disclosure

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