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Primary results of a randomized phase II study of osimertinib plus bevacizumab versus osimertinib monotherapy for untreated patients with non-squamous non-small cell lung cancer harboring EGFR mutations: WJOG9717L study

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Background

Osimertinib (Osi) has been a standard treatment for untreated patients (pts) with non-small-cell lung cancer (NSCLC) harboring an *EGFR* mutation. Previous studies showed that the addition of anti-VEGF inhibitors to erlotinib prolonged progression-free survival (PFS) in *EGFR* mutated non-squamous NSCLC (Ns-NSCLC) pts. This phase II, open-label, randomized trial was conducted to compare Osi plus bevacizumab (Bev) with Osi monotherapy for untreated pts with advanced *EGFR* mutated Ns-NSCLC.

Methods

This study enrolled untreated pts with advanced Ns-NSCLC harboring an *EGFR* sensitizing mutation (Del19 or L858R), and without symptomatic brain metastases. 122 eligible pts were randomized in a 1:1 ratio to receive either Osi (80 mg, daily) plus Bev (15 mg/kg, every 3 weeks) (OB arm) or Osi monotherapy (O arm), and stratified according to sex, stage and *EGFR* mutation status. The primary endpoint was PFS, assessed by blinded, independent central radiologic reviewer (BICR). Assuming that the median PFS in the OB arm and the O arm were 27 and 18 months, planned sample size was 120 in total to give a power of 80% with a one-sided alpha of 20%, with an accrual period of 1.5 years and a follow-up period of 2 years.

Results

Between January 2018 and September 2018, 122 pts were enrolled (OB arm, 61 pts O arm, 61 pts). At a median follow-up of 19.8 months, median PFS by BICR was 22.1 months for OB arm and 20.2 months for O arm, with a hazard ratio (HR) of 0.862 (60% CI, 0.700–1.060; 95% CI, 0.531–1.397; one-sided stratified log-rank p=0.213). In subgroup analysis, ex-smoker (HR 0.481) and pts with 19del (HR 0.622) showed better trend of PFS in OB arm. Objective response rate was 82% in OB arm and 86% in O arm. Grade 3-4 adverse events were observed in 34 pts (56%) for OB arm and in 29 (48%) for O arm. Any grade paronychia, rash acneiform, hypertension, epistaxis and proteinuria were frequently observed in OB arm. Among them, 3% and 18% experienced any grade pneumonitis, and grade 3 pneumonitis in 1 pt for each arm.

Conclusions

This study failed to show the efficacy of OB arm for improving PFS in untreated pts with EGFR mutated Ns-NSCLC.

Clinical trial identification

UMIN000030206.

Legal entity responsible for the study

West Japan Oncology Group.

Funding

AstraZeneca.

Disclosure

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