

LBA73

PACE-LUNG: A multicenter, single-arm, phase II clinical trial evaluating the efficacy of additional chemotherapy for patients with EGFRm NSCLC with the continued presence of plasma ctDNA EGFRm at week 3 after start of osimertinib first-line treatment (AIO-TRK-0422/ass)

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Background

In patients (pts) with common EGFR-mutant (EGFRm) advanced/metastatic non-small cell lung cancer (NSCLC), persisting EGFRm positivity in circulating tumor DNA (ctDNA) after 3 weeks on osimertinib is associated with an unfavorable outcome with a median progression-free survival (PFS) of 11.3 months (mo) (FLAURA). Recently, the addition of chemotherapy (CTx) to osimertinib has significantly improved PFS and overall survival (OS) with added toxicity compared with osimertinib alone. As no predictive biomarker is available for treatment stratification in these pts, PACE-LUNG aims to explore feasibility and clinical utility of a biomarker-guided treatment intensification strategy in pts with EGFRm NSCLC.

Methods

PACE-LUNG is an academic multicenter, single-arm, investigator-initiated phase II trial. Pts with untreated advanced/metastatic NSCLC and persistent ctDNA EGFRm by Guardant360® after 3 weeks osimertinib monotherapy received treatment escalation with 4 cycles of additional CTx, followed by osimertinib maintenance. Primary endpoint is investigator-assessed PFS1 per RECIST 1.1 from start of CTx. Secondary endpoints include PFS0, measured from start of osimertinib, OS1, safety, and others.

Results

Between Jan 2022 and Sep 2025, 255 pts were screened; 74 (29%) had persistent ctDNA EGFRm after 3 weeks of osimertinib. Thereof, 50 pts received additional CTx. Median age was 63 yrs (range, 39-85), ECOG PS was 0 or 1 (94%) at CTx initiation. Median PFS1 was 16.3 mo (95% CI, 10.8-18.9) with 57.8% (42.0-70.6) and 21.7% (10.2-36.1) of pts progression-free and alive at 12 and 24 mo after start of CTx, respectively. Median PFS0 was 17.8 mo (12.9 – 20.5). Median OS1 was 29.2 mo (95% CI, 23.2-42.4) with 87.4%(74.1-94.2) and 65.4% (48.0-78.2) of pts alive at 12 and 24 mo, respectively. No new safety signals were observed.

Conclusions

PACE-LUNG demonstrates that ctDNA-guided treatment intensification is feasible and results in a PFS that compares favorably with

historical data. This approach should be used in future trials to enable personalized therapy in pts with EGFRm NSCLC.

Clinical trial identification

EudraCT 2019-004757-88.

Legal entity responsible for the study

Goethe University Frankfurt, Germany.

Funding

AstraZeneca.

Disclosure

M. Sebastian: Financial Interests, Personal, Advisory Board: AstraZeneca, Boehringer Ingelheim, Takeda, Gilead, Daiichi Sankyo, Regeneron Pharmaceuticals; Financial Interests, Personal, Other, DSMB Member: Amgen; Financial Interests, Personal, Invited Speaker: BeOne; Financial Interests, Personal, Other, Travel cost and accommodation: Pfizer, Merck, Takeda; Financial Interests, Personal, Other, DSMB: CureVac; Financial Interests, Institutional, Funding, IIT funding: Gilead, BeOne; Financial Interests, Institutional, Coordinating PI, IIT funding: AstraZeneca; Non-Financial Interests, Member of Board of Directors: AIO. M. 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