P14-15780

O-2. A randomized phase III trial of afatinib（A）+paclitaxel（P）vs investigator's choice chemotherapy（CT）in patients（pts）with metastatic non-small-cell lung cancer（NSCLC）progressed on erlotinib/gefitinib（E/G）and A：LUX-Lung 5

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Background：Improved disease control with continuation of EGFR inhibition after progression has been suggested in non-randomized studies. The Phase III Lux-Lung 5 trial assessed the efficacy of continuation of the irreversible ErbB family blocker, A, plus P in NSCLC pts who had progressed after benefit from reversible EGFR tyrosine kinase inhibitors（E/G）and A.
Methods：Pts who had failed ≥1 line of CT and E/G（after ≥12 wks treatment）were treated with A（50 mg/day）in Part A（n=1154）. On progression, pts with ≥12 wks on A were eligible to be randomized 2：1 to A+P（40 mg/day；80 mg/m^2/wk）or single agent investigator's choice CT in Part B. Primary endpoint was progression-free survival（PFS）. Other endpoints included objective response rate（ORR）, overall survival（OS）and safety.
Results：202 pts were randomized（A+P, n=134；CT, n=68）and baseline characteristics were well balanced（median age 60 yrs, females 49%, ECOG PS 0-1 91%）. A significant increase in median PFS occurred on A+P vs CT（5.6 vs 2.8 mo, HR[95% CI]0.60[0.43-0.85]；

p=0.003）. ORR was significantly higher on A+P vs CT（32.1% vs 13.2%；p=0.005）. Median OS was similar in both arms（12.2 vs 12.2 mo, HR[95% CI]1.00[0.70-1.43]；p=0.994）. Median exposure to study medication was 133 days with A+P and 51 days with CT. Most common related adverse events（AEs）with A+P vs CT were diarrhea（54% vs 7%）, alopecia（33% vs 15%）and asthenia（27% vs 28%）.

Conclusions：Continued ErbB family blockade with A+P significantly improved PFS and ORR vs CT alone in heavily pretreated pts with acquired resistance to E/G and progression on A monotherapy. Our data support that tumors progressing on E/G and A still depend on signalling via ErbB family receptors and benefit from continuous treatment with A.