Introduction

- Genotyping is required to identify patients with advanced cancer eligible for targeted therapy.
- Many do not receive biomarker testing due to limitations of tissue analysis, in part due to limitations associated with tissue-only genotyping practices, the growing list of biomarkers recommended to be tested and long turnaround time.1,2
- Next generation sequencing (NGS) liquid biopsy overcomes some of these limitations but is not yet fully adopted.3,4
- We report here the clinical performance of a comprehensive liquid biopsy test based on next generation sequencing (NGS) of circulating tumor DNA (ctDNA) for the identification of NSCLC patients with EGFR exon 19 deletions (ex19del) or L858R mutations (collectively (EGFRm) or EGFR T790M, eligible for treatment with osimertinib.

- Osimertinib is a third-generation, irreversible, oral EGFR-TKI that potently and selectively inhibits both EGFRm and EGFR T790M and has demonstrated efficacy in NSCLC CNS metastases.5,9

Methods

- Patients: 441 (79%) of 556 pts randomized in the FLAURA trial (NCT012151981; 6. Global Medicines Development, AstraZeneca, Cambridge, UK; 7. Translational Medicine, Early Research and Development, AstraZeneca, Boston, Massachusetts, USA; 8. Medical Affairs, Guardant Health, Redwood City, California, USA; 9. Guangdong Provincial Peoples Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China; 10. Emory University School of Medicine Worship Cancer Institute, Atlanta, Georgia, USA; 11. Clinical Development, Guardant Health, Redwood City, California, USA)

Conclusions

- Guardant360 demonstrated clinical performance similar to cobas® EGFR Mutation Test for identifying EGFRm or T790M positive NSCLC patients for treatment with osimertinib in retrospective analysis of plasma samples from patients randomized in the pivotal FLAURA and AURA3 studies.

Discussion

- The ability of G360 to detect EGFRm and T790M positive NSCLC patients for treatment with osimertinib was associated with statistically significant PFS benefit relative to control therapy in NSCLC patients with EGFRm ex19del or EGFR T790M (FLAURA) and T790M positive patients were similar to those obtained for the Full Analysis Set and for patients with these mutations as detected by the cobas test using tissue or plasma specimens (Figure 2 and 3).

- Due to trial design, efficacy analyses were limited to tissue positive patients.

- Osimertinib and T790M are not detected in liquid biopsy of all tissue positive NSCLC patients, as not all tumors shed detectable levels of mutated ctDNA in the blood.

Results

- Baseline patient demographics and clinical characteristics were balanced between treatment arms considering randomization ratio (FLAURA, 1:1; AURA3, 2:1; Table 1).

- PFS HR results in G360 EGFRm and EGFR T790M positive patients were similar to those obtained for the Full Analysis Set and for patients with these mutations as detected by the cobas test using tissue or plasma specimens (Figure 2 and 3).

- Table 1. Baseline Patient Demographics and Clinical Characteristics

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