

P3.243: Osimertinib With or Without Savolitinib as 1L treatment in De Novo *MET* aberrant, *EGFR*m Advanced NSCLC: An Updated Analysis From FLOWERS

Jin-Ji Yang^{1#}, Anna Li¹, Zong-Kun Shi², Ke-Jing Tang³, Jun Zhao⁴, Yun Jia⁵, Hao Sun¹, Yong-Sheng Li⁶, Cheng-Zhi Zhou⁷, Yun Fan⁸, Wei-Neng Feng⁹, Hai-Yan Tu¹⁰, Juan Li¹¹, Bing-Fei Xu¹, Xiao-Ling Chen¹⁰, Chong-Rui Xu¹⁰, Hua-Jun Chen¹, Hong-Hong Yan¹⁰, Dan-Dan Cao²

¹Division 1 of Pulmonary Oncology, Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Southern Medical University, Guangzhou, China; ²Genetron Health (Beijing) Co. Ltd., Beijing, China;

³Division of Pulmonary and Critical Care Medicine, the First Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China. ⁴Key laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department I of Thoracic Oncology, Peking University Cancer Hospital and Institute, Beijing, China. ⁵Dongguan People's Hospital, Dongguan, China. ⁶Chongqing University Cancer Hospital, Chongqing, China.

⁷The First Affiliated Hospital of Guangzhou Medical University, National Clinical Research Center for Respiratory Disease, State Key Laboratory of Respiratory Disease, Guangzhou Institute of Respiratory Health, Guangzhou, China. ⁸Zhejiang Cancer Hospital, Hangzhou, China. ⁹The First People's Hospital of Foshan, Foshan, China. ¹⁰Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China.

¹¹Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, Affiliated Cancer Hospital of University of Electronic Science and Technology of China, Chengdu, China

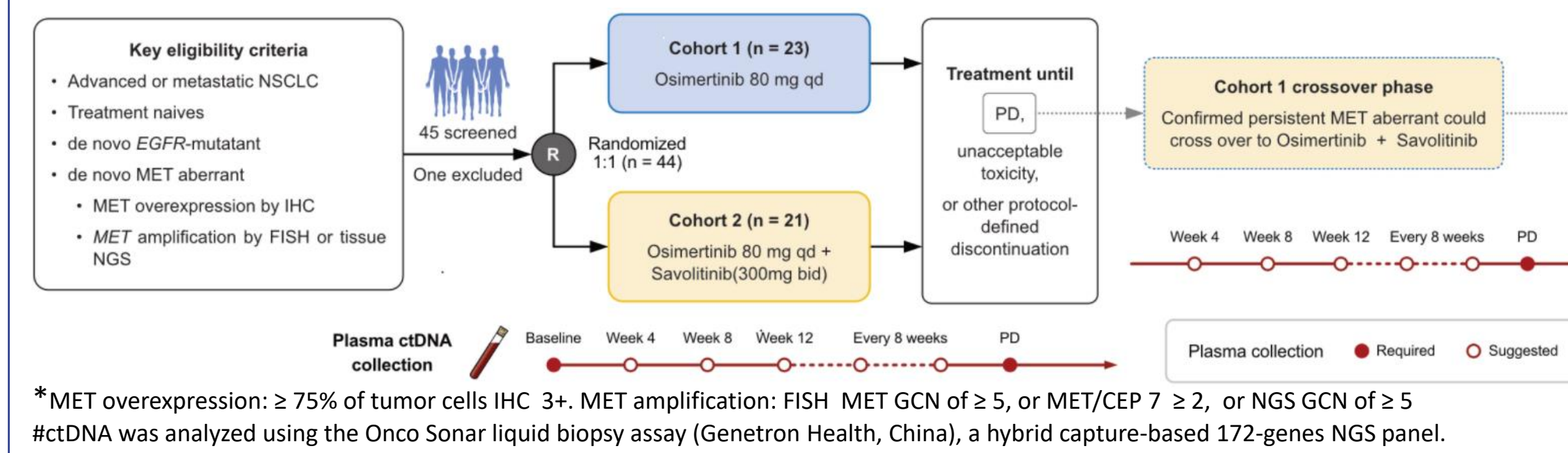
INTRODUCTION

- EGFR*m advanced non-small cell lung cancer (NSCLC) patients with co-existing de novo *MET* amplification and/or overexpression were observed to have a limited efficacy on first-line *EGFR*-TKI monotherapy¹⁻².
- In primary analysis from this prospective phase II FLOWERS study (CTONG 2008, NCT05163249), osimertinib plus savolitinib as 1L treatment showed preliminary promising antitumor activity with a manageable safety profile in these patients³.
- Here, the updated efficacy and safety results with longer follow-up alongside exploratory biomarker analyses are reported.

METHODS

- FLOWERS is a phase 2, prospective, non-comparative, randomized trial (Figure 1).
- Patients with advanced *EGFR*m NSCLC harboring de novo *MET* amplification and/or overexpression were randomized to receive either osimertinib monotherapy (Cohort 1) or osimertinib plus savolitinib (Cohort 2)
- Exploratory ctDNA and acquired resistance mechanism analyses were conducted to characterize baseline plasma molecular profiles, early on-treatment molecular dynamics, molecular clearance at Week 4, and acquired resistance mechanism.

Figure 1. FLOWERS study design



Primary endpoint	Secondary endpoints	Exploratory endpoints
ORR in each cohort	• PFS, DoR, DCR, OS • Safety and tolerability	• Acquired resistance mechanism • Biomarker analysis (ctDNA clearance, etc.)

Correspondence

Jin-Ji Yang, Email: yangjinji@gdph.org.cn

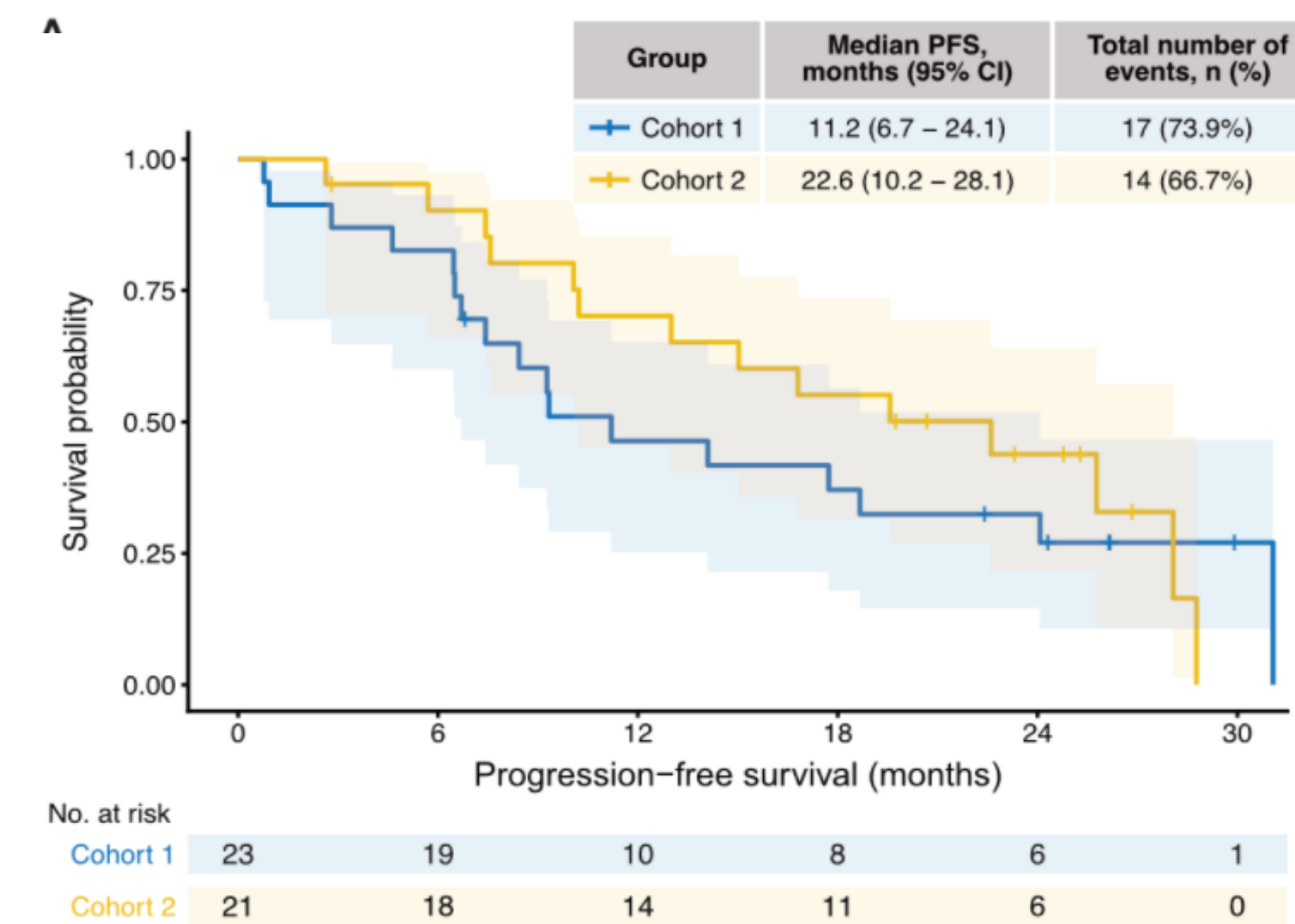
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RESULTS

Efficacy

Figure 2. Progression-free survival



- Overall, 44 patients were randomized (Cohort 1, n=23; Cohort 2, n=21). As of November 13, 2025, the median follow-up was 24.3 months.
- The median PFS was 11.2 months (95% CI: 6.7–24.1) in Cohort 1 and 22.6 months (95% CI: 10.2–28.1) in Cohort 2 (Figure 2). The median DOR was 12.9 months (95% CI: 8.3–NE) and 20.1 months (95% CI: 10.2–NE), respectively.
- OS data remained immature.

Safety

- Grade ≥3 TRAEs were reported in 17.4% (4/23) of patients in Cohort 1 and 61.9% (13/21) in Cohort 2.
- The most common grade ≥3 TRAEs were blood creatine phosphokinase increased (8.7%) in Cohort 1 and alanine aminotransferase increased (19%) in Cohort 2.
- No new safety signals or treatment-related deaths were observed.

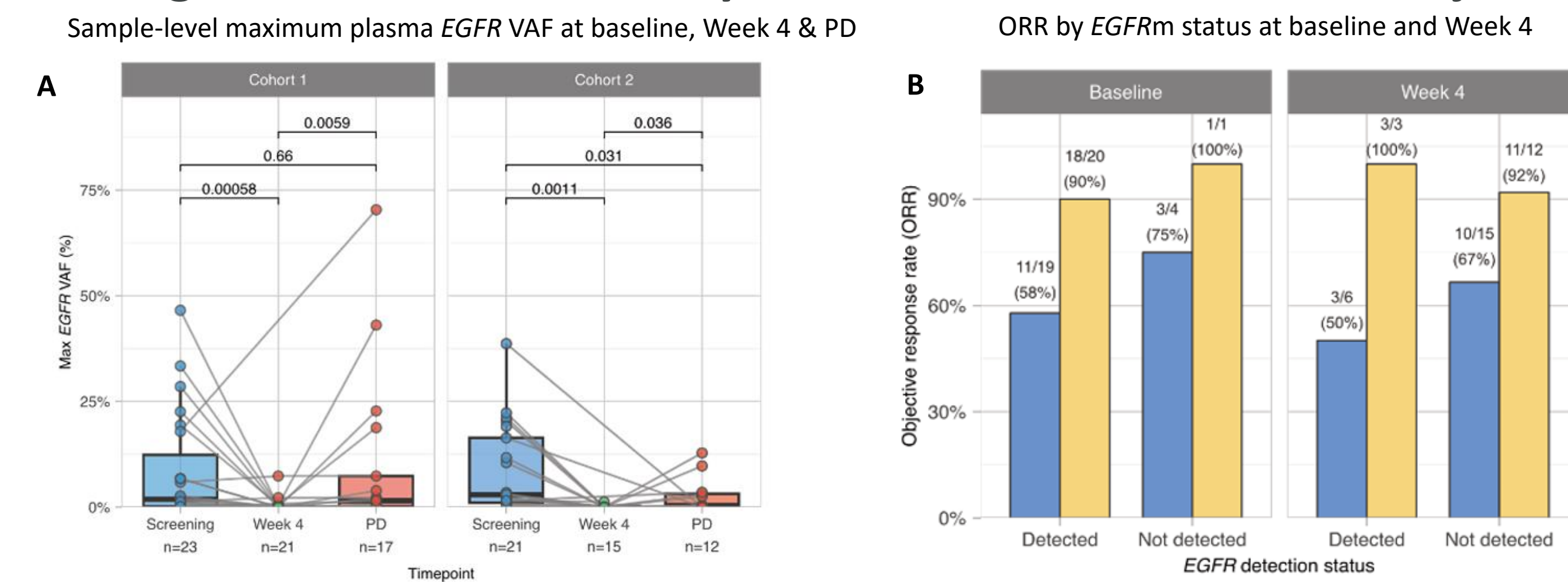
CONCLUSION

- Osimertinib plus savolitinib demonstrates clinical meaningful efficacy and manageable safety with longer follow-up in treatment naïve patients with advanced NSCLC harboring *EGFR*m and concurrent de novo *MET* abnormalities.
- These findings suggest reduction in frequency of detection of *EGFR* and *MET* resistance in dual inhibition of osimertinib plus savolitinib and demonstrate preliminary proof of mechanism with potent inhibition of resistance via the *EGFR* and *MET* pathways. These results support its potential as a 1L treatment option for these patients.

AI Use Disclaimer: No artificial intelligence (AI) tools were used in the development of this poster.

ctDNA analysis & Acquired resistance mechanisms

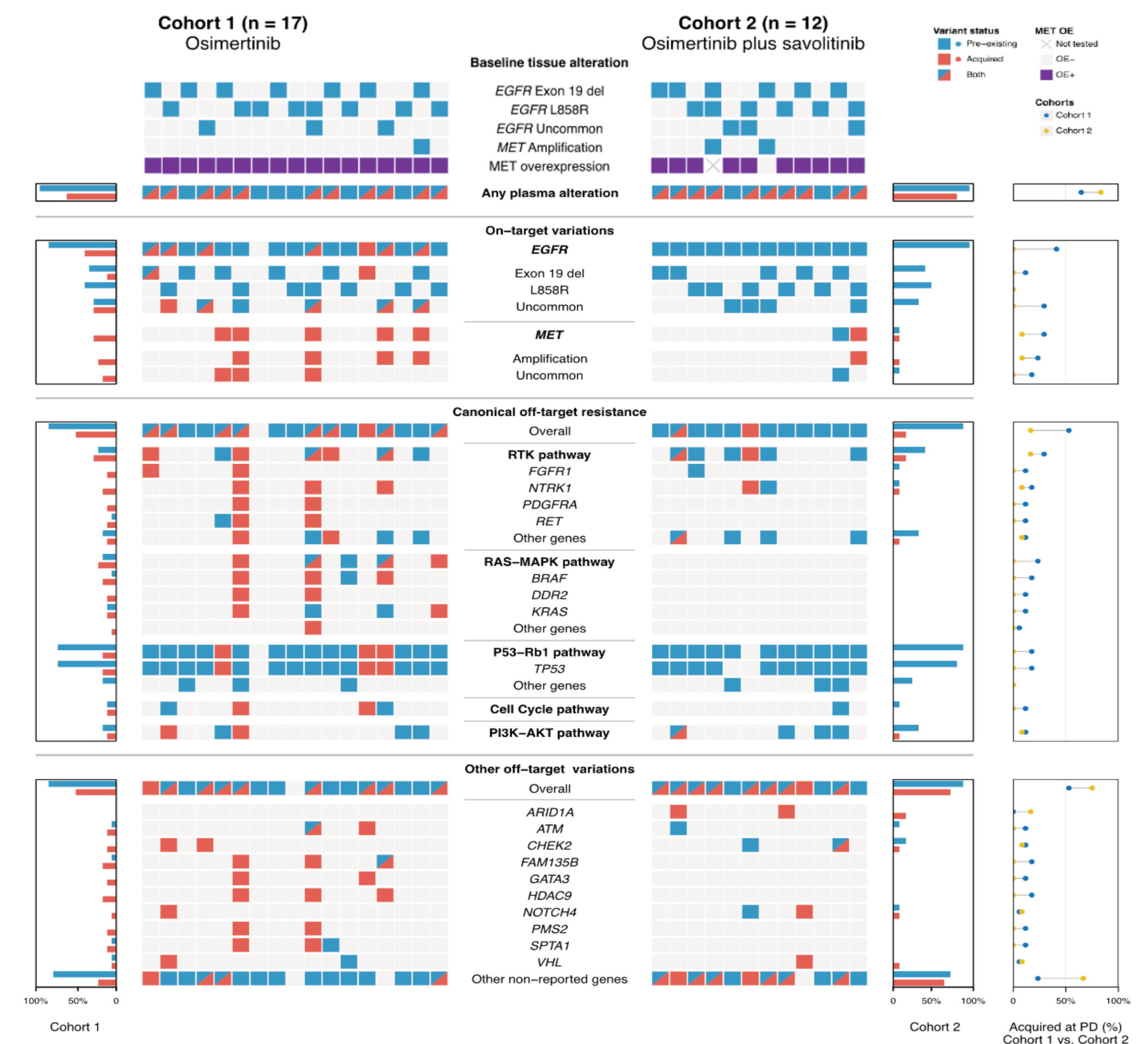
Figure 3. Plasma *EGFR*m dynamics and association with objective response



- At Week 4, patients with persistent ctDNA *EGFR*m detection had ORRs of 50% (3/6) and 100% (3/3), whereas those achieving ctDNA *EGFR*m clearance had ORRs of 67% (10/15) and 92% (11/12), respectively (Figure 3, B).

- Acquired resistance mechanisms of Cohort 1 were similar with previously reported, with no novel mechanisms detected.
- Acquired *EGFR* or *MET* alterations were observed in 52.9% and 8.3% of patients in Cohort 1 and Cohort 2. Cohort 2 had lower rates of acquired *MET* amplification (8.3% vs. 23.5%) and other *EGFR* resistance alterations (0% vs. 17.6%) (Figure 4).
- Alterations involving canonical off-target resistance were also numerically lower for Cohort 2 vs. Cohort 1 (16.7% vs. 52.9%), while there was an enrichment of unknown alterations in Cohort 2 (66.7% vs. 47.1%) (Figure 4).

Figure 4. Pre-existing and acquired plasma variations in paired samples



Disclosures

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