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2022 World Conference
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AUGUST 6-9, 2022 | VIENNA, AUSTRIA



Real-World Landscape of EGFR C797X Mutation as a Resistance Mechanism to Osimertinib in NSCLC

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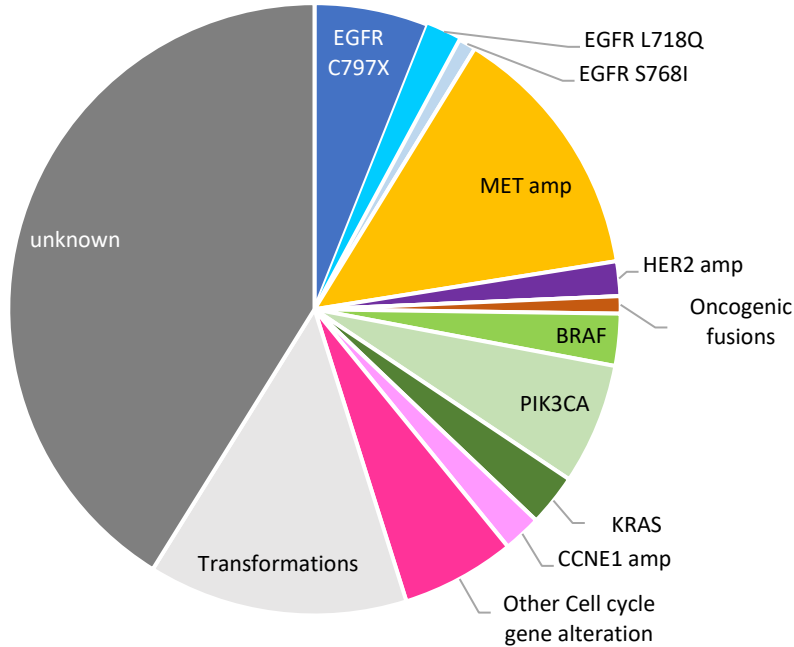
DISCLOSURES

Commercial Interest	Relationship(s)
Amgen, GSK, Eisai, BMS	Consultancy/advisory board
Astra Zeneca, BMS, Amgen, Genmab, Takeda, Merck, GSK	Research support

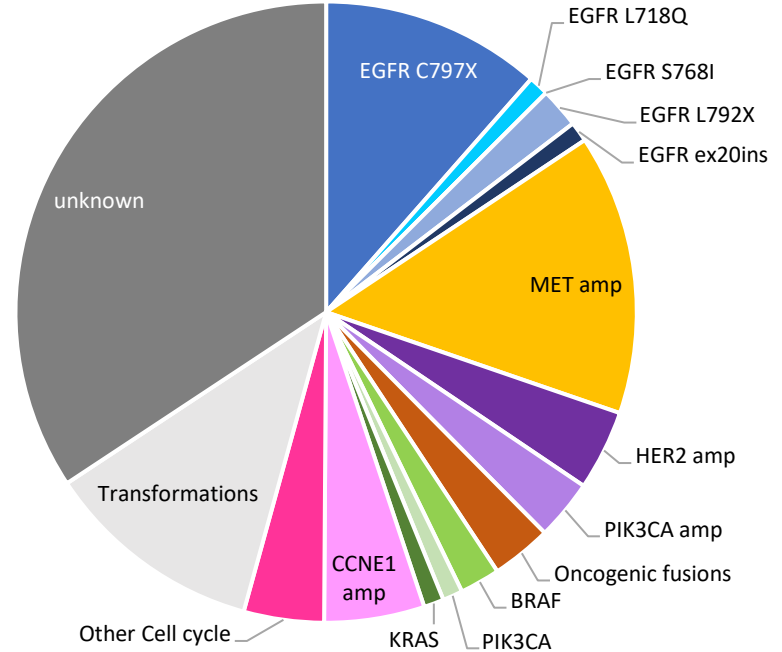
Resistance to osimertinib is complex with multiple mechanisms

- 3rd-gen EGFR TKI Osimertinib is the standard of care for NSCLC patients with common EGFR mutations
- After osimertinib, EGFR C797X mutations are one of the major resistance mechanisms
- The dynamics of the appearance of resistance mechanisms remains poorly studied

Resistance mechanisms to 1L Osimertinib



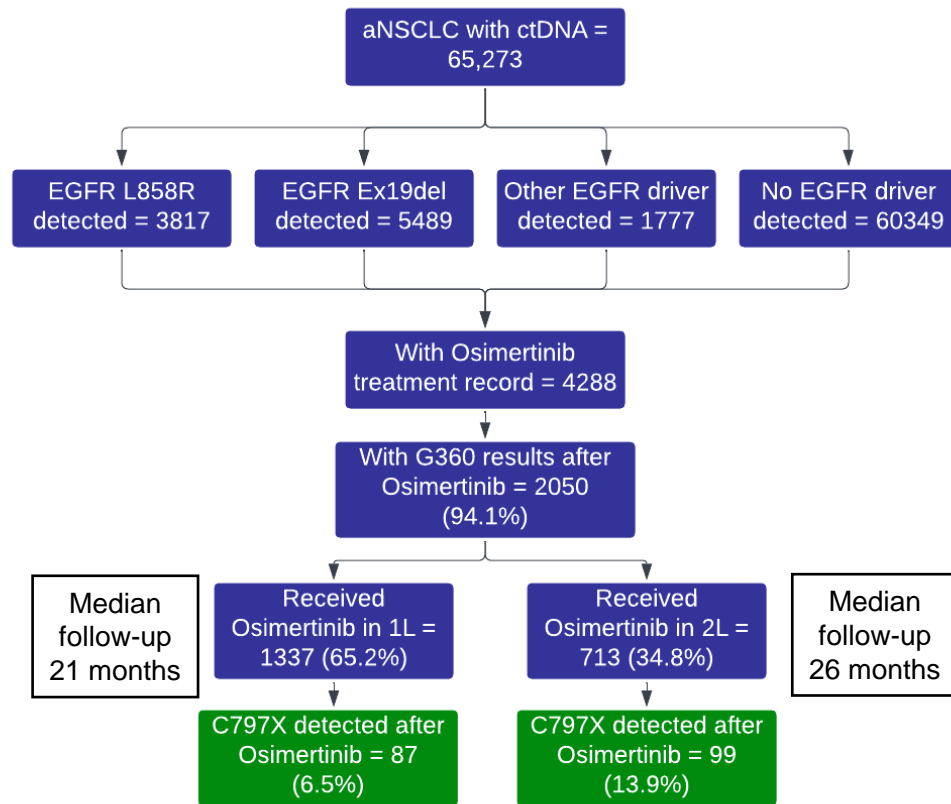
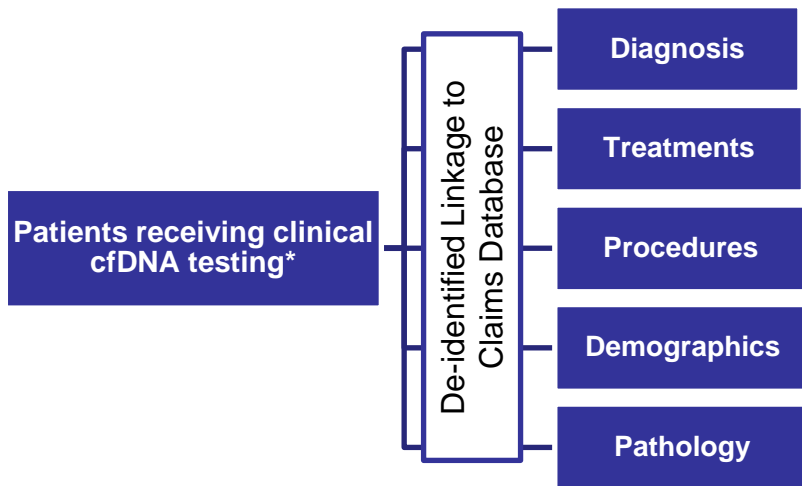
Resistance mechanisms to 2L Osimertinib



Leonetti et al. *British Journal of Cancer*, 2019.

Real world data integrating Guardant360 cfDNA and INFORM data

- INFORM is an aggregated commercial payer claims database with de-identified records of over 174,000 U.S.-based advanced cancer patients with clinical cfDNA* results.

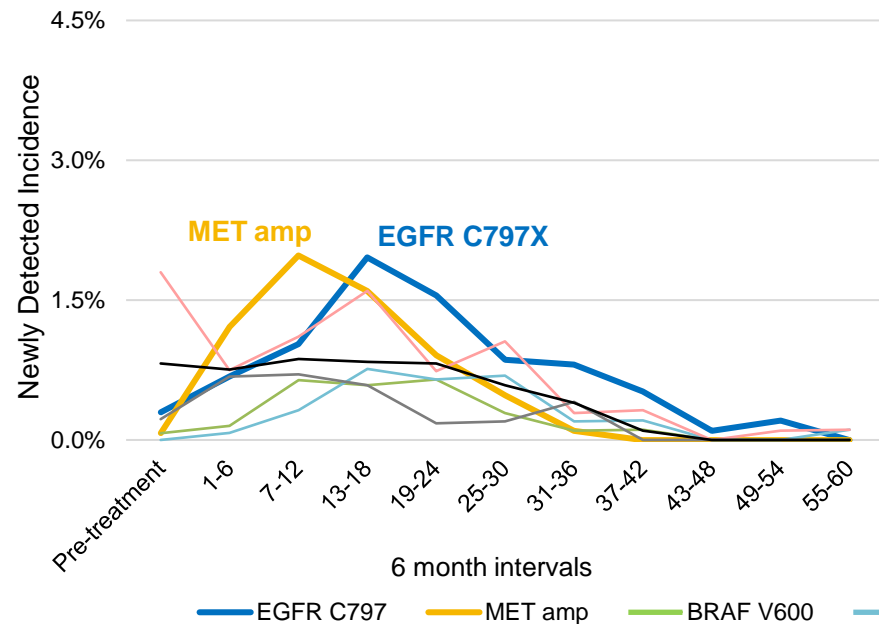


*cfDNA testing done via either Guardant360 CDx or Guardant360

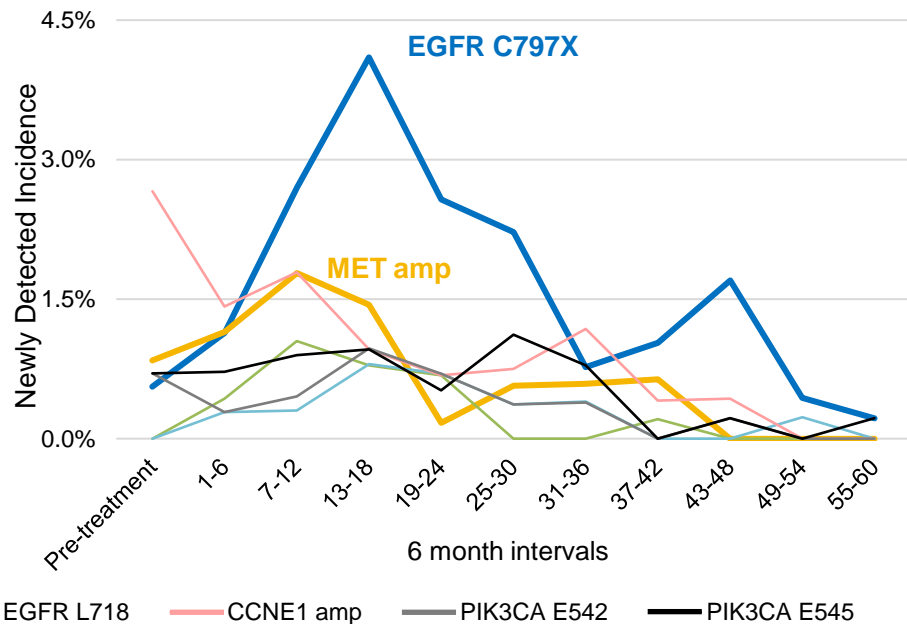
MET amp is most common acquired resistance mechanism in 1st year of 1L osimertinib, while EGFR C797X is most common after the 1st year

6-month Incidence of Common Acquired Resistance Mutations after osimertinib

After 1L osimertinib (n=1337)



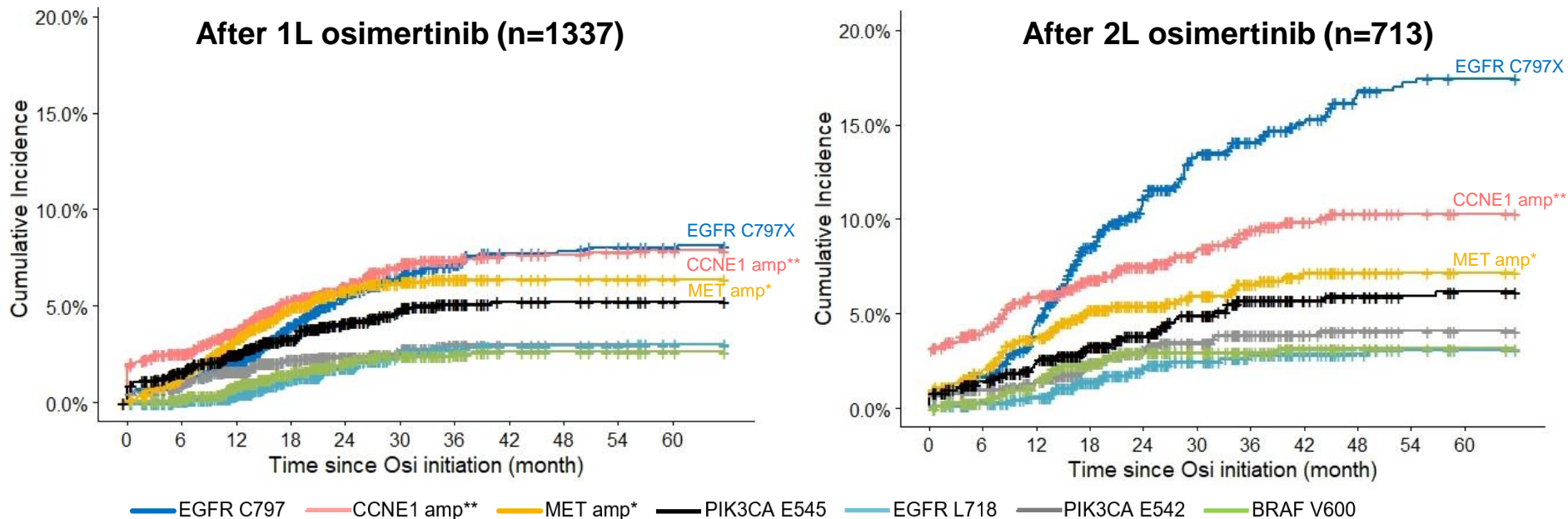
After 2L osimertinib (n=713)



*Plasma copy number ≥ 2.1 , per clinical reporting

EGFR C797X is the most common on-target or off-target resistance mutation, cumulatively, after osimertinib treatment

Cumulative incidence of common resistance mutations after osimertinib initiation[#]



- The cumulative incidence of EGFR C797X in a subset of likely 1L osi progressors (n=600) was 12.5%[&]

[#]Including pts who were sequenced anytime after osimertinib. [&]When analysis limited to those who discontinued osimertinib within 60 days of G360 (likely progressors).

*Including focal MET amp, per clinical reporting. **including both focal and aneuploidy of CCNE1 amplification, per clinical reporting.



Conclusions and Limitations

- MET amplification is the most common initial resistance mutation in the first year of 1L osimertinib, but EGFR C797X mutations subsequently emerge and are the most common resistance after the first year
- Cumulatively, EGFR C797X mutations were 1.25 times more common than MET amplification after 1L osimertinib and 2.4 times more common after 2L osimertinib
- In patients likely progressing after 1L osimertinib, the cumulative incidence of EGFR C797X was 12.5%
- This study demonstrates the needs for novel targeted therapy to address resistance mechanisms in patients who progressed on Osimertinib, with EGFR C797, MET amp and CCNE1 amp having the highest incidence
- Limitations inherent to healthcare claims data include: missing clinical information not routinely reported, potential for misclassification, representativeness of the study cohort