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Efficacy of Sequential ALK- and MET-TKI Combinations for Treating *ALK*-Rearranged NSCLC with Acquired *MET* Amplification

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Disclosure

Artificial Intelligence (AI) Use Disclaimer

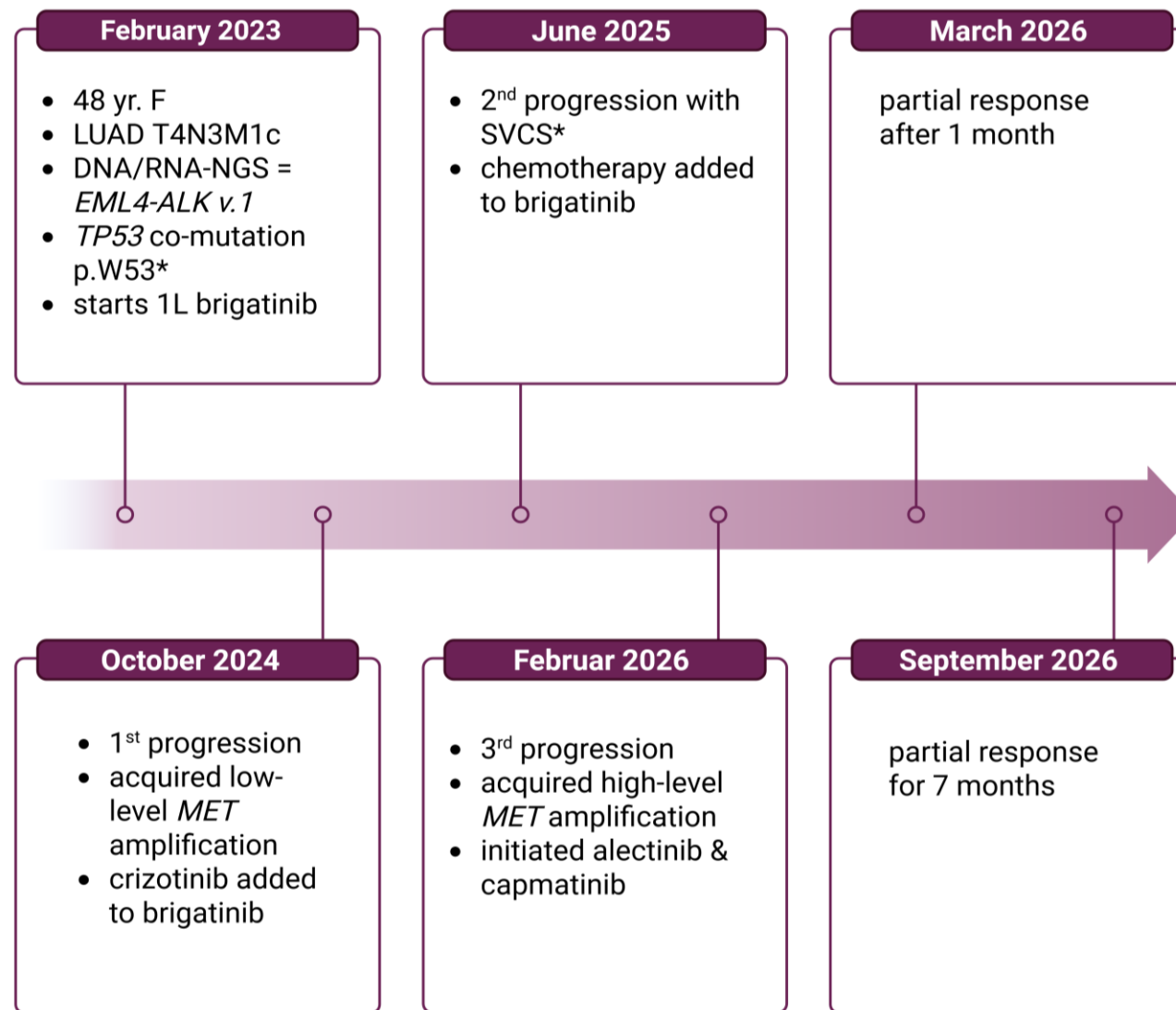
DeepL was used for language refinement, grammar, and organizational clarity in the preparation of this presentation.

All scientific content, data, analyses, interpretations, and conclusions were developed and verified by the authors.

MET amplification (ampl): an actionable bypass resistance mechanism

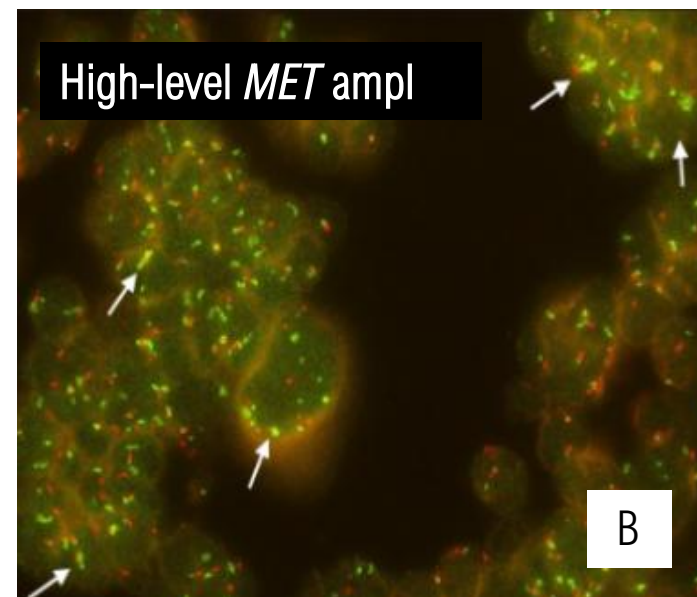
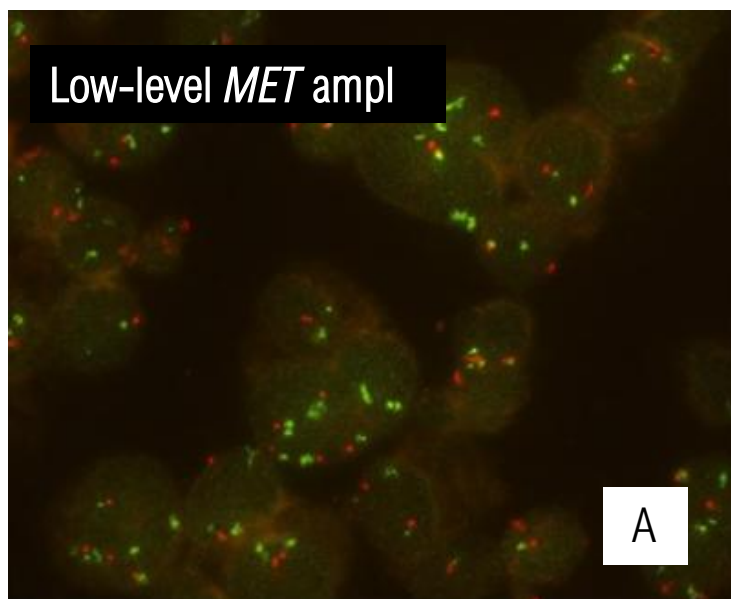
- Acquired *MET* ampl occurs in 5-15% of *ALK*-rearranged NSCLC at progression on *ALK*-TKIs
- Combined *ALK* + *MET* inhibition may overcome this bypass resistance
- We report a case of low- to high-level *MET* ampl retargeted sequentially with *ALK/MET*-TKIs

Clinical course: from ALK control to MET-driven resistance & ALK/MET retargeting



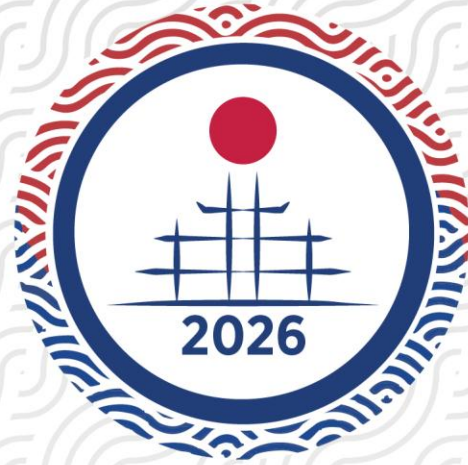
Molecular evolution & response

- A: Low-level *MET* amplification [(median (m)GCN 5, MET:CEN7 = 1.6)] → brigatinib + crizotinib → 9 months' disease control
- Progression → chemotherapy + brigatinib → further progression
- B: High-level *MET* amplification [mGCN 9, MET:CEN7 > 2, >10% cx with "*MET* clusters" = >15 copies (arrows)] → alectinib + capmatinib → PR ongoing at 7 months



Conclusions: Retargeting evolving resistance

- *MET* amplification evolved from low- to high-level during ALK-TKI treatment
- Sequential combinations of ALK- and MET-TKIs may provide meaningful clinical benefits in patients with *ALK*-rearranged NSCLC acquiring *MET* amplification at increasing levels



Thank You.