

EP17.01: First-Line Treatment of De Novo MET Amplification with High PD-L1 Expression in NSCLC: A Case Series

Anna Li1, Hao Sun1, Ji-Lin Guang2, Bing-Fei Xu1, Hua-Jun. Chen1, Jin-Ji. Yang1
1Division 1 of Pulmonary Oncology, Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Southern Medical University, Guangzhou, China;
2 Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Southern Medical University, Guangzhou, China;
Correspondence: Anna Li, 39439307@qq.com;

INTRODUCTION

MET amplification occurs in 1%–5% of treatment naïve NSCLC and is now recognized as a druggable driver following the KUNPENG trial, in which vebreltinib achieved an ORR of 51.8% and mPFS of 8.3 months in treatment naïve patients, leading to its conditional approval in June 2025 as the first MET TKI for this indication. The optimal 1st line strategy for patients with concurrent MET amplification and high PD-L1 expression remains unclear. We report four cases of treatment naïve MET amplified NSCLC with PD-L1 high expression who received different 1st line sequencing strategies.

DISCUSSION AND CONCLUSION

We present a series of four advanced NSCLC cases harboring concurrent MET amplification and high PD-L1 expression, highlighting the therapeutic dilemma between targeted therapy and immunotherapy. *De novo* MET amplification frequently co-occurs with high PD-L1 expression and predominates in male smokers. Patients derive clinical benefit from either immunotherapy or targeted therapy; Further investigations are warranted to optimize first-line therapeutic strategies in this patient population.

REFERENCES & ACKNOWLEDGEMENTS

1. Hsu C C, Huang D D, Hsu W H, et al. PD-L1 regulates c-MET phosphorylation and contributes to MET-dependent resistance to osimertinib in EGFR-mutant NSCLC [J]. Journal of biomedical science, 2025, 32(1): 94.
2. Zhang Y, Yang Q, Zeng X, et al. MET Amplification Attenuates Lung Tumor Response to Immunotherapy by Inhibiting STING [J]. Cancer discovery, 2021, 11(11): 2726-37.
3. Yoshimura K, Inoue Y, Inui N, et al. MET Amplification and Efficacy of Nivolumab in Patients With NSCLC [J]. JTO Clin Res Rep, 2021, 2(11): 100239.
4. Khan A, Imeh M, Barad P, et al. Targeting MET in 2025: From Exon 14 Skipping to MET-Amplified Acquired Resistance in Non-Small Cell Lung Cancer [J]. International journal of molecular sciences, 2026, 27(13).
5. Yong Z, Qin Y, Xiang Z, et al. MET Amplification Attenuates Lung Tumor Response to Immunotherapy by Inhibiting STING. Cancer Discov . 2021 Nov;11(11):2726-2737.
6. Federica P, Hui L, Alessandro F, et al. First-Line MET Tyrosine Kinase Inhibitors versus Immunotherapy ± Chemotherapy for Patients with MET Exon 14 Skipping Mutant Metastatic NSCLC. Clin Cancer Res . 2025 Nov 14;31(22):4802-4813.
We sincerely thank all the patients and their families and caregivers.

Case Description:

Case 1: 67-year-old male, heavy smoker. He presented in June 2024 with cough and shortness of breath, and a CT scan revealed a large mass in the left upper lobe measuring 8.8cm. Biopsy confirmed lung adenocarcinoma. Diagnosed cT4N3M1c(Stage IVB) with malignant pleural effusion, axillary lymph node, and rib metastases. IHC showed MET overexpression (90%, 3+) and high PD-L1 expression (TPS 95%). NGS revealed MET copy number gain (CN 6.17), and FISH confirmed clustered amplification. The first line savolitinib started in July 12, 2024. And achieved a partial response with manageable Grade 1 edema, PFS was 10 months(Fig1). At progression in May 2025, a re-biopsy was performed. While MET IHC remained high (95%, 3+) and PD-L1 was 95%, NGS revealed the MET D1228N resistance mutation along with increased copy number (CN 9.19). He received second-line pembrolizumab; however, the patient derived no benefit from immunotherapy.

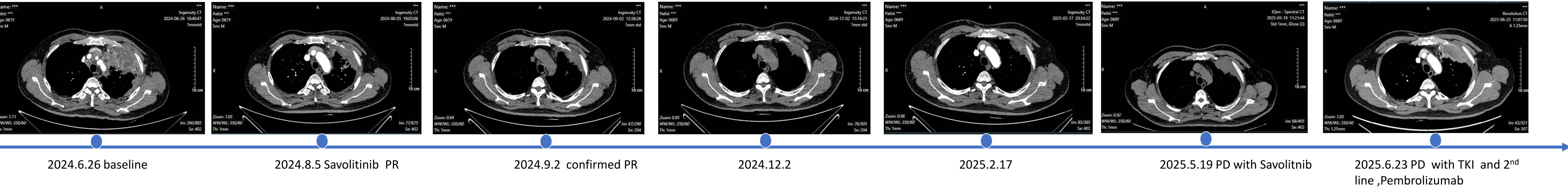


Fig1:Case 1 radiological evaluations

Case2: 65-year-old male, heavy smoker, Biopsy in January 2022 confirmed adenocarcinoma. Diagnosed Stage IVB disease with metastases to the bone, adrenal gland, and retroperitoneal nodes. Biomarkers showed PD-L1 TPS 85% and MET clustered amplification by FISH and CN 3.2 by NGS. The first-line chemo-immunotherapy with sintilizumab, nab-paclitaxel, and carboplatin, achieving a PR with a PFS of 8 months. He progressed with new brain metastases. For second-line treatment, he was started on savolitinib combined with radiosurgery for the brain lesions. Response is PR, but discontinuation of the TKI due to interstitial lung disease (ILD), and PFS was 6m(Fig2).

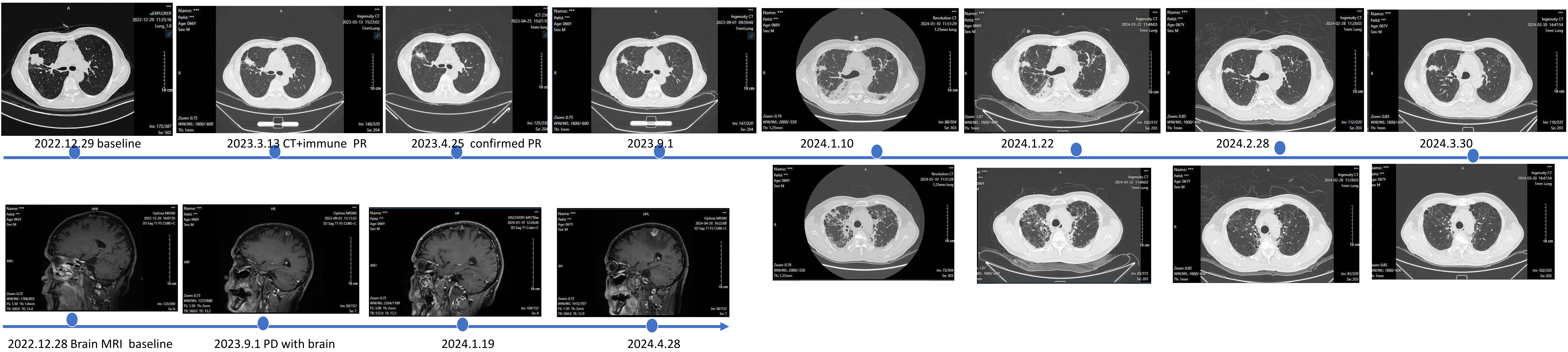


Fig2:Case 2 radiological evaluations

Case 3: 72-year-old male. ever smoker. CT showed a left lower lobe mass with extensive nodal involvement and pleural effusion in June 2023. Biopsy confirmed adenocarcinoma. Biomarkers revealed high PD-L1 (85%), MET clustered amplification by FISH and CN 3.0 by NGS. The first-line treatment is savolitinib. best response is PR with PFS 6m.He received pemetrexed, carboplatin, and pembrolizumab for 2nd line therapy, achieving a durable PR till now more than 2 years .

Case 4: 65-year-old male, heavy smoker. who presented in February 2023 with dyspnea and an incidental lung mass. PET-CT revealed a left apical lesion with extensive spread, including brain metastases. Biopsy confirmed adenocarcinoma. Biomarkers showed high PD-L1 (95%) and MET IHC (95%, 3+), with NGS revealing MET CN 3.8 and MET cluster amplification by FISH. He received 1st line pemetrexed, carboplatin, and sintilimab for six cycles and then maintenance with pemetrexed+sintilimab achieving PR with PFS for 14 months. No subsequent anti-tumor therapy was pursued after progression.

Anna Li has nothing to disclose

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