AUCTORES
Globalize your Research

International Journal of Clinical Case Reports and Reviews
Andrea Marini *

Open Access

Case Report

Response to Capmatinib in A Patient with Advanced Nsclc with Met Exon 14 Skipping Mutation and Sars-Cov-2 Infection: A Case Report

Andrea Marini [1]*, Irene Stasi [1], Antonio Pellino [1], Enrico Sammarco [1], Azzurra Farnesi [1], Gianna Musettini [1], Cecilia Barbara [1], Ermelinda De Maio [1], Samanta Cupini [1], Filomena Marrelli [3], Andrea Giusti [4], Giacomo Allegrini [1,2]

[1]Division of Medical Oncology, Livorno Hospital, Azienda USL Toscana Nord Ovest, Livorno, Italy.

[2]Department of Oncology, Azienda USL Toscana Nord Ovest, Pisa, Italy.

[3]Division of Pneumology, Livorno Hospital, Azienda USL Toscana Nord Ovest, Livorno, Italy.

[4]Department of Molecular Pathology, Carrara Hospital, Azienda USL Toscana Nord Ovest, Carrara, Italy.

***Corresponding Author:** Andrea Marini, Division of Medical Oncology, Livorno Hospital, Azienda USL Toscana Nord Ovest, Livorno, Italy.

Received Date: August 18, 2025 | **Accepted Date:** August 26, 2025 | **Published Date:** September 23, 2025

Citation: Andrea Marini, Irene Stasi, Antonio Pellino, Enrico Sammarco, Azzurra Farnesi, et al., (2025), Response to Capmatinib in A Patient with Advanced Nsclc with Met Exon 14 Skipping Mutation and Sars-Cov-2 Infection: A Case Report, *International Journal of Clinical Case Reports and Reviews*, 30(1); **DOI:10.31579/2690-4861/950**

Abstract:

The approval and mainstreaming of targeted therapies have decreased the mortality of non-small cell lung cancers (NSCLC). Notably, MET exon 14 (METex14) skipping mutations constitute driver alterations that occur in 3-4% of these cancers and capmatinib, a MET inhibitor, arrests cell proliferation when this mutation occurs; however, this agent has also shown antiviral activity against coronaviruses in preclinical studies.

An 82-year-old man admitted with epileptic seizures and loss of consciousness was diagnosed with stage IVB NSCLC, harboring a METex14 skipping mutation. He underwent locoregional treatment for his brain metastases and systemic chemotherapy. The patient later developed a SARS-CoV-2 infection concomitant to his worsening NSCLC. He was then treated with remdesivir and capmatinib and eventually recovered from SARS-CoV-2 along with radiological and clinical NSCLC regression within two months of initiating capmatinib.

This case highlights the clinical benefit of capmatinib in NSCLC with METex14 mutations in patients with SARS-CoV- 2 and the importance of testing for METex14 with DNA- and RNA-based methods as early as possible following advanced NSCLC diagnosis.

Key words: NSCLC; METex14 skipping; capmatinib; SARS-CoV-2; case report

Introduction

Lung cancer remains the most common cause of cancer-related death worldwide, with an estimated 1.8 million fatalities reported each year [1]. Non-small cell lung cancer (NSCLC) accounts for nearly 85% of all cases, and despite improvements in early detection and the development of novel treatments, the overall 5-year survival rate is still below 25% [2]. Among the molecular subtypes of NSCLC, alterations in the mesenchymal-epithelial transition (MET) gene—particularly MET exon 14 (METex14) skipping mutations—are detected in approximately 3–4% of cases and are associated with poor prognosis [3,4].

Capmatinib, a selective MET inhibitor, has demonstrated clinically meaningful activity in METex14-positive advanced NSCLC, with overall response rates of around 40–68% depending on prior treatment status, and has become a standard targeted therapeutic option [5].

In parallel, the coronavirus disease 2019 (COVID-19) pandemic has posed significant challenges in the management of patients with lung cancer, who are at increased risk of severe outcomes. The antiviral agent remdesivir remains one of the most commonly used treatments in hospitalized patients with COVID-19, although data on its concomitant use with targeted anticancer therapies are lacking [6,7].

The case described herein shows a remarkable therapeutic response to second-line capmatinib for advanced NSCLC harboring a MET exon 14

(METex14)-skipping mutation administered concomitantly with remdesivir due to SARS- CoV-2 infection. The combination of these agents was safe and hypothesis-generating regarding the potential benefit of capmatinib in lung cancer patients with SARS-CoV-2 infections.

Case Presentation

In January 2024, an 82-year-old man was admitted to the Livorno Hospital following an epileptic seizure with loss of consciousness (see Table 1 for detailed findings throughout the development of the case). The patient's NSCLC was stage IVB based on imaging scans showing two lesions on the right and left frontal brain lobes with perilesional edema, a right lung lesion, and mediastinal lymphadenopathies (Figure 1). Pathologic and molecular testing indicated adenocarcinoma histology and programmed cell death ligand 1 (PD-L1) expression of 40%. Next-generation sequencing (NGS) revealed a MET exon 15 mutation. Subsequent RNA-based NGS analysis detected a METex14 skipping mutation [4].

In January 2024, the patient underwent stereotactic radiosurgery for his brain lesions. He started first-line chemotherapy with gemcitabine combined with carboplatin in February 2024. Consequently, he experienced nausea (grade 3), asthenia (grade 2), anemia (grade 3), and thrombocytopenia (grade 2). In May, imaging showed a pleural effusion, the lung lesion (Figure 2B), and three new brain lesions (Figure 3 A1, A2, A3). The patient's clinical condition declined with intense asthenia, anorexia, and dyspnea on light exertion.

In June 2024, the patient was admitted to the emergency room due to fever and persistent cough. A SARS-CoV-2 infection was diagnosed and he was treated with oxygen therapy and remdesivir. During this hospitalization, imaging revealed a diffuse parenchymal thickening in the right lung (Figure 2C). Thus, concomitant capmatinib was initiated. After five days, he tested negative for SARS-CoV-2 and in the following weeks, his dyspnea and cough significantly improved. His capmatinib dose was reduced due to nausea (grade 2), peripheral edema (grade 2), and elevated serum creatinine (grade 2). In August 2024, two months after initiating capmatinib, imaging revealed the lung lesion with partial remission and significantly reduced brain metastases (Figures 2D and 3B2).

In November 2024, imaging showed further reductions in the target lesions. The patient survives in good overall health, without signs of disease progression, and is still being treated and in follow-up.

DATE	EVENT/TEST PERFORMED	DETAILS
01/2024	Patient's initial presentation and hospital admission to the Medical Oncology Division of the Livorno Hospital (Azienda USL Toscana Nordovest, Italy)	• Presenting symptoms: Epileptic seizure with loss of consciousness • ECOG PS 0 • No significant comorbidities and denied smoking history. • Diagnosed with NSCLC IVB (cT3 N2 M1c; TNM staging, 8th edition)
	Full-body CT scan with contrast	• Two lesions on the right and left frontal brain lobes with perilesional edema • One right lung lesion • Mediastinal lymphadenopathies
	Pathologic and molecular testing	• NSCLC, adenocarcinoma • PD-L1 expression of 40% (Ventana (SP263) assay) • DNA-based NGS: MET exon 15 mutation (allele frequency, 62.3%; MET exon 15 c.3082G>A; p.D1028N) • RNA-based NGS analysis: METex14 skipping mutation
	Treatment: • Stereotactic radiosurgery for brain lesions	• Stereotactic radiosurgery: 30 gray in 3 fractions
02/2024	Treatment: • First-line chemotherapy	• Chemotherapy: Gemcitabine (3-week cycles, 1000 mg/m2 on day 1 and 8) + carboplatin (per AUC4, 150 mg/m2 on day 1 for 4 cycles) • Adverse events: Nausea (grade 3), asthenia (grade 2), anemia (grade 3), and thrombocytopenia (grade 2) per the CTCAE
05/2024	Full-body CT scan and clinical deterioration	• Pleural effusion • One 45 mm lung lesion (Figure 2B) • Three new brain lesions (Figure 3 A1, A2, A3) • Clinical condition declined with intense asthenia, anorexia, and dyspnea on light exertion (ECOG PS 2)
06/2024	Emergency room admission at Livorno Hospital	• Fever and persistent cough (ECOG PS 3) • Diagnosed with SARS-CoV-2 infection: SpO2 of 88%, PaO2 of 56 mmHg. • Received oxygen therapy and remdesivir (loading dose, 200 mg; 100 mg/day for five days)

Table 1: Detailed case information and findings throughout the development of the case.

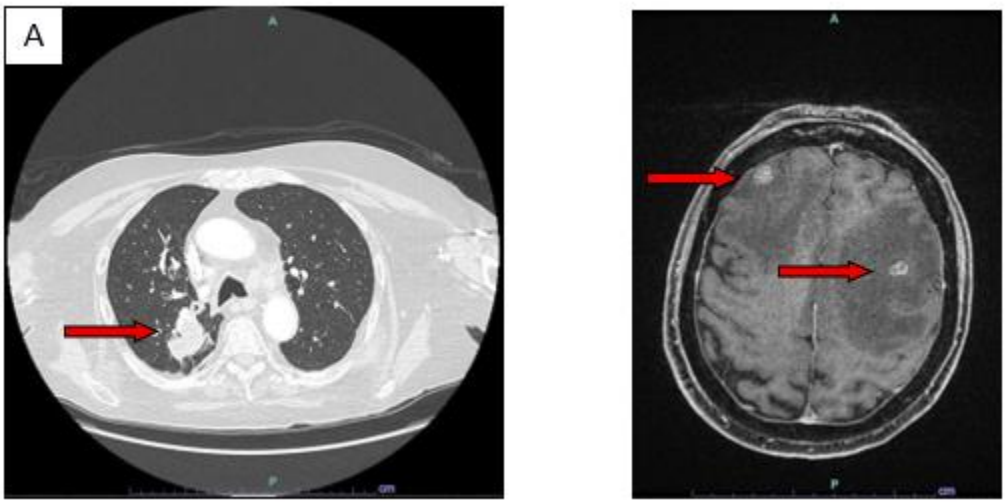

Figure 1: Chest (A) and brain (B) computed tomography (CT) images on January 2024. The chest CT shows a lesion close to the right costal pleura (40 x 43 x 43 mm) and multiple mediastinal lymphadenopathies. The brain CT shows two focal lesions on the right and left frontal brain lobes with perilesional edema.

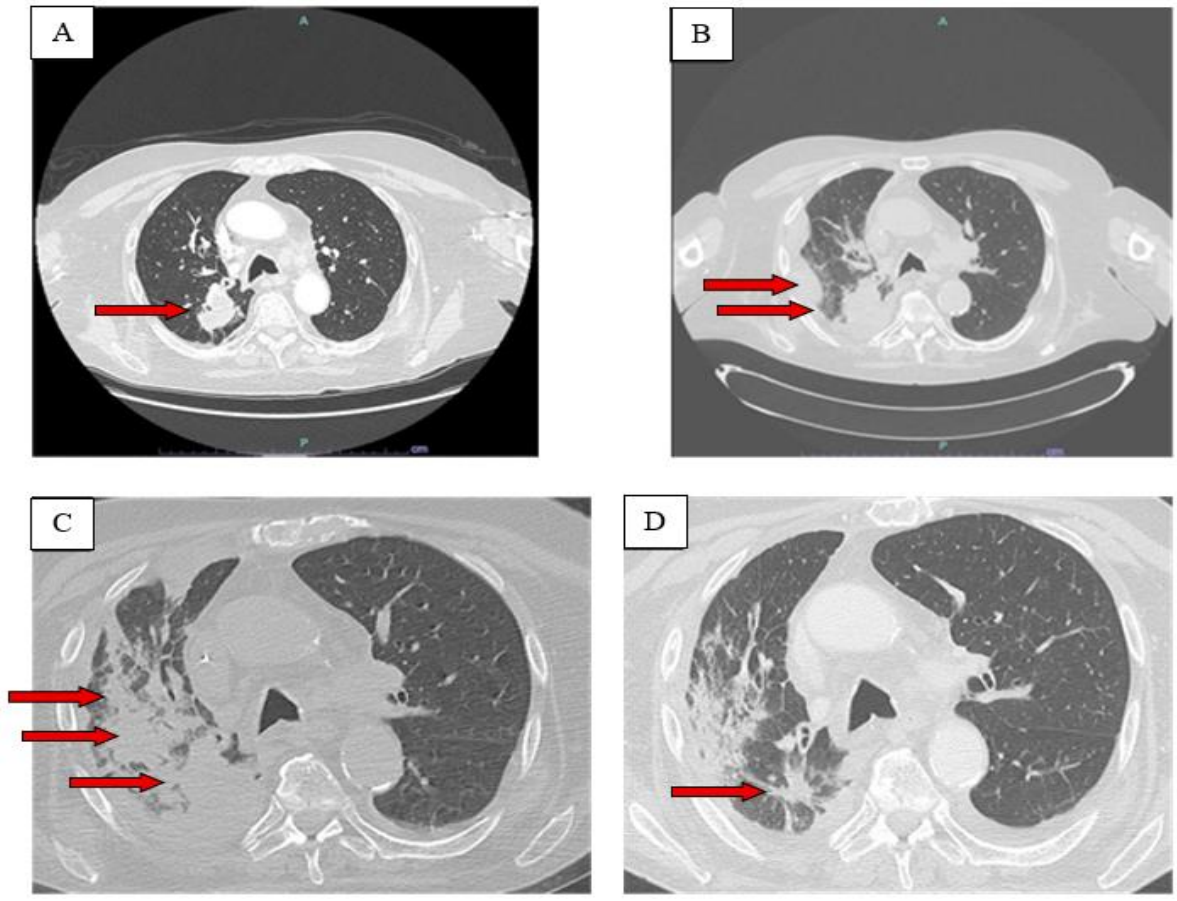

Figure 2: Chest CT images from January 2024 (A) and in May 2024 (B), three months after starting chemotherapy; (C) shows CT images of the chest before (June 2024) and after (August 2024 (D)) starting treatment with capmatinib. The largest diameter of the right lung lesion is 43.12 mm in A, 45.02 mm in B, 47.09 in C, and 15.26 in D. Figure B shows the right-sided pleural effusion in addition to the lung lesion. Figure C, shows a diffuse confluent parenchymal thickening in the right lung that could have been due to COVID-19, cancer progression, or both.

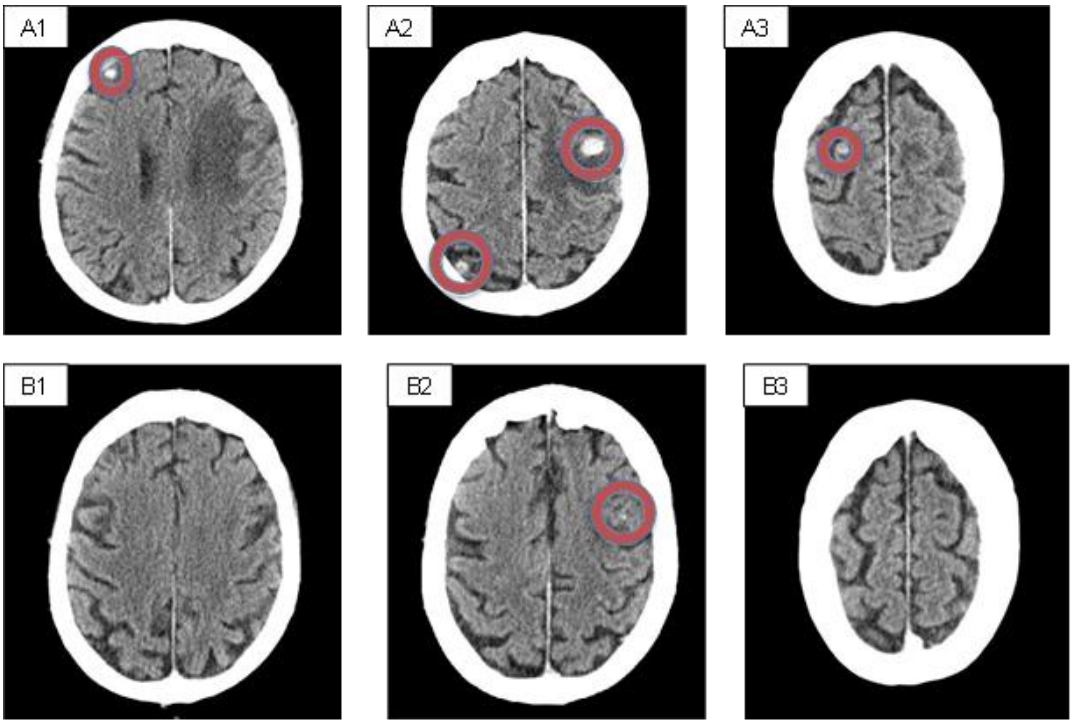

Figure 3: CT images of the brain before (June 2024, A) and two months after (August 2024, B) starting treatment with capmatinib. A1 shows the small right frontal lesion, A2 shows the largest lesion which was located in the left frontal lobe (largest diameter, 12.61 mm), and A3 a small right parietal lesion. B1 and B3 show no lesions and B2 shows the left frontal lesion greatly decreased in size (largest diameter, 7 mm).

Discussion

One of NSCLC's known driver alterations is the METex14 skipping mutation, occurring in 3-4% of them. The exon 14 of the MET gene encodes the juxtamembrane domain, preventing MET receptors' from over-signaling; thus, skipping mutations increase oncogenicity. [3] These mutations usually occur in older patients with lung squamous carcinoma and adenocarcinoma, with or without smoking history, and are associated with poor prognosis. [3]

In our case, the DNA-based NGS revealed a point mutation in the exon 15 of the MET gene. Only subsequent RNA- based analysis showed that this mutation was associated with exon 14 skipping, which as reported by Davies et al., identifies a higher percentage of METex14 skipping than amplicon-mediated DNA-based testing. This results from overcoming an inherent limitation of DNA-based approaches where primer design does not detect all METex14 events. [4] For this reason, DNA- and RNA-based NGS using hybrid capture-mediated target enrichment are preferred to avoid the allele dropout issue often seen with amplicon-based methods. [3]

Capmatinib, a potent and selective MET receptor inhibitor, has antitumor activity against MET-dysregulated NSCLC and crosses the blood-brain barrier with relatively low-grade toxicity. [5] Indeed, in the phase II GEOMETRY mono-1 trial, the overall response rate and median progression-free survival were 41% and 5.4 months in previously-treated patients and 68% and 12.4 months in treatment-naive patients.5 Capmatinib also showed promising intracranial activity and predictable and reversible adverse events consisting of mostly grade 1 or 2 peripheral edema, nausea, vomiting, and increased serum creatinine. [5]

Our patient received capmatinib concomitantly with remdesivir for a SARS-CoV-2 infection in the context of NSCLC progression because the lung's parenchymal thickenings on his chest CT could have represented either SARS-CoV-2 infection signs or further NSCLC progression. In addition to this rationale, the decision was based on reports of capmatinib's possible antiviral activity. For instance, Reza et al. showed that capmatinib can be active against selected SARS-CoV-2 proteins [6] and Jade et al. found that capmatinib binds to SARS-CoV-2's RNA-dependent RNA polymerase, essential for viral replication, and can thus limit the viral infection by inhibiting RNA synthesis. [7] Therefore, we can reasonably hypothesize that in our case capmatinib could have exerted antiviral action in addition to antitumor activity, and perhaps interacted synergistically with remdesivir,

Conclusion

Our case highlights the clinical benefit of capmatinib against NSCLC with METex14 skipping mutations and the importance of early molecular testing using DNA- and RNA-based methods. This case also underlines capmatinib's safety profile and efficacy even in patients with SARS-CoV-2, on which it may contribute to treating this infection. This potential role of capmatinib deserves further investigation.

Disclosure of funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement: All the authors declare that the they do not have any conflicts of interest to disclose.

Reviewer suggestions: The authors declare that the following manuscript was realized with the support of Novartis and prefer that the journal assigns the reviewers for their manuscript.

References

1. Siegel Rebecca L, Miller Kimberly D, Fuchs Heather (2021). Cancer statistics, 2021. *CA Cancer J Clin;* 71(1): 7-33.
2. Howlader Nadia, Forjaz Gabriel, Mooradian Matthew J, et al. (2020). The effect of advances in lung-cancer treatment on population mortality. *N Engl J Med;* 383(7): 640-649.
3. Nathany Shubham, Batran Usama (2022). MET: A narrative review of exon 14 skipping mutation in non-small-cell lung carcinoma. Cancer Res Stat Treat; 5(2): 284-292.
4. Davies Kimberly D, Lomboy Anthony, Lawrence Craig A, et al. (2019). DNA-based versus RNA-based detection of MET exon 14 skipping events in lung cancer. *J Thorac Oncol;* 14(4): 737-741.
5. Wolf Juergen, Takashi Shunichi, Han Ji-Youn, et al. (2020). Capmatinib in MET Exon 14–Mutated or MET-Amplified Non–Small-Cell Lung Cancer. *N Engl J Med;* 383(10): 944-957.
6. Reza Rashed, Dutta Tanmoy, Baildya Nirjhar, et al. (2022). Repurposing of anti-lung cancer drugs as multi-target inhibitors of SARS-CoV-2 proteins: An insight from molecular docking and MD-simulation study. Microb Pathog; 169: 105615.
7. Jade Dileep, Alzahrani Abdullah, Critchley William, et al. (2023). Identification of FDA-approved drugs against SARS-CoV-2 RNA-dependent RNA polymerase (RdRp) through computational virtual screening. Struct Chem; 34(3): 1005-1019.
8. Gondi Vinai, Bauman Glenn, Bradfield Luke, et al. (2022). Radiation therapy for brain metastases: An ASTRO clinical practice guideline. *Pract Radiat Oncol;* 12(4): 265-282.
9. Scagliotti Giorgio V, De Marinis Filippo, Rinaldi Maurizio, et al. (2003). Phase III randomized trial comparing three platinum-based doublets in advanced non–small-cell lung cancer. *J Clin Oncol;* 20(21): 4285–4291.
10. Planchard David, Popat Sanjay, Kerr Keith, et al. (2018). Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol; 29(Suppl 4): iv192–iv237.
11. U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Insti-tute. Common Terminology Criteria for Adverse Events (CTCAE) v5.0. November 27, 2017.

DOI:10.31579/2690-4861/950