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MET Crusaders is a community of Lung Cancer patients and care givers collaborating with advocates and medical professionals collectively dedicated to helping patients with a MET alteration live normal lives.

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Defining comprehensive biomarker-related testing and treatment practices for advanced non-small-cell lung cancer: results of a survey of US oncologists

Objective:

- To understand biomarker ordering/testing and barriers, as well as practices and treatment decisions for patients with advanced NSCLC

Design:

- Survey
- Available July to September 2020

Population:

- 2,374 US oncologists, NPs, and PAs with 170 eligible responses
- 98% of respondents were physicians
- 60% of respondents practiced within an academic institution
- Respondents were asked to report on pre-pandemic practice

Results:

- Non-squamous NSCLC:
 - 97% of respondents ordered testing for EGFR, ALK, ROS1, and BRAF
 - MET, RET, and NTRK testing was higher within academic institutions (95%, 91%, 89%) compared to community practices (81%, 80%, 81%) and among specialized thoracic practitioners (95%, 93%, 93%) compared to generalist practitioners (84%, 82%, 79%)
 - KRAS and HER2 testing was more than 70% for all respondents and more than 85% among specialized practitioners and at academic institutions
 - 95% of respondents ordered testing for biomarkers and PD-L1 prior to starting immunotherapy

• Squamous NSCLC:

- 69-80% frequency of testing for EGFR, BRAF, NTRK, MET, RET, KRAS, ROS1, ALK, and HER2
- No significant difference between practitioner group
- 67% of respondents changed treatment from immunotherapy to targeted therapy if patient was started on immunotherapy based on PD-L1 expression and targetable mutation was identified later on
- 46-52% of respondents considered 1-2 weeks an acceptable turnaround time for test results, 37% waited at least 3 weeks for test results, and 63% deferred treatment until they had test results
- Community and generalist practitioners were more likely to initiate non-targeted treatment if it took 3 or more weeks to get test results
- 42% of practitioners who were in practice for less than 5 years did not order biomarker testing due to concerns about waiting for results, compared to 19% of practitioners who were in practice for 6 or more years
- Barriers to biomarker testing included inadequate tumor sample (34%), concern for delay in treatment (23%)
- 71% of respondents reported implementing strategies to increase biomarker testing, most of which did so via multidisciplinary teams (85%)

Conclusions:

- Results indicate high biomarker testing rates in patients with NSCLC
- Biomarker test turnaround time impacted practitioner's treatment decisions
- Treatment decisions and biomarker testing differed between practice setting, type of practitioner, and years in practice

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Capmatinib successfully overcomes tepotinib-induced intolerable peripheral edema

Drug(s): capmatinib

Objective:

- To present a case of intolerable tepotinib-induced peripheral edema that improved with switching to capmatinib

Design:

- Case report

Population:

- 72-year-old male with MET-mutated lung adenocarcinoma

Results:

- Initially treated with tepotinib 500mg orally once daily
- Developed grade 3 edema in extremities which was not responsive to diuretics and caused gait disturbance
- Tepotinib was held for 2 weeks with improvement in edema
- Tepotinib was resumed at reduced dose of 250mg orally once daily, grade 3 edema developed again

- Tepotinib was reduced to 250mg orally every other day, edema continued to worsen
- Received tepotinib for 151 days
- Switched to capmatinib at reduced dose of 400mg orally once daily, no edema noted
- Received capmatinib for 100 days without edema present and with treatment response

Conclusions:

- Edema with MET inhibitors may not be dose related
- Differences in tolerance of the two agents in terms of edema may be due to metabolism (capmatinib is metabolized by CYP3A whereas tepotinib is not)
- Peripheral edema is a common and often difficult to tolerate side effect of MET inhibitors
- If intolerable edema occurs on one type of MET inhibitor, it may be reasonable to switch to a different MET inhibitor as an attempt to improve tolerance

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An alert to possible false positives with a commercial assay for MET exon 14 skipping

Objective:

- To describe discordant results among three commercial METex14 assays.

Design:

- Retrospective analysis of METex14 testing results among a cohort of patients with NSCLC at a single center in Japan
- Samples originally tested using Oncomine DxTT, a multiplex gene panel test for NSCLC using NGS. Identical unstained sections then submitted to ArcherMET and laboratory-developed reverse-transcriptase polymerase chain reaction (LDT RT-PCR)

Population:

- Included 50 patients with NSCLC and METex14 results available. Per Oncomine DxTT, 26 positive for METex14 and 24 negative.

Results:

- ArcherMET and LDT RT-PCR had identical results for all 50 samples tested. However, 8 samples differed between these and Oncomine DxTT—all 8 were positive per Oncomine DxTT and negative per ArcherMET and LDT RT-PCR.
- Alterations in other driver genes were detected in 2 of the 8 discordant samples.

- Most of the discordant samples had read counts less than 800 (73.3 vs 7478, $P < 0.001$). Based on this finding, the authors examined 6 more samples with METex14 detected by Oncomine DxTT. Three were concordant with ArcherMET and LDT RT-PCR, but the remaining 3 low read counts were not concordant with ArcherMET/LDT RT-PCR.
- In 5 of 8 discordant samples, a certain thymidine repeat at the METex14 donor site was deleted and the number of deletions matched the read count, therefore potentially the cause of the variant.

Conclusion:

- False negatives have historically been of greater concern with METex14, due to the complexity of DNA alterations that result in METex14 skipping. However, this article highlights a concerning risk for false positives in a widely-approved NGS panel. Clinicians should use caution and consider validating positive METex14 results obtained via the Oncomine DxTT panel. Alternative NGS panels and MET-specific tests have been validated in clinical trials—several have also been approved by various regulatory agencies as companion diagnostics for capmatinib and tepotinib.
- Readers should be aware that the senior and corresponding author of the reports receiving financial support from ArcherDx

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Landscape and clonal dominance of co-occurring genomic alterations in non-small-cell lung cancer harboring MET exon 14 skipping

Objective:

- To describe co-occurring genetic alterations in MET exon 14 skipping mutation (METex14) altered NSCLC and the potential impact on therapeutic sensitivities.

Design:

- Retrospective analysis of genetic alterations among patients with MET exon 14 NSCLC. Data was combined from three independent data sets: Guardant360, GenePlus, and VISION ctDNA cohort
- Analyses performed on either tissue or circulating tumor DNA (ctDNA) with three different panels. Altogether, 48 genes were covered in all patients across the three data sets.

Population:

- Total of 692 patients with METex14 NSCLC, representing 3.2% of a total 40,824 patients tested.
- The majority of cases (N= 557) had ctDNA results

Results:

- MET amplification co-occurred with METex14 in 8.4% of patients. The number of patients in the VISION trial (tepotinib) was too small to determine whether MET amplification correlated with response, although the number was numerically higher (80% in MET amplified group vs 46% without).
- Secondary mutations in the MET kinase domain (KD) may be associated with resistance (H1094C/Y, D1228H/N, Y1230C/H). KD mutations occurred in 5% of the Guardant360 cohort and 6% of the GenePlus cohort, but none were identified in the VISION trial (TKI-naïve patients).
- No mutations in other cancer genes occurred more frequently in the METex14 group compared to NSCLC without METex14. Certain mutations (EGFR, KRAS, TP53) occurred more frequently in the non-METex14 group, supporting the idea that METex14 is a de novo driver mutation.

- Only 7 patients with concomitant alterations had outcome information with tepotinib. One patient with METex14 and ERBB2 mutation had reduction in tumor size. None of the remaining six patients had a response to tepotinib (2 PIK3CA, 2 K/NRAS, 2 PTEN).
- Among patients with multiple ctDNA samples over time (23 in Guardant360 and 6 in GenePlus), 4 acquired resistance mutations in MET KDs, all following treatment with crizotinib. One of these also acquired EGFR exon 20 insertion and an EGFR amplification, although another patient had both present along with METex14 before treatment. EGFR driver alterations were also detected in 3 other cases, suggesting METex14 as a resistance mutation. Another patient acquired a RET fusion as a resistance mutation after treatment with crizotinib.
- Only 10 cases had both tissue and ctDNA in the GenePlus cohort. These demonstrated perfect concordance for METex14, although the co-occurring alterations varied between tissue and ctDNA in 6.

Conclusion:

- The strength of this analysis lies in the large number of patients with METex14 NSCLC, allowing for hypothesis generation regarding co-occurring alterations.
- Several probable resistance mutations to MET TKI therapy are described: MET KD mutations, EGFR amplification or exon 20 insertion, and RET fusion.
- Although co-occurring alterations in other genes are rare in METex14, this seems to correlate with lack of benefit from MET targeted therapy.
- Concomitant MET amplification and METex14 could indicate a tumor dependent on MET signaling for survival and may predict sensitivity to MET inhibition, but the sample size is too small to make any strong conclusions.

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Budget impact of capmatinib for adults with metastatic non-small cell lung cancer harboring a MET exon 14 skipping mutation in the United States

Drug(s): capmatinib

Objective:

- To estimate the budget impact of capmatinib in US commercial and Medicare health plans for patients with metastatic non-small cell lung cancer (mNSCLC) harboring a MET exon 14 (METex14) skipping mutation.

Design:

- Budget impact analysis (BIA)
- Eligible patients entered the model with progression-free survival (PFS) and outcomes were tracked over 3 years
- Total budget impact and per member per month (PMPM) budget impact were estimated as cost differences with and without capmatinib

Population:

- Hypothetical plan population of 1 million enrollees over three years (2020-2022)
- Treatment-naïve and previously treated adult patients with mNSCLC with METex14 skipping mutations
- The model included estimated capmatinib market share uptake for each year
- Drug and drug administration costs were estimated from national references. In the model without capmatinib, other percentages of patients on other treatments (pembrolizumab, platinum-doublet based regimens, single-agent chemotherapy with docetaxel, gemcitabine, etc.) were estimated
- Drug cost for oral capmatinib was \$17,950 per 28-day supply
- Estimates were made based on estimates for various costs of illness: drug acquisition, drug administration, pre-progression monitoring, adverse event, progression and terminal care, mutation testing

- Relative dose intensities were estimated in the model to account for variance in drug dosing, including: dose interruptions, dose reductions due to adverse events, and non-compliance
- Costs related to disease progression were also estimated

Results:

- For commercial payers, the authors estimate an expense of \$0.0008 to \$0.0056 per health plan member over the first three years. PMPM increases in drug and drug administration costs were \$0.0011, \$0.0040, and \$0.0064 for the first, second, and third years, respectively. These costs were found to be partially offset by cost reductions related to adverse event management, progression, and terminal care when comparing the model with and without capmatinib.
- For Medicare payers, the authors estimate \$0.0118 to \$0.0821 per health plan member in the first three years. Increased PMPM costs ranged from \$0.0154 to \$0.0928 and were offset by cost reductions in adverse event management, progression and terminal care costs of -\$0.0042 to \$0.0141 per year.
- The total budget impact of capmatinib in a Medicare health plan was \$141,350 in the first year, \$576,706 in the second year, and \$985,695 in the third year.

Strengths:

- Thoughtful budget analysis design that tried to estimate costs from existing trial data
- Because the model was comprehensive, the analysis provides a good estimate to payers' in support of including capmatinib in formularies. This is beneficial for patients from an access perspective

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Continued:

Weaknesses:

- Budget impact analysis was funded by the capmatinib manufacturer
- Results are all based on assumptions that are applied to the model, which may not account for all real-world costs
- Costs for lower grade or less common adverse events were not included in the model
- Relative dose intensity and treatment durations were based on clinical trial data, which may not account for real-world outcomes
- Estimates for wasted intravenous drugs were not considered in the model

- Capmatinib costs may not have been completely captured due to other out-of-pocket costs and co-payments not estimated

Conclusion:

- Increases in PMPM budget with capmatinib entry were partially offset by cost reductions in progression-related, terminal care, and adverse event management costs.
- In the future, analyses would need to be updated to reflect current practices and costs.

[LINK TO ARTICLE](#)

A novel c-mesenchymal-epithelial transition factor intergenic fusion response to crizotinib in a Chinese patient with lung adenocarcinoma: a case report

Drug(s): crizotinib

Objective:

- To describe the response to crizotinib in a patient with a rare MET intergenic fusion

Design:

- Case report

Population:

- 72yo male with poorly differentiated lung adenocarcinoma diagnosed in June 2020
- Stage IIIB (pT1N3M0), no extrapulmonary metastasis but mediastinal/hilar lymph nodes involved
- Deemed inoperable due to underlying history of interstitial lung disease (ILD) and locally advanced spread
- Intergenic MET fusion detected on next generation sequencing
 - Identified a fusion of random sequences to MET gene, with breakpoints located on chr7_g1000195_random: 6974 and chr7:116423550 in intron 19 of the MET gene, and the sequence of MET reversed

Results:

- Crizotinib 250mg twice daily initiated in August 2020.
- Scans at 3 months demonstrated partial response in primary tumor and lymph nodes.
- ILD worsened in November 2020 and crizotinib could not be ruled out as cause of exacerbation. Crizotinib discontinued and patient continued with observation alone.
- Patient had ongoing partial response in February 2021 after 3 months off crizotinib.
- Unfortunately, the patient progressed 5 months after discontinuing crizotinib.

Conclusion:

- This interesting report illustrates crizotinib activity in a patient with a rare, complex MET intergenic fusion. It is unfortunate that the patient experienced potential toxicity that required discontinuing treatment, as it would have been interesting to know the duration of response and/or if the patient was able to tolerate other MET inhibitors. It is important to note that these results are not necessarily generalizable to patients with other rare MET fusions.

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Case report: sequential combination targeted therapy with type I and II MET inhibitors in a metastatic EGFR-mutated, MET-amplified NSCLC patient with acquired MET Y1230H mutation

Drug(s): erlotinib, gefitinib, crizotinib, cabozantinib, pembrolizumab, cisplatin, pemetrexed, bevacizumab, carboplatin, cetuximab, paclitaxel

Objective:

- To report the sequential use of type I and II MET inhibitors in a patient with EGFR-mutated and MET-amplified NSCLC

Design:

- Case report

Population:

- 49-year-old female with stage IV NSCLC

Results:

- Initial genetic testing revealed EGFR exon 19 deletion
- Received erlotinib 150mg daily with progression after 1 month
- Changed to cisplatin, pemetrexed, and bevacizumab for 6 cycles with partial response followed by maintenance pemetrexed and bevacizumab for 5 cycles with progression
- Discovered MET overexpression (IHC 3+) and another EGFR deletion on biopsy
- Changed to crizotinib 250mg twice daily plus gefitinib 250mg every other day with partial response followed by progression
- Changed to carboplatin, paclitaxel, and cetuximab for 2 cycles which was discontinued due to grade 4 myelosuppression
- Rechallenged with reduced dose crizotinib (250mg daily) and gefitinib for 3 months with stable disease followed by progression

- Biopsy confirmed original EGFR exon 19 deletion and MET amplification, so increased crizotinib to 250mg twice daily with partial response followed by progression
- Discovered acquired MET Y1230H mutation and high expression of PD-L1 (TPS 75%)
- Literature at the time demonstrated MET Y1230H mutation was resistant to type I but not type II MET inhibitors, so changed to gefitinib 250mg every other day, cabozantinib 40mg daily, and pembrolizumab 100mg every 2 weeks with partial response for 13 months
- Upon progression, added bevacizumab which resulted in stable disease
- After additional progression, biopsy confirmed original EGFR mutation and TP53 mutation with no expression of MET amplification or MET Y1230H mutation
- Patient decided to continue gefitinib and cabozantinib and remained on this combination for 2 months
- Overall survival of 54 months

Conclusions:

- Gefitinib and crizotinib is effective in EGFR-mutated, MET-amplified, and erlotinib-resistant NSCLC and is a viable treatment option in patients who cannot afford or access MET-specific agents
- Switching from type I to type II MET inhibitors is effective in overcoming type I MET inhibitor resistance

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Canadian consensus recommendations on the management of MET-altered NSCLC

Objective:

- To develop evidence-based consensus recommendations for the management and use of targeted therapies for patients with MET-altered non-small cell lung cancer (NSCLC) in Canada

Population:

- Patients with NSCLC and one of three clinically-relevant MET alterations:
 - METex14 skipping mutations
 - De novo MET amplification
 - MET amplification in acquired resistance to EGFR inhibitors

Questions addressed and recommendations:

- How should the patients most likely to benefit from MET-targeted therapies be identified?
 - Multigene panel testing (next generation sequencing; NGS) is the most appropriate approach to allow for detection of MET alongside other actionable mutations
 - Testing for MET exon 14 skipping mutations should be performed for all treatment-eligible patients with advanced non-squamous NSCLC.
 - In patients with squamous NSCLC, consider testing on demand in non-smoking treatment-eligible patients with advanced disease.
 - Liquid biopsy can be considered if tissue biopsy is not feasible, if it yields inadequate samples, or when urgent treatment decisions are required. Mutations found by liquid biopsy (both MET exon 14 skipping and MET amplification) are considered actionable.
 - Rapid turnaround time is critical. The maximum turnaround time from acquisition of tissue to delivery of the report should not exceed 21 calendar days.
 - Biomarker tests should be compiled and reported comprehensively by the pathologist, including PD-L1 status.
- What are the preferred first-line and subsequent therapies for patients with MET exon 14 skipping mutations?
 - Patients with advanced MET exon 14 NSCLC should be offered MET targeted therapy. Caution is encouraged when initiating TKI after an immune checkpoint inhibitor due to potential increased risk of toxicity.
 - Type 1b MET inhibitors (capmatinib, tepotinib, or savolitinib) are preferred over crizotinib skipping due to more robust efficacy. The choice among the type 1b inhibitors should be based on patient-specific factors and availability. However, crizotinib may be considered if other therapies are unavailable.
 - A MET inhibitor is the preferred first-line therapy in non-smokers with NSCLC and MET exon 14 skipping mutations. However, other guideline-recommended standard of care may also be offered.
 - For patients who have already received MET-targeted therapy, guideline-recommended standard of care for NSCLC without driver mutations should be offered as subsequent treatment.
- MET exon 14 testing based on DNA alone risks missing some actionable mutations. This risk is lower when combined with RNA sequencing. Tests should undergo validation before clinical implementation.
- MET IHC is not recommended as a screening tool for MET exon 14 or MET amplification as this correlates poorly to the presence of these alterations.
- Pathologists are encouraged to utilize an assay that provides MET copy number status and/or copy number ratio when selecting a NGS panel. Data are emerging on the cutpoints that define MET amplification.
- Single-gene tests for MET amplification can be used in select scenarios, such as patients with resistance to EGFR TKI.

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Continued:

- e. Among patients with MET exon 14 mutations and brain metastases, tepotinib and capmatinib may be considered reasonable options in addition to other multidisciplinary approaches.
- 3. What are the preferred first-line and subsequent therapies for advanced NSCLC patients with de novo MET amplification?
 - a. MET-targeted therapy can be considered through a clinical trial at any line of therapy.
 - b. Although data are emerging on MET inhibitors in MET amplification, the data are not robust or consistent enough to recommend targeted therapy over standard of care. MET targeted therapy can be considered for these patients after standard therapies have been exhausted or when deemed ineligible for these therapies.
- 4. What is the preferred therapy for patients with advanced epidermal growth factor receptor (EGFR)-mutated NSCLC with acquired MET amplification progressing on EGFR inhibitors?
 - a. Patients with advanced EGFR-mutated NSCLC who have a MET amplification should be considered for a clinical trial with a MET inhibitor after progression on either: first and second

generation EGFR TKI without T790M resistance mutation OR after osimertinib regardless of line of therapy.

- 5. What are the potential strategies for overcoming resistance to MET inhibitors?
 - a. Enrollment in clinical trials should be encouraged for patients with MET alterations resistant to MET inhibitors.
 - b. Resistance profiling after MET targeted therapy has not yet been demonstrated to impact outcomes. This is not recommended outside of clinical trials.

Conclusions:

- Accurate and timely detection of MET alterations along with other targetable mutations is critical. MET inhibitors should be considered first-line for patients with MET exon 14 skipping mutations. Enrollment in clinical trials should be considered at all times, but especially to answer open questions on the role of MET inhibitors in de novo and treatment-emergent MET amplifications.

[LINK TO ARTICLE](#)

Tepotinib efficacy and safety in patients with MET exon 14 skipping NSCLC: outcomes in patient subgroups from the VISION study with relevance for clinical practice

Drug(s): tepotinib | NCT: 02864992

Objective

- To provide updated outcome data on the VISION study that assessed tepotinib and its effect on patients with MET exon 14 skipping (METex14) non-small cell lung cancer (NSCLC)

Design

- Phase II, single-arm, multi-cohort, open-label clinical trial
- Intervention: tepotinib 500mg once daily
- Primary endpoint: objective response rate (ORR) by independent review committee (IRC)

- Secondary endpoint: investigator-assessed objective response, duration of response (DOR), progression-free survival (PFS), overall survival (OS), and safety

Population

- 152 patients with METex14 skipping mutation
- Median age: 73.1 years
- Histology: Adenocarcinoma (86.2%), squamous cell carcinoma (9.9%), sarcomatoid (2%)
- Lines of prior therapy: 0 (45.4%), 1 (32.2%), 2+ (22.4%)

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Continued:

Effectiveness

- IRC results
 - ORR (44.7%), median DOR (11.1 months), median PFS (8.9 months), median OS (17.6 months)
 - Age <75 years: ORR (48.8%), Age ≥ 75 years: ORR (39.7%), Age ≥ 80 years: ORR (35.1%)
- Investigator-assessed outcomes
 - ORR (53.3%), median DOR (12.5 months), median PFS (8.5 months), median OS (17.6 months)
 - Age <75 years: ORR (54.8%), Age ≥ 75 years: ORR (51.5%), Age ≥ 80 years: ORR (54.1%)

Safety

- Patients experiencing any side effect (86.3%), swelling of extremities (54.1%), nausea (20.0%), diarrhea (19.6%), increased kidney damage indicators (17.6%), increased markers for liver damage (8.6%), 3 events of death due to adverse effect

Conclusion

- This study provides an updated look at the safety and effectiveness of tepotinib in METex14 skipping NSCLC patients. The data outlined here supports earlier analysis that suggests favorable efficacy in this subset of patients.

[LINK TO ARTICLE](#)

Immunotherapy in non-small cell lung cancer with actionable mutations other than EGFR

Drug(s): immunotherapy

Objective:

- To review current literature on immune checkpoint inhibitor (ICI) therapies for treatment of NSCLC with ALK, ROS1, BRAF, MET, RET, NTRK, KRAS and HER2 alterations.

Design

- Review of 5 studies that investigated the effect of ICIs in NSCLC with MET mutations

Findings specific to MET

- Sabari JK. et al. (METex14 skipping mutation, 147 included patients)
 - ORR: 17%, PFS: 1.9 months, OS: 18.2 months
- Mazieres J., et al. (METex14 skipping mutation and MET amplification, 36 included patients)
 - ORR: 49%, PFS: 3.4 months, OS: 18.4 months
- Guisier F., et al. (MET mutation, 30 included patients)
 - ORR: 36%, PFS: 4.9 months, OS: 13.4 months
- Dudnik-E, et al. (METex14 skipping mutation, 148 included patients; MET amplification, 54 included patients)

- METex14 skipping: ORR: 12%, PFS: 4 months
- MET amplification: ORR: 25%, PFS: 4.9 months
- Mayenga M., et al. (METex14 skipping mutation, 2nd line of ICI, 13 included patients)
 - ORR: 46.2%

Strengths

- The review was able to compile relevant research of ICI therapy and MET NSCLC

Weaknesses

- Specific ICI therapies used in the studies not mentioned
- Reviews without meta-analysis limit the ability to generalize information

Conclusion

- In the studies included that assessed MET mutated NSCLC, ICI therapies appear to show benefit in some cases. A more comprehensive systematic review with meta-analysis is required to better understand the correlation between MET altered NSCLC and ICI therapy.

[LINK TO ARTICLE](#)



Overcoming acquired resistance mutation MET D1228N to crizotinib with cabozantinib in NSCLC with MET exon 14 skipping mutation

Drug(s): crizotinib, cabozantinib

Objective:

- To describe a response to cabozantinib in a patient who developed a MET exon 14 skipping resistance mutation while on crizotinib therapy

Design:

- Case report

Population:

- 70 year old male, former smoker
- Originally diagnosed with stage 1b lung adenocarcinoma and underwent lobectomy
- One year later, imaging revealed recurrent lung cancer, spread to nodes and throughout lung.

Results:

- Biopsy demonstrated adenosquamous carcinoma with PD-L1 expression 90-100%. Next generation sequencing detected a MET exon 14 skipping mutation.
- Crizotinib was initiated and the patient responded with a 61% decrease in lesions.
- After 6 months of crizotinib, patient unfortunately progressed. Repeat biopsy demonstrated a new MET D1228N mutation.
- Patient was switched to standard-of-care (SOC) pembrolizumab due to high PD-L1 expression, 3-month scans showed progression. The patient was also treated with carboplatin plus pemetrexed and docetaxel as 3rd and 4th line treatments but progressed on both.

- Given lack of remaining SOC options, preserved performance status, and new data, cabozantinib 60mg daily was initiated. Treatment was tolerated well despite hypertension requiring treatment. Patient experienced a partial response to cabozantinib at 6 weeks (30% decrease), but imaging after 4 months of cabozantinib demonstrated progression.
- Biopsy after cabozantinib progression no longer detected MET D1228N, but did show EGFR amplification. In retrospect, this had been there in a small subpopulation of cells after progression on crizotinib.
- Patient passed away 2 weeks after discontinuing cabozantinib.

Conclusion:

- This report describes a response to cabozantinib (a type II MET inhibitor) after progression on crizotinib (a type Ia MET inhibitor) and several SOC treatments in the presence of a suspected MET resistance mutation D1228N. The response was short lived however - cabozantinib may have selected for a subpopulation of EGFR-amplified cells resulting in progression. These results are certainly hypothesis-generating. More data on effective treatments for MET exon 14 resistance mutations are needed.

[LINK TO ARTICLE](#)



Multicenter real-world data of patients harboring rare mutations other than EGFR or ALK in advanced or metastatic non-small cell lung cancer

Drug(s): platinum, pemetrexed, crizotinib

Objective:

- To investigate the therapeutic response of conventional chemotherapy for patients with advanced or metastatic non-small cell lung cancer (NSCLC) with rare mutations

Design:

- Retrospective, multicenter, cohort study
- 9 tertiary hospitals in Korea
- Results analyzed according to liquid biopsy or tissue biopsy used to confirm MET mutation
- Progression free survival (PFS) and overall survival (OS) were compared in patients with ROS1, RET, MET, ERBB2, and BRAF mutations

Population:

- 118 patients
- Nonsquamous NSCLC diagnosis from January 2015 to September 2020
- Median age 61 years
- Male: 44%
- Smoking history: 39%
- Presence of brain metastasis: 14%
- Mutations included (n, %): ROS1 (46, 39%), RET (27, 22.9%), MET (14, 11.9%), ERBB2 (14, 11.9%), BRAF (10, 8.5%), FGFR (5, 4.2%), and NTRK (2, 1.7%)
- Tumor histology: 90% adenocarcinoma; 7% squamous
- Presence of brain metastases: 11%
- Treatments: 107 patients received palliative chemotherapy. 88 (82%) received platinum-based first-line chemotherapy (of which, 58 (54%) were platinum-pemetrexed and 30 (28%) were platinum-other), 13 (12%) received crizotinib, 6 (5.6%) received other treatments

Effectiveness Results:

- Median PFS 9.6 months
 - BRAF 10.9 months
 - ERBB2 5.3 months
 - MET 7.2 months
 - RET 11.4 months
 - ROS1 10 months
- Median OS 36.9 months
 - BRAF 14.1 months
 - ERBB2 34.5 months
 - MET 22.7 months
 - RET 29.8 months
 - ROS1 not reached

Safety Results:

- Not reported

Strengths:

- Reported outcomes of chemotherapy in patients with rare mutations

Weaknesses:

- Retrospective trial: this type of trial has many potential issues with patient selection, potential misclassification, and confounding of the outcome (PFS, OS)
- Non-controlled trial: this limits comparisons to other potential therapies and could introduce bias because investigators knew what patients are receiving.
- Small cohort: this limits applicability to other patients

Conclusion:

- There is some durable benefit of platinum-based chemotherapy if targeted treatments for rare mutations cannot be obtained.

[LINK TO ARTICLE](#)



Oncogenic switch and single-agent MET inhibitor sensitivity in a subset of EGFR-mutant lung cancer

Objective:

- Case reports and clinical trials have combined EGFR and MET inhibitors as a treatment to overcome MET amplification-mediated resistance to EGFR tyrosine kinase inhibitor (TKI) therapy. This study sought to find a way to identify patients with EGFR-mutated cancer who might respond to single-agent MET TKI therapy.

Design:

- Three patient-derived lines were created
- All three models had mutant EGFR and MET amplification
- Each model was treated with either a MET inhibitor (crizotinib or savolitinib) or EGFR inhibitor (erlotinib or osimertinib), or a combination of both

Population:

- Three patient-derived xenografts (PDX) were created from cells of patients who developed resistance to single-agent EGFR TKI therapy. Cells from different patients were used to create tumors, then implanted into mice for studies.
 - Acquired resistance after initial long-term response to treatment with EGFR TKI therapy
 - De novo resistance to EGFR TKI therapy
- EGFR mutations included mutation in exon 19 (ELREA, LREAT deletions) and exon 21 (L858R point mutation)
- All had a MET copy number gain
- Cell lines were also developed from these samples

Effectiveness Results:

- All three models showed sensitivity to single-agent MET inhibition along with sustained tumor regression
- All three models showed resistance to single-agent EGFR inhibition

- When MET was inhibited, proapoptotic proteins were upregulated
- When EGFR inhibition was combined with MET inhibition, there was no evidence that the EGFR inhibitor improved the efficacy of the MET inhibitor. In two of the models, average tumor volume decrease was not different when comparing single to combination inhibition. One treatment was discontinued, there was also no difference in tumor outgrowth
- In cell line models, researchers also confirmed that samples were resistant to EGFR inhibitors. However, they were found to be highly sensitive to single MET inhibition, and sufficient enough to inhibit downstream growth signals
- Researchers also found that in MET-dependent EGFR-mutated models, MET activates downstream oncogenic signaling through ERBB3 phosphorylation
- Researchers also identified low EGFR:MET expression ratio as a predictor of single-agent MET inhibitor sensitivity

Strengths:

- Very extensive study in both mouse PDX and cell line models that assesses molecular growth pathway signaling changes with single or combination TKI therapy

Weaknesses:

- Pre-clinical study: These experiments were done in mice and cells in a lab. Results need to be validated in clinical trials

Conclusion:

- Some EGFR-mutated, MET-amplified lung cancers develop dependence on MET activation alone and may potentially be treated with single-agent MET TKI therapy instead of combination therapy with an EGFR TKI.

[LINK TO ARTICLE](#)



MET amplification and efficacy of nivolumab in patients with NSCLC

Drug(s): nivolumab

Objective:

- To assess the association of MET amplification, gene copy number gains, and MET expression with Nivolumab's effect in patients with NSCLC

Design

- Retrospective analysis of a previous multicentered cohort study that evaluated Nivolumab's effectiveness related to PD-L1 gene copy number status
- MET copy number status and MET gene signals per cell were utilized to assess MET amplification

Population

- 175 patients enrolled
 - MET copy number status: non-amplified (92.6%), amplified (7.4%)
 - MET gene signal: no gain (89.7%), low gain (8.0%), high gain (2.3%)
 - MET expression: Positive (25.7%), negative (74.3%)
- Average age: 69 years
- Sex: Male (80.6%), female (19.4%)
- Histology: Adenocarcinoma (57.7%), squamous cell carcinoma (35.4%), other (4.0%)
- Stage: III (18.9%), IV (70.3%), postoperative recurrent (10.8%)
- Number of previous regimens: 1 (46.3%), 2 (29.7%), ≤ 3 (24.0%)

Effectiveness

- Amplified patients: ORR: 23.1%, PFS: 3.5 months
- Non-amplified patients: ORR: 19.1%, PFS: 2.6 months
- High gain/ low gain/no gain (respectively): ORR: 25.0%/28.6%/18.5%
- MET expression: ORR: Positive (24.4%), negative (17.7%)
- Average OS for all patients in study: 14.1 months

Strengths

- Inclusion of data from both definitions of MET amplification
- Perhaps the only study known that explores Nivolumab's effects associated with the impacts of MET amplification

Weaknesses

- Lack of complete co-mutation status of the included patients
- Retrospective analysis on a study with different objectives limits the quality of this study

Conclusion

- This exploratory study sheds light on how MET amplified NSCLC may have varying results with Nivolumab. Future prospective studies are required to better understand the impact that MET status may have on Nivolumab and who is best suited for this therapy.

[LINK TO ARTICLE](#)



Mesenchymal-epithelial transition exon 14 skipping mutation and amplification in 5,008 patients with lung cancer

Objective:

- To examine the correlation between mesenchymal-epithelial transition (MET) genomic alterations and the clinical characteristics of lung cancer

Design:

- Analysis of lung cancer patients treated at China's Affiliated Hospital of Qingdao University
- MET alterations and characteristics studied: MET exon 14 skipping mutation, MET amplification, co-mutation with MET alterations, DNA splicing site with MET exon 14 skipping mutation

Population:

- 5,008 patients
- Age: >60 years (51.3%), ≤ 60 years (48.7%)
- Histology: Adenocarcinoma (92.1%), squamous cell carcinoma (5.93%), adenosquamous carcinoma (0.67%)
- Tumor stage: I (65.6%), II (12.8%), III (5.3%), IV (16.1%)

Results:

- MET exon 14 skipping mutation: (45/5,008 = 0.91%)
 - Age: > 60 years (1.32%), ≤ 60 years (0.45%)
 - Histology: adenocarcinoma (0.9%), Squamous cell carcinoma (1.02%), other (1.03%)
 - Tumor stage: 0+I+II (0.96%), III+IV (0.77%)
- MET amplification: (23/2,927 = 0.79%)
 - Age: > 60 years (9.40%), ≤ 60 years (0.62%)
 - Histology: adenocarcinoma (0.78%), squamous cell carcinoma (1.07%)
 - Tumor stage: 0+I+II (0.43%), III+IV (2.41%)

Strengths:

- Large cohort of patients with an in-depth genomic analysis helps to shed light on the correlation between mutation type and clinical characteristics

Weaknesses:

- Single-center study limits ability to generalize results
- Lack of survival data for the included patients

Conclusion :

- This study found a significant association between MET exon 14 skipping mutation and older age, and that MET amplification had a higher incidence in advanced tumor stages.

[LINK TO ARTICLE](#)



ADDITIONAL READING

In the construction of the MET Crusader newsletter, the research team searches content from across the Internet. In that process, they come across articles that don't reasonably fit our criteria but are still significant. The following are the articles found in preparation of this newsletter.

Preclinical Readings

- [Combination of type I and type II MET tyrosine kinase inhibitors as therapeutic approach to prevent resistance](#)
Molecular Cancer Therapeutics, November 17th 2021
- [Correlation of MET-receptor overexpression with MET gene amplification and patient outcome in malignant mesothelioma](#)
International Journal of Molecular Sciences, November 29th 2021

Additional Readings

- [Therapeutic strategies in METex14 skipping mutated non-small cell lung cancer](#)
Journal of Hematology & Oncology, August 23rd 2021
- [Cancer therapy guided by mutation tests: current status and perspectives international](#)
Journal of Molecular Sciences, October 10th 2021
- [Drug resistance of targeted therapy for advanced non-small cell lung](#)
Journal of Cancer Research and Clinical Oncology, October 18th 2021
- [Targeted treatment of non-small cell lung cancer: focus on capmatinib with companion diagnostics](#) OncoTargets and Therapy, November 23rd 2021
- [The treatment of advanced pulmonary sarcomatoid carcinoma](#)
Future Oncology, December 9th 2021
- [MET gene dysregulation as a promising therapeutic target in lung cancer—a review](#)
Journal of Personalized Medicine, December 14th 2021
- [Targeting un-MET needs in advanced non-small cell lung cancer](#)
Lung Cancer, December 29th 2021



MET Clinical Trials

IMPORTANT

Below is a list of clinical trials involving MET alterations on **ClinicalTrials.gov**. This list is a summary snapshot of emerging therapeutic strategies, details of these trials can be found at **ClinicalTrials.gov**. Recruitment for clinical trials is constantly changing, and many eligibility criteria are typically required in order to participate. The treatments being studied in the clinical trials listed here are meant for reference only and do not replace medical advice. Always have a discussion with your oncologist if you have questions about clinical trial participation.

This list was last updated on January 30, 2022.

TKI TRIALS

NIH Identifier: NCT04084717

Link: <https://clinicaltrials.gov/ct2/show/NCT04084717>

Title: Study of Crizotinib for ROS1 and MET Activated Lung Cancer
Status: Recruiting
Drug: Crizotinib
Phase: P2
Countries: Canada

NIH Identifier: NCT03693339

Link: <https://clinicaltrials.gov/ct2/show/NCT03693339>

Title: Capmatinib in Patients With Non-small Cell Lung Cancer Harboring cMET exon14 Skipping Mutation
Status: Recruiting
Drug: Capmatinib
Phase: P2
Countries: Republic of Korea

NIH Identifier: NCT03993873

Link: <https://clinicaltrials.gov/ct2/show/NCT03993873>

Title: Phase 1 Study of TPX-0022, a MET/CSF1R/SRC Inhibitor, in Patients With Advanced Solid Tumors Harboring Genetic Alterations in MET
Status: Recruiting
Drug: TPX-0022
Phase: P1
Countries: US, Republic of Korea

NIH Identifier: NCT02864992

Link: <https://clinicaltrials.gov/ct2/show/NCT02864992>

Title: Tepotinib Phase II in Non-small Cell Lung Cancer (NSCLC) Harboring MET Alterations (VISION)
Status: Active, Not Recruiting
Drug: Tepotinib
Phase: P2
Countries: US, Austria, Belgium, France, Germany, Israel, Italy, Japan, Republic of Korea, Netherlands, Poland, Spain, Switzerland, Taiwan

NIH Identifier: NCT03175224

Link: <https://clinicaltrials.gov/ct2/show/NCT03175224>

Title: APL-101 Study of Subjects With NSCLC With c-Met EXON 14 Skip Mutations and c-Met Dysregulation Advanced Solid Tumors (SPARTA)
Status: Recruiting
Drug: APL-101
Phase: P1/P2
Countries: US, Australia, Canada, Italy, Puerto Rico, Singapore, Spain, Taiwan, Ukraine, United Kingdom

NIH Identifier: NCT04258033

Link: <https://clinicaltrials.gov/ct2/show/NCT04258033>

Title: A Study of PLB1001 in Non-small Cell Lung Cancer With c-Met Dysregulation
Status: Recruiting
Drug: PLB1001 also known as Bozitinib and APL-101
Phase: P2
Countries: China

NIH Identifier: NCT01639508

Link: <https://clinicaltrials.gov/ct2/show/NCT01639508>

Title: Cabozantinib in Patients With RET Fusion-Positive Advanced Non-Small Cell Lung Cancer and Those With Other Genotypes: ROS1 or NTRK Fusions or Increased MET or AXL Activity
Status: Recruiting
Drug: Cabozantinib
Phase: P2
Countries: US

NIH Identifier: NCT03088930

Link: <https://clinicaltrials.gov/ct2/show/NCT03088930>

Title: Evaluating Crizotinib in the Neoadjuvant Setting in Patients With Non-small Cell Lung Cancer
Status: Completed
Drug: Crizotinib
Phase: P2
Locations: US

NIH Identifier: NCT04693468

Link: <https://clinicaltrials.gov/ct2/show/NCT04693468>

Title: Talazoparib and Palbociclib, Axitinib, or Crizotinib for the Treatment of Advanced or Metastatic Solid Tumors, TalaCom Trial
Status: Recruiting
Drug: Talazoparib + Palbociclib, Axitinib or Crizotinib
Phase: P1
Countries: US

NIH Identifier: NCT02414139

Link: <https://clinicaltrials.gov/ct2/show/NCT02414139>

Title: Clinical Study of Oral cMET Inhibitor INC280 in Adult Patients With EGFR Wild-type Advanced Non-small Cell Lung Cancer (Geometry Mono-1)
Status: Active Not Recruiting
Drug: Capmatinib
Phase: P2
Countries: US, Argentina, Austria, Belgium, Brazil, Canada, France, Germany, Israel, Italy, Japan, Republic of Korea, Lebanon, Mexico, Netherlands, Norway, Poland, Russia, Singapore, Spain, Sweden, Switzerland, Taiwan, Turkey, United Kingdom

NIH Identifier: NCT02219711

Link: <https://clinicaltrials.gov/ct2/show/NCT02219711>

Title: Phase 1/1b Study of MGCD516 in Patients with Advanced Cancer
Status: Unknown
Drug: MGCD516
Phase: P1
Countries: US, Republic of Korea

NIH Identifier: NCT04270591

Link: <https://clinicaltrials.gov/ct2/show/NCT04270591>

Title: Assess the Anti-tumor Activity and Safety of Glumetinib in Patient with Advanced c-MET-positive Non-Small Cell Lung Cancer
Status: Recruiting
Drug: Glumetinib
Phase: P1/P2
Countries: US, China, Japan



TKI TRIALS (CONTINUED)

NIH Identifier: NCT02920996

Link: <https://clinicaltrials.gov/ct2/show/NCT02920996>

Title: Merestinib In Non-Small Cell Lung Cancer And Solid Tumors

Status: Active, Not Recruiting

Drug: Merestinib

Phase: P2

Countries: US

NIH Identifier: NCT02867592

Link: <https://clinicaltrials.gov/ct2/show/NCT02867592>

Title: Cabozantinib-S-Malate in Treating Younger Patients With Recurrent, Refractory, or Newly Diagnosed Sarcomas, Wilms Tumor, or Other Rare Tumors

Status: Active, not recruiting

Phase: P2

Locations: US

NIH Identifier: NCT002650375

Link: <https://clinicaltrials.gov/ct2/show/NCT002650375>

Title: Study of Metatinib

Tromethamine Tablet

Status: Recruiting

Drug: Metatinib Tromethamine

Phase: P1

Countries: China

NIH Identifier: NCT02499614

Link: <https://clinicaltrials.gov/ct2/show/NCT02499614>

Title: Crizotinib in Pretreated Metastatic Non-small-cell Lung Cancer With MET Amplification or ROS1 Translocation (METROS) (METROS)

Status: Recruiting

Drug: Crizotinib

Phase: P2

Countries: Italy

UMBRELLA TRIALS

NIH Identifier: NCT03574402

Link: <https://clinicaltrials.gov/ct2/show/NCT03574402>

Title: Phase II Umbrella Study Directed by Next Generation Sequencing (TRUMP)

Status: Recruiting

Trial Name: Umbrella (TRUMP)

Phase: P2

Countries: China

NIH Identifier: NCT02693535

Link: <https://clinicaltrials.gov/ct2/show/NCT02693535>

Title: TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)

Status: Recruiting

Trial Name: TAPUR

Phase: P2

Countries: US

NIH Identifier: NCT02664935

Link: <https://clinicaltrials.gov/ct2/show/NCT02664935>

Title: National Lung Matrix Trial: Multi-drug Phase II Trial in Non-Small Cell Lung Cancer

Status: Active, not recruiting

Trial Name: Matrix

Phase: P2

Countries: United Kingdom

NIH Identifier: NCT02465060

Link: <https://clinicaltrials.gov/ct2/show/NCT02465060>

Title: Targeted Therapy Directed by Genetic Testing in Treating Patients With Advanced Refractory Solid Tumors, Lymphomas, or Multiple Myeloma (The MATCH Screening Trial)

Status: Recruiting

Trial Name: Match

Phase: P2

Countries: US, Guam, Puerto Rico

NIH Identifier: NCT03297606

Link: <https://clinicaltrials.gov/ct2/show/NCT03297606>

Title: Canadian Profiling and Targeted Agent Utilization Trial (CAPTUR)

Status: Recruiting

Trial Name: CAPTUR

Phase: P2

Countries: Canada

NIH Identifier: NCT04116541

Link: <https://clinicaltrials.gov/ct2/show/NCT04116541>

Title: A Study Evaluating the Activity of Anti-cancer Treatments Targeting Tumor Molecular Alterations/ Characteristics in Advanced / Metastatic Tumors. (MegaMOST)

Status: Recruiting

Phase: P2

Countries: France

ANTIBODY-ADC TRIALS

NIH Identifier: NCT03539536

Link: <https://clinicaltrials.gov/ct2/show/NCT03539536>

Title: Study of Telisotuzumab Vedotin (ABBV-399) in Subjects with Previously Treated c-Met+ Non-Small Cell Lung Cancer

Status: Recruiting

Drug: ABBV-399

Phase: P2

Countries: US, Australia, Belgium, Canada, China, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Japan, Republic of Korea, Romania, Russia, Spain, Taiwan, Turkey, United Kingdom

NIH Identifier: NCT04077099

Link: <https://clinicaltrials.gov/ct2/show/NCT04077099>

Title: REGN5093 in Patients With MET-Altered Advanced Non-Small Cell Lung Cancer

Status: Recruiting

Drug: REGN5093

Phase: P1, P2

Countries: US, Republic of Korea

NIH Identifier: NCT04484142

Link: <https://clinicaltrials.gov/ct2/show/NCT04484142>

Title: Study of DS-1062a in Advanced or Metastatic Non-small Cell Lung Cancer With Actionable Genomic Alterations (TROPION-Lung05)

Status: Recruiting

Drug: DS-1062a also known as Datopotamab

Phase: P2

Countries: US, France, Germany, Hungary, Italy, Japan, Republic of Korea, Netherlands, Spain, Taiwan

NIH Identifier: NCT00585195

Link: <https://clinicaltrials.gov/ct2/show/NCT00585195>

Title: A Study Of Oral PF-02341066, A C-Met/Hepatocyte Growth Factor Tyrosine Kinase Inhibitor, In Patients With Advanced Cancer (PROFILE 1001)

Status: Active, not recruiting

Drug: PF-02341066

Phase: P1

Countries: US, Austria, Japan, Republic of Korea



EGFR + MET TRIALS

NIH Identifier: NCT03944772

Link: <https://clinicaltrials.gov/ct2/show/NCT03944772>

Title: Phase 2 Platform Study in Patients With Advanced Non-Small Lung Cancer Who Progressed on First-Line Osimertinib Therapy (ORCHARD)
Status: Recruiting
Drug: Osimertinib + Savolitinib
Phase: P2
Countries: US, Denmark, Japan, Republic of Korea, Netherlands, Norway, Spain, Sweden

NIH Identifier: NCT03778229

Link: <https://www.clinicaltrials.gov/ct2/show/NCT03778229>

Title: Osimertinib Plus Savolitinib in EGFRm+/MET+ NSCLC Following Prior Osimertinib (SAVANNAH)
Status: Recruiting
Drug: Osimertinib + Savolitinib
Phase: P2
Countries: US, Brazil, Canada, Chile, Denmark, France, India, Israel, Italy, Japan, Puerto Rico, Republic of Korea, Spain, Taiwan, Vietnam

NIH Identifier: NCT03940703

Link: <https://clinicaltrials.gov/ct2/show/NCT03940703>

Title: A Study of Tepotinib Plus Osimertinib in Osimertinib Relapsed Mesenchymal-epithelial Transition Factor (MET) Amplified Non-small Cell Lung Cancer (NSCLC) (INSIGHT 2)
Status: Recruiting
Drug: Tepotinib + Osimertinib
Phase: P2
Countries: US, Belgium, China, France, Germany, Hong Kong, Italy, Japan, Republic of Korea, Malaysia, Netherlands, Russia, Singapore, Spain, Taiwan, Thailand, Vietnam

NIH Identifier: NCT02609776

Link: <https://clinicaltrials.gov/ct2/show/NCT02609776>

Title: Study of Amivantamab, a Human Bispecific EGFR and cMet Antibody, in Participants with Advanced Non-Small Cell Lung Cancer (CHRYSLIS)
Status: Recruiting
Drug: Amivantamab
Phase: P1
Countries: US, Australia, Canada, China, France, Italy, Japan, Republic of Korea, Spain, Taiwan, United Kingdom

NIH Identifier: NCT03797391

Link: <https://clinicaltrials.gov/ct2/show/NCT03797391>

Title: A Dose Escalation With Expansion Study of EMB-01 in Participants With Advanced/Metastatic Solid Tumors
Status: Recruiting
Drug: EMB-01
Phase: P1/P2
Countries: US, China

NIH ID: NCT04606771

Link: <https://clinicaltrials.gov/ct2/show/NCT04606771>

Title: A Study Comparing Savolitinib Plus Osimertinib vs Savolitinib Plus Placebo in Patients with EGFRm+ and MET Amplified Advanced NSCLC (CoC)
Status: Recruiting
Drug: Osimertinib + Savolitinib
Phase: P2
Countries: US, Argentina, Brazil, Chile, India, Republic of Korea, Taiwan, Thailand, Vietnam

IMMUNOTHERAPY AND COMBINATION TRIALS

NIH Identifier: NCT03983954

Link: <https://clinicaltrials.gov/ct2/show/NCT03983954>

Title: Naptumomab Estafenatox in Combination With Durvalumab in Subjects With Selected Advanced or Metastatic Solid Tumors
Status: Recruiting
Drug: Naptumomab Estafenatox + Durvalumab
Phase: P1
Countries: Israel

NIH Identifier: NCT04310007

Link: <https://clinicaltrials.gov/ct2/show/NCT04310007>

Title: Testing the Addition of the Pill Chemotherapy, Cabozantinib, to the Standard Immune Therapy Nivolumab Compared to Standard Chemotherapy for Non-small Cell Lung Cancer
Status: Recruiting
Drug: Cabozantinib + Nivolumab
Phase: P2
Countries: US

NIH ID: NCT02954991

Link: <https://clinicaltrials.gov/ct2/show/NCT02954991>

Title: Phase 2 Study of Glesatinib, Sitravatinib or Mocetinostat in Combination with Nivolumab in Non-Small Cell Lung Cancer
Status: Active, Not Recruiting
Drug: Glesatinib, Sitravatinib or Mocetinostat + Nivolumab
Phase: P2
Countries: US

NIH ID: NCT03666143

Link: <https://clinicaltrials.gov/ct2/show/NCT03666143>

Title: A Phase 1b Study to Assess Sitravatinib in Combination with Tislelizumab in Patients With Advanced Solid Tumors.
Status: Active, Not Recruiting
Drug: Sitravatinib + Tislelizumab
Phase: P1
Countries: Australia, China

NIH ID: NCT04323436

Link: <https://clinicaltrials.gov/ct2/show/NCT04323436>

Title: Study of Capmatinib and Spaltalizumab/Placebo in Advanced NSCLC Patients with MET Exon 14 Skipping Mutations
Status: Active, not recruiting
Drug: Capmatinib + Spaltalizumab
Phase: P2
Countries: Belgium, France, Germany, Japan

NIH ID: NCT04139317

Link: <https://clinicaltrials.gov/ct2/show/NCT04139317>

Title: Safety and Efficacy of Capmatinib (INC280) Plus Pembrolizumab vs Pembrolizumab Alone in NSCLC With PD-L1 ≥ 50%
Status: Active, Not Recruiting
Drug: Capmatinib + Pembrolizumab
Phase: P2
Countries: Australia, Belgium, Czechia, France, Germany, Hong Kong, India, Italy, Japan, Malaysia, Spain, Taiwan, Thailand



MET Cell Lines, PDX and CDX models

Cell lines and mouse models are fundamental to MET cancer research. We need these tools to assist researchers in finding a cure for MET mutated cancer.

The following is a list of known cell lines and mouse models that are generally available, subject to the terms and conditions of the institution sharing the biologics. Please check with the contact for additional information. MET Crusaders does not verify or validate the quality of the materials offered.

If you are a researcher with a METex14 or other MET mutated cell line, and you would be willing to share and have listed below, please contact John Hallick at john.hallick@metcrusaders.org or call 608-209-6682 John's cell phone.

If you are a patient and interested in donating tissue or pleural fluid to create cell lines or mouse models, please contact John Hallick at john.hallick@metcrusaders.org or call 608-209-6682 John's cell phone. We desperately need your donation.

CELL LINES/PDX MODELS/CDX MODELS

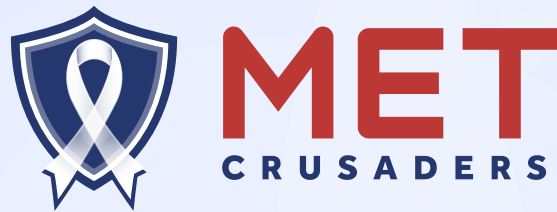
Genetic Alteration: MET 14 Skipping
Identifier: MSK-LX439
Type: PDX Model
Source: Lung
Institution: Memorial Sloan Kettering Cancer Center
Contact: Charles Rudin, MD PhD
Memorial Sloan Kettering Cancer Center
1275 York Avenue, New York, NY 10065
Email: rudinc@mskcc.org

Genetic Alteration: MET 14 Skipping
Identifier: MSK-LX461
Type: PDX Model
Source: Lung
Institution: Memorial Sloan Kettering Cancer Center
Contact: Charles Rudin, MD PhD
Memorial Sloan Kettering Cancer Center
1275 York Avenue, New York, NY 10065
Email: rudinc@mskcc.org

Genetic Alteration: MET 14 Skipping
Identifier: Lung-21
Type: PDX Model
Source: Brain
Institution: University of Wisconsin Hospital
Contact: Andrew M. Baschnagel, M.D.
University of Wisconsin School of Medicine and Public Health
600 Highland Avenue, Madison, WI 53792
Email: baschnagel@humonc.wisc.edu

Genetic Alteration: MET Asp-1000 Frame Shift
Identifier: Lung-20
Type: PDX Model
Source: Brain
Institution: University of Wisconsin Hospital
Contact: Andrew M. Baschnagel, M.D.
University of Wisconsin School of Medicine and Public Health
600 Highland Avenue, Madison, WI 53792
Email: baschnagel@humonc.wisc.edu

Genetic Alteration: MET 14 Skipping
Identifier: CUTO47
Type: Cell Line
Source: Lung
Institution: University of Colorado
Contact: Robert C. Doebele, MD, PhD
University of Colorado
12801 East 17th Avenue 8122, Aurora, CO 80045
Email: ROBERT.DOEBELE@CUANSCHUTZ.EDU



The MET Crusader newsletter is written for the benefit of MET patients, caregivers, clinicians and researchers. It contains an outlined summary of MET related abstracts, posters and articles. The outline summaries provide key metrics and improve readability. The summaries are not intended to replace the abstracts, posters and articles. Where possible, links are provided to the source materials. Where links are not possible, a reference is made to help locate the source documents. If you need help in finding a document contact us.

Where possible, the outlined summaries contain the NIH ID that links to the actual clinical trial. This helps our community in the evaluation of clinical trials. The drug under trial is also provided.

*The MET Crusader newsletter can be freely shared. Pass it along. If you are a MET patient or caregiver and would like to be on our email list, go to **Join Us** on www.metcrusaders.org and register. If you are a clinician or researcher, email your information to info@metcrusaders.org.*

Your comments and suggestions are always welcome.

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Come Join Us!

www.metcrusaders.org

