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CRUSADER NEWSLETTER

Q1 2022 RESEARCH EDITION



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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Safety of Tepotinib in Patients With MET Exon 14 Skipping NSCLC and Recommendations for Management

Drug(s): tepotinib

Objective

- To describe in detail adverse events of interest in the VISION trial

Design

- Multicenter open-label phase II trial (VISION)
- Patients received tepotinib 500mg (450mg of active moiety) once a day
 - Dose could be reduced if required for tolerability

Population

- 255 patients with advanced non-small cell lung cancer (NSCLC) with MET exon 14 skipping
- Up to 2 prior lines of therapy allowed
- Median age 72yo, range 41-94
- Majority of patients had ECOG performance status of 1 (72%)
- Majority adenocarcinoma (81.2%)
- Slight majority previously treated (51%)

Safety Results

- 96.5% of patients experienced adverse effects, with 52.9% experiencing grade ≥ 3 effects
 - Peripheral edema (60%, 7.8% grade ≥ 3) or edema events (69.8%, 9.4% grade ≥ 3)
 - Median time to onset 7.9 weeks (any grade) and 18.9 weeks (grade 3)
 - Median time to resolution not reported due to the low number of patients with completely resolved peripheral edema
 - More common in older patients, white vs Asian patients, and those with higher BMI
 - Led to dose reduction (18.8%), holds (23.1%), or both (25.9%) in many patients. There were 11 patients (4.3%) who permanently discontinued due to edema.
 - No clear association with hypoalbuminemia (70.2% of patients with edema had normal albumin)

- Hypoalbuminemia (23.9%, 5.5% grade ≥ 3)
 - Median time of onset 9.4 weeks
 - More common in men, smokers, and patients with hypertension
- Pleural effusion (13.3%, 4.7% grade ≥ 3)
 - Median time to onset 16.6 weeks; median time to resolution 56.1 weeks
 - More common in white vs Asian patients and those with hypertension
 - May have been either attributable to drug or to underlying disease
 - Led to dose reduction (2.7%), holds (4.3%), or permanent discontinuation (2%) in a handful of patients.
- Increased creatinine (25.1%, 0.4% grade ≥ 3)
 - Median time to onset 3.1 weeks
 - Slightly more common in Asian patients
 - Did not seem to be associated with renal impairment, although more common in those with baseline renal impairment
 - Led to dose reduction (2.7%), holds (6.1%), or permanent discontinuation (0.8%) in a handful of patients.
- Nausea (26.7%, 0.8% grade ≥ 3)
 - Median time to onset 4 weeks; median time to resolution 5.9 weeks
 - More common in women, white patients and those with obesity
 - Led to dose reduction (0.8%), holds (2%), or permanent discontinuation (0.4%) in a couple patients.
 - Vomiting reported in 12.9% with only 1.2% having grade 3 vomiting. Typically short-lived (median time to resolution 0.3 weeks). Led to a hold in 1 patient.

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- Diarrhea (26.3%, 0.4% grade ≥ 3)
 - Median time to onset 2.4 weeks; median time to resolution 1.8 weeks
 - More common in women and in obese patients
 - Led to holds (2%) or permanent discontinuation (0.4%) in a couple patients.
- ALT and/or AST increase (12.2%, 2.4% grade ≥ 3)
 - Median onset 6.1 weeks
 - Typically asymptomatic and consistent across subgroups
 - Led to dose reduction (0.8%), holds (3.5%), or permanent discontinuation (3.5%) in a few patients.
- Other all-cause adverse effects were less common, but included eye disorders, dyspnea, constipation, decreased appetite, fatigue, pleural effusion, asthenia, cough, increased ALT, back pain, and pneumonia
- Impact on treatment course
 - 29.8% required dose reduction
 - 43.9% required treatment interruption

- 20.4% required discontinuation
- Three patients (1.2%) died from treatment-related causes (interstitial lung disease, severe worsening of dyspnea, and acute hepatic failure)
- Most common serious adverse effects were pleural effusion (6.7%), pneumonia (4.7%), and progression (4.7%)

Conclusion

- These detailed safety results can give clinicians and patients a better idea of what to expect with tepotinib treatment. Although tepotinib is associated with a low rate of serious adverse effects, some patients may require dose adjustment, treatment pauses, or additional supportive care to assist with adverse effects such as peripheral edema and nausea. Notably, peripheral edema typically takes several weeks to occur, may worsen with time, and may be slow to resolve. Some patients may not be able to tolerate tepotinib and may require discontinuation. An ongoing, active collaboration between the patient and the care team is vital for early detection and treatment of side effects.

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The Impact of Driver Mutation on the Treatment Outcome of Early-Stage Lung Cancer Patients Receiving Neoadjuvant Immunotherapy and Chemotherapy

Drug(s): platinum agent, pembrolizumab

Objective

- Outcomes of treatment with immunotherapy and chemotherapy in operable, early stage non-small cell lung cancer (NSCLC) are mixed. This study aimed to analyze treatment outcomes of combination neoadjuvant pembrolizumab and chemotherapy, and determine the efficacy of treatment based on PD-L1 expression and other genomic alterations.

Design

- Single center, tertiary hospital
- Retrospective review

Population

- Stage I to III NSCLC in Taiwan
- Excluded patients with unresectable disease, poor performance status, or relatively limited disease that did not require extensive surgical resection
- Patients treated with neoadjuvant (before surgery) chemotherapy received 4 cycles of platinum-doublet chemotherapy, with 2 doses of pembrolizumab at the physician's discretion
- Average age was 64 years
- Included 23 patients total treated neoadjuvantly, 11 with chemo-immunotherapy (combination treatment) and 12 with chemotherapy alone. Of patients treated with chemo-immunotherapy:
 - 9 males
 - 5 adenocarcinoma histology
 - 10 with tumor size that was 3 cm or greater
 - 3 with N1 nodal involvement, 8 with N2 nodal involvement
 - 1 stage II, 4 stage IIIA, 6 stage IIIB

Efficacy Results

- Median follow-up was 18.3 months
- Radiologic objective response rate (ORR): 45.5% with combination treatment, 58.3% with chemotherapy alone
- Disease-free survival (from date of surgery to disease recurrence): 100% in both groups
- Major pathological response (MPR): 63.% with combination treatment, 8.3% with chemotherapy alone
- Responses to combination chemo-immunotherapy based on mutation status were also reported. Of 11 individuals, 3 experienced cancer recurrence (cancer came back). All of these individuals had an adenocarcinoma histology, a PD-L1 greater than 50%, and either a MET amplification or MET exon 14 skipping mutation.
 - One patient had a MET amplification, EGFR exon 20 insertion.
 - One patient had a MET exon 14 skipping mutation. Initially found with a major pathologic response and clear lymph nodes after surgery.
 - One patient had a MET amplification, EGFR exon 18 E709G mutation, and EGFR exon 21 L858R mutation. Initially also found with a major pathologic response and clear lymph nodes after surgery.

Safety Results

- Not reported

Conclusion

- Limited data exist to guide neoadjuvant treatment with immunotherapy in patients with oncologic mutation drivers. This data suggests that immunotherapy may not be effective for patients with MET alterations, but larger, prospective studies are needed to further prove this.

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Amivantamab in Patients With NSCLC With MET Exon 14 Skipping Mutation: Updated Results From the CHRYSALIS Study

Drug(s): amivantamab

Objective

- Evaluate efficacy of amivantamab, a humanized, bispecific antibody targeting both EGFR and MET, in NSCLC patients with a primary MET exon 14 (METex14) skipping mutation.

Design

- Phase 1 dose escalation/dose expansion
- Treated with amivantamab with either 1050 mg (patients less than 80 kg) or 1400 mg (patients 80 kg or more) weekly for 1 cycle, then biweekly thereafter
- Response measured by RECIST

Population

- 43 patients with advanced NSCLC with a primary METex14 skipping mutation who progressed on or declined standard of care therapy
- Median age 70 years
- Female 58%
- Median prior lines of therapy: 2, including crizotinib, capmatinib, tepotinib, anti-MET antibody
 - 36 patients had at least 1 post-baseline disease assessment: 6 patients had no prior treatment, 11 patients had no prior MET inhibitor, 19 had a prior MET inhibitor
- Brain metastases 23%

Efficacy Results

- Median duration of follow-up 5.8 months
- Overall response rate 33%: 50% if those with no prior treatment, 46% in those with no prior MET inhibitor, 21% in those with some prior MET inhibitor treatment
- Duration of response was 6 months or greater in 67% of patients

Safety Results

- Similar to previously reported experience with amivantamab
- Treatment-related adverse events led to 3 dose reductions and 3 discontinuations

Conclusion

- Amivantamab seems to have anti-tumor activity in METex14 skipping mutated NSCLC, even after prior MET inhibitor therapy. Updated data is needed to further validate these results.

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A Lung Adenocarcinoma Patient Harboring MET c. 3028 + 2 T>A Variant Sensitive to Crizotinib Treatment

Drug(s): crizotinib

Objective

- To describe a response to crizotinib in a patient with a specific MET exon 14 skipping variant verified by multiple methodologies

Design

- Case report

Description

- 71yoM diagnosed with metastatic poorly differentiated lung adenocarcinoma after presenting with shortness of breath and chest pressure
- Next generation sequencing (NGS) testing was performed upon diagnosis, which demonstrated METex14 3028 + 2 T>A. This was predicted to be an activating mutation.

- Hyperactivation of MET was confirmed via quantitative polymerase chain reaction (qPCR) measurement of DNA expression and immunohistochemistry (IHC) measurement of protein expression.

Results

- Patient started crizotinib 250 mg twice daily.
- CT revealed a response 1 month later, which correlated with improved symptoms. The patient continued to have a response at time of publication, with 6 months of total treatment.

Conclusion

- The combination of NGS, PCR, and IHC testing taken with a clinical response to crizotinib supports the hypothesis that the 3028 + 2 T>A variant of METex14 is an activating mutation sensitive to MET inhibitors.

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Targeted RNA Sequencing for Upfront Analysis of Actionable Driver Alterations in Non-Small Cell Lung Cancer

Objective

- To compare targeted RNA-based Next-Generation Sequencing (tRNA-seq) detection of actionable drivers against targeted DNA-based Next-Generation Sequencing (tDNA-seq) and to evaluate their clinical application

Design

- NSCLC tissue sample divided into retrospective and prospective testing groups
 - Validation cohort (retrospective) analyzed using tDNA-seq, used as reference
 - Diagnostic test cohort prospectively tested using tDNA-seq and tRNA-seq
- Actionable driver alterations included single nucleotide variants (SNVs), small insertions/deletions (indels) or ALK gene fusion

Population

- 126 NSCLC tumor samples from individuals with stage IV adenocarcinoma
 - Validation cohort (N=20)
 - Diagnostic test cohort (N-106)

Results

- Compared to tDNA-seq:
 - tRNA-seq able to identify all 28 SNVs and indels
 - tRNA-seq able to identify 34/35 mutations
 - tRNA-seq identified driver fusion variant that tDNA-seq was unable to identify

Conclusion

- tRNA-seq could potentially be used in the future to identify molecular biomarkers while saving time and tumor tissue compared to tDNA-seq

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Crizotinib in MET Exon 14-Mutated or MET-Amplified in Advanced Disease Non-Small Cell Lung Cancer - A Retrospective, Single Institution Experience

Drug(s): crizotinib

Objective

- To describe outcomes with crizotinib in MET-altered non-small cell lung cancer (NSCLC)

Design:

- Retrospective case series of patients with NSCLC treated with crizotinib for MET alterations at a single institution between January 2015 and January 2020.

Population:

- Of 403 patients with advanced or metastatic lung cancer treated at the institution, 374 received molecular testing
- A total of 16 patients received crizotinib for a MET alteration
 - METex14 mutation (7 patients)
 - Median age 67, range 48-78
 - All adenocarcinoma; one with sarcomatoid features
 - A minority of patients (n = 3) received crizotinib as first-line treatment
 - MET amplification (9 patients)
 - Median age 63, range 50-70
 - 3 with squamous cell carcinoma; 6 adenocarcinoma
 - Only 1 patient received crizotinib as first-line treatment

Results:

- METex14
 - Median overall survival 22.8 months (3 – 52 months)
 - Median progression-free survival 12.4 months
- MET amplification
 - Median overall survival 5.4 months (0 – 33 months)
 - Median progression-free survival 2.6 months

Conclusion:

- As corroborated in other studies, patients with the METex14 mutation seemed to respond better to crizotinib compared to those with MET amplifications. However, it should be noted that more patients with the METex14 mutation received crizotinib as first-line treatment and it is difficult to draw conclusions given the small and heterogeneous population included.

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Efficacy of First-Line Immune Checkpoint Inhibitors in Patients With Advanced NSCLC With KRAS, MET, FGFR, RET, BRAF, and HER2 Alterations

Drug(s): pembrolizumab, nivolumab, ipilimumab

Objective

- Evaluate the effects of first-line immune checkpoint inhibitor (ICI) therapy in NSCLC patients who have oncogenic mutations.

Design

- Single-center, retrospective cohort study at a center in Japan

Population

- 78 Asian patients with NSCLC harboring driver mutations in *KRAS* (n=21), *MET* (n=6), *FGFR* (n=3), *RET* (n=2), *BRAF* (n=2), *HER2* (n=1), as well as those without mutations (driver negative)
- Median age was 72 years (range 31-89)
- 67% male
- 15% never-smokers
- 83% adenocarcinoma
- High PD-L1 (50% or more) found in 40% of patients
- Treatment options included: pembrolizumab, ICI with chemotherapy, nivolumab/ipilimumab, and nivolumab/ipilimumab with chemotherapy

Efficacy Results

- Median progression free survival was 10.1 months in the overall group
 - *KRAS*: 16.2 months (95% CI 6.3-not reached [NR])
 - *MET*: 2.8 months (2.7-NR)
 - Other alterations: 11.7 months (5.9-NR)

- Median overall survival was 22.6 months in the overall group
 - *KRAS*: 31.3 months (9-NR)
 - *MET*: NR
 - Other alterations: 23.5 months (18.3-NR)
 - Drive negative: 21.1 months (15.2-NR)
- Driver mutation status (drive positive vs. driver negative) was not significantly associated with median overall survival (23.5 vs. 23.1 months, p=0.35)

Safety Results

- Not reported

Conclusion

- First-line ICI treatment outcomes were similar in advanced NSCLC harboring driver mutations, except for those with *MET* alterations. mPFS was 2.8 months, which is consistent with other reports of patients harboring *MET* alterations that were treated with ICI therapy. These data suggest that initial treatment with ICI should be avoided in patients with *MET* alterations – *MET* inhibitors should be trialed first.

[ARTICLE LINK](#)



Clinical Outcomes of EGFR+/METamp+ vs. EGFR+/METamp- Untreated Patients With Advanced Non-Small Cell Lung Cancer

Objective

- MET overexpression may cause primary resistance to EGFR-TKI therapies with EGFR-mutated advanced NSCLC. This study examined outcomes with first-line TKI monotherapy in *MET* amplified patients. It also examined the tumor inhibition rate and drug sensitivity in different patient-derived lung cancer organoids (LCOs) models derived from malignant pleural effusion.
- First-line treatments were predominantly first-generation EGFR TKI monotherapy (95.5%, 61.1%). Other treatments included:
 - Second-generation EGFR TKIs (4.5%, 11.1%)
 - Third-generation EGFR TKIs (0%, 5.6%)
 - MET TKIs (0%, 5.6%)
 - Dual targeted therapy (4.5%, 50%)

Design:

- Single-center, retrospective review at a hospital in China
- Survival rates estimated via Kaplan-Meier curves and log-rank statistics
- MET immunohistochemistry (IHC) was done to score MET positivity.
 - MET overexpression was positive if more than 50% of tumor cells
- *MET* amplification was determined by *MET* FISH. MET positivity was defined if *MET* gene copy number was ≥ 5 , *MET/CEP7* ratio ≥ 2 , and focal amplification was present in $>10\%$ of tumor cells.
- LCOs were prepared by a previously described protocol and analyzed with a drug sensitivity assay

Population:

- 54 patients with advanced NSCLC with *EGFR* sensitizing mutations and/or de novo *MET* amplifications.
- *MET* FISH (to detect *MET* amplification, METamp) was assessed in 40 patients:
 - EGFR+/METamp- (n=22)
 - EGFR+/METamp+ (n=18)
- METamp- and METamp+
 - 63.6% and 66.7% never smokers
 - 22.7% and 33.3% brain metastases
- All patients were stage 4 and had adenocarcinoma

Efficacy Results:

- Median progression free survival (mPFS) was 12.1 months for METamp- patients, and 1.9 months for METamp+ patients ($P < 0.001$)
- Median overall survival (mOS) was 33.2 months for METamp- patients and 12.7 months for METamp+ patients
- 9 of 12 EGFR+/METamp+ patients were treated with dual targeted therapy as subsequent-line treatment. Only 1 patient maintained a partial response, but all others developed progressive disease.

Objective response rate was 66.7%.

- Drug sensitivity showed potential efficacy:
 - One sample suggested potential efficacy of combination osimertinib and crizotinib treatment ($IC = 0.34 \mu M$).
 - Another sample showed potential sensitivity to osimertinib ($IC_{50} = 0.57 \mu M$). It also demonstrated that dual therapy did not enhance osimertinib activity.

Safety Results:

- Not reported

Conclusion:

- EGFR+/METamp+ patients with advanced NSCLC had worse responses to EGFR-TKI monotherapy and poorer survival. In vitro testing suggests better anticancer activity with dual targeted therapy.

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Mutation-Tailored Treatment Selection in Non-Small Cell Lung Cancer Patients in Daily Clinical Practice

Objective

- To paint a real-world picture of molecular testing and treatment selection for patients with metastatic NSCLC in the Netherlands from 2017 – 2019.

Design

- Retrospective review of pathology and treatment in the Netherlands utilizing the Dutch Pathology Registry (PALGA) and the Netherlands Cancer Registry (NCR).

Population

- Because the NCR and PALGA registries cover 99% of the Dutch population, this study included virtually all new NSCLC diagnoses in the country within the given time period

Testing

- Among 5038 patients with NSCLC who had molecular testing performed, the majority were adenocarcinoma. Molecular testing was performed in 85.0% of adenocarcinomas, 60.4% of NSCLC-not otherwise specified (NOS) and 17.4% of squamous cell carcinomas.
- The presence of alterations in genes of interest varied significantly with lung cancer histology (see figure).
- MET exon 14 skipping was relatively rare:
 - 2.1% of patients with adenocarcinoma
 - 0.9% in squamous cell carcinoma
 - 1.8% in NSCLC not otherwise specified

- Actionable alterations were detected at a higher frequency by NGS versus non-NGS-approaches (adenocarcinoma: 62.4% versus 56.5%, respectively ($P = 0.004$)) due to a lower failure rate, more comprehensive testing and higher sensitivity.
- There was variability in testing practices and strategies among pathology centers.

Treatment

- Treatment with targeted therapy in eligible patients varied depending on the target:
 - EGFR: 85.8%
 - ALK: 74.7%
 - ROS1: 33.7%
 - BRAF: 51.5%
- MET inhibitors were not approved at the time and available only through clinical trials and compassionate use programs – nevertheless 22.8% of MET altered patients received a targeted treatment

Conclusion

- Gaps still exist in NSCLC testing and targeted therapy in the Netherlands, although the rates of access to MET therapy are surprisingly high given the lack of approved drugs for this target in the studied time period. Next-generation sequencing was also superior to non-NGS-approaches.

[ARTICLE LINK](#)



Durable Response of Dabrafenib, Trametinib, and Capmatinib in an NSCLC Patient With Co-Existing BRAF-KIAA1549 Fusion and MET Amplification: A Case Report

Drug(s): dabrafenib, trametinib, capmatinib

Objective

- To describe a patient with NSCLC and an unusual BRAF fusion plus MET amplification, including response to treatment.

Design

- Case report

Population

- 67-year-old male diagnosed with metastatic poorly differentiated lung adenocarcinoma in December 2018
- EGFR-, ALK-, and ROS-1-specific testing performed and negative, PD-L1 3%, NGS not performed due to insufficient tissue

Results

- Cisplatin + pemetrexed + pembrolizumab initiated. Disease progressed after 12 months.
- Repeat biopsy performed on the right and yielded KIAA1549-BRAF fusion and MET amplification (copy number gain 10).
- Second-line chemotherapy of docetaxel and ramucirumab administered. Disease progressed after 8 months.
- Third-line capmatinib administered to target MET amplification, but had progression after 3 months of the left pleural effusion.
- Repeat biopsy of the left pleura demonstrated persistent KIAA1549-BRAF fusion but no MET amplification.

- Dabrafenib + trametinib administered. After 3 months, the left pleural effusion resolved, but the right pleural effusion significantly increased.
- Since the patient's performance status was too poor for chemotherapy and discordance in response on two different sides, initiated dabrafenib + trametinib + capmatinib after multidisciplinary discussion.
- The right effusion responded to the triple combination and the patient continued to experience a response at time of publication, 6 months after treatment was initiated.
- The patient also experienced more side effects with combination therapy than either regimen by itself – symptoms included nausea, fatigue, rash, and fever. The patient required a dose reduction of capmatinib to 100mg twice daily due to grade 3 peripheral edema and grade 2 fatigue.

Conclusion

- This report is an interesting example of two different clonal populations responding differently to treatment – with the left clone harboring only the BRAF fusion but the right clone expressing both a BRAF fusion and MET amplification, which responded only to triple therapy of BRAF/MEK/MET inhibitors. This also gives us some idea of the additive toxicities of BRAF/MEK inhibitors plus MET inhibitors – fatigue, peripheral edema, and rash were experienced more significantly with triple therapy compared to either regimen alone.

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Successful and Prompt Treatment With Tepotinib for Lung Adenocarcinoma Harboring MET Exon 14 Skipping Mutation Combined with Lung Abscess Formation: A Case Report

Drug(s): tepotinib

Objective:

- To describe a case of successful treatment of tepotinib after prompt diagnosis of MET exon 14 skipping mutation (METex14) NSCLC

Design:

- Case report

Population:

- 65-year-old man diagnosed with lung adenocarcinoma METex14 NSCLC after presentation to hospital

Results:

- At initial evaluation, chest CT showed a lung tumor in right middle lobe which was identified as adenocarcinoma after transbronchial biopsy of lung 9 days after initial visit.
- 4 days later, he developed a spiking fever at home accompanied by right chest pain and yellow sputum production.

- He returned to the hospital where rapid lung cancer growth and multiple bone metastases were detected on CT imaging.
- Further genomic workup using AmoyDx® Pan Lung Cancer PCR Panel revealed a MET exon 14 skipping mutation and Tepotinib was initiated.
- His fever improved and chest CT showed tumor shrinkage. Only adverse effect experienced was mild leg edema, but no severe effects. Treatment was continued for 2 months.

Conclusion:

- This rare case of NSCLC was able to demonstrate the effectiveness of prompt genomic workup after the diagnosis of lung adenocarcinoma was made. While the patient initially experienced worsening of symptoms due to tumor growth, Tepotinib was shown to be a viable treatment option for this patient that improved his overall performance status and promoted tumor shrinkage.

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Clinical and Pathological Characteristics of 11 NSCLC Patients With MET Exon 14 Skipping

Objective

- To summarize the findings of 11 patients with mesenchymal-epithelial transition factor exon 12 skipping (METex14) NSCLC

Design

- Retrospective analysis of patients identified from the Affiliated Hospital of Guangdong Medical University in China from 2018-2021
- Tissue samples analyzed using next-generation sequencing (NGS)

Population

- 11 patients with METex14 NSCLC analyzed
- Sex: Male (81%), Female (19%)
- Average age: 77 years
- Smoking history: Yes (45%), No (55%)
- Histology: Adenocarcinoma (64%), Sarcomatoid (27%), Adenosquamous (9%)

- Overall survival (OS): 22.4 months
- Treatment types included crizotinib, crizotinib + chemotherapy, capmatinib, savolitinib,

Results

- Progression-free survival (PFS) of individuals treated with crizotinib ranged from 3-24 months
- Selective therapy showed better prognosis than multitargeted tyrosine kinase inhibitors (TKIs) such as crizotinib or standard therapy

Conclusion

- Even with the small cohort of patients in this study, their findings support the careful consideration of treatment specific to the patient's tumor profile and to take into consideration acquired resistance mechanisms.

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Case Report: A Lung Adenocarcinoma With Brain Metastasis Harbored Novel MET 14 Skipping Alteration Sensitive to Savolitinib

Drug(s): savolitinib

Objective

- To present a case on a patient with MET amplified and MET exon 14 skipping NSCLC who benefited from savolitinib

Design

- Case report

Population

- 61-year-old woman with concomitant MET amplified and MET exon 14 skipping NSCLC
- Patient declined chemotherapy and only wanted targeted treatment
- Next generation sequencing (NGS) identified MET amplification and MET exon 14 skipping mutation
- Based on NGS results, patient was started on savolitinib 600 mg daily

Efficacy Results

- Achieved partial response (PR) after 2 months on savolitinib
 - Shortness of breath and cough improved
 - CT demonstrated significant reduction in volume of lung and brain lesions
- At 5-month follow-up, patient was tolerating savolitinib with no progression

Safety Results

- No treatment-related adverse effects (TRAEs) except mild edema in lower extremities

Conclusion

- This is the first known report of a patient with MET-altered NSCLC with brain metastases who demonstrated a significant response to savolitinib

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Tepotinib Improves Prognosis in an Elderly Patient With Poor Performance Status and MET Exon 14 Skipping Mutation-Positive Non-Small Cell Lung Cancer

Drug(s): tepotinib

Objective

- To describe a case of patient with poorly differentiated MET exon 14 skipping (METex14) who had favorable performance status (PS) improvement with tepotinib

Design

- Case report

Population

- 84-year-old man with 62 pack year history of smoking, type 2 diabetes, and high cholesterol diagnosed with METex14 NSCLC
- Initial stage: IVB (cT3N2M1c)

Results

- Patient referred to hospital because of generalized pain and abnormal chest shadows. Chest CT showed multiple nodules in left lung and fracture of left 5th rib. Body CT also showed enlarged lymph nodes and mass in the pelvis.
- Bronchoscopy performed where biopsy was taken. Diagnosis of NSCLC was made, tumor negative for EGFR, ALK and ROS oncogene mutations.

- First-line chemotherapy of carboplatin and nab-paclitaxel was initiated. Despite this, patient experienced tumor growth and overall PS worsened from 1 to 3.
- Further genomic assessment made with ArcherMET, METex14 skipping NSCLC confirmed. Tepotinib initiated with patient consent.
- PS improved to 0-1 after 1 week, and partial response (PR) was maintained for more than 12 months. No serious adverse effects reported aside from mild lower leg edema.

Conclusion

- Tepotinib was able to demonstrate an improvement in this patient's performance status along with sustaining a partial response greater than 12 months at time of case report publishing. Tepotinib may provide patients with METex14 NSCLC benefit when cytotoxic agents are unable to elicit improvement.

[ARTICLE LINK](#)



Real-World Experience With Capmatinib in MET Exon 14-Mutated Non-Small Cell Lung Cancer (RECAP): A Retrospective Analysis From an Early Access Program

Drug(s): capmatinib

Objective

- To determine the safety and efficacy of capmatinib in a real-world setting in patients with METex14 NSCLC

Design

- Retrospective, non-interventional, multicenter, international, real-world analysis

Population:

- Patients with advanced METex14 NSCLC treated with capmatinib through an early access program between March 2019 and December 2021 (N = 81)
- 37 treatment-naive and 44 pre-treated patients
 - Pre-treated received a median number of one prior treatment to capmatinib (range 1-5)
 - ECOG \geq 2 represented 43% in treatment-naive group vs 21% in pre-treated group
- 86% had stage IV NSCLC
- 27% had brain metastases

Efficacy Results:

- ORR
 - All patients = 58%
 - Treatment-naive patients = 68%
 - Pre-treated patients = 50%
- Median PFS
 - All patients = 9.5 months
 - Treatment-naive patients = 10.6 months
 - Pre-treated patients = 9.1 months

- Median OS
 - All patients = 18.2 months
 - Treatment-naive patients = not reached
 - Pre-treated patients = 17.2 months
- Intracranial ORR = 46%
- Intracranial PFS = 9.1 months

Safety Results:

- 75% of patients experienced TRAEs
 - Most were grade \leq 2
 - Peripheral edema (48%), fatigue / weakness (20%), nausea (17%), elevated creatinine (12%)
- Grade \geq 3 treatment-related adverse events (TRAEs)
 - Peripheral edema (13%), elevated creatinine (4%), elevated liver enzymes (3%)

Conclusion:

- Capmatinib demonstrated durable responses in patients with advanced METex14 NSCLC (including those with brain metastases) and had a tolerable safety profile
- These results confirm that what was reported in previous phase II studies also occurred in the real-world setting

[ARTICLE LINK](#)



Phase Ia/Ib Study of the Selective MET Inhibitor, Savolitinib, in Patients With Advanced Solid Tumors: Safety, Efficacy, and Biomarkers

Drug(s): savolitinib

NCT: 0198555

Objective

- To confirm the recommended phase II dose of savolitinib and assess overall safety, tolerability, and benefit in MET-altered solid tumors

Design

- Open-label, multi-center, two-part phase I study (dose escalation + dose expansion)
- Dose escalation phase was a 3+3 design in which patients received one of the following doses:
 - 600 mg daily, 800 mg daily, 400 mg twice daily, 500 mg twice daily, or 600 mg twice daily (all on a 21-day cycle)
- Dose expansion phase:
 - 600 mg daily (N = 18)
 - 500 mg twice daily (N = 46)

Population

- Chinese patients with advanced / metastatic MET-altered gastric cancer or NSCLC (N = 64) with at least 2 prior lines of therapy

Efficacy Results

- MET exon 14 skipping NSCLC
 - Target lesion shrinkage (55% and 27%) observed in 2 of 4 patients
 - PR not achieved
- ORR = 9.4%
- Disease control rate = 39.1%
- All PRs occurred in patients with MET-amplified gastric cancer

Safety Results

- Most frequent treatment-related adverse effects (TRAEs):
 - Nausea (29.4%), vomiting (27.1%), peripheral edema (21.2%)
- 83.5% of patients reported TRAEs during savolitinib treatment
 - Most were grade 1 or 2
- Patients in twice daily cohort experienced more nausea / vomiting

Conclusion

- Recommended phase II dose = 600 mg daily or 500 mg twice daily
- Good tolerability and signs of antitumor activity of savolitinib were seen in patients with MET exon 14 skipping NSCLC; however, demonstration of efficacy in this population is limited by small sample size
- Safety results were similar to those demonstrated in previous Australian study
- Further studies are warranted to assess the activity of savolitinib in MET-altered solid tumors

[ARTICLE LINK](#)



Matching-Adjusted Indirect Comparison (MAIC) of Tepotinib with Other MET Inhibitors for the Treatment of Advanced NSCLC with MET Exon 14 Skipping Mutations

Drug(s): tepotinib, capmatinib, savolitinib, crizotinib

Objective

- To compare outcomes data between tepotinib, capmatinib, savolitinib, and crizotinib in patients with advanced NSCLC with a MET exon 14 skipping mutation

Design

- Matching-adjusted indirect comparison (MAIC)
 - Can minimize patient population / characteristic bias by weighting data between trials to more closely resemble one another and allow for cross trial comparison of outcomes
- Data from the VISION study (tepotinib) were weighted for comparison with data from the following studies using MAIC:
 - GEOMETRY mono-1 (capmatinib)
 - NCT02897479 (savolitinib)
 - PROFILE 1001 (crizotinib)

Population

- Patients with METex14 advanced NSCLC who received tepotinib, capmatinib, savolitinib, or crizotinib in one of the above studies

Efficacy Results

- Previously treated patients only
 - Odds ratios (ORs) for overall response rate (ORR) comparison between tepotinib and capmatinib suggested overall neither MET inhibitor was superior to the other
 - Median progression-free survival (PFS) comparison indicated considerable increase with tepotinib as opposed to capmatinib (11.0 vs 5.5 months)
 - Median duration of response (DOR) was similar between tepotinib and capmatinib
 - Using MAIC of Kaplan-Meier curves, the data favors tepotinib with separation from the capmatinib curve up to around 24 months (PFS) and 21 months (overall survival, OS)

- Line-agnostic patients
 - OR for ORR between tepotinib and capmatinib was close to 1, indicating no difference between the two agents
 - ORR for tepotinib was higher than savolitinib and crizotinib, with ORs favoring tepotinib
 - Predicted trends via MAIC suggest prolonged survival with tepotinib compared with capmatinib
 - Estimated median PFS and DOR were slightly higher for tepotinib than savolitinib
 - Kaplan-Meier curve comparison between tepotinib and crizotinib suggests longer PFS with tepotinib
 - Predicted median OS was slightly longer with tepotinib compared with crizotinib (22.3 vs 20.5 months)
 - Predicted median DOR was considerably longer with tepotinib compared with crizotinib (15.4 vs 9.1 months)
- Treatment-naive patients
 - ORR with capmatinib was higher than tepotinib (66.7-67.9% vs 54.7-60.7%)
 - MAIC ORRs for tepotinib considerably increased compared to unweighted ORRs
 - OR for ORR comparisons were not significant
 - Kaplan-Meier curves for PFS and OS for tepotinib and capmatinib suggested no difference between the agents
 - Considerable difference in median DOR between tepotinib (32.7 months) and capmatinib (12.6 months)

Safety Results

- Not reported / compared

Continued on next page



Continued:

Conclusion:

- The MAIC determined possible differences in efficacy between tepotinib, capmatinib, savolitinib, and crizotinib in patients with advanced METex14 NSCLC, with a trend toward favorable PFS with tepotinib compared with capmatinib and crizotinib
- Results must be interpreted cautiously as the MAIC method cannot account for all confounding variables
- Further studies are needed in order to determine patient-specific characteristics that can be used to select a MET inhibitor

[ARTICLE LINK](#)

Foretinib Can Overcome Common On-Target Resistance Mutations After Capmatinib/Tepotinib Treatment in NSCLCs with MET Exon 14 Skipping Mutation

Drug(s): foretinib, capmatinib, tepotinib

Objective

- To analyze agents that are active against secondary MET mutations (D1228X or Y1230X) that lead to acquired resistance in patients treated with tepotinib or capmatinib and subsequently suggest a subsequent treatment option after tepotinib / capmatinib treatment failure in patients with METex14 NSCLC

Design

- Inhibitory effects of 33 MET inhibitors were screened for activity in cells carrying D1228X or Y1230X mutations and identified the following MET inhibitors for further evaluation:
 - Altiratinib, CEP-40783, foretinib, sitravatinib, cabozantinib, and merestinib

Murine and human cell lines carrying METex14 were

- • transfected to create in vitro models of METex14 cells plus a secondary mutation (D1228X or Y1230X)
 - MET inhibitors were then added to wells containing these cell lines to assess in vitro activity
- An in vivo study was also performed using mice to confirm in vitro findings with a D1228N secondary mutation (selected due to clinical relevance)

Efficacy Results:

- In vitro analysis
 - All 6 MET inhibitors demonstrated potent activity against Y1230X
 - Foretinib was the only agent with potent activity against D1228X
 - CEP-40783 and altiratinib had some activity against D1228X
- In vivo analysis
 - Foretinib showed a major partial response (PR) with up to 90% tumor shrinkage
 - Cabozantinib showed up to 20% difference in tumor shrinkage compared to control

Safety Results:

Not evaluated

Conclusion:

- Foretinib may be an acceptable subsequent treatment option for patients with METex14 NSCLC who fail capmatinib or tepotinib due to Y1230X or D1228X mutations
- Cabozantinib and merestinib may not be able to overcome resistance due to D1228X mutations
- This warrants further investigation of foretinib in the subsequent line setting after failure of capmatinib or tepotinib due to secondary mutations conferring resistance

[ARTICLE LINK](#)



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

- [c-Met specific CAR-T cells as a targeted therapy for non-small cell lung cancer cell A549](#)
Bioengineered, April 4th 2022
- [Licochalcone A promotes the ubiquitination of c-MET to abrogate gefitinib resistance](#)
BioMed Research International, March 10th 2022
- [Cancer cells haploinsufficient for ATM are sensitized to PARP inhibitors by MET inhibition](#)
International Journal of Molecular Sciences, May 21st 2022
- [METΔ14 promotes a ligand-dependent, AKT-driven invasive growth](#)
Life Science Alliance, May 30th 2022

Additional Readings

- [MET-targeted therapies and clinical outcomes: a systematic literature review](#)
Molecular Diagnosis & Therapy, March 10th 2022
- [Safety of MET tyrosine kinase inhibitors in patients with MET exon 14 skipping non-small cell lung cancer: a clinical review](#) Clinical Lung Cancer, May 1st 2022
- [MET exon 14 skipping mutations: essential considerations for current management of non-small cell lung cancer](#) The Journal of Molecular Diagnostics, May 9th 2022
- [Spotlight on tepotinib and capmatinib for non-small cell lung cancer with MET exon 14 skipping mutation](#) Lung Cancer (Auckl), May 13th 2022
- [NSCLC as the paradigm of precision medicine at its finest: the rise of new druggable molecular targets for advanced disease](#) International Journal of Molecular Sciences, June 17th 2022
- [Non-small-cell lung cancer: how to manage MET exon 14 skipping mutant disease](#)
Drugs In Context, June 29th 2022



MET Clinical Trials

IMPORTANT

Below is a list of clinical trials involving MET alterations on [ClinicalTrials.gov](https://clinicaltrials.gov). This list is a summary snapshot of emerging therapeutic strategies, details of these trials can be found at [ClinicalTrials.gov](https://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 August 11, 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/P2
Countries: US, France, Spain, 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, Netherland, 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 also known as Volitinib
Phase: P1/P2
Countries: US, Australia, Canada, Italy, Finland, Hungary, Russia, 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, APL-101 and Volitinib
Phase: P2
Countries: China

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: 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: 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: 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: 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: Unknown
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: Unknown
Drug: Crizotinib
Phase: P2
Countries: Italy

NIH Identifier: NCT04739358

Link: <https://clinicaltrials.gov/ct2/show/NCT04739358>

Title: CNS Dose Escalation/Expansion of Tepotinib in MET-driven NSCLC
Status: Recruiting
Drug: Tepotinib
Phase: P1/2
Countries: US

NIH Identifier: NCT04992858

Link: <https://clinicaltrials.gov/ct2/show/NCT04992858>

Title: Nintetinib in Advanced NSCLC Skipping Mutations With MET Exon 14 Skipping Mutations
Status: Not Yet Recruiting
Drug: Nintetinib
Phase: P2
Countries: TBD

NIH Identifier: NCT04677595

Link: <https://clinicaltrials.gov/ct2/show/NCT04677595>

Title: Study of Capmatinib in Chinese Adult Patients With Advanced Non-small Cell Lung Cancer Harboring MET Exon 14 Skipping Mutation (GeoMETry-C)
Status: Recruiting
Drug: Capmatinib
Phase: P2
Countries: China

NIH Identifier: NCT04926831

Link: <https://clinicaltrials.gov/ct2/show/NCT04926831>

Title: Phase II of Neoadjuvant and Adjuvant Capmatinib in NSCLC (Geometry-N)
Lung Cancer Harboring MET Exon 14 Skipping Mutation (GeoMETry-C)
Status: Recruiting
Drug: Capmatinib
Phase: P2
Countries: US

NIH Identifier: NCT02929290

Link: <https://clinicaltrials.gov/ct2/show/NCT02929290>

Title: Safety, Efficacy and Pharmacokinetic of BPI-9016M in Patients With c-Met- Dysregulated Advanced NSCLC
Status: Recruiting
Drug: BPI-9016M
Phase: P1
Countries: China

NIH Identifier: NCT04398940

Link: <https://clinicaltrials.gov/ct2/show/NCT04398940>

Title: A Study of TQ-B3139 Capsules in Subjects With MET-Altered Advanced Non-small Cell Lung Cancer
Status: Recruiting
Drug: TQ-B3139
Phase: P2
Countries: China

NIH Identifier: NCT04647838

Link: <https://clinicaltrials.gov/ct2/show/NCT04647838>

Title: Tepotinib in Solid Tumors Harboring MET Alterations
Status: Recruiting
Drug: Tepotinib
Phase: P2
Countries: Republic of Korea

NIH Identifier: NCT05110196

Link: <https://clinicaltrials.gov/ct2/show/NCT05110196>

Title: Study of Capmatinib in Indian Patients With MET Exon 14 Skipping Mutation Positive Advanced NSCLC.
Status: Not Yet Recruiting
Drug: Capmatinib
Phase: P4
Countries: India

NIH ID: NCT04030429

Link: <https://clinicaltrials.gov/ct2/show/NCT04030429>

Title: Crizotinib in c-MET Mutation Metastatic/Recurrent/Persistent Endometrial Cancer
Status: P2
Drug: Crizotinib
Phase: P2
Countries: Taiwan

NIH ID: NCT05120960

Link: <https://clinicaltrials.gov/ct2/show/NCT05120960>

Title: A Phase 1a/1b Study to Determine the Recommended Phase 2 Dose, of Tepotinib in Participants With MET Alterations and Brain Tumors
Status: Not yet Recruiting
Drug: Tepotinib
Phase: P1
Countries: US

NIH ID: 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: Carbozantnib
Phase: P2
Countries: US



TKI TRIALS (CONTINUED)

NIH ID: NCT04052971

Link: <https://clinicaltrials.gov/ct2/show/NCT04052971>

Title: To Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, and Antitumor Activity of ABN401 in Patients With Advanced Solid Tumors and Non-Small Cell Lung Cancer Harboring c-MET Dysregulation
Status: Recruiting
Drug: ABN401
Phase: P1/P2
Countries: Australia, Republic of Korea

NIH ID: NCT004322578

Link: <https://clinicaltrials.gov/ct2/show/NCT004322578>

Title: Crizotinib or Standard Chemotherapy in Met Exon 14 Skipping Advanced NSCLC
Status: Recruiting
Drug: Crizotinib
Phase: None Listed
Countries: China

NIH ID: NCT03040973

Link: <https://clinicaltrials.gov/ct2/show/NCT03040973>

Title: Study to Allow Patients Previously Participating in a Novartis Sponsored Trial to Continue Receiving Capmatinib Treatment as Single Agent or in Combination With Other Treatments or the Combination Treatment Alone
Status: Recruiting
Drug: Capmatinib
Phase: P2
Countries: US, Canada, Denmark, France, Germany, Italy, Republic of Korea, Singapore, Spain

NIH ID: NCT004923932

Link: <https://clinicaltrials.gov/ct2/show/NCT004923932>

Title: Savolitinib for Treating Gastric Cancer and Esophagogastric Junction Adenocarcinoma Patients
Status: Recruiting
Drug: Savolitinib
Phase: P2
Countries: China

NIH ID: NCT004923945

Link: <https://clinicaltrials.gov/ct2/show/NCT004923945>

Title: Savolitinib for Treating Locally Advanced or Metastatic Non-small Cell Lung Cancer (NSCLC) Patients
Status: Recruiting
Drug: Savolitinib
Phase: P3
Countries: China

NIH ID: NCT05088070

Link: <https://clinicaltrials.gov/ct2/show/NCT05088070>

Title: Clinical Study of SPH3348 Tablets, a c-Met Inhibitor, in Patients With Advanced Solid Tumors
Status: Recruiting
Drug: SPH3348
Phase: P1
Countries: China

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: 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: 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, Quam, Puerto Rico

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: Teliso Vedotin (ABBV-399)
 Phase: P2
 Countries: US, Australia, Belgium, Bulgaria, Canada, China, Czechia, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Japan, Republic of Korea, Poland, Puerto Rico, Romania, Russia, Spain, Switzerland, Taiwan, Turkey, United Kingdom

NIH Identifier: NCT05029882

Link: <https://clinicaltrials.gov/ct2/show/NCT05029882>

Title: Study to Assess Adverse Events and Change in Disease Activity in Adult Participants With Advanced Solid Tumors Receiving Intravenous (IV) ABBV-400
 Status: Recruiting
 Drug: ABBV-400
 Phase: P1
 Countries: US, Japan, Puerto Rico, France, Israel, Republic of Korea, Spain

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: P1/2
 Counties: US, Republic of Korea, France

NIH Identifier: NCT04982224

Link: <https://clinicaltrials.gov/ct2/show/NCT04982224>

Title: Study of REGN5093-M114 (METxMET Antibody-Drug Conjugate) in Adult Patients With Mesenchymal Epithelial Transition Factor (MET) Overexpressing Advanced Cancer
 Status: Recruiting
 Drug: REGN5093-M114
 Phase: P1/2
 Counties: US

NIH ID: NCT04169178

Link: <https://clinicaltrials.gov/ct2/show/NCT04169178>

Title: Evaluate Safety, Tolerability and PK of HLX55 in Patients With Advanced Solid Tumors With Different cMET Status
 Status: Recruiting
 Drug: HLX55
 Phase: P1
 Countries: Taiwan

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: **Active, Not Recruiting**
 Drug: DS-1062a also known as Datopotamab
 Phase: P2
 Countries: US, France, Germany, Hungary, Italy, Japan, Republic of Korea, Netherlands, Spain, Taiwan

NIH ID: NCT05323045

Link: <https://clinicaltrials.gov/ct2/show/NCT05323045>

Title: A First-in-human Dose-escalation and Expansion Study With the Antibody-drug Conjugate BYON3521
 Status: Recruiting
 Drug: BYON3521
 Phase: P1
 Countries: Belgium, Italy, Netherlands, United Kingdom

NIH ID: NCT05117931

Link: <https://clinicaltrials.gov/ct2/show/NCT05117931>

Title: A Study of Amivantamab in People With Esophagogastric Cancer
 Status: Recruiting
 Drug: Amivantimab
 Phase: P2
 Countries: US

NIH ID: NCT04928846

Link: <https://clinicaltrials.gov/ct2/show/NCT04928846>

Title: A Study to Assess Disease Activity and Adverse Events of Intravenous (IV) Telisotuzumab Vedotin Compared to IV Docetaxel in Adult Participants With Previously Treated Non-Squamous Non-Small Cell Lung Cancer (NSCLC)
 Status: Recruiting
 Drug: Telisotuzumab Vedotin
 Phase: P3
 Countries: US, Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, Chile, China, Czechia, Denmark, France, Germany, Greece, Israel, Italy, Japan, Republic of Korea, Mexico, Netherlands, Poland, Portugal, Romania, Slovakia, South Africa, Spain, Sweden, Taiwan, Turkey, United Kingdom



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) (ORCHARD)

Status: Recruiting

Drug: Osimertinib + Salvitinib

Phase: P2

Countries: US, Denmark, Japan, Republic of Korea, Netherlands, Norway, Spain, Sweden

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 (CHRYSALIS)

Status: Recruiting

Drug: Amivantamab

Phase: P1

Countries: US, Australia, Canada, China, France, Italy, Japan, Republic of Korea, Spain, Taiwan, United Kingdom

NIH Identifier: NCT03778229

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

Title: Osimertinib Plus Savolitinib in EGFR+/MET+ NSCLC Following Prior Osimertinib (SAVANNAH)

Status: Recruiting

Drug: Osimertinib + Salvitinib

Phase: P2

Countries: US, Brazil, Canada, Chile, Denmark, France, India, Israel, Italy, Japan, Puerto Rico, Republic of Korea, Spain, Taiwan, Vietnam

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 EGFR+ 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

NIH ID: NCT04868877

Link: <https://clinicaltrials.gov/ct2/show/NCT04868877>

Title: A Phase 1/2 Study Evaluating MCLA-129, a Human Anti-EGFR and Anti-c-MET Bispecific Antibody, in Patients With Advanced NSCLC and Other Solid Tumors

Status: Recruiting

Drug: MCLA-129

Phase: P1/2

Countries: US

NIH ID: NCT05163249

Link: <https://clinicaltrials.gov/ct2/show/NCT05163249>

Title: Osimertinib With or Without Savolitinib as 1L in de Novo MET+, EGFR+ NSCLC (FLOWERS)

Status: **Not Yet Recruiting**

Drug: Osimertinib, Savolitinib

Phase: P2

Countries: China

NIH ID: NCT0430432

Link: <https://clinicaltrials.gov/ct2/show/NCT0430432>

Title: Study of MCLA-129, a Human Bispecific EGFR and cMet Antibody, in Patients With Advanced NSCLC and Other Solid Tumors

Status: Recruiting

Drug: MCLA-129

Phase: P1/2

Countries: China

NIH ID: NCT05015608

Link: <https://clinicaltrials.gov/ct2/show/NCT05015608>

Title: Study on Savolitinib Combined With Osimertinib in Treatment of Advanced NSCLC With MET Amplification (SACHI)

Status: Recruiting

Drug: Savolitinib and Osimertinib

Phase: P3

Countries: China

NIH ID: NCT05009836

Link: <https://clinicaltrials.gov/ct2/show/NCT05009836>

Title: Clinical Study on Savolitinib + Osimertinib in Treatment of EGFR+/MET+ Locally Advanced or Metastatic NSCLC (SANOVO)

Status: Recruiting

Drug: Savolitinib + Osimertinib

Phase: P3

Countries: China



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: 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: NCT05261399

Link: <https://clinicaltrials.gov/ct2/show/NCT05261399>

Title: Savolitinib Plus Osimertinib Versus Platinum-based Doublet Chemotherapy in Participants With Non-Small Cell Lung Cancer Who Have Progressed on Osimertinib Treatment (SAFFRON)
Status: **Not Yet Recruiting**
Drug: Savolitinib + Osimertinib
Phase: P3
Countries: US, Argentina, Australia, Austria, Belgium, Brazil, Canada, China, France, Italy, Japan, Poland, Spain, Turkey, United Kingdom

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 \geq 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

NIH ID: NCT04323436

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

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

NIH ID: NCT005435846

Link: <https://clinicaltrials.gov/ct2/show/NCT005435846>

Title: Capmatinib Plus Trametinib for the Treatment of Metastatic Non-small Cell Lung Cancer With MET Exon 14 Skipping Mutation
Status: Not Yet Recruiting
Drug: Capmatinib + Trametinib
Phase: P1
Countries: US

NIH ID: NCT05039736

Link: <https://clinicaltrials.gov/ct2/show/NCT05039736>

Title: A Phase II Study to Evaluate the Effects of Sequential Therapy With the Anti c-MET/VEGFR Tyrosine Kinase Inhibitor (TKI), Cabozantinib, Followed by an Anti-PD-1 Antibody (Nivolumab) in Patients With Advanced HCC Who Progressed on First-line Therapy
Status: Not Yet Recruiting
Drug: Cabozantinib + Nivolumab
Phase: Phase 2
Countries: US

NIH ID: NCT04427072

Link: <https://clinicaltrials.gov/ct2/show/NCT04427072>

Title: Study of Capmatinib Efficacy in Comparison With Docetaxel in Previously Treated Participants With Non-small Cell Lung Cancer Harboring MET Exon 14 Skipping Mutation (GeoMETry-III)
Status: Recruiting
Drug: Capmatinib + Docetaxel
Phase: P3
Countries: Australia, Belgium, Brazil, Bulgaria, France, Germany, Hungary, India, Italy, Republic of Korea, Malaysia, Lithuania, Netherlands, Portugal, Russia, South Africa, Spain, Thailand, Vietnam

NIH ID: NCT05439993

Link: <https://clinicaltrials.gov/ct2/show/NCT05439993>

Title: Tepotinib Plus Paclitaxel in MET Amplified or MET Exon 14 Altered Gastric and GEJ Carcinoma
Status: P1/P2
Drug: Tepotinib + Paclitaxel
Phase: P12/P2
Countries: Republic of Korea
NIH ID: NCT04533321
Link: <https://clinicaltrials.gov/ct2/show/NCT04533321>
Title: A Biomarker-implemented Clinical Study Evaluating Mutations in MET and TP53 in a Population of Treatment-refractory Squamous Cell Carcinoma
Status: Not Yet Recruiting
Drug: Afatinib
Phase: P2
Countries: Singapore

NIH ID: NCT05015608

Link: <https://clinicaltrials.gov/ct2/show/NCT05015608>

Title: Study on Savolitinib Combined With Osimertinib in Treatment of Advanced NSCLC With MET Amplification (SACHI)
Status: Recruiting
Drug: Savolitinib + Osimertinib
Phase: P3
Countries: China

NIH ID: NCT005043090

Link: <https://clinicaltrials.gov/ct2/show/NCT005043090>

Title: Savolitinib Plus Durvalumab Versus Sunitinib and Durvalumab Monotherapy in MET-Driven, Unresectable and Locally Advanced or Metastatic PRCC (SAMETA)
Status: Recruiting
Drug: Savolitinib + Durvalumab
Phase: P3
Countries: US, Argentina, Australia, Brazil, Canada, Chile, Cheznia, France, Germany, Hong Kong, India, Israel, Italy, Republic of Korea, Netherlands, Poland, Romania, Russia, Singapore, Spain, Taiwan, Turkey, Ukraine, United Kingdom

NIH ID: NCT05243641

Link: <https://clinicaltrials.gov/ct2/show/NCT05243641>

Title: Neratinib and Capmatinib Combination (Phase Ib/II) in Metastatic Breast Cancer and Inflammatory Breast Cancer Patients With Abnormal HER2 and c-Met Pathway Activity as Measured by the CELSignia Signaling Analysis Test
Status: **Not Yet Recruiting**
Drug: Capmatinib + Neratinib
Phase: P1/P2
Countries: US

NIH ID: NCT05038839

Link: <https://clinicaltrials.gov/ct2/show/NCT05038839>

Title: Cabozantinib and Pamiparib for the Treatment of Advanced of Refractory Solid Tumors
Status: Recruiting
Drug: Cabozantinib + Pamiparib
Phase: P1
Countries: US

NIH ID: NCT05374603

Link: <https://clinicaltrials.gov/ct2/show/NCT05374603>

Title: Savolitinib Combine With Durvalumab in EGFR Wild-type Locally Advanced or Metastatic NSCLC (SOUND)
Status: **Not Yet Recruiting**
Drug: Savolitinib + Durvalumab
Phase: P2
Countries: US



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.



Come Join Us!

www.metcrusaders.org

