



Your resource for the latest research into the MET alteration.

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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Lung Cancer and Self-Management Interventions: A Systematic Review of Randomized Controlled Trials

Objective

- To gather the available evidence on the effectiveness of self-management (SM) interventions in people experiencing symptoms associated with lung cancer.

Design

- Systematic review of multiple studies

Methods

- Primary question: “how effective are SM interventions at improving outcomes among patients with lung cancer”
 - Included only randomized controlled trials
 - Excluded studies that did not have a control arm utilizing standard or usual care
 - Included only studies that looked at patients with lung cancer separately or exclusively, but included all stages and histologies of lung cancer
 - Included only studies that measured the effectiveness of the SM intervention
- Self-management was defined as “a person’s ability to manage their disease symptoms including treatment, physical, social, and lifestyle changes... includes problem solving, decision making, resource utilization, patient/provider relationship development, and taking action”
- Robust and replicable systematic search of several databases was performed. Two reviewers came to a consensus on inclusion in the systematic review.

Results

- Of 587 studies that appeared in the initial search, 10 RCTs met the criteria for inclusion, representing a total of 1089 patients
- Most studies (n = 6) studied exercise as an intervention, with or without supplementary diary use and/or counseling. This was successful in 5 of these studies, improving symptoms such as fatigue, anxiety, depression, sleep quality, and exercise capacity.

- The other interventions included SM education (n = 2), a telephone-based symptoms reporting tool (n = 1), and a quality-of-life diary (n = 1). Among these, only one of the SM education studies met the primary endpoint.
- The majority of studies (6/10) met their primary endpoint demonstrating a positive effect of the SM intervention.

Strengths

- Strong and transparent search criteria and techniques were used to identify studies for the systematic review

Weaknesses

- This review included studies with a wide variety of patient populations, interventions, and primary endpoint measures. This makes it difficult to generalize the results to a specific population, intervention, or symptom.
- Most of these studies were small and performed at a single center, which further complicates application to a broader patient population.
- Some of the studies that did not identify an impact may not have had an adequate number of patients to identify a significant difference.

Conclusion

- Acknowledging the limitations of the available literature, exercise seems to be the SM intervention with the best results in patients with lung cancer. Investigators and professionals caring for patients with lung cancer may find this publication helpful when prioritizing SM interventions to study and/or implement in their facilities.

[ARTICLE LINK](#)



A Case Report of Successful Treatment With Crizotinib to Overcome Resistance to Osimertinib in an EGFR Mutated Non-Small-Cell Lung Cancer Patient Harboring an Acquired MET Exon 14 Mutation

Drug(s): crizotinib, osimertinib

Objective

- To describe a case of acquired MET exon 14 mutation as a resistance mechanism to osimertinib treatment and subsequent successful treatment with crizotinib.

Design

- Case report

Population

- 56yo nonsmoking Caucasian male diagnosed with metastatic lung adenocarcinoma on initial presentation
- Initial testing revealed EGFR exon 21 L858R mutation

Results

- Initial palliative radiation to the brain and painful bone metastases, then gefitinib initiated.
- Gefitinib quickly switched to erlotinib due to grade 3 liver toxicity. Patient experienced an objective response to erlotinib for 12 months
- Upon progression, PCR testing was done on plasma cell-free DNA (cfDNA), which revealed a new EGFR T790M mutation
- Osimertinib was initiated. Five months into treatment, the patient had solitary progression in hip bone with response in other tissues, so radiation was given to hip bone. Patient received a total of 8 months of osimertinib before new liver metastases were identified.

- Carboplatin and pemetrexed were initiated and the patient had stable disease for 7 months until new pleural effusion.
- Next generation sequencing on pleural cfDNA revealed a new METex14 skipping mutation, confirmed in plasma cfDNA. The original EGFR L858R mutation was present, but the T790M mutation was not identified.
- Patient received one cycle of salvage bevacizumab/paclitaxel, but had rapid progression
- Due to METex14 mutation, crizotinib monotherapy was initiated with rapid symptomatic relief and confirmed response on imaging. Crizotinib monotherapy was chosen due to the lack of safety data with combination EGFR and MET TKI therapy along with the patient's rapidly declining performance status.
- Unfortunately, the patient died from worsening respiratory failure 4 months after crizotinib initiation.

Conclusion

- This is a rare instance of a treatment-emergent METex14 mutation (rather than MET amplification) as a resistance mechanism to EGFR TKIs. It is also interesting that the patient responded to MET TKI monotherapy, rather than combination therapy with an EGFR inhibitor. Prospective trials would be needed to determine if combination therapy offers more side effects and/or a longer response compared to monotherapy in these treatment-emergent mutations.

[ARTICLE LINK](#)



Biomarker Testing Patterns and Treatment Outcomes in Patients With Advanced Non-Small Cell Lung Cancer (NSCLC) and MET Exon 14 Skipping Mutations: A Descriptive Analysis From the US

Objective

- To describe real-world testing patterns in advanced NSCLC and assess the clinical outcomes of first- and second-line therapies for patients with MET exon 14 mutations in a pre-MET TKI time period.

Design

- Retrospective study conducted using data from the Flatiron Health medical record and Foundation Medicine database
 - Flatiron Health provides medical record services to over 280 cancer clinics (largely in community practice), representing 800 sites of care and more than 2.4 million patients with cancer
 - Foundation Medicine offers comprehensive genomic profiling (CGP) to patients across the US, with >400,000 sequenced tumor samples available for this study
 - Data were matched between the two databases in a HIPAA-compliant fashion and de-identified
- Collected progression-free survival data for patients who received either chemotherapy or immune checkpoint inhibitors first-line

Population

- Included 91 patients with MET exon 14 advanced NSCLC diagnosed January 1, 2021 – October 2, 2019
 - Stage IIIB – IVB or recurrent/progressive early stage NSCLC
 - Treated with at least 1 line of therapy (1L)
 - MET exon 14 confirmed from solid tumor biopsy
 - Excluded patients enrolled in clinical trials or receiving chemotherapy + immune-oncology drug (IO) for first-line treatment
- Median age 75, range 48 – 85, and 89% were non-squamous
- 5 patients (5%) had concurrent KRAS mutations

Results

- Testing
 - 62% had PD-L1 testing; PD-L1 was $\geq 50\%$ in 46% and 1-49% in 20%
 - 34% of patients received their testing reports before initiating 1L treatment, which increased over time
 - PD-L1 results came back faster than NGS results, median of 20 days vs 27 days between specimen collection and reporting results
- First line real-world progression free survival (PFS) and overall survival (OS) - n = 77
 - Chemotherapy (n = 59): PFS median 5.7 months; OS median 20 months
 - IO (n = 18): PFS median 2.4 months; OS median not reached
 - Not calculated for other treatments due to low numbers (MET inhibitor n = 11, erlotinib n = 3)
- Second line real-world progression free survival (n = 39)
 - Chemotherapy (n = 16): median PFS 3.5 months; median OS 15.3 months
 - IO (n = 23): median PFS 4.7 months; median OS 19.3 months
 - Not calculated for other treatments due to low numbers (MET inhibitor n = 7, clinical trial n = 6, afatinib n = 2, ceritinib n = 1, crizotinib + pembrolizumab n = 1)

Strengths

- Interesting data set gives insight into real-world practice and outcomes for patients with advanced METex14 NSCLC in a pre-MET TKI era

Continued on p8



Continued:

Weaknesses

- There were no FDA-approved MET inhibitors available during the time period of the study. Also, the KEYNOTE-189 trial results that brought pembrolizumab plus chemotherapy into first-line were not available until the last year or two of the study, so there were few patients who received triple therapy up front and the authors excluded them. The standard of care here (either chemotherapy or IO) does not represent the current standard of care. This makes the results of this trial hard to interpret in our current climate.
- The authors do not compare characteristics of the patients who received chemotherapy versus immunotherapy. There are significant factors that would make oncologists choose one therapy or the other, so it is difficult to interpret the differences in outcomes between the two groups.

- The MET TKIs used for patients in the study are not listed, but would likely be the early nonselective TKIs such as crizotinib and cabozantinib, which are less selective for MET inhibition compared to currently available therapies.

Conclusion

- CGP testing results became available prior to starting 1L treatment for more patients as time went on throughout the study
- The response to immunotherapy in METex14 NSCLC was underwhelming, although a small portion of patients did have durable responses.

[ARTICLE LINK](#)

Case Report: A 91-Year-Old Patient With Non-Small Cell Lung Cancer Harboring MET Y1003S Point Mutation

Drug(s): crizotinib

Objective

- To present a case report on an elderly patient with non-small cell lung cancer and a MET Y1003S mutation

Design

- Case report

Population

- One 91-year-old patient
- Lung adenocarcinoma with a MET Y1003S mutation who was treated with crizotinib 250 mg by mouth twice daily
- No other mutations found (EGFR, ALK, ROS1, BRAF, NRAS, KRAS, ERBB2, PIK3CA, MET exon 14 skipping)

- No history of smoking or drinking
- Both parents died of lung cancer

Efficacy

- After 1 month of treatment, a repeat chest CT showed a partial response
- Patient was on treatment for 8 months

Safety

- None reported

Conclusion

- Crizotinib may have meaningful clinical activity in lung cancers carrying a MET Y1003S mutation

[ARTICLE LINK](#)



Acquired MET-DSTN Fusion Mediated Resistance to EGFR-TKIs in Lung Adenocarcinoma and Responded to Crizotinib Plus Gefitinib: A Case Report

Drug(s): crizotinib, gefitinib

Objective

- To describe a novel MET-DSTN fusion after the occurrence of osimertinib resistance that responds well to crizotinib plus gefitinib

Design

- Case report

Population

- 52-year-old Chinese female, never smoked
- Originally diagnosed with stage IV lung adenocarcinoma in August 2018
- Extensive bone and lymph node metastases observed

Efficacy & Safety

- Tumor biopsy showed EGFR-L858R mutation identified through next generation sequencing (NGS)
- Subsequently placed on gefitinib and achieved stable disease
- Four months later, disease progression was seen and patient was treated with 6 cycles of pemetrexed plus cisplatin, followed by 2 cycles of paclitaxel plus bevacizumab and achieved partial response

- Further disease progression observed, and patient was placed on osimertinib treatment for EGFR-T790M mutation, identified by NGS, and achieved partial response
- Ten months later, PET/CT disease progression confirmed and repeat NGS showed EGFR-L858R mutation and MET-DSTN fusion
- Patient placed on crizotinib 250 mg twice daily and gefitinib 250 mg once daily. Chest CT 1 week later showed shrinkage of lesions in both lungs. Complete response was achieved 1 month later and has been maintained for more than 6 months with no severe adverse effects reported.

Conclusion

- This patient case report suggests the observed MET-DSTN fusion may be a novel mechanism to EGFR-TKI resistance. In this patient, treatment with combined MET inhibitor and EGFR-TKIs was shown to be effective.

[ARTICLE LINK](#)



Treatment Response to Immunotherapy After Crizotinib Resistance in a Patient With Pulmonary Sarcomatoid Carcinoma Harboring MET Exon 14 Skipping Mutation: A Case Report

Drug(s): crizotinib, anlotinib, chemoimmunotherapy

Objective

- To present a case of a pulmonary sarcomatoid carcinoma carrying a MET exon 14 skipping mutation treated with crizotinib and then chemo-immunotherapy

Design

- Case report

Population

- One 58-year-old male patient
- No smoking, drinking, or family history of cancer
- Masses found in the lung, pericardium, brain, and colon
- CA125, tumor-specific growth factor, and PSA were all elevated
- PD-L1 tumor proportion score (TPS) >90%, MET exon 14 skipping mutation, and somatic mutations in ATR and TP53 found prior to initial treatment with crizotinib

Efficacy

- After about 1 month of treatment, the patient was found with a partial response
- After about 1 week, the lung tumor grew and new tumors were seen
- A medication called anlotinib (not available in the U.S.) was started, but discontinued due to skin rash
- Repeat sequencing found a new MET point mutation, MET amplification, NRAS mutation, CD274 amplification, and losses in CDKN2A/B
- Combination chemotherapy and immunotherapy was started, and the patient had a partial response for 15 months

Safety

- Rash reported from anlotinib

Conclusion

- Crizotinib treatment was short and resulted in early resistance in this MET-mutated case of pulmonary sarcomatoid carcinoma
- Prolonged response (progression free survival of 15 months) was seen with chemo-immunotherapy, given PD-L1 TPS >90%

[ARTICLE LINK](#)



Successful Tepotinib Challenge After Capmatinib-Induced Interstitial Lung Disease in a Patient With Lung Adenocarcinoma Harboring MET Exon 14 Skipping Mutation: Case Report

Drug(s): tepotinib, capmatinib

Objective

- To report the first successful case of treatment with tepotinib after capmatinib-induced interstitial lung disease (ILD)

Design

- Case report

Population

- 75-year-old Japanese female with stage IVA lung adenocarcinoma
 - Negative for EGFR, ALK, and ROS1
 - PD-L1 tumor proportion score (TPS) = 90%

Efficacy & Safety

- Patient received several lines of treatment over 4 years
 - Pembrolizumab, carboplatin + pemetrexed + bevacizumab, carboplatin + nab-paclitaxel
 - Relapsed with single brain metastasis so received radiation
 - Relapsed with lymph node metastases
 - Next generation sequencing identified MET exon 14 skipping mutation

- Two months after discontinuation of fourth line treatment, patient had progression in brain metastases
- Patient was started on capmatinib 400mg twice daily
 - Patient was diagnosed with grade 2 capmatinib-induced ILD six days after starting capmatinib
 - Capmatinib was discontinued and her symptoms improved
- Two months after discontinuation of capmatinib, CT chest showed progression
 - Started low dose tepotinib at 250mg once daily
 - Reduction in enlarged lymph nodes seen 7 weeks after starting tepotinib
 - No side effects reported including ILD
- Six months later, the patient was still demonstrating a response to tepotinib

Conclusion

- This is the first report of a successful transition of capmatinib to tepotinib after capmatinib-induced ILD in terms of safety and efficacy
- Rechallenging with a MET inhibitor can be considered if carefully observed

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Has the Enemy “MET” Its Match? Subgroup Analysis Results from VISION Study

Drug(s): tepotinib

Objective

- To present results of subgroup analyses from the VISION study and identify patients who are most likely to benefit from MET-targeted treatment

Design

- Subgroup analysis from the open-label, phase 2 VISION study

Population

- Patients with MET exon 14 skipping NSCLC

Efficacy & Safety

- Encouraging results in patients ≥ 75 and ≥ 80 years old
 - Patients ≥ 75 required more frequent dose reduction than younger patients (23.3% vs 33.9%) with few discontinuing treatment (7.5% vs 14.7%)
 - Edema led to discontinuation in 10.6% of patients ≥ 75 years old who experienced this side effect, which is a higher rate than the general population
- Pre-treated and treatment-naive patients had similar objective response rates (ORR) of 44.9% and 44.6% and progression-free survival (PFS) of 10.9 months and 8.5 months

- Patients who received prior chemotherapy versus immunotherapy had similar PFS of 11 months and 10.9 months
- 71% of patients with measurable intracranial disease achieved a partial response (PR)
 - Of the patients with evaluable intracranial disease, 92% achieved intracranial disease control and 54% responded with 31% complete responses (CR)
- Most common side effect was peripheral edema (54.1% any grade)

Conclusion

- Tepotinib is safe and effective in the older patient population with encouraging initial results for patients with intracranial disease
- The safety and efficacy of MET inhibitors like tepotinib may be more favorable for older patients compared to chemoimmunotherapy
- These results reinforce the importance of genetic testing to guide treatment decisions in patients with NSCLC

[ARTICLE LINK](#)



Integrating Comprehensive Genomic Sequencing of Non-Small Cell Lung Cancer into a Public Healthcare System

NCT: 03558165

Objective

- To evaluate the impact of comprehensive genomic profiling (GCP) in Canada's publicly funded health system

Design

- Prospective, single center study with participants from Princess Margaret Cancer Center Thoracic Clinic
- Outcomes measured
 - New actionable genomic alterations identified, clinical trial eligibility as a result of undergoing CGP, and patient willingness to pay

Population

- 134 patients included for CGP analysis
- Average age at diagnosis: 61.5 years
- Sex: Male (40.3%), Female (59.7%)
- Race: Caucasian (64.1%), Asian/pacific islander (32.3%), Black (4.5%)
- Histology: Adenocarcinoma (91.7%), squamous (2.3%), other (6.1%)
- Past targeted therapy: EGFR therapy (16.4%), ALK therapy (3.7%)

Efficacy

- New actionable genomic alterations identified in 48% of cohort that were previously unknown
- New actionable genomic alterations identified in 5/27 (18.5%) of cohort with known EGFR and ALK aberrations
- 75% of patients met inclusion criteria for at least one clinical trial as a result of undergoing CGP
 - ERBB2, KRAS and METex14 skipping mutation and amplification were most common genomic identifiers for inclusion
- Willingness to pay
 - 99% indicated they would choose to undergo testing if publicly funded
 - The median willingness to pay for CGP was \$200

Conclusion

- CGP testing was able to identify additional actionable targets that could play a role in patients overall treatment options but may be limited by cost barriers in non-public funded healthcare systems

[ARTICLE LINK](#)

A Phase 1b Study of Telisotuzumab Vedotin in Combination With Nivolumab in Patients With NSCLC

Drug(s): telisotuzumab vedotin, nivolumab | NCT: 02099058

Objective

- To evaluate the safety, tolerability, and efficacy of telisotuzumab vedotin combined with nivolumab in patients with advanced MET-altered NSCLC

Design

- Phase 1b multicenter, open-label study

Population

- Patients with advanced MET-altered NSCLC
 - Initially enrolled patients with any level of MET expression (N=37)
 - Modified criteria to only patients with MET+ NSCLC (membrane H-score 150, N=27)
 - Patients with MET- NSCLC were included in the safety population only

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Continued:

- Patients who were previously treated with treatment targeting PD-1 or PD-L1 were excluded
- Patients received telisotuzumab vedotin (1.6, 1.9, or 2.2 mg/kg IV) + nivolumab (3 mg/kg or 240mg IV) every 2 weeks
 - Patients with complete response (CR), partial response (PR), or stable disease (SD) could continue treatment for up to 24 months if tolerating
 - Patients who discontinued nivolumab due to side effects related to nivolumab continued telisotuzumab vedotin
- Additional characteristics (total N=27)
 - Three groups - PD-L1+ (n=15), PD-L1- (n=9), and PD-L1 unknown (n=3)
 - Majority non-squamous histology (n=24)
 - MET H-score 150-224 (n=15) or ≥ 225 (n=12)
 - Received at least 2 prior lines of therapy (n=16)

Efficacy

- Telisotuzumab vedotin was discontinued by all patients in the efficacy population due to progressive disease
- Overall response rate (ORR) = 7.4%
 - Two patients with confirmed partial response (PR)
 - These patients had MET IHC H-scores of 190 and 290
 - 23 patients had stable or progressive disease
 - One patient had a 30% reduction in lesions from baseline
 - 67% of patients had tumor size reduction
- Median progression free survival (PFS) = 7.2 months
- None of the patients with MET amplification had a response to treatment
- No difference in response rates between PD-L1+ and PD-L1- populations, but duration of treatment and PFS trended longer for PD-L1+ patients

Safety

- Regardless of relationship to telisotuzumab vedotin
 - 97% of patients experienced at least one adverse event
 - 62% of patients experienced a grade 3 or higher adverse event
 - 41% of patients experienced a serious adverse event
 - Most common adverse events included fatigue (46%), decreased appetite (30%), cough (27%), and hypoalbuminemia (27%)
- Reasonable possibility of relationship to telisotuzumab vedotin
 - 78% of patients experienced at least one adverse event
 - 32% of patients experienced a grade 3 or higher adverse event
 - 16% of patients experienced a serious adverse event
 - Most common adverse events included fatigue (27%), peripheral sensory neuropathy (19%), decreased appetite (16%), and hypoalbuminemia (16%)
- Peripheral sensory neuropathy was the most common reason for dose reduction of telisotuzumab vedotin, and peripheral neuropathy was the most common reason for dose interruption or discontinuation
 - Of note, 14 patients had baseline neuropathy

Conclusion

- The combination of telisotuzumab vedotin and nivolumab was overall well tolerated with manageable adverse events including peripheral neuropathy
- Disappointing overall response rate for the combination, especially compared to response rates for monotherapy of each treatment

[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

- [Functional analysis of MET exon 14 skipping alteration in cancer invasion and metastatic dissemination](#)
American Association for Cancer Research, April 1st 2022
- [Anthrax toxin receptor 2 is a potential therapeutic target for non-small cell lung carcinoma with MET exon 14 skipping mutations](#)
Experimental Cell Research, February 19th 2022
- [The natural product berberine synergizes with osimertinib preferentially against MET-amplified osimertinib-resistant lung cancer via direct MET inhibition](#)
Pharmacological Research, January 2022

Additional Readings

- [Targeted therapies for lung cancer patients with oncogenic driver molecular alterations](#)
Journal of Clinical Oncology, January 5th 2022
- [Targeting un-MET needs in advanced non-small cell lung cancer](#)
Lung Cancer, December 27th 2021
- [MET-targeted therapies and clinical outcomes: a systematic literature review](#)
Molecular Diagnosis & Therapy, March 10th 2022
- [KRAS and MET in non-small cell lung cancer: two of the new kids on the 'drivers' block](#)
Therapeutic Advances in Respiratory Disease, January 31st 2022
- [The impact of driver mutation on the treatment outcome of early-stage lung cancer patients receiving neoadjuvant immunotherapy and chemotherapy](#)
Nature, February 28th 2022
- [Multimodality treatment of pulmonary sarcomatoid carcinoma: a review of current state of art](#)
Journal of Oncology, March 25th 2022



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 April 18, 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, 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: 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: Active Not 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: 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: Not Yet Recruiting
Drug: Tepotinib
Phase: P1/2
Countries: US

NIH Identifier: NCT04992858

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

Title: Ningetinib in Advanced NSCLC Skipping Mutations With MET Exon 14 Skipping Mutations
Status: Not Yet Recruiting
Drug: Ningetinib
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



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](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: NCT04116541

Link: [HTTPS://CLINICALTRIALS.GOV/CT2/SHOW/NCT04116541](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

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

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](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

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
Countries: US, Republic of Korea

NIH Identifier: NCT04982224

Link: [HTTPS://CLINICALTRIALS.GOV/CT2/SHOW/NCT04982224](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
Countries: US

NIH Identifier: NCT04484142

Link: [HTTPS://CLINICALTRIALS.GOV/CT2/SHOW/NCT04484142](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



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: 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 + Salvitinib

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 (CHRYSALIS)

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

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: Recruiting

Drug: Osimertinib, Savolitinib

Phase: P2

Countries: China

NIH ID: NCT0430432

Link: <https://clinicaltrials.gov/ct2/show/NCT04930432>

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-128

Phase: P1/2

Countries: China

NIH ID: NCT02335944

Link: <https://clinicaltrials.gov/ct2/show/NCT02335944>

Title: Study of Safety and Efficacy of EGFR-TKI EGF816 in Combination With cMET Inhibitor INC280 in Adult Patients With EGFR Mutated Non Small Cell Lung Cancer.

Status: Recruiting

Drug: EGF816 + Capmatinib

Phase: P1/2

Countries: US, Australia, Canada, France, Germany, Italy, Republic of Korea, Norway, Singapore, Spain, Taiwan



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: Glestatinib, Sitravastinib 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 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: 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



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

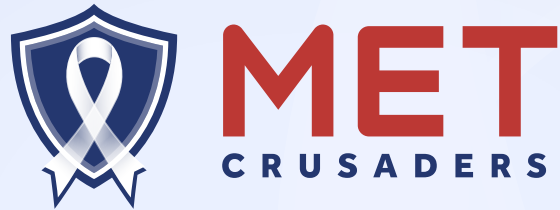
Institution: University of Colorado

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

