Your resource for the latest research into the MET alteration.

CRUSADER NEWSLETTER

Q3 2021 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.

Come Join Us!

www.metcrusaders.org

Contact us at

info@metcrusaders.org

EDITOR

Jessica McKernan, PharmD
Atrium Health, Charlotte, NC

CONTRIBUTING EDITORS

Julia Stevens, PharmD
Beth Israel Deaconess Medical Center, Boston, MA

Emmeline Academia, PharmD
Beth Israel Deaconess Medical Center, Boston, MA

Brandon Lengel
Pharmacy Student
University of Wisconsin

In this edition

Phase I Study of 2- or 3-Week Dosing of Telisotuzumab Vedotin, an Antibody–Drug Conjugate Targeting c-Met, Monotherapy in Patients with Advanced Non–Small Cell Lung Carcinoma

Drug: Telisotuzumab Vedotin | NCT: 02099058

Objective:

- To report the safety and efficacy of telisotuzumab vedotin monotherapy in patients with NSCLC

Design:

- Open-label, multicenter, phase I/Ib study
- Telisotuzumab vedotin IV once every 2 weeks (28 day cycle) or once every 3 weeks (21 day cycle) until disease progression or unacceptable tolerability
- Two parts: dose escalation and dose expansion
- Dose escalation to assess safety, maximum tolerated dose (MTD), and kinetics
- Dose expansion to assess safety, tolerability, and efficacy of recommended phase II dose (determined from dose escalation phase)

Population:

- Total 58 patients
- Telisotuzumab vedotin once every 2 weeks (n = 28)
- Telisotuzumab vedotin once every 3 weeks (n = 24)
- Characteristics
- 40 patients were MET+
- Histology: 33 non-squamous, 6 squamous, 1 mixed
- Average prior therapies: 3 (range 0 to 7+)
- 65% of patients previously received antimicrotubule agents (same mechanism of action as the “vedotin” part of Telisotuzumab vedotin)
- Dose escalation
- Advanced solid tumor of multiple types
- Dose expansion
- MET+ NSCLC (MET H-score ≥ 150 or MET amplification/MET exon 14 skipping mutation)

Efficacy Results:

- 9 out of 40 MET+ patients
- Median duration of response: 8.7 months
- Median progression-free survival (PFS): 5.2 months

Safety Results:

- Most common adverse effects included fatigue (54%), peripheral neuropathy (42%), nausea (38%)
- No dose limiting toxicities (DLTs) observed for telisotuzumab vedotin once every 2 weeks up to 2.2 mg/kg and once every 3 weeks up to 2.7 mg/kg

Strengths:

- Well designed open-label multicenter trial
- Included patients who previously received antimicrotubule agents which may help determine sequencing of therapy in the future

Weaknesses:

- Small sample size
- Still unknown correlation of MET expression with tumor response so predefined MET+ H-score may miss patients who could potentially respond to telisotuzumab vedotin

Conclusion:

- Telisotuzumab vedotin demonstrated safety and efficacy in MET+ NSCLC
- Telisotuzumab vedotin 1.9 mg/kg IV once every 2 weeks and 2.7 mg/kg IV once every 3 weeks were chosen for further development in future studies

LINK TO ARTICLE

Oncogene-specific differences in tumor mutational burden, PD-L1 expression, and outcomes from immunotherapy in non-small cell lung cancer

Objective:

- To characterize the impact of oncogene mutations on tumor mutational burden (TMB) and programmed death ligand-1 (PD-L1) in a cohort of NSCLC patients from various databases.

Design:

- Multicenter, open-label, non-controlled phase 2 study
- Results analyzed according to liquid biopsy or tissue biopsy used to confirm MET mutation
- In the FMI biomarker cohort (defined below), the following oncogene alterations were assessed: *BRAF* (both V600E and non-V600E), *HER2, KRAS*, classic *EGFR* (exon 19 deletions, exon 21 L858R mutation; ± T790M mutation), *MET* (exon 14 skipping mutations), *ALK, ROS1*, and *RET* gene fusion/rearrangements
- In both the FMI biomarker cohort and CDGB cohorts defined below, tumor mutational burden (TMB) was assessed, which was defined as the number of all mutations per megabase (Mb). High TMB was defined as ≥10 or 16 mutations/Mb
- In the MDACC cohort defined below, PD-L1 expression was measured by tumor proportion score (TPS) and defined as positive (≥1%) or negative (<1%), and high (≥50%) or low (1%–49%)
- Outcomes assessed included progression free survival (PFS) and overall survival (OS)

Population:

- 4017 NSCLC patients from the FMI FoundationCORE database with molecular data (FMI biomarker cohort),
- 172 patients in one clinical cohort of NSCLC from the MD Anderson Cancer Center (MDACC cohort)
- 894 patients in another clinical cohort of NSCLC patients from the Clinico-Genomic Database from Flatiron Foundation Medicine, either treated with immune-checkpoint blockade (ICB) therapy (CDGB immunotherapy cohort) or combination chemotherapy therapy with or without immunotherapy (CDGB chemotherapy cohort)

Effectiveness Results:

- In the CGDB immunotherapy cohort:
  - Higher TMB was associated with longer PFS and OS
  - Positive PD-L1 expression was associated with longer PFS but no statistically significant difference in OS
- In the CGDB immunotherapy cohort and MDACC cohorts:
  - *BRAF* and *KRAS* were enriched for smokers
  - *EGFR*-mutated patients received more prior treatment lines
  - The *BRAF* group had the longest PFS and OS
  - The *EGFR* group had shorter PFS
  - Patients with fusions (*ALK, ROS1, RET*) had shorter PFS compared to KRAS
  - The *MET* exon 14 mutation group had a short PFS (2.7 months) which was not statistically different from the *KRAS* group. OS for *MET*-mutated tumors was 12.3 months
- In the MDACC cohort:
  - When assessed for the impact of mutations on ICB outcomes:
    - The *BRAF* group had the longest PFS
    - The *EGFR* and *HER2* groups had the shortest PFS
    - The *BRAF* group had longer OS but this difference was not statistically significant
    - The *EGFR* group had the shortest OS
    - There were 3 patients with *MET* exon 14 skipping mutations, 2 of which had stable disease
- In the CGDB chemotherapy cohort:
  - The fusion group (*ALK, ROS1, RET*), had the longest OS with chemotherapy (27.2 months vs. 11.7 months in the *KRAS* group)
  - PFS and OS was not different between mutations

Continued on p7

Continued:

- The *KRAS*-mutant group was the largest group, and no difference was seen between different *KRAS*-mutant alleles (G12C, G12D, G12V)
- In the FMI biomarker cohort:
  - High PD-L1 positivity was seen in *MET, RET, BRAF V600E, ROS1*, and *ALK*
  - Low PD-L1 positivity was seen in *EGFR* exon 20, *HER2*, classic *EGFR*, and *BRAF* non-V600E
  - Compared to *KRAS*, *MET*-mutant tumors had higher PD-L1 positivity and *EGFR*-mutant tumors had lower PD-L1 positivity
  - *MET*-mutant tumors also had higher prevalence of high PD-L1 expression (high TPS)
  - TMB was highest in the BRAF non-V600E group compared to *KRAS, ALK*, classic *EGFR, HER2, RET*, and *ROS1*

Strengths:

- Larger sample size, including patients from different sites
- In depth analysis of markers for immunotherapy efficacy and oncogene alterations

Weaknesses:

- Non-controlled trial: this limits comparisons to other potential therapies, but can be hypothesis generating for future clinical trials.
- Retrospective
- Very small numbers of *MET*-mutated patients

Conclusion:

- *BRAF*-mutant NSCLC was found to have higher TMP and PD-L1 expression, potentially making this group more sensitive to ICB therapies.
- Classic *EGFR, EGFR* exon 20, and *HER2*-mutated tumors were associated with less benefit from ICB, highlighting the need for further development of effective immunotherapies for *EGFR*-mutant NSCLC.
- Tumors with *ALK, ROS1*, or *RET* fusions or *MET* exon 14 skipping mutations had high PD-L1 expression and low TMB, which did not translate to better clinical outcomes on ICB therapy. This suggests that there are other mechanisms besides TMB and PD-L1 expression that affect ICB therapy outcomes.

LINK TO ARTICLE

Response to gefitinib/crizotinib combination in a pulmonary sarcomatoid carcinoma patient harboring concurrent EGFR mutation and MET amplification

Drugs: gefitinib, crizotinib

Objective:

- To describe a case of successful gefitinib + crizotinib treatment in a rare and aggressive subtype of non-small cell lung cancer (NSCLC), pulmonary sarcomatoid carcinoma (PSC)

Design:

- Case report

Population:

- 74yo female diagnosed with metastatic PSC

History:

- June 2017: Presented with dyspnea, cough, and swollen face. PET scan and biopsy led to the diagnosis of PSC, metastatic to mediastinal lymph nodes. DNA-based next generation sequencing (NGS) revealed EGFR exon 21 L858R mutation and MET amplification.
- Due to advanced age and poor performance status, she was not a candidate for chemotherapy. Instead, gefitinib 250mg orally daily and crizotinib 250mg orally twice daily (full dose of both drugs) were both started to target the EGFR and MET alterations.
- First follow-up CT 2 months later demonstrated a response.
- The patient has continued to respond as of time of publication, a total of 9.7 months.

Critique:

- No tolerability or safety information is presented in this paper.

Conclusions:

- MET amplification is a known mechanism of resistance to EGFR inhibitors in NSCLC, although this is less well described in PSC. This case report suggests that giving an EGFR inhibitor with a MET inhibitor might be an effective approach in some patients with PSC harboring both EGFR and MET alterations.

LINK TO ARTICLE

PD-L1 Expression and Comprehensive Molecular Profiling Predict Survival in Non-Small Cell Lung Cancer: A Real-World Study of a Large Chinese Cohort

Objective:

- To investigate how the molecular phenotype and tumor features impact PD-L1 expression in Chinese patients with non-small cell lung cancer (NSCLC)

Design:

- Evaluation of tumor by immunohistochemistry testing to determine PD-L1 expression and next-generation sequencing to identify genomic mutations
- Statistical analysis to determine correlation between PD-L1 expression and genetic alteration along with survival

Population:

- 819 Chinese patients with NSCLC
- Histology: Adenocarcinoma (91.8%), squamous cell carcinoma (5.7%), large cell carcinoma (0.5%)
- Staging: Stage I-IIIa (98.1%), stage IIIb-IV (1.8%)

Results:

- PD-L1 expression (N = 800)
  - Negative (75.3%), low (17.5%), high (7.2%)
  - High expression significantly elevated in male patients with squamous cell carcinoma
- Next-generation sequencing analysis
  - At least 1 mutation (94.1%), up to 4 mutations (43.2%), no alterations (5.9%)
  - EGFR mutation (66.8%), TP53 mutation (40.3%), KRAS (8.9%), MET (3.0%)
- Connection between mutations and PD-L1 expression
  - High PD-L1 expression significantly associated with METex14 skipping mutations
- Survival analysis (N = 710)
  - Median recurrence free survival (RFS)
    - PD-L1 negative (43.9 months), PD-L1 low (35.2 months), PD-L1 high (25.5 months)
  - Median overall survival (OS)
    - PD-L1 negative (46.5 months), PD-L1 low (36.3 months), PD-L1 high (30.2 months)

Strengths:

- Comprehensive investigation looking at PD-L1 expression and genetic mutation in terms of outcomes

Weaknesses:

- Short follow up time of 1-48 months

Conclusion:

- PD-L1 expression is a useful diagnostic tool to help determine therapeutic options
- This study suggests that individuals with high PD-L1 expression along with negative PD-L1 expression with accompanying suppressor gene mutations correlate with inferior outcomes

LINK TO ARTICLE

Frequency of actionable molecular drivers in lung cancer patients with precocious brain metastases

Objective:

- To determine the prevalence of actionable mutations in lung cancer patients who experience neurological symptoms of brain metastases as their first symptom of lung cancer (precocious brain metastases)

Design:

- Retrospective analysis from a single hospital
- Patients underwent neurosurgery to address symptoms from brain metastases and the surgical specimens were analyzed

Population:

- 33 Caucasian patients with non-small cell lung cancer (NSCLC – 24) or small cell lung cancer (SCLC – 9)
- Brain metastases as first manifestation of disease, no prior diagnosis or treatment
- Median age 63 (range 48-85 years)
- Most patients with single brain metastasis (84%)

Results:

- Mutation prevalence:
  - MET amplification: 26.7%
  - FGFR1 amplification: 16.1%
  - KRAS: 15.6%
  - EGFR: 9.1%
  - No ROS1, RET, or EML4/ALK were present
- In SCLC patients, one MET amplification and one FGFR1 mutation
- One patient with both an EGFR mutation and MET amplification despite no prior treatment
- Overall survival:
  - Mean: 17.4 months
  - Median: 10 months
  - Range: 0-53 months
- No significant association was found between mutational status and any other characteristic

Conclusion:

- It is difficult to draw significant conclusions about the overall prevalence of targetable mutations in this population due to the small size of the cohort. However, it continues to demonstrate that even patients with brain metastases as their presenting symptom should be tested for targetable driver mutations.

LINK TO ARTICLE

Real-world insights into patients with advanced NSCLC and MET alterations

Objective:

- To report characteristics, treatments, and outcomes of patients with MET exon 14 mutated (METex14) or MET amplified NSCLC

Design:

- Non-interventional retrospective cohort study
- Extracted data from electronic medical records in multiple countries between January 2010 and September 2018

Population:

- 117 patients with MET altered advanced NSCLC
  - 70 patients with MET exon 14 skipping mutation
  - 47 patients with MET amplification

Results:

- Characteristics
  - Concomitant oncogenic driver mutations more common in MET amplified NSCLC than METex14 NSCLC
  - Patients with METex14 NSCLC were older and majority were never smokers
- First line therapy
  - Chemotherapy: 44% METex14, 41% MET amplified
  - MET inhibitor: 33% METex14, 29% MET amplified
  - Immunotherapy (monotherapy): 12% METex14, 15% MET amplified
  - Combination therapy: 8% METex14, 3% MET amplified
- Second line therapy
  - Chemotherapy: 35% METex14, 30% MET amplified
  - MET inhibitor: 30% METex14, 39% MET amplified
- Objective response rate (ORR)
  - METex14: first line 28%, second line 30%
    - No patient responded to immunotherapy
  - MET amplified: first line 36%, second line 22%
- Overall survival (OS)
  - METex14: 12 months
  - MET amplified: 22 months

Strengths:

- Contributes to body of evidence on tumor response across different lines of therapy in advanced NSCLC
- Describes routine clinical practice for patients with MET altered NSCLC

Weaknesses:

- Retrospective design
- Small sample size
- Very heterogeneous group of patients so higher risk for confounding variables contributing to results
- Potential risk of data extraction errors which increases risk for information bias

Conclusions:

- This study supports the use of MET targeted therapy vs non-MET targeted therapy for patients with MET altered NSCLC
- The treatment landscape for patients with MET altered NSCLC is very diverse and heterogeneous
- Larger prospective studies are needed to further define what is occurring in routine clinical practice across countries and therapies in patients with MET altered NSCLC

LINK TO ARTICLE

Characterization of Non-Small-Cell Lung Cancers With MET Exon 14 Skipping Alterations Detected in Tissue or Liquid: Clinicogenomics and Real-World Treatment Patterns

Objective:

- To characterize the coalterations and signatures of MET Exon 14 skipping mutated NSCLC to predict resistance and sensitivity to combination therapies

Design:

- Large-scale analysis of tumor tissue or circulating tumor DNA samples from 69,219 patients with primary advanced NSCLC
- Comprehensive genomic profiling (CGP) done on samples with MET exon 14 (METex14) skipping alterations to assess coalterations that may predict sensitivity or resistance

Population:

- Advanced NSCLC with METex14 skipping mutations: METex14 found in 1,592 (2.3%) of patients
- Median age 75 years

Genomics Results:

- Objective response rate 46% (all partial responses, no complete responses)
- Low tumor mutational burden (TMB; median 3.8 mutations per megabase) was found in METex14-altered NSCLC tumor samples compared to wild-type (7.0 mutations per megabase)
- More METex14-altered samples had high tumor proportion scores (TPS) compared to wild-type samples (84% versus 59%). High TPS (>/= 50%)) was found in METex14-altered samples.
- The most frequent coalterations seen in METex14-altered samples were TP53 alterations (42%), MDM2 amplification (34%), CDK4 amplification (19%), MET amplification (11%).
- Small percentages of KRAS, EGFR, ERBB2, RET, and ROS alterations were found, which may represent acquired resistance in some cases.
- No BRAF, ALK, or NTRK fusions were found.
- Real-world response rate to MET inhibitors was 45%.
- Time to discontinuation of treatment was 4.4 months.

Strengths:

- This study provides an in-depth analysis of METex14-altered NSCLC. It includes a breakdown of TMB, TPS, histologic subtype, coalterations, functional sites of coalterations. This analysis helps researchers understand the biology of METex14-altered lung cancers better.

Weaknesses:

- Non-controlled trial: Treatment patterns and outcomes reported in this trial are not from a controlled study. This makes it difficult to apply outcomes to other settings.

Conclusion:

- METex14 alterations were found in 2-3% of NSCLC cases.
- This study highlights the diversity of MET alterations and the need for genomic analyses to detect them.
- Information from this study may help researchers understand the biology of this alteration, in order to better tailor treatments of METex14-altered NSCLC patients.

LINK TO ARTICLE

Dramatic response to osimertinib combined with crizotinib in EGFR T790M mutation only in blood and MET amplification only in tumor tissue expressive non-small cell lung cancer

Drugs: osimertinib, crizotinib

Objective:

- Case report describing a patient's response to third line osimertinib combined with crizotinib in EGFR T790m mutated NSCLC

Design:

- Case report

Population:

- A 53-year-old Asian man with no history of smoking diagnosed with left lung adenocarcinoma in June 2017

History:

- June 2017: Presented with productive cough, scan and biopsy confirmed left lung adenocarcinoma (stage cT4N2M0). Biopsy sent for next-generation sequencing (NGS). Received six cycles of cisplatin and pemetrexed while awaiting genotyping results.
- September 2017: Reached a partial response. NGS results showed EGFR exon 21 L858R point mutation. Patient declined further chemotherapy due to fatigue and loss of appetite.
- November 2017: Started on gefitinib 250 mg daily.
- April 2018: Scan showed disease progression.
- May 2018: Afatinib started, but progression was seen a month later.
- June-August 2018: Two cycles of cisplatin and pemetrexed with addition of bevacizumab resulted in disease stability. Further progression seen at the end of August.
- September 2018: EGFR T790M mutation found only in blood specimen and MET amplification found only in tumor tissue. High expression of PD-L1 found.
- October 2018: Osimertinib 80 mg daily combined with crizotinib 250 mg twice daily started.
- December 2018: Scans showed dramatic tumor reduction, patient achieved partial response.

Conclusions:

- Resistance to first- and second-generation tyrosine kinase inhibitor (TKI) medications can often be seen in EGFR mutated NSCLC
- This case highlights the pronounced response seen with the combination of a MET and EGFR inhibitor in the setting of EGFR resistance with MET amplified NSCLC

LINK TO ARTICLE

Correlation between PD-L1 expression and MET gene amplification in patients with advanced non-small cell lung cancer and no other actionable oncogenic driver

Objective:

- To determine the relationship between MET amplification and PD-L1 expression in patients with advanced NSCLC

Design:

- Retrospective observational study
- Single institution
- July 2015 to February 2019

Population:

- 48 patients
- No other actionable driver mutations
- Histology: adenocarcinoma (76%), squamous (8%), unknown (16%)

Results:

- Patients with MET amplification showed higher proportion of PD-L1 expression (93% vs 39%, $p < 0.001$) than those with no MET amplification
- Patients with MET amplification showed higher proposed of PD-L1 overexpression (64% vs 27%, $p = 0.02$) than those with no MET amplification
- Of note, PD-L1 overexpression defined as > 50% PD-L1
- Overall survival (OS) rates did not significantly differ based on MET amplification or PD-L1 expression
- Median OS: 16.3 months

Strengths:

- First study to find a positive correlation between MET amplification and PD-L1 expression in patients with NSCLC
- Homogeneous population with no other actionable driver mutations which allowed for minimization of confounding variables to focus on correlation between MET amplification and PD-L1 expression

Weaknesses:

- Small sample size
- Retrospective design
- Single institution so may be prone to some level of bias
- Used arbitrary MET cutoffs to define amplification since there is still no consensus

Conclusion:

- There is a positive correlation between MET amplification and PD-L1 expression in patients with advanced NSCLC, which may help guide treatment decisions for this specific patient population in the future
- Need larger prospective studies to confirm correlation and subsequently inform providers on how to approach treatment of this patient population

LINK TO ARTICLE

Acquired Tertiary MET Resistance (MET D1228N and a Novel LSM8-MET Fusion) to Selpercatinib and Capmatinib in a Patient With KIF5B-RET-positive NSCLC With Secondary MET Amplification as Initial Resistance to Selpercatinib

Drugs: selpercatinib, capmatinib

Objective:

- To report a case of a patient with KIF5B-RET-positive NSCLC who developed a MET amplification after treatment with selpercatinib

Design:

- Case report

Population:

- Metastatic NSCLC with KIF5B-RET mutated NSCLC with secondary MET amplification
- Prior treatments: Selpercatinib, Cabozantinib + Carboplatin + Pemetrexed + Bevacizumab
- Started on combination Selpercatinib + Capmatinib at full doses after MET amplification was identified

Effectiveness and Safety Results:

- The patient was treated with Selpercatinib + Capmatinib for 4.5 months.
- Upon start increasing abdominal pain, repeat plasma genotyping found a MET D1228N mutation with KIF5B-RET fusion, so patient was switched back to Cabozantinib while continuing Selperecatinib.
- A small bowel perforation developed at the site of a large metastasis, and the patient elected hospice care about 1 month later.
- The abdominal metastasis was sequenced and found with the following mutations: MET D1228N, MET amplification, KIF5B-RET, and a novel LSM8-MET fusion.

Strengths:

- This report outlines the case of a patient with a MET D1228N mutation as an on-target resistance mutation after combination RET and MET therapy.

Weaknesses:

- Case report: this limits comparisons to other patients or therapies.

Conclusion:

- This case report highlights the importance of repeat sequencing and junctures of progression. It also demonstrates that the MET D1228N mutation can occur as a mechanism of on-target resistance, in addition to the previously reported tertiary resistance mechanism.

LINK TO ARTICLE

ADDITIONAL READING

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

Preclinical Readings

- Multiple Blockades of the HGF/MET Signaling Pathway for Metastasis Suppression Using Nanoinhibitors, American Chemical Society, July 7th 2021
- KRAS Inhibitor Resistance in MET-Amplified KRAS-G12C NSCLC Induced by RAS- and Non-RAS-Mediated Cell Signaling Mechanisms, American Association for Cancer Research, August 7th 2021

Additional Readings

- Therapeutic Strategies in METex14 Skipping Mutated NSCLC, Journal of Hematology and Oncology, August 23rd 2021
- Current Landscape of Non-Small Cell Lung Cancer: Epidemiology, Histological Classification, Targeted Therapies, and Immunotherapy, Cancers (Basel), September 20th 2021
- Savolitinib: First Approval, Drugs, August 29th 2021
- FDA Approval Summary: Capmatinib and Tepotinib for the Treatment of Metastatic NSCLC Harboring MET Exon 14 Skipping Mutations or Alterations, American Association for Cancer Research, August 3rd 2021
- Tumor-Infiltrating Lymphocyte Treatment for Anti-PD1-Resistant Metastatic Lung Cancer: A Phase 1 Trial, Nature Medicine, August 12th 2021
- An Alert to Possible False Positives with a Commercial Assay for MET Exon 14 Skipping, Journal of Thoracic Oncology, July 16th 2021

MET Clinical Trials

IMPORTANT

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

This list was last updated on November 10, 2021.

TKI TRIALS

NIH Identifier: NCT04084717
Link: https://clinicaltrials.gov/ct2/show/NCT04084717
Title: Study of Crizotinib for ROS1 and MET Activated Lung Cancer
Status: Recruiting
Drug: Crizotinib
Phase: P2
Countries: Canada

NIH Identifier: NCT03693339
Link: https://clinicaltrials.gov/ct2/show/NCT03693339
Title: Capmatinib in Patients With Non-small Cell Lung Cancer Harboring cMET exon14 Skipping Mutation
Status: Recruiting
Drug: Capmatinib
Phase: P2
Countries: Republic of Korea

NIH Identifier: NCT03993873
Link: https://clinicaltrials.gov/ct2/show/NCT03993873
Title: Phase 1 Study of TPX-0022, a MET/CSF1R/SRC Inhibitor, in Patients With Advanced Solid Tumors Harboring Genetic Alterations in MET
Status: Recruiting
Drug: TPX-0022
Phase: P1
Countries: US, Republic of Korea

NIH Identifier: NCT02864992
Link: https://clinicaltrials.gov/ct2/show/NCT02864992
Title: Tepotinib Phase II in Non-small Cell Lung Cancer (NSCLC) Harboring MET Alterations (VISION)
Status: Active, Not Recruiting
Drug: Tepotinib
Phase: P2
Countries: US, Austria, Belgium, France, Germany, Israel, Italy, Japan, Republic of Korea, 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
Phase: P1/P2
Countries: US, Australia, Canada, Italy, Puerto Rico, Singapore, Spain, Taiwan, Ukraine, United Kingdom

NIH Identifier: NCT04258033
Link: https://clinicaltrials.gov/ct2/show/NCT04258033
Title: A Study of PLB1001 in Non-small Cell Lung Cancer With c-Met Dysregulation
Status: Recruiting
Drug: PLB1001 also known as Bozitinib and APL-101
Phase: P2
Countries: China

NIH Identifier: NCT02750215
Link: https://clinicaltrials.gov/ct2/show/NCT02750215
Title: A Study of Capmatinib (INC280) in NSCLC Patients With MET Exon 14 Alterations Who Have Received Prior MET Inhibitor
Status: Completed
Drug: Capmatinib
Phase: P2
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: 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: 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: NCT04258033
Link: https://clinicaltrials.gov/ct2/show/NCT04258033
Title: A Study of PLB1001 in Non-small Cell Lung Cancer With c-Met Dysregulation
Status: Recruiting
Drug: PLB1001 also known as Bozitinib and APL-101
Phase: P2
Countries: China

TKI TRIALS (CONTINUED)

NIH Identifier: NCT02219711
Link: https://clinicaltrials.gov/ct2/show/NCT02219711
Title: Phase 1/1b Study of MGCD516 in Patients with Advanced Cancer
Status: Active, Not Recruiting
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

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

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: 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

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

ANTIBODY-ADC TRIALS

NIH Identifier: NCT03539536
Link: https://clinicaltrials.gov/ct2/show/NCT03539536
Title: Study of Telisotuzumab Vedotin (ABBV-399) in Subjects with Previously Treated c-Met+ Non-Small Cell Lung Cancer
Status: Recruiting
Drug: ABBV-399
Phase: P2
Countries: US, Australia, Belgium, Canada, China, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Japan, Republic of Korea, Romania, Russia, Spain, Taiwan, Turkey, United Kingdom

NIH Identifier: NCT04077099
Link: https://clinicaltrials.gov/ct2/show/NCT04077099
Title: REGN5093 in Patients With MET-Altered Advanced Non-Small Cell Lung Cancer
Status: Recruiting
Drug: REGN5093
Phase: P1, P2
Counties: US, Republic of Korea

NIH Identifier: NCT04484142
Link: HTTPS://CLINICALTRIALS.GOV/CT2/SHOW/NCT04484142
Title: Study of DS-1062a in Advanced or Metastatic Non-small Cell Lung Cancer With Actionable Genomic Alterations (TROPION-Lung05)
Status: Recruiting
Drug: DS-1062a also known as Datopotamab
Phase: P2
Countries: US, France, Germany, Hungary, Italy, Japan, Republic of Korea, Netherlands, Spain, Taiwan

EGFR + MET TRIALS

NIH Identifier: NCT03944772
Link: https://clinicaltrials.gov/ct2/show/NCT03944772
Title: Phase 2 Platform Study in Patients With Advanced Non-Small Lung Cancer Who Progressed on First-Line Osimertinib Therapy (ORCHARD)
Status: Recruiting
Drug: Osmeritinib + Salvotinib
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: Osmeritinib + Salvotinib
Phase: P2
Countries: US, Brazil, Canada, Chile, Denmark, France, India, Israel, Italy, Japan, 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 + Osmeritinib
Phase: P2
Countries: US, Belgium, China, France, Germany, Hong Kong, 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: Amivantimab
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: P2
Countries: US, China

NIH ID: NCT04606771
Link: https://clinicaltrials.gov/ct2/show/NCT04606771
Title: A Study Comparing Savolitinib Plus Osimertinib vs Savolitinib Plus Placebo in Patients with EGFRm+ and MET Amplified Advanced NSCLC (CoC)
Status: Recruiting
Drug: Osimertinib + Savolitinib
Phase: P2
Countries: US, Argentina, Brazil, Chile, India, Republic of Korea, Taiwan, Thailand, Vietnam

IMMUNOTHERAPY TRIALS

NIH Identifier: NCT02323126
Link: https://clinicaltrials.gov/ct2/show/NCT02323126
Title: Study of Efficacy and Safety of Nivolumab in Combination with EGF816 and of Nivolumab in Combination With INC280 in Patients With Previously Treated Non-small Cell Lung Cancer (EGF816)
Status: Completed
Drug: Nivolumab + EGF816 + Capmatinib
Phase: P2
Countries: US, Australia, France, Germany, Italy, Netherlands, Singapore, Spain, Switzerland

NIH Identifier: NCT01911507
Link: https://clinicaltrials.gov/ct2/show/NCT01911507
Title: INC280 and Erlotinib Hydrochloride in Treating Patients With Non-small Cell Lung Cancer
Status: Completed
Drug: Capmatinib + Erlotinib
Phase: P1
Countries: US

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: 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≥ 50%
Status: Active, Not Recruiting
Drug: Capmatinib + Pembrolizumab
Phase: P2
Countries: US, Australia, Belgium, Czechia, France, Germany, Hong Kong, India, Italy, Japan, Malaysia, Spain, Taiwan, Thailand

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 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

MET CRUSADERS

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