



Your resource for the latest research into the MET alteration.

CRUSADER

NEWSLETTER

Q4 2020 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.

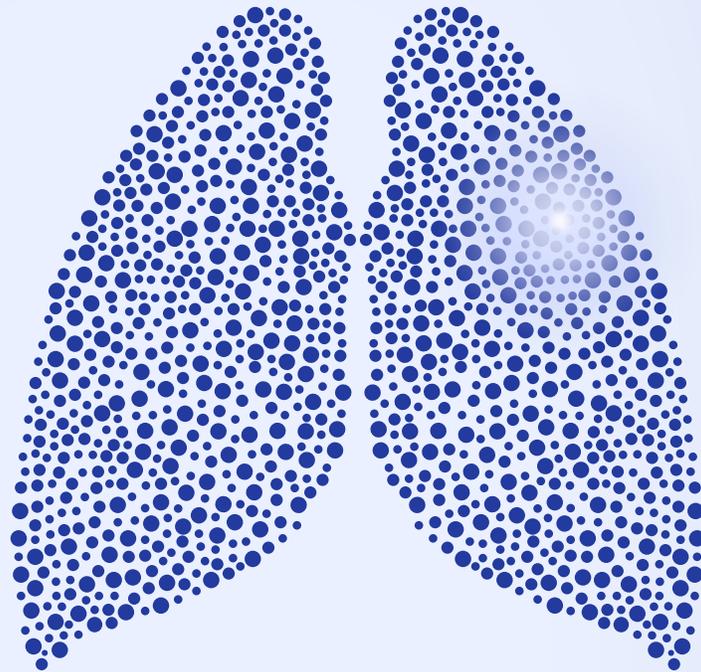
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SRC and PIM1 as potential co-targets to overcome resistance in MET deregulated non-small cell lung cancer

Objective:

- To better understand the role of proviral integration site for Moloney murine leukemia virus (PIM-1) and Src in EGFR inhibitor resistance.

Design:

- Four cell lines with MET amplification (EBC-1 and H1993), MET exon 14 skipping mutation (Hs746T), and MET exon 7-8 skipping mutation (E98) were treated with varying doses of MET-TKIs (tepotinib, savolitinib, crizotinib and cabozantinib), pan-PIM inhibitors (AZD1208 and PIM447) and SRC inhibitor (dasatinib)
- Retrospective analysis of pretreated tumor samples gathered from patients diagnosed with advanced NSCLC with squamous cell carcinoma, sarcomatoid characteristics, and EGFR mutant adenocarcinoma

Population:

- Median age of 70 years old
- Histology: adenocarcinoma EGFR+ (25.8%), squamous cell carcinoma (58.8%), sarcomatoid (15.4%)
- Total presence of MET alteration: 9/97 patients (9.3%)
 - Adenocarcinoma EGFR+ (0%), squamous cell carcinoma (77.8%), sarcomatoid (22.2%)
- Prior lines of treatment received: 0 (18.9%), 1 (47.8%), ≥ 2 (33.3%)

[LINK TO ARTICLE](#)

Results:

- PIM-1 and SRC inhibitors displayed no activity in MET addicted cell lines when used as single therapy
- Combination treatment of MET and PIM-1 inhibitors demonstrated an additive effect against all cell lines
- All MET inhibitors alone in combination with dasatinib showed synergism against all cell lines with the exception of tepotinib + dasatinib in the H1993 cell line
- Dasatinib in combination with tepotinib resulted in partial reversal of pre-existing single MET inhibitor resistance mechanisms
- Patient tumor samples analyzed for MET alterations fall in line with previous reported data trends. Suggests EGFR resistance may be acquired rather than exist at baseline

Strengths:

- Researchers had full access to data on retrospective tumor samples
- Cell viability experiments included different MET alteration types

Weaknesses

- Claims of EGFR resistance mechanism based off of small sample size
- Most of the patients analyzed did not have MET alterations

Conclusion:

- Based on the cell line results, the combination of PIM-1 or SRC inhibitors with MET TKIs warrants further investigation as it appears to be a potential combatant against EGFR inhibitor resistance.



SHP2 Inhibition Influences Therapeutic Response to Tepotinib in Tumors with MET Alterations

Drug: tepotinib

Objective:

- To discuss the various influences that factor into resistance of MET TKIs and to look at the role of SHP inhibition in tepotinib response.

Design:

- Parent cell lines and cell lines with acquired tepotinib resistance were introduced to investigational SHP inhibitor compounds (SHPi-01, SHPi-02) and MET TKIs under varying conditions
- Molecular and clinical profile analysis of 10 NSCLC patients

Population:

- Cell lines:
 - EBC-1 (MET amplified) and tepotinib resistant cell lines termed TR1 and TR2
 - Hs746T (METex14/MET amplified) and tepotinib resistant cell lines termed TR3
- 6 patients with METex14 skipping mutation and 4 patients with MET amplification treated with tepotinib
- 90% adenocarcinoma, 10% large cell carcinoma
- 60% received tepotinib first line

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Effectiveness:

- Median tumor burden change: -38.30%
- Gene copy number (GCN) gain was greater in MET amplification than METex14 skipping patients
- Tepotinib plus either SHP inhibitor showed synergy in each parent cell line and high efficacy in mice models
- Exposure to tepotinib + SHPi-02 almost fully inhibited cell growth in SHPi-02 doses ≥ 200 nmo/L

Strengths:

- Article provides thorough look into the possible relationship of MET TKI resistance and other RTK activity
- Cell line data obtained from multiple forms of cell culturing

Weaknesses:

- Small cohort of patients available to do clinical analysis
- Dosing schedule may not be representative of human tolerability dosing

Conclusion:

- Tepotinib plus an SHP inhibitor may prove to be a new alternative to attenuate MET TKI resistance in patients with MET14ex and MET amplification alterations. This article provides potential pathways of resistance between the two alterations, but still requires larger scale studies to be conducted to better understand them.

A phase Ib study of the highly selective MET-TKI savolitinib plus gefitinib in patients with EGFR-mutated, MET-amplified advanced non-small-cell lung cancer

Drugs: savolitinib, gefitinib **NCT ID:** 02374645

Objective:

- To report the safety and tolerability of savolitinib plus gefitinib, and the identification of the recommended phase II dose for the combination, in patients with EGFRm NSCLC who have progressed on EGFR-TKI therapy.

Design:

- Multicenter, open-label, phase 1b study of savolitinib plus gefitinib
- Safety run-in phase with dose escalation, followed by an expansion phase
- Expansion phase dosing was savolitinib 600 mg plus gefitinib 250 mg

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Population:

- Chinese patients
- Safety run-in phase included locally advanced or metastatic NSCLC with EGFR mutations, progressed during previous treatment with an EGFR-TKI; Expansion phase included patients with MET-amplified tumors (characteristics below)
- 60 patients with MET-amplification, 51 received study treatment
- Median age 61 years
- EGFR mutations: 51% with Exon 19 deletion, 39% with L858R, 6% with other
- EGFR T790M mutation: 45% positive, 45% negative, and 10% unknown
- Number of prior treatments: 57% received 1 prior therapy, 8% received 2 prior therapies, 24% received 3 prior therapies, 4% received 4 prior therapies, 8% received 5 prior therapies
- Prior treatments: 41% of patients previously received cytotoxic chemotherapy, 25% of patients received radiotherapy, 94% of patients previously received an EGFR-TKI (including afatinib, dacomitinib, erlotinib, gefitinib, icotinib, osimertinib)

Effectiveness Results (Expansion Phase only):

- Objective response rate 46% (all partial responses, no complete responses)
- Median actual combined treatment duration 2.9 months (range 0.099-13.57 months)
- Overall objective response rate 52%
- Confirmed partial response 31%, no complete response, stable disease 27%
- Amongst EGFR-T790M subgroups: objective response rate 52% in T790M-negative patients, 9% in T790M-positive patients, 40% in T790M-unknown status patients
- Median time to onset of response from first dose: 1.4 months
- Median duration of response: 5.6 months

- Amongst EGFR-T790M subgroups, median duration of response: 7.2 months in T790M-negative patients, 5.5 months in T790M-positive patients
- Median progression-free survival: 4 months
- Amongst EGFR-T790M subgroups, median progression-free survival: 4.2 months in T790M-negative patients, 2.8 months in T790M-positive patients

Safety Results:

- Common adverse effects: vomiting (39%), nausea (37%), aspartate aminotransferase (AST) increased (35%), rash (37%), alanine aminotransferase (ALT) increased (35%), gamma-glutamyltransferase (GGT) increased (31%), hypoalbuminemia (29%), amylase increased (24%), blood alkaline phosphatase (Alk Phos) increased (24%), diarrhea (18%), peripheral edema (14%)
- Serious adverse effects (grade ≥ 3): nausea (2%), AST increased (8%), ALT increased (8%), GGT increased (6%), blood Alk Phos increased (4%)

Strengths:

- Provides preliminary information on activity of savolitinib plus gefitinib in EGFR-mutated, MET-amplified NSCLC

Weaknesses:

- Non-controlled trial: this limits comparisons to other MET-directed therapies and could introduce bias because investigators know what patients are receiving
- Small sample size, Chinese population: this limits ability to generalize results to a broader population
- Does not include patients who harbor MET mutations or amplifications alone, without EGFR mutations

Conclusion:

- Savolitinib plus gefitinib yielded responses in a portion of Chinese patients with EGFR-mutated, MET-amplified NSCLC. Side effects appear to be comparable to other MET-directed therapies and typically manageable.

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NSCLC patients with MET non-exon 14 mutations rather than MET exon 14 mutations response to immune checkpoint inhibitors

Objective:

- To examine patients with METex14 and MET-non-ex14 mutations and assess the role that immune checkpoint inhibitors (ICIs) exhibit.

Design:

- Retrospective analysis of ICI treated NSCLC patients from clinical and genomic data obtained from cBioPortal database

Population:

- Total of 385 ICI treated NSCLC patients
- MET altered NSCLC: 4.4%
 - METex14: 58.8%
 - MET-non-ex14: 35.3%
 - MET-non-ex14/METex14 co-mutation: 5.9%

Effectiveness:

- Durable clinical benefit: 66.7% in MET-non-ex14 versus 14.3% in METex14

[LINK TO ARTICLE](#)

- Progression free survival: 9.1 months in MET-non-ex14 versus 2.1 months in METex14
- Overall survival: (unable to calculate*) in MET-non-ex14 versus 18 months in METex14

Strengths:

- This analysis was able to differentiate MET subtype data and acknowledged conflicting data that exists between ICI treatment in MET-non-ex14 and METex14 NSCLC.

Weaknesses:

- Not all patients had available DCB, PFS, or PD-L1 expression data available
- Small cohort of MET NSCLC patients

Conclusion:

- Differences in ICI treatment effectiveness among MET subtypes may exist given this data. Larger scaled studies are needed to better describe the relationship between MET NSCLC subtypes and ICIs.

Phase 1/2 study of the safety and efficacy of APL-101, a specific c-MET inhibitor

Drug: APL-101 NCT ID: 03993873

Objective:

- To identify the safety and recommended phase 2 dose of APL-101, a selective type 1b c-MET inhibitor

Design:

- Phase 1 dose-escalation study
- APL-101 100 – 400 mg orally divided twice daily

Population:

- Patients with c-MET dysregulated solid tumors
- Mean age 60.9 years
- Median prior lines of therapy 3.5 (range 1-10)
- Of 17 subjects, 8 had c-MET amplification, 7 had c-MET overexpression, 1 had c-MET exon 14-mutated cancer (not NSCLC), and 1 had c-MET kinase domain mutation.

[LINK TO ABSTRACT](#)

Results:

- No dose-limiting toxicities or grade 3 or higher adverse events
- Most common side effects were fatigue (35%), diarrhea (24%), edema (24%)
- One patient with partial response and 9 with stable disease
- Median progression-free survival 84 days
- Recommended phase 2 dose is 400mg (200mg orally twice daily)

Conclusion:

- This poster available in abstract version only – key data on solid tumor types and other characteristics are missing
- Due to dose-escalation structure and small sample size, cannot make conclusions at this point about efficacy
- Safety information very preliminary due to small sample size, dose-escalation structure, and short follow up, but no harm signals (either dose-limiting toxicity or grade 3 or higher adverse events)



Multi-line treatment with tyrosine kinase inhibitors enabled in 4-year survival for patient with stage IV lung adenocarcinoma: a case report

Drugs: gefitinib, osimertinib, crizotinib

Objective:

- To report a case of patient with multiple targetable mutations with advanced NSCLC who received multiple lines of tyrosine kinase inhibitors and achieved prolonged survival

Design:

- Case report

Population:

- One patient with advanced NSCLC who was ALK positive with EGFR exon 19 deletion and MET amplification treated with cisplatin with pemetrexed, followed by gefitinib, osimertinib, crizotinib, and crizotinib with gefitinib

Efficacy Results:

- Patient achieved 4-year survival

Safety Results:

- Patient experienced clots in lungs and lower limb at end of follow up, unsure if related to treatment or underlying disease process

Strengths:

- This is one of the few reports demonstrating multi-line tyrosine kinases inhibitors in patients with advanced NSCLC, contributing to a gap in the literature

Weaknesses:

- These results are demonstrated in one patient in this case report, so need more robust studies to confirm safety and efficacy in this patient population

Conclusion:

- Multi-line tyrosine kinase inhibitors may be a reasonable approach in patients with advanced NSCLC who have multiple targetable mutations, but additional and larger studies are needed to confirm the safety and efficacy of this approach
- Additional studies are needed to understand the mechanisms of tyrosine kinase inhibitor resistant in this patient population

[LINK TO ARTICLE](#)



MET exon 14-altered lung cancers and MET inhibitor resistance

Objective:

- To determine the mechanisms of primary resistance to MET tyrosine kinase inhibitors

Design:

- Single-center, open-label study
- Genomic (DNA sequencing, RNA sequencing, and cell-free DNA sequencing) and proteomic (mass spectrometry and immunohistochemistry) analysis on pre-treatment patient samples

Population:

- MET exon 14-altered lung cancers treated with a MET TKI: 169 patients reviewed, 75 with prior receipt of a MET TKI
- Median age 73 years
- Tumor histology: 79% adenocarcinoma; 9% sarcomatoid; 12% other
- MET mutations type: 48% base substitution, insertion/deletion 35%, large deletion (>35 base pairs) 8%, fusion 3%, other 3%, not detected by DNA-based Next Generation Sequencing 4%
- Prior MET TKIs: 75% of patients previously received 1 TKI; 25% of patients with 2 or more TKIs
- First MET TKI receive: 88% crizotinib, 1% cabozantinib, 11% tepotinib

Effectiveness Results:

- No genomic characteristics examined correlated with overall response rate (ORR) or progression free survival (PFS)
- Tumor responses varied in subclonal (0%) versus clonal ones, though not statistically significant
- Tumor mutational burden did not affect MET TKI ORR or PFS
- Pretreatment concurrent genomic alterations such as TP53, MDM2, CDK4, TERT, and CDKN2A did not impact ORR or PFS, though ORR was numerically (but not significantly) lower in tumors with PI3K or PTEN co-mutations

- Of those with MET exon 14 alterations, only 67% had detectable MET expression by mass spectrometry. MET protein expression by mass spectrometry correlated with high immunohistochemistry H-scores
- Overall response rate per MET detected by mass spectrometry: 60% in cases with detectable MET vs. 0% with undetectable MET
- Overall response rate per immunohistochemistry H-score: 62% with high H-scores 200 or greater versus 33% with lower H-scores 1-149
- Median progression free survival per immunohistochemistry H-score: 10.4 months with H-scores 200 or greater, 5.5 months with H-scores less than 200
- No differences seen in clinicopathologic characteristics, such as treatment with crizotinib or tepotinib, seen in different H-score groups
- Overall response rate per MET copy number or high H-score: 64% with higher copy number or H-score versus 0% in low copy number and H-score
- Median progression free survival per MET copy number: 13.8 months with higher copy number or H-score versus 4.6 months in low copy number and H-score

Safety Results:

- Not reviewed in this study

Strengths:

- In depth analysis of genomic and proteomic factors that may predict treatment outcomes and resistance

Weaknesses:

- Non-controlled, single-center experience limits the ability to generalize this to a broader population
- The small sample size is insufficient to support routine MET protein analysis
- Assays used to assess genomic and proteomic changes in this study may not be widely available in the community

Conclusion:

- No correlation was found between additional genomic factors (zygosity, clonality, whole genome duplication, and tumor mutational burden) and response or survival. However, proteomic factors may modify response to MET TKI therapy.

[LINK TO ARTICLE](#)



Genetic Heterogeneity of MET-aberrant Non-Small Cell Lung Cancer and its Impact on the Outcome of Immunotherapy

Objective:

- To describe the characteristics of different MET alterations and the activity of immune therapy among these MET subgroups

Design:

- Retrospective analysis of a single-center cohort
- Included patients with MET-altered NSCLC diagnosed over a 3-year period
- FISH, NGS, and PD-L1 IHC were performed on the biopsies

Patients:

- 337 patients included
 - MET exon 14 = 59 (17.5%)
 - MET amplified = 278 (82.5%)
- Mean age 67 overall, but higher in MET exon 14 (77)
- MET exon 14 more likely to be never-smokers (36% vs 4%)
- Most patients either metastatic (70%) or stage III B/C (13.6%) at diagnosis, with MET exon 14 more likely metastatic (76% vs 69%)
- 37% of patients received an immune checkpoint inhibitor (similar between groups), most commonly as second-line therapy after progression on chemotherapy
- 45% of patients received chemotherapy without a checkpoint inhibitor, more common in MET amplified vs MET exon 14 (47% vs 45.1%)

Results:

- Co-alterations were less common with MET exon 14 mutations versus MET amplifications (42% vs 87%). No patients had EGFR, ALK, or ROS co-alterations.
- There were no differences in PD-L1 expression between MET exon 14 vs MET amplification. PD-L1 expression did not well separate out subgroups with and without benefit from immune therapy in these patients.

- Overall survival with immune therapy versus chemotherapy
 - MET amplified: better survival with immune therapy
 - Gene copy number <10: median survival 19 months vs 8 months
 - Gene copy number \geq 10: median survival 36 months vs 4 months
 - MET exon 14: no significant difference between immune therapy and chemotherapy (16 mos vs 10 months, HR 0.62, 95% CI 0.32-1.22, P = 0.147)

Strengths:

- Helpful to see the differences in prevalence and immune therapy response between MET exon 14 mutations and MET amplification
- Relatively large cohort for a single-center analysis of a rare mutation

Weaknesses:

- Although no statistically significant difference with immune therapy versus chemotherapy for MET exon 14 subgroup, this may just be due to small sample size. Small cohort may also have impacted other endpoints.

Conclusion:

- MET alterations and MET exon 14 mutations are not equivalent in their prevalence, patient characteristics, or response to immune therapy
- Better response to immune therapy in MET amplified group is not surprising given what we know overall about immune therapy prolonging overall survival in NSCLC generally.
- Difficult to make conclusions about immune therapy versus chemotherapy in MET exon 14 mutated NSCLC due to small cohort.

[LINK TO ARTICLE](#)



First-in-human safety, pharmacokinetics, and preliminary efficacy of TPX-0022, a novel inhibitor of MET/SRC/CSF1R in patients with advanced solids tumors harboring genetic alterations in MET

Drug: TPX-0022 NCT ID: 03993873

Objective:

- To determine the maximum tolerated dose, safety, pharmacokinetics (absorption, distribution, metabolism, and excretion), and tumor activity of TPX-0022 in patients with solid tumors with MET alterations

Design:

- 3 + 3 dose escalation phase
- Expansion phase using doses that were shown to have anti-tumor activity

Population:

- Adults (median age 63) with advanced solid tumors with MET alterations
 - 9 patients with amplification, 7 patients with METex14, 2 patients with fusion
- Previous treatment with a MET inhibitor was allowed
 - Median number of therapies = 3
 - 39% of patients were previously on a MET inhibitor
- Total 18 patients enrolled across different doses (range 20 to 120mg daily)
 - 11 patients with NSCLC, 4 patients with colorectal cancer, 3 patients with gastric cancer

Efficacy Results:

- One patient with METex14 NSCLC achieved a partial response (PR)
- Two patients with MET amplified gastric cancer achieved a PR
- One patient with MET amplified colorectal cancer achieved a PR

Safety Results:

- Most common side effects included dizziness (61%), increase in amylase (33%), increase in lipase (33%), fatigue (33%), nausea (33%)
- No grade 3 or higher side effects
- One dose-limiting toxicity of grade 2 dizziness occurred at 120mg daily

Conclusion:

- TPX-0022 had a tolerable safety profile overall and showed anti-tumor activity in a variety of solid tumors and MET alterations
- TPX-0022 is currently in phase 2 studies

[LINK TO ABSTRACT](#)



Acquired MET Amplification in Non-Small Cell Lung Cancer Is Highly Associated with the Exposure of EGFR inhibitors and May Not Affect Patients' Outcome

Objective:

- To determine if acquired MET amplification impacts outcomes among patients with non-small cell lung cancer (NSCLC)

Design:

- Retrospective analysis of tumor samples and outcomes

Population:

- Patients with NSCLC who had a FISH test for MET at least 2 or more times
- Median age 65 years (range 32-87)
- Majority adenocarcinoma (85)
- Median interval between initial and second biopsy 10.5 months

Results:

- 99 patients with NSCLC had FISH 2 or more times at this institution in the 5-year period
- Initial biopsy – 77% stage III/IV disease at this point
 - 41% EGFR mutated
 - 4% MET amplification
 - 17% polysomy 7
 - 78% MET-negative
- Second biopsy – 93% Stage III/IV disease at this point, all had progressed
 - 16 acquired MET amplification (4 had polysomy 7 and 12 MET-negative initially)
 - Most common in EGFR-mutated patients exposed to EGFR inhibitors (40%)
 - 5 acquired TP53 mutations

- No MET exon 14 detected in any specimen
- MET-amplified group had lower rate of other mutations (including KRAS, PIK3CA, ATM, and others)
- No statistically significant difference in overall survival for MET-amplified patients versus MET-negative (96.9 vs 48.3 months, $P = 0.2766$) or acquired MET versus never MET-amplified (not reached vs 48.3 months, $P = 0.4957$)
- No survival differences with MET amplification among EGFR mutated or TP53 mutated subgroups
- In multivariate analysis, only tumor stage (I/II vs III/IV) was independent predictor of survival

Weaknesses:

- This study can not be applied to patients with MET exon 14-mutated NSCLC as no patients with this mutation were included in the analysis

Conclusion:

- Acquired MET amplification is associated with exposure to EGFR inhibitors
- Patients with acquired MET amplification had a trend towards longer overall survival, although results were not statistically significant
- Although other studies have indicated that initial MET amplification is a negative prognostic indicator in NSCLC, acquired MET amplification does not seem to carry the same negative connotation.

[LINK TO ARTICLE](#)



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 February 21, 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: NCT003088930

Link: <https://clinicaltrials.gov/ct2/show/NCT003088930>

Title: Evaluating Crizotinib in the Neoadjuvant Setting in Patients With Non-small Cell Lung Cancer
Status: Active, Not Recruiting
Drug: Crizotinib
Phase: P2
Countries: US

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: 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: 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: 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: 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: Active, Not Recruiting
Drug: Capmatinib
Phase: P2
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: 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: 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: 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



UMBRELLA TRIALS

NIH Identifier: NCT03574402

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

Title: Phase II Umbrella Study Directed by Next Generation Sequencing (TRUMP)
Status: Recruiting
Trial Name: Umbrella (TRUMP)
Phase: P2
Countries: China

NIH Identifier: NCT02693535

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

Title: TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer (TAPUR)
Status: Recruiting
Trial Name: TAPUR
Phase: P2
Countries: US

NIH Identifier: NCT02664935

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

Title: National Lung Matrix Trial: Multi-drug Phase II Trial in Non-Small Cell Lung Cancer
Status: Recruiting
Trial Name: Matrix
Phase: P2
Countries: United Kingdom

NIH Identifier: NCT02465060

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

Title: Targeted Therapy Directed by Genetic Testing in Treating Patients With Advanced Refractory Solid Tumors, Lymphomas, or Multiple Myeloma (The MATCH Screening Trial)
Status: Recruiting
Trial Name: Match
Phase: P2
Countries: US, Guam, Puerto Rico

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: Active, Not Recruiting
Drug: Nivolumab + EGF816 + Capmatinib
Phase: P2
Countries: US, Australia, France, Germany, Italy, Netherlands, Singapore, Spain, Switzerland

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: Recruiting
Drug: Glesatinib, Sitravatinib or Mocetinostat + Nivolumab
Phase: P2
Countries: US

NIH ID: NCT03666143

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

Title: A Phase 1b Study to Assess Sitravatinib in Combination with Tislelizumab in Patients With Advanced Solid Tumors.
Status: Recruiting
Drug: Sitravatinib + Tislelizumab
Phase: P1
Countries: Australia, China

NIH ID: NCT04323436

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

Title: Study of Capmatinib and Spatalizumab/Placebo in Advanced NSCLC Patients with MET Exon 14 Skipping Mutations
Status: Recruiting
Drug: Capmatinib + Spatalizumab
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: Recruiting
Drug: Capmatinib + Pembrolizumab
Phase: P2
Countries: US, Australia, Belgium, Czechia, France, Germany, Hong Kong, India, Italy, Japan, Malaysia, Spain, Taiwan, Thailand

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: Active, Not Recruiting
Drug: Capmatinib + Erlotinib
Phase: P1
Countries: US



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: Osmertinib + Salvotinib

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) (INSIGHT 2)

Status: Recruiting

Drug: Tepotinib + Osmertinib

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 JNJ-61186372, a Human Bispecific EGFR and cMet Antibody, in Participants with Advanced Non-Small Cell Lung Cancer (CHRYSALIS)

Status: Recruiting

Drug: JNJ-61186372

Phase: P1

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

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 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: Osmertinib + Salvotinib

Phase: P2

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

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>

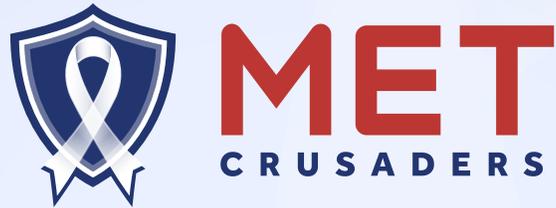
Title: REGN5093 in Patients With MET-Altered Advanced Non-Small Cell Lung Cancer

Status: Recruiting

Drug: REGN5093

Phase: P1, P2

Counties: US, Republic of Korea



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 improves readability while providing key metrics. The summaries are not intended to replace the abstracts, posters or 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(s) under trial is also provided.

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