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NEWSLETTER

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

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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*

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Co-occurring MET amplification predicts inferior clinical response to first line erlotinib in advanced stage EGFR-mutated NSCLC patients

Drug: erlotinib

Objective:

- To determine the predictive potential of co-occurring genetic alterations on the response to first-line erlotinib

Design:

- Prospective, observational, multicenter study in West Denmark
- Circulating cell-free DNA (cfDNA) isolated from patients and sequenced to assess for mutations and other oncogenic drivers; co-occurring oncogenic drivers included mutations or increases in copy numbers of known oncogenes other than EGFR

Population:

- Advanced or metastatic NSCLC with EGFR mutations who received erlotinib as first line treatment: 76 patients
- Median follow-up time: 23.3 months
 - 52 patients (68%) progressed
 - 58 patients (76%) died
- Median age: 68 years
- Without other oncogenic driver, 36% male; with other oncogenic driver, 44% male
- Without other oncogenic driver, 46% former smoker, 36% never smoker; with other oncogenic driver, 38% former smoker, 44% never smoker
- EGFR mutations in both groups included predominantly Del19 and L858R; no T790M mutations in pretreatment samples found

Results:

- Other mutations found in pretreatment samples: TP53 (43%), MET (12%), KRAS (3%), PIK3CA (7%), ERBB2 (3%), CTNNB1 (8%)
- Median progression free survival (PFS) was shorter with the presence of co-occurring oncogenic drivers (n=16, 21%) when compared to those without co-occurring oncogenic drivers: 6.9 months vs. 14.4 months, respectively, HR 2.088, P = 0.0355
- Overall survival (OS) was shorter with the presence of co-occurring oncogenic drivers when compared to those without co-occurring oncogenic drivers: 9.2 months vs. 28.3 months, respectively, HR 2.127, P = 0.0128

- MET amplification without other concurrent mutations was associated with an inferior PFS (5.5 months vs. 14.4 months, HR 4.750, P = 0.0007) and OS (7.6 months vs. 28.3 months, HR 3.952, P = 0.0005)
- In those with one other concurrent oncogenic driver that was not MET, there was no statistically significant association with shorter PFS or OS
- TP53 was not found to be associated with resistance to EGFR TKIs
- Presence of co-occurring oncogenic drivers in patients who cleared EGFR-mutated ctDNA after treatment was associated with a shorter PFS (8.7 months vs. 16.1 months) though this was not statistically significant (HR 1.703, CI 0.5347-5.424, P = 0.2508)

Strengths:

- Provides insight into potential predictors of erlotinib or EGFR TKI response through in-depth analysis of mutations at baseline and after treatment. This study confirms the value in genetic sequencing to assess co-occurring mutations and further understand intrinsic resistance
- Demonstrates that MET amplifications are associated with inferior clinical response

Weaknesses:

- Non-controlled trial: limits comparisons to other potential treatments
- Small sample size: differences in PFS and OS may not be clinically meaningful
- Population included patients treated with first-line erlotinib, which has fallen out of favor in the United States. Standard first-line treatment is typically with osimertinib; further studies are needed to assess the role of MET amplifications with osimertinib treatment

Conclusion:

- Co-occurring oncogenic drivers, particularly MET amplification, were associated with shorter progression free and overall survival
- Data confirm the need to identify co-occurring oncogenic drivers in order to understand mechanisms of resistance and furthermore, identify potential treatments to overcome them

[LINK TO ARTICLE](#)



Tepotinib in patients with NSCLC harbouring MET exon 14 skipping: Japanese subset analysis from the Phase II VISION study

Drug: Tepotinib | NCT ID: 02864992

Objective:

- To assess tepotinib's efficacy and tolerability in Japanese patients with advanced NSCLC METex14 skipping mutation

Design:

- Phase II, single arm, open-label, multicenter trial investigating tepotinib 500 mg once daily

Population:

- 15 Japanese patients identified with METex14 skipping mutations
- Median age of 69.4 years
- Histology: adenocarcinoma (93.3%), NSCLC not specified (6.7%)
- Number of lines of prior treatment: 0 (46.7%), 1 (20.0%), 2 (33.3%)

Effectiveness:

(evaluation by both investigator and independent review committee)

- Objective response rate: 60.0% (IRC), 73.3% (investigator)
- Complete response: 0% (IRC), 6.7% (investigator)
- Partial response: 60% (IRC), 66.7% (investigator)
- Stable disease: 6.7% (IRC and investigator)
- Progressive disease: 26.7% (IRC), 13.3% (investigator)

- Median progression free survival: 11.0 months (IRC), 11.1 (investigator)
- Median duration of treatment: 10.4 months

Safety:

- Any adverse event of all grades due to treatment (94.7%)
 - Elevated blood creatinine (63.2%), hand or lower leg swelling (47.4%), diarrhea (36.8%)
- Grade ≥ 3 adverse events (47.4%)
 - Hand or lower leg swelling (5.3%), diarrhea, (5.3%), increased amylase (5.3%)

Strengths:

- Few studies exist involving Japanese patients and this study aids in the understanding of NSCLC in this population

Weaknesses:

- Small cohort of patients with varying outcomes data shown between the IRC and the investigator

Conclusion:

- Tepotinib was shown to have clinical benefit in this cohort of Japanese patients with NSCLC harboring METex14 mutation identify the patients who would benefit most from crizotinib treatment

[LINK TO ARTICLE](#)



A Phase II Study of Telisotuzumab Vedotin in Patients With c-MET-positive Stage IV or Recurrent Squamous Cell Lung Cancer (LUNG-MAP Sub-study S1400K, NCT03574753)

Drug: Telisotuzumab vedotin | NCT: 03574753

Objective:

- To determine the safety and response rate of telisotuzumab vedotin in patients with c-MET overexpressing squamous NSCLC

Design:

- Phase II trial, no control arm
- Subgroup of the Lung-MAP umbrella trial for NSCLC
- Patients received telisotuzumab vedotin 2.7 mg/kg IV over 30 minutes on day 1 of each 21-day cycle until progression or significant toxicity

Population:

- Previously treated patients with squamous NSCLC and measurable disease
 - Cohort 1: never treated with immune checkpoint inhibitor (ICI-naïve)
 - Cohort 2: previously treated with immune checkpoint inhibitor (ICI-refractory)
- c-MET overexpression (by IHC staining)
- Patients were excluded if they had significant peripheral neuropathy or extensive liver involvement

Results:

- A total of 28 patients were enrolled, 15 into ICI-naïve group and 13 into ICI-refractory group
 - Median age 65 years, with 57% male and 91% white
 - 39% received 2 or more prior lines of treatment
- Of 23 evaluable patients, 1 experienced a complete response, 1 had partial response, and 10 had stable disease. The patient with initial partial response had progressive disease at the next scan. Disease control rate = 52%.

- The study was closed early at the interim analysis due to low response rate.
- One patient had a MET exon 14 mutation and progressed at the first assessment. Neither responders had MET exon 14 mutations.

Safety:

- 3 deaths possibly related to treatment: 1 due to pulmonary hemorrhage, and 2 due to pneumonitis, an unexpected effect
 - Both patients who died from pneumonitis had been exposed to immunotherapy previously
- Grade 3-4 adverse effects: anemia, low neutrophils, low sodium, low phosphate, neuropathy

Strengths:

- Given that ~30% of squamous NSCLC is positive for MET expression, this trial investigated a targeted approach that could significantly impact patient care

Weaknesses:

- It is unclear whether MET-IHC is the best biomarker to select patients for treatment with MET-directed antibodies

Conclusion:

- Although telisotuzumab vedotin did not meet the criteria to continue past the interim analysis, the manufacturer felt that the effectiveness justified performing another phase II study (NCT03539536)
- Patients should be monitored for pneumonitis closely – ongoing studies will continue to elucidate the risk factors for pneumonitis from telisotuzumab

[LINK TO ARTICLE](#)



Durvalumab consolidation therapy in a patient with stage IIIB unresectable NSCLC harboring a MET exon 14 splice site alteration

Drug: durvalumab

Objective:

- To assess the benefit of immunotherapy and targeted therapy in earlier stage unresectable NSCLC with both PDL1 expression and actionable driver mutations

Design:

- Case report

Population:

- 83-year-old patient with stage IIIB NSCLC with high PDL1 expression (80%) and MET exon 14 skipping
- Received concurrent chemoradiotherapy (platinum and pemetrexed with radiation) followed by consolidation with durvalumab
- Switched to crizotinib 250mg twice daily after durvalumab

Efficacy Results:

- Rapid progression after chemoradiotherapy followed by durvalumab
- Partial response (PR) with crizotinib
- Maintained on crizotinib for 8 months before developing progression

Safety Results:

- No reported side effects from crizotinib

Strengths:

- Demonstrates the need for more studies to assess the use of targeted therapy in earlier stage, non-metastatic, unresectable lung cancer
- Illustrates no increased risk of side effects with sequential immunotherapy followed by targeted therapy, unlike what has been reported in other studies
- Contributes to the gap in literature regarding use of targeted therapy in earlier stage NSCLC, particularly the lack of data of targeted therapy in patients with earlier stage MET mutated NSCLC
- Provides support for testing for driver mutations before locally advanced or metastatic stage of NSCLC

Weaknesses:

- Case report, only have data on one patient so need more research to confirm findings

Conclusion:

- Targeted therapy has demonstrated response in earlier stage unresectable NSCLC with driver mutations and thus warrants further research to determine safety and efficacy in this patient population

[LINK TO ARTICLE](#)



Early Alectinib Resistance From MET Amplification in ALK Rearranged NSCLC: Response to Crizotinib with Re-response to Alectinib and Crizotinib

Drugs: alectinib, crizotinib

Objective:

- To report a case of a patient with metastatic NSCLC harboring an EML4-ALK rearrangement who was treated with alectinib, carboplatin/paclitaxel, crizotinib, and then crizotinib/alectinib

Design:

- Case report

Population:

- One patient with stage IV NSCLC with left vocal cord paralysis, a large left hilar mass with mediastinal extension, large pericardial effusion with pericardial tamponade, and a right pelvis/hip lesion, initially treated with alectinib and radiation to the bone metastases.

Efficacy Results:

- Initial very good partial response
- At 6 months, CT of the chest, abdomen, and pelvis showed progressive disease. Repeat PET/CT showed continued response of the hilar mass, but progression elsewhere, so alectinib was stopped
- Carboplatin and paclitaxel were then started while repeat molecular results were pending
- Repeat sequencing showed a high level of MET amplification with no ALK mutation
- After four cycles of carboplatin and paclitaxel, the patient had stable disease, and crizotinib (dual ALK and MET) inhibitor was started
- After 10 months, PET/CT showed disease progression
- Repeat sequencing showed an increase in the MET copy number, and an EML4-ALK rearrangement with no resistance mutations

- Combination alectinib and crizotinib were then started, which was complicated by pulmonary embolism, resulting in a treatment hold and dose reduction
- After 6 months, intracranial metastatic disease was seen

Safety Results:

- Bilateral pleural effusions and new pulmonary embolus were seen after starting dual alectinib and crizotinib therapy, resulting in a treatment hold. Repeat PET/CT after 2 weeks of treatment showed response in multiple areas, so treatment was continued at a reduced dose

Strengths:

- Detailed overview of patient response to dual alectinib and crizotinib therapy
- Degree of MET amplification (high) reported

Weaknesses:

- Results are demonstrated in only one patient in this case report, larger studies are needed to confirm response in patients who develop MET amplification as a resistance mechanism to ALK-directed therapy

Conclusion:

- Addition of alectinib to crizotinib (ALK-directed therapy with MET-directed therapy) in MET-mediated resistance to ALK-rearranged NSCLC is a potential treatment combination
- Repeated molecular analysis during treatment can be useful in guiding therapy
- Other studies have already demonstrated treatment possibilities for patients with ALK rearrangements and de novo MET amplifications. Larger, randomized studies are needed to further confirm these findings

[LINK TO ARTICLE](#)



Crizotinib for c-MET-amplified advanced NSCLC: a single-center experience

Drug: crizotinib

Objective:

- To evaluate the efficacy of crizotinib in MET-amplified metastatic NSCLC

Design:

- Retrospective observational chart review

Population:

- 8 patients with locally advanced or metastatic NSCLC
- All patients had MET amplification
- All patients received crizotinib 500mg daily

Efficacy Results:

- Partial response (PR) in 4 patients
- Progressive disease (PD) in 4 patients
- Median progression-free survival (PFS) = 9.4 months
- Median overall survival (OS) = 10.9 months

Safety Results:

- 37% of patients had diarrhea (grade 1-2)
- 37% of patients had nausea (grade 2-4)
- 25% of patients had visual impairment (grade 1)

- Other side effects included edema, fatigue, elevated liver tests, elevated creatinine
- No patients discontinued crizotinib or required a dose reduction due to side effects

Strengths:

- Contributes to data that crizotinib may be an effective treatment option for patients with MET amplified NSCLC
- Demonstrates importance of performing more robust studies to confirm safety and efficacy of crizotinib in this patient population

Weaknesses:

- Retrospective observational study
- Small number of patients

Conclusion:

- Crizotinib may be a safe and effective treatment option for patients with locally advanced or metastatic MET amplified NSCLC, but more robust studies are needed to verify this

[LINK TO ARTICLE](#)



Combination of Crizotinib and Osimertinib in T790M+ EGFR-Mutant Non-Small Cell Lung Cancer with Emerging MET Amplification Post-Osimertinib Progression in a 10-Year Survivor: A Case Report

Drug: crizotinib, osimertinib

Objective:

- To report a case of long-term survival and successful use of crizotinib and osimertinib.

Design:

- Case report

Population:

- A never-smoking Caucasian woman who was diagnosed with metastatic lung cancer in 2010 at the age of 61 years old

History:

- May 2010: Presented with shortness of breath and right-sided chest pain. CT and biopsy demonstrated metastatic lung adenocarcinoma (NSCLC) with EGFR exon 19 deletion on PCR. Treated with gefitinib 250 mg daily for 4 years, achieving a partial response
- August 2014: Progression demonstrated on CT. Pemetrexed was added, resulting in stable disease for 6 months.
- May 2015: Palliative chest radiation for chest wall infiltration
- December 2015: Progressive disease. Re-biopsy performed and demonstrated EGFR T790M mutation. Treated with osimertinib 80mg daily through a study, achieving a partial response. Response maintained for 2 years.

- August 2018: Progression on imaging, re-biopsy performed. EGFR exon 19 deletion and T790M mutation still present, with low-level MET amplification. Crizotinib was added in November 2018.
 - Osimertinib switched to 80/40mg on alternate days and crizotinib started at 200 mg twice daily out of precaution for drug interactions and side effects given low body weight
 - CT scan at 4 weeks demonstrated partial response with complete response of left lung nodules
 - Crizotinib dose reduced to 20mg twice daily alternating with once daily for fatigue, vomiting, and decreased appetite
- March 2020: Patient developed shortness of breath, cough, and pain. CT scan demonstrated progression. Re-biopsy confirmed the same EGFR mutations and MET amplification. Doses were increased to osimertinib 80mg daily and crizotinib 200mg twice daily, with subsequent symptom improvement and partial response.
 - Side effects returned, but the patient felt these were tolerable enough to continue treatment.

Conclusions:

- MET amplification is a known mechanism of resistance to EGFR inhibitors. This case report suggests that administration of an EGFR inhibitor with a MET inhibitor may be an effective approach in some patients with MET-driven EGFR resistance.

[LINK TO ARTICLE](#)



MET amplification attenuates lung tumor response to immunotherapy by inhibiting STING

Drug: nivolumab

Objective:

- To understand how MET gene amplification affects immunotherapy effectiveness.

Design:

- Case report of two patients followed by multiple analyses of tissues from larger groups of patients and mouse models

Case reports:

- 57 year old male with stage IIIC lung adenocarcinoma, negative EGFR and ALK
 - Treated with cisplatin and paclitaxel, but progressed
 - Tissues positive for MET amplification, PD-L1 positive also (TPS 55%)
 - Treated with nivolumab without response – new brain metastasis
- 28 year old male with metastatic lung adenocarcinoma, negative for EGFR and ALK
 - Treated with cisplatin and paclitaxel, but progressed
 - Tissues positive for MET amplification, PD-L1 positive also (TPS 75%)
 - Treated with nivolumab without response – new bone metastasis

Tissue, database, and animal model results:

- Expression of immune markers was measured in NSCLC samples with MET amplification (n = 11) compared to not MET amplified (n = 12)
 - MET amplified patients had lower STING, CCL5, CD8, and GZMB expression
 - This indicates an immune-suppressive environment – cancers with MET amplification can more easily escape from immune killing of cancer cells
- MET amplification then correlated with immunotherapy response in larger NSCLC population (n = 81) → excluded patients with EGFR, RAS, ALK, or MET mutations

- Patients who did not respond were more likely to have higher MET copy number
- Patients with longer progression-free survival likely to have a low MET copy number
- Analysis also done on patients from two clinical trial cohorts of NSCLC patients treated with immunotherapy.
 - Relatively few patients with MET amplification received immunotherapy in these trials (4 patients in one and 6 in the other)
 - MET amplification was an independent risk factor for poor immunotherapy response. None of the MET-amplified patients had durable clinical benefit from immunotherapy.
- A cancer genome database was analyzed for the correlation between MET amplification and immune marker expression. MET amplification was correlated with low STING levels and cytolytic scores.
- The number and function of immune cells were evaluated in MET-amplified NSCLC samples. MET-amplified samples had lower numbers of immune cells and had higher levels of immune cell exhaustion.
- In a mouse model, MET overexpression corresponded with lack of immunotherapy effectiveness. Combining a MET inhibitor with immunotherapy was effective in mice, although it was not clear whether this was just an effect of the MET inhibitor alone.
- Additional experiments were performed in mouse models to describe and confirm the mechanisms by which MET amplification can lead to immunotherapy resistance.

Conclusion:

- MET amplification (defined as MET copy number >5 in this paper) predicts minimal benefit from immunotherapy. This paper indicates that this happens through reduced STING activity and less immune cell infiltration into the tumor. Ongoing studies are needed to determine whether the combination of MET inhibitors and immunotherapy can be safe and effective for patients with MET-amplified NSCLC.

[LINK TO ARTICLE](#)



Once-daily savolitinib in Chinese patients with pulmonary sarcomatoid carcinomas and other non-small-cell lung cancers harbouring MET exon 14 skipping alterations: a multicentre, single-arm, open-label, phase 2 study

Drug: savolitinib | NCT ID: NCT02897479

Objective

- To analyze the objective response rate (ORR), through evaluation by an independent review committee (IRC) and the investigator, of savolitinib in Chinese patients with NSCLC METex14 skipping mutation

Design

- Multicenter, single-arm, open-label, phase II study involving 70 patients in the full analysis
- Savolitinib dosing: weight of <50 kg received 400 mg daily or ≥50 kg received 600 mg daily

Population

- Mean age of 68.7 years
- Histology: adenocarcinoma (57%), pleomorphic carcinoma (21%), spindle cell carcinoma (11%), squamous cell carcinoma (4%)
- Number of previous lines of treatment: 0 (40%), 1 (46%), 2 (7%), 3 (4%), ≥4 (3%)

Effectiveness

- ORR: 42.9% (IRC), 47.1% (investigator)
- Disease control rate: 82.9% (IRC), 81.4% (investigator)
- Median time to response: 1.4 months (IRC and investigator)
- Median duration of response: 8.3 months (IRC), 6.9 months (investigator)

- Median progression free survival: 6.8 months (IRC), 6.9 months (investigator)
- Median overall survival: 12.5 months

Safety

- Any adverse event of all grades due to treatment (100%)
 - Swelling in the extremities (54%), nausea (46%), low albumin (23%), increased liver enzymes (AST: 37%, ALT: 39%)
- Grade ≥ 3 adverse events (46%)
 - Swelling in the extremities (9%), increased liver enzymes (AST: 13%, ALT: 10%), low potassium levels (3%)

Strengths

- This trial conducted analysis from a large cohort of patients and was the first trial investigating savolitinib as treatment for METex14 altered NSCLC

Weaknesses

- Analysis conducted only on cohort 1 which was patients naïve to MET inhibitor treatment

Conclusion

- Savolitinib's response rate and safety profile in this patient cohort suggests that it may be a viable treatment option in METex14 NSCLC

[LINK TO ARTICLE](#)



Phase I results of S49076 plus gefitinib in patients with EGFR TKI-resistant non-small cell lung cancer harbouring MET/AXL dysregulation

Drug: S49076, gefitinib

Objective:

- To investigate the safety and tolerability of S49076 in combination with gefitinib in patients with EGFR mutated NSCLC that have developed MET/AXL dysregulation resistance

Design:

- International, multicenter, single-arm, open-label, non-randomized, non-comparative Phase I study in Italy, Japan, Korea, Singapore, Spain, and Taiwan
- S49076 is a novel tyrosine kinase inhibitor (TKI) with activity against MET, AXL, and FGFR, which can block downstream signalling to inhibit cell growth and migration
- Sought to determine safety and tolerability of S49076 in combination with gefitinib by assessing dose-limiting toxicities (DLT), adverse events (AE), and establishing the recommended phase II dose in EGFR-mutated NSCLC patients who have developed resistance to EGFR TKIs with MET and/or AXL dysregulation, and without EGFR exon 20 T790M mutations

Population:

- 92 patients pre-screened with IIIB/IV NSCLC, who have progressed after first- or second-line single-agent first- or second-generation EGFR TKI therapy
- 22 patients were negative for EGFR exon 21 T790M mutation and had either MET and/or AXL dysregulation
- 14 patients were included
- Median age was 61.5 years; 40% males, 50% smokers
- Tumor histology: 100% adenocarcinoma
- Tumor staging: 100% stage IV disease
- Prior EGFR TKIs: 30% gefitinib, 60% erlotinib, 20% afatinib

Safety Results:

- All 14 patients experienced at least one AE
- The most frequent AEs (43-50%) in the study included: diarrhea, paronychia, asthenia, peripheral edema, nausea

- The most frequent AEs related to S49076 included: diarrhea, paronychia, asthenia, and nausea, most of which were mild (91% grade 1)
- Serious AEs in 9 patients were attributed to both S49076 and gefitinib and included: febrile neutropenia, diarrhea, stomatitis
- Serious AEs in 2 patients were attributed to S49076: atrial fibrillation and asthenia
- 1 death occurred, and was deemed related to progression, not treatment

Effectiveness Results:

- Responses were evaluable in 12/14 patients
- Best overall response (BOR) was:
 - Partial response (PR) in 2/14
 - Stable disease (SD) in 8/14
 - Progressive disease (PD) in 2/14
- Overall response rate (ORR) was 14.3% (2/14 patients)
- Median progression-free survival (PFS) 24.6 weeks
- In patients with both MET and AXL dysregulation (2 patients), 1 PR and 1 SD was observed
- In patients with MET dysregulation only (9 patients), 1 PR and 6 SD was observed
- In patients with SD and PD, other mechanisms of resistance to EGFR TKIs were identified

Strengths:

- The study suggests that those with co-occurring MET and/or AXL dysregulation, combination therapy with S49076 and gefitinib did not restore sensitivity to the EGFR TKI
- This was further assessed through an depth analysis of additional biomarkers, such as other EGFR mutations, and at different time points, in order to determine relation to BOR
- Provides additional insight into resistance mechanisms of EGFR TKI treatment

Continued on p12



Continued:

Weaknesses:

- Small sample size due to phase I study design and narrow inclusion criteria requiring lack of EGFR exon 20 T790M mutations with either MET or AXL dysregulation
- Non-controlled trial limits comparison to other potential therapies

Conclusion:

- S49076 and gefitinib may not be a potential treatment option for NSCLC patients with MET and/or AXL dysregulation as a result of resistance to EGFR TKI therapy, but may be of interest in treating resistance to MET dysregulation alone
- Larger, prospective, controlled trials are needed to further evaluate potential benefit

[LINK TO ARTICLE](#)

Case Report: High-Level MET Amplification as a Resistance Mechanism of ROS1-Tyrosine Kinase Inhibitors in ROS1-Rearranged Non-Small Cell Lung Cancer

Drugs: crizotinib, lorlatinib

Objective:

- To report a case of ROS1 resistance due to MET amplification

Design:

- Case report

Population:

- 62-year-old patients with ROS1-rearranged metastatic NSCLC
- Received crizotinib 250mg twice daily followed by lorlatinib 75mg daily
- Found to have high level MET amplification after progression on lorlatinib

Efficacy Results:

- Achieved partial response (PR) on crizotinib for 19 months
- Maintained on lorlatinib for 1 month

Safety Results:

- Good tolerance of crizotinib

Strengths:

- First report of ROS1 targeted therapy resistance via MET amplification

Weaknesses:

- Unable to validate resistance mechanism as patient was not able to receive MET inhibitor
- Case report so need more studies to confirm resistance mechanism

Conclusion:

- MET amplification may be a resistance mechanism to ROS1 inhibitors; however, further research is needed to confirm this utilizing a combination of crizotinib with a MET inhibitor after progression on crizotinib in patients with ROS1 mutated NSCLC who acquire MET amplification

[LINK TO ARTICLE](#)



Savolitinib ± Osimertinib in Japanese Patients with Advanced Solid Malignancies or EGFRm NSCLC: Ph1b TATTON Part C

Drugs: savolitinib, osimertinib | NCT: 02143466

Objective:

- To assess the safety and efficacy of savolitinib in patients with EGFR mutated NSCLC who developed MET-based resistance to osimertinib

Design:

- Phase Ib, multi-arm, open-label, multicenter study

Population:

- Patients with advanced EGFR mutated advanced NSCLC who progressed on osimertinib
- Received osimertinib 80mg daily with savolitinib (300mg, 400mg, or 600mg) daily
- 12 patients received the combination of osimertinib and savolitinib

Efficacy Results:

- Overall response rate (ORR) was 42%
- Partial response (PR) in 5 of 12 (42%) of patients
- Of the 7 patients who did not respond to combination therapy, 6 patients had stable disease (SD) for at least 6 weeks

Safety Results:

- Osimertinib + savolitinib 300mg daily - none reported
- Osimertinib + savolitinib 400mg daily - fatigue, nausea, myalgia
- Osimertinib + savolitinib 600mg daily - pyrexia, skin reaction, anaphylactic shock
- 33% of patients experienced a grade 3 or higher adverse effect

Strengths:

- Demonstrated safety of patients on osimertinib and savolitinib combination therapy
- Determined maximum tolerated dose of savolitinib when combined with osimertinib

Weaknesses:

- Low patient enrollment, so need larger studies to confirm findings
- No MET status data, so cannot confirm savolitinib's activity in MET amplified NSCLC
- Cannot confirm that efficacy is from the combination of osimertinib and savolitinib versus osimertinib alone, so need follow up studies to assess the activity of this combination in this patient population

Conclusion:

- Maximum tolerated dose of savolitinib is 400mg daily
- Savolitinib and osimertinib combination therapy has an acceptable safety profile
- Savolitinib plus osimertinib may be a treatment option for patients with EGFR mutated NSCLC who progress on an EGFR inhibitor
- More to come with the SAVANNAH trial, which is evaluating the combination of savolitinib and osimertinib in EGFR mutated and MET amplified NSCLC

[LINK TO ARTICLE](#)



Phase I/II Study of Capmatinib Plus Erlotinib in Patients With MET-Positive Non-Small-Cell Lung Cancer

Drug: capmatinib, erlotinib

Objective:

- To determine the safety and the recommended doses of capmatinib plus erlotinib in patients with MET-positive NSCLC, as well as preliminary effectiveness.

Design:

- Dose escalation phase followed by dose expansion phase
 - Dose escalation trial (phase I): Patients were treated with low doses first, then the dose was gradually increased with subsequent groups of patients. The goal is to try to find the highest dose that does not cause harmful side effects.
- Patients received capmatinib 100 – 600 mg twice daily with erlotinib 100 – 150 mg daily
 - Dose expansion (phase II - at recommended dose of capmatinib 400 mg twice daily plus erlotinib 150 mg daily):
- Cohort A: EGFR-mutated tumors resistant to erlotinib
- Cohort B: tumors with no EGFR mutations, erlotinib-naïve

Population (total of 35 patients):

- Advanced or metastatic NSCLC with measurable disease
- MET alterations, including increased MET copy number, increased MET expression, or MET exon 14 mutation

Effectiveness Results:

- Objective response occurred in 8 of 26 evaluable patients overall, including both dose escalation and dose expansion (ORR 31%)
 - In Cohort A (MET and EGFR-mutated, resistant to erlotinib): objective response in 4/8 patients
 - In Cohort B (MET altered, no EGFR mutation): objective response in 3/4 patients
- Erlotinib and capmatinib did not significantly change the drug levels of each other in the body

Safety Results:

- Most common side effects overall: acneiform rash (63%), fatigue (51%), nausea (46%), vomiting (37%), diarrhea (37%), and edema/swelling (37%)
 - When just looking at the patients who received a full dose of both drugs, rates of fatigue and nausea/vomiting were mildly higher
- Most common grade 3 (serious) side effects: anorexia (6%), increased lipase (6%), edema (56%)
- Dose modifications required for capmatinib, erlotinib, or both: 6/35, 5/35, and 4/35

Strengths:

- Gives valuable safety information for a frequently asked question – is it safe to add a targeted drug to a patient who develops a “targetable” resistance mutation?

Weaknesses:

- Erlotinib is no longer standard of care for EGFR-mutated tumors – this change happened during the study and limited ability to enroll patients. Most patients with EGFR mutations should now receive osimertinib, which is active against several mutations including T790M which are resistant to erlotinib. Some patients harbored T790M mutations in this study.
- Inclusion of patients with multiple different MET alterations makes it difficult to determine the impact of this drug combination in a specific MET alteration, given the small number of patients

Conclusion:

- Erlotinib and capmatinib can safely be combined at standard doses. The side effect profiles are as expected when the drugs are given together. Patients may need dose reductions.
- Patients with EGFR alterations who were resistant to erlotinib due to MET alteration seemed to benefit from the combination of erlotinib and capmatinib.
- It is unclear what benefit erlotinib provided in non-EGFR-mutated cases.
- Larger studies should be performed in a more selected population to better determine the effectiveness of this combination. Full doses of capmatinib and erlotinib could be used in such a study.

[LINK TO ARTICLE](#)



Prognosis and Concurrent Genomic Alterations in Patients With Advanced NSCLC Harboring MET Amplification or MET Exon 14 Skipping Mutation Treated With MET Inhibitor: A Retrospective Study

Drugs: crizotinib, bozitinib, volitinib

Objective:

- To explore the mutation profile of patients with METex14 skipping mutation or MET amplified NSCLC who are on MET tyrosine kinase inhibitor (TKI) therapy.

Design:

- Retrospective study of patients with MET amplification or METex14 skipping mutation
- MET TKIs prescribed included 250 mg crizotinib twice daily, 200 mg bozitinib twice daily or 600 mg volitinib once daily

Population:

- 43 patients with MET amplified NSCLC and 31 patients with METex14 NSCLC
- Median age of 56 in MET amplification and 61 in METex14 skipping cohorts
- Histology: MET amplification (adenocarcinoma-83.7%, SCC-16.3%), METex14 skipping (adenocarcinoma-83.9%, SCC-16.1%)
- 83.7% of patients with MET amplification and 90.3% of patients with METex14 skipping had stage IV disease

Effectiveness:

- No difference in progression free survival (PFS) and overall survival (OS) between intermediate and high MET amplification in patients receiving MET TKI therapy
- PFS was statistically shorter in the MET amplification cohort versus METex14 skipping mutation cohort

- MET amplification
 - Partial response: 34.5%
 - Stable disease: 48.3%
 - Progressive disease: 17.2%
 - ORR: 34.5% and disease control rate: 82.8%
- METex14 skipping mutation
 - Partial response: 51.7%
 - Stable disease: 34.5%
 - Progressive disease: 13.8%
 - ORR: 51.7% and disease control rate: 86.2%
- 60.5% of MET amplification cohort and 64.5% of METex14 skipping mutation cohort had other concurrent mutations

Strengths:

- One of the only retrospective studies that compares survival outcomes and concurrent mutations in NSCLC

Weaknesses:

- Retrospective study with incomplete clinical data

Conclusion:

- Patients with METex14 skipping mutation were found to have longer PFS than patients with MET amplification. While this study suggests that TP53 and PIK3CA mutations appear to play a large role in resistance and survival outcomes, larger prospective studies are still needed

[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

- [MET Exon 14 Skipping: A Case Study for the Detection of Genetic Variants in Cancer Driver Genes by Deep Learning International](#), Journal of Molecular Sciences, April 19th 2021
- [Discovery of amivantamab \(JNJ-61186372\), a bispecific antibody targeting EGFR and MET](#), Journal of Biological Chemistry, April 8th 2021
- [HIF-1 Inhibitor YC-1 Reverses the Acquired Resistance of EGFR-Mutant HCC827 Cell Line with MET Amplification to Gefitinib](#), Oxidative Medicine and Cellular Longevity, March 3rd 2021

Additional Readings

- [MET alterations are enriched in lung adenocarcinoma brain metastases and define a distinct molecular and transcriptomic subtype](#), American Association for Cancer Research, April 10th 2021
- [Tyrosine Kinase Inhibitors, Antibody-Drug Conjugates, and Proteolysis-Targeting Chimeras: The Pharmacology of Cutting-Edge Lung Cancer Therapies](#), American Society of Clinical Oncology, May 27th 2021
- [MET Exon 14 Skipping Mutations in Non-Small-Cell Lung Cancer: An Overview of Biology, Clinical Outcomes, and Testing Considerations](#), JCO Precision Oncology, April 13th 2021
- [Racial and socioeconomic disparities in lung cancer screening in the United States: A systematic review](#), American Cancer Society Journals, May 20th 2021
- [Oncogenic driver mutations in non-small cell lung cancer: Past, present and future](#), World Journal of Clinical Oncology, April 24th 2021
- [MET alterations and their impact on the future of non-small cell lung cancer \(NSCLC\) targeted therapies](#), Expert Opinion on Therapeutic Targets, April 30th 2021
- [A narrative review of MET inhibitors in non-small cell lung cancer with MET exon 14 skipping mutations](#), Translational Lung Cancer Research, March 10th 2021
- [Novel Therapies for Metastatic Non-Small Cell Lung Cancer with MET Exon 14 Alterations: A Spotlight on Capmatinib](#), Lung Cancer: Targets and Therapy, March 18th 2021
- [Capmatinib for patients with non-small cell lung cancer with MET exon 14 skipping mutations: A review of preclinical and clinical studies](#), Cancer Treatment Reviews, March 1st 2021
- [Anti-PD1/PD-L1 Immunotherapy for Non-Small Cell Lung Cancer with Actionable Oncogenic Driver Mutations](#), International Journal of Molecular Sciences, June 22nd 2021
- [Heterogeneity in MET-Aberrant NSCLC](#), International Association for the Study of Lung Cancer, April 1st 2021
- [When the MET receptor kicks in to resist targeted therapie](#), Oncogene, May 24th 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 August 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: NCT02920996

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

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

Status: **Active, Not Recruiting**

Drug: TalaMerestinib

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: **Active, Not Recruiting**

Drug: Tepotinib

Phase: P2

Countries: US, Austria, Belgium, France, Germany, Israel, Italy, Japan, Republic of Korea, Netherlands, Poland, Spain, Switzerland, Taiwan

NIH Identifier: NCT03175224

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

Title: APL-101 Study of Subjects With NSCLC With c-Met EXON 14 Skip Mutations and c-Met Dysregulation Advanced Solid Tumors (SPARTA)

Status: Recruiting

Drug: APL-101

Phase: P1/P2

Countries: US, Australia, Canada, Italy, Puerto Rico, Singapore, Spain, Taiwan, Ukraine, United Kingdom

NIH Identifier: NCT04258033

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

Title: A Study of PLB1001 in Non-small Cell Lung Cancer With c-Met Dysregulation

Status: Recruiting

Drug: PLB1001 also known as Bozitinib and APL-101

Phase: P2

Countries: China

NIH Identifier: 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: 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: 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: 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



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: **Completed**
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: **Active, Not Recruiting**
Drug: Glesatinib, 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 Spaltalizumab/Placebo in Advanced NSCLC Patients with MET Exon 14 Skipping Mutations
Status: Recruiting
Drug: Capmatinib + Spaltalizumab
Phase: P2
Countries: Belgium, France, Germany, Japan

NIH ID: NCT04139317

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

Title: Safety and Efficacy of Capmatinib (INC280) Plus Pembrolizumab vs Pembrolizumab Alone in NSCLC With PD-L1 ≥ 50%
Status: **Active, Not Recruiting**
Drug: Capmatinib + Pembrolizumab
Phase: P2
Countries: 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: Osimertinib + 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 + Osimertinib
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 (CHRYSLIS)
Status: Recruiting
Drug: Amivantamab
Phase: P1
Countries: US, Australia, Canada, China, France, Italy, Japan, Republic of Korea, Spain, Taiwan, United Kingdom

NIH Identifier: NCT03778229

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

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

NIH ID: NCT04606771

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

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

ANTIBODY-ADC TRIALS

NIH Identifier: NCT03539536

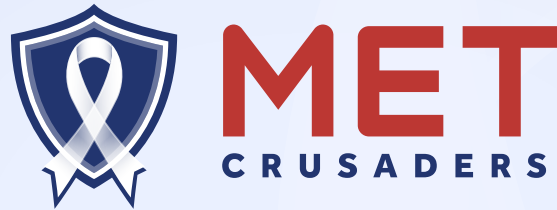
Link: <https://clinicaltrials.gov/ct2/show/NCT03539536>

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

NIH Identifier: NCT04077099

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

Title: REGN5093 in Patients With MET-Altered Advanced Non-Small Cell Lung Cancer
Status: Recruiting
Drug: REGN5093
Phase: P1, P2
Countries: US, Republic of Korea



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.

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Your comments and suggestions are always welcome.

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