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Osimertinib + Savolitinib in pts with EGFRm MET-Amplified/Overexpressed NSCLC: Phase Ib TATTON Parts B and D Final Analysis

Drugs: osimertinib, savolitinib | NCT02143466

Overview
- Final data from the expansion cohorts of the TATTON study
- Analyzing the combination of savolitinib (MET inhibitor) plus osimertinib (EGFR inhibitor) in overcoming MET-driven resistance to EGFR inhibitors in locally advanced or metastatic MET amplified or overexpressed EGFR-mutated NSCLC

Safety Results
- Grade ≥ 3 adverse events were experienced in 50-62% of patients
- Serious adverse events occurred in 38-49% of patients

Efficacy Results
- Overall response rate (ORR) varied from 33-67% and median PFS varied from 5.5-11.1 months depending on T790M status and history of treatment with a 3rd generation EGFR inhibitor.

Conclusion
- Safety of savolitinib combined with osimertinib is similar to what has been previously reported
- Efficacy outcomes suggest this combination may overcome MET-based resistance in patients with NSCLC who progressed on an EGFR inhibitor
- This combination is being explored further in the SAVANNAH (NCT03778229) and ORCHARD (NCT03944772) studies

Resistance to MET Inhibition in MET Driven NSCLC and Response after Switching from Type I to Type II MET Inhibitors

Drugs: crizotinib, cabozantinib

Overview
- The authors identified 7 patients with MET-driven NSCLC who were treated with type I MET inhibitors and assessed the expression of MET from tumor biopsies at baseline and progression
- Three patients had MET exon 14 skipping, 3 had MET amplification, 1 had KIF5B-MET fusion
- Identified both on- and off-target resistance mechanisms, including KRAS mutations, HER2 amplifications, and MET kinase domain p.D1246N and p.Y1248H mutations.

Results
- In one patient, both MET exon 14 skipping and the MET p.D1246N mutation was present at baseline (before the patient started crizotinib) as well as after the patient progressed on crizotinib
  ○ Patient was switched to type II MET inhibitor cabozantinib which resulted in progression
- Patient with KIF5B-MET fusion progressed on crizotinib and was found to have a MET p.Y1248H mutation
  ○ Patient was switched to cabozantinib with an initial response but subsequently progressed

Conclusion
- This highlights the need for further investigation into resistance mechanisms in patients with MET-driven NSCLC who progress on type I MET inhibitors
Tepotinib Safety in MET Exon 14 (METex14) Skipping NSCLC: Updated Results from the VISION Trial

Drug: tepotinib | NCT02864992

Overview
- Updated safety data from the VISION trial
- Analyzed tepotinib (MET inhibitor) in patients with advanced MET exon 14 skipping NSCLC

Safety Results
- Most common treatment-related adverse events (TRAEs) included peripheral edema, nausea, diarrhea, increased creatinine, and hypoalbuminemia
  - Majority of which were mild to moderate in severity
- Adverse events led to dose reduction in 27.8% of patients, treatment interruption in 35.3% of patients, and treatment discontinuation in 10.6% of patients
- Most common TRAE leading to treatment modification was peripheral edema
- Serious TRAEs (mostly pleural effusion or peripheral edema) were reported in 12.2% of patients
- Two patients had TRAEs that led to death (dyspnea and acute respiratory failure)

Activity of Tepotinib in Brain Metastases (BM): Preclinical and Clinical Data in MET Exon 14 (METex14) Skipping NSCLC

Drug: tepotinib | NCT02864992

Overview
- Researchers investigated tumor activity of tepotinib in preclinical models and patients with brain metastases and MET exon 14 skipping NSCLC in the VISION study
- Brain penetration of tepotinib was assessed in rats, and was found to have high binding in rat brain tissue
- Tumors in the patient-derived xenograft (PDX) models both regressed significantly

Efficacy Results
- A total of 21 patients with brain metastases in the VISION study received tepotinib
- Best overall response was a partial response in 52.4% of patients, which was similar to 45.2% in the overall population
- Median duration of response was 9.5 months
- Median progression-free survival was 9.5 months
- Tepotinib activity in brain metastases will continue to be assessed with brain scans in this cohort
**PD-L1 Expression and Efficacy of Immunotherapy in Japanese Patients with NSCLC Harboring MET Exon 14 Skipping Mutation**

**Drug:** immune checkpoint inhibitors

**Overview**
- Evaluated PD-L1 expression and how it relates to efficacy of immune checkpoint inhibitors (ICIs) in 23 patients with MET exon 14 skipping NSCLC

**Results**
- One patient had 0% PD-L1 expression, 6 patients had 1-49% PD-L1 expression, and 16 patients had more than 50% PD-L1 expression
- Seven of these patients received an ICI with an objective response rate (ORR) of 42.9%
- Early disease progression was observed in all patients within two months of initiating an ICI

**Neutrophil Counts Deregulated by C-met TKIs and the Variation Predicts Treatment Response in NSCLC**

**Drug:** MET inhibitors

**Overview**
- Investigated the theory that MET inhibitors impair neutrophil recruitment to the tumor, implying that measuring changes in circulating neutrophils could potentially correlate with treatment response

**Results**
- MET inhibitors deregulated absolute neutrophil counts in peripheral blood
- Variations in neutrophil count were not correlated with progression-free survival

**Conclusion**
- Circulating neutrophil counts may predict treatment response but do not impact survival outcomes

**Telisotuzumab Vedotin (ABBV 399, Teliso-V) Combined with Erlotinib**

**Drug:** telisotuzumab vedotin | NCT02099058

**Overview**
- Phase I trial that assessed the safety and efficacy of ABBV 399 with erlotinib (EGFR inhibitor) in patients with MET exon 14 skipping/MET amplified and EGFR-mutated metastatic NSCLC

**Safety Results**
- Most common adverse events included peripheral neuropathy (52%), rash (38%), diarrhea (38%), fatigue (31%), shortness of breath (31%), and low albumin (31%)

**Efficacy Results**
- Objective response rate (ORR) was 34.5%

**Conclusion**
- Results suggest the combination of ABBV 399 and erlotinib has promising antitumor activity with a tolerable safety profile
Telisotuzumab Vedotin (ABBV 399, Teliso-V) Monotherapy

Drug: telisotuzumab vedotin | NCT02099058

Overview
- Phase I trial that assessed the safety and efficacy of ABBV 399, an antibody drug conjugate (ADC) that combines an anti-MET monoclonal antibody with a cytotoxic chemotherapy molecule (MMAE), in patients with MET-driven NSCLC

Safety Results
- Most common treatment-related adverse events (TRAEs) included fatigue (25%), nausea (23%), neuropathy (15%), decreased appetite (13%), vomiting (13%), and diarrhea (10%)

Efficacy Results
- Eight patients experienced a grade 3 or higher adverse event including fatigue, low albumin, anemia, and neutropenia
- No treatment-related deaths were reported

First-in-human (FIH) study of SCC244, a novel potent and highly selective c-MET inhibitor, in patients (pts) with advanced non-small cell lung cancer (NSCLC)

Drug: SCC244 | NCT03466268

Overview
- Results of the first-in-human phase I study of a new MET inhibitor SCC244 in 19 patients with advanced NSCLC (enrolled regardless of MET status)

Safety Results
- Most common treatment-related adverse events (TRAEs) included peripheral edema (36.8%), decreased appetite (36.8%), headache (31.6%), dizziness (31.6%), nausea/vomiting (31.6%), increased bilirubin (26.3%), and weakness (26.3%)

Efficacy Results
- In 17 evaluable patients, two patients experienced a partial response (PR) with a duration of response from 7.3 to 11.1 months
- One of these patients had MET exon 14 skipping, and the other patient had MET amplification

Conclusion
- This study showed a manageable safety profile and antitumor activity of SCC244. SCC244 is being studied further in patients with MET exon 14 skipping NSCLC
**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 April 28, 2021.

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**TKI TRIALS**

**NIH Identifier: NCT04084717**
Link: [https://clinicaltrials.gov/ct2/show/NCT04084717](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](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: NCT02864992**
Link: [https://clinicaltrials.gov/ct2/show/NCT02864992](https://clinicaltrials.gov/ct2/show/NCT02864992)
Title: A Study of Crizotinib for ROS1 and MET Activated Lung Cancer
Status: Recruiting
Drug: Crizotinib
Phase: P2
Countries: Canada

**NIH Identifier: NCT03993873**
Link: [https://clinicaltrials.gov/ct2/show/NCT03993873](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: NCT02684992**
Link: [https://clinicaltrials.gov/ct2/show/NCT02684992](https://clinicaltrials.gov/ct2/show/NCT02684992)
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, Netherlands, Poland, Spain, Switzerland, Taiwan

**NIH Identifier: NCT03175224**
Link: [https://clinicaltrials.gov/ct2/show/NCT03175224](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, Argentina, Australia, Canada, Italy, Puerto Rico, Singapore, Spain, Taiwan, Ukraine, United Kingdom

**NIH Identifier: NCT04258033**
Link: [https://clinicaltrials.gov/ct2/show/NCT04258033](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](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: NCT02414139**
Link: [https://clinicaltrials.gov/ct2/show/NCT02414139](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

**NIH Identifier: NCT01639508**
Link: [https://clinicaltrials.gov/ct2/show/NCT01639508](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: P1
Countries: US

**NIH Identifier: NCT00219711**
Link: [https://clinicaltrials.gov/ct2/show/NCT00219711](https://clinicaltrials.gov/ct2/show/NCT00219711)
Title: Phase 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](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](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](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](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](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](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](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 + Cabozantinib  
**Phase:** P2  
**Countries:** US, Australia, France, Germany, Italy, Netherlands, Singapore, Spain, Switzerland

**NIH Identifier:** NCT03983954  
Link: [https://clinicaltrials.gov/ct2/show/NCT03983954](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](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 Identifier:** NCT02954991  
Link: [https://clinicaltrials.gov/ct2/show/NCT02954991](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 Identifier:** NCT04323436  
Link: [https://clinicaltrials.gov/ct2/show/NCT04323436](https://clinicaltrials.gov/ct2/show/NCT04323436)  
**Title:** Study of Capmatinib and Sunitizumab/Placebo in Advanced NSCLC Patients with MET Exon 14 Skipping Mutations  
**Status:** Recruiting  
**Drug:** Capmatinib + Sunitizumab  
**Phase:** P2  
**Countries:** Belgium, France, Germany, Japan

**NIH Identifier:** NCT01911507  
Link: [https://clinicaltrials.gov/ct2/show/NCT01911507](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

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<td>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)</td>
<td>Title: Study of Amivantamab, a Human Bispecific EGFR and cMet Antibody, in Participants with Advanced Non-Small Cell Lung Cancer (CHRYSALIS)</td>
<td>Title: Osimertinib Plus Savolitinib in EGFRm+/MET+ NSCLC Following Prior Osimertinib (SAVANNAH)</td>
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## ANTIBODY-ADC TRIALS

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<td>Title: REGN5093 in Patients With MET-Altered Advanced Non-Small Cell Lung Cancer</td>
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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 improve 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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Your comments and suggestions are always welcome.