MET CRUSADERS

Your resource for the latest research into the MET alteration.

CRUSADER NEWSLETTER

ESMO, TARGETED THERAPIES, ASCO 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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In this edition

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

LINK TO ARTICLE

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

LINK TO ARTICLE

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)

LINK TO ARTICLE

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

LINK TO ARTICLE

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

LINK TO ARTICLE

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

LINK TO ARTICLE

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

LINK TO ARTICLE

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

Efficacy Results

- Of the 16 patients who were treated, 3 patients had a partial response (PR)
- Mediation duration of response was 4.8 months
- Median progression-free survival (PFS) was 5.7 months

LINK TO ARTICLE

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

LINK TO ARTICLE

MET Clinical Trials

IMPORTANT

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

This list was last updated on April 28, 2021.

TKI TRIALS

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

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

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

NIH Identifier: NCT02864992
Link: https://clinicaltrials.gov/ct2/show/NCT02864992
Title: Tepotinib Phase II in Non-small Cell Lung Cancer (NSCLC) Harboring MET Alterations (VISION)
Status: Recruiting
Drug: Tepotinib
Phase: P2
Countries: US, Austria, Belgium, France, Germany, Israel, Italy, Japan, Republic of Korea, Netherland, Poland, Spain, Switzerland, Taiwan

NIH Identifier: NCT03175224
Link: https://clinicaltrials.gov/ct2/show/NCT03175224
Title: APL-101 Study of Subjects With NSCLC With c-Met EXON 14 Skip Mutations and c-Met Dysregulation Advanced Solid Tumors (SPARTA)
Status: Recruiting
Drug: APL-101
Phase: P1/P2
Countries: US, Australia, Canada, Italy, Puerto Rico, Singapore, Spain, Taiwan, Ukraine, United Kingdom

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

NIH Identifier: NCT02750215
Link: https://clinicaltrials.gov/ct2/show/NCT02750215
Title: A Study of Capmatinib (INC280) in NSCLC Patients With MET Exon 14 Alterations Who Have Received Prior MET Inhibitor
Status: Active, Not Recruiting
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: 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
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

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, Quam, 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: Glestatinib, Sitravastinib or Mocetinostat + Nivolumab
Phase: P2
Countries: US

NIH ID: NCT03666143
Link: https://clinicaltrials.gov/ct2/show/NCT03666143
Title: A Phase 1b Study to Assess Sitravatinib in Combination with Tislelizumab in Patients With Advanced Solid Tumors.
Status: Recruiting
Drug: Sitravatinib + Tislelizumab
Phase: P1
Countries: Australia, China

NIH ID: NCT04323436
Link: https://clinicaltrials.gov/ct2/show/NCT04323436
Title: Study of Capmatinib and Spartalizumab/Placebo in Advanced NSCLC Patients with MET Exon 14 Skipping Mutations
Status: Recruiting
Drug: Capmatinib + Spartalizumab
Phase: P2
Countries: Belgium, France, Germany, Japan

NIH ID: NCT04139317
Link: https://clinicaltrials.gov/ct2/show/NCT04139317
Title: Safety and Efficacy of Capmatinib (INC280) Plus Pembrolizumab vs Pembrolizumab Alone in NSCLC With PD-L1≥ 50%
Status: 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: Osmeritinib + 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 + Osmeritinib
Phase: P2
Countries: US, Belgium, China, France, Germany, Hong Kong, Japan, Republic of Korea, Malaysia, Netherlands, Russia, Singapore, Spain, Taiwan, Thailand, Vietnam

NIH Identifier: NCT02609776
Link: https://clinicaltrials.gov/ct2/show/NCT02609776
Title: Study of Amivantamab, a Human Bispecific EGFR and cMet Antibody, in Participants with Advanced Non-Small Cell Lung Cancer (CHRYSALIS)
Status: Recruiting
Drug: Amivantimab
Phase: P1
Countries: US, Australia, Canada, China, France, Italy, Japan, Republic of Korea, Spain, Taiwan, United Kingdom

NIH Identifier: NCT03778229
Link: https://www.clinicaltrials.gov/ct2/show/NCT03778229
Title: Osimertinib Plus Savolitinib in EGFRm+/MET+ NSCLC Following Prior Osimertinib (SAVANNAH)
Status: Recruiting
Drug: Osmeritinib + Salvotinib
Phase: P2
Countries: US, Brazil, Canada, Chile, Denmark, France, India, Israel, Italy, Japan, Republic of Korea, Spain, Taiwan, Vietnam

NIH 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

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

MET CRUSADERS

The MET Crusader newsletter is written for the benefit of MET patients, caregivers, clinicians and researchers. It contains an outlined summary of MET related abstracts, posters and articles. The outline summaries 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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