



# BioDSA Analysis Report

Report Generated:	2026-01-25 16:23:49
Total Iterations:	27
Code Executions:	0
Artifacts Generated:	0

## User Query

Please find clinical trials for this patient:

58-year-old female with metastatic NSCLC (adenocarcinoma).

EGFR mutation positive (exon 19 deletion).

Previously treated with erlotinib with progression after 14 months.

ECOG PS 1. No brain metastases.

# Agent Exploration Process

The following shows the agent's reasoning and exploration process. Code blocks are truncated for readability - full implementations are in the Supplementary Materials section.

## Step 2: AI

Tool call: clinical\_trial\_search

Tool call input: {'conditions': 'Non-Small Cell Lung Cancer', 'required\_mutations': 'EGFR', 'terms': 'exon 19 deletion, metastatic, adenocarcinoma', 'prior\_therapies': 'erlotinib, EGFR TKI', 'age\_group': 'ADULT', 'recruiting\_status': 'OPEN', 'page\_size': 100}

Tool call: clinical\_trial\_search

Tool call input: {'conditions': 'Non-Small Cell Lung Cancer', 'interventions': 'osimertinib', 'required\_mutations': 'EGFR', 'age\_group': 'ADULT', 'recruiting\_status': 'OPEN', 'page\_size': 100}

Tool call: clinical\_trial\_search

Tool call input: {'conditions': 'Non-Small Cell Lung Cancer', 'interventions': 'amivantamab,lazertinib', 'required\_mutations': 'EGFR', 'age\_group': 'ADULT', 'recruiting\_status': 'OPEN', 'page\_size': 100}

Tool call: clinical\_trial\_search

Tool call input: {'conditions': 'Non-Small Cell Lung Cancer', 'interventions': 'patritumab deruxtecán,HER3-DXd,U3-1402', 'required\_mutations': 'EGFR', 'age\_group': 'ADULT', 'recruiting\_status': 'OPEN', 'page\_size': 100}

Tool call: clinical\_trial\_search

Tool call input: {'conditions': 'Non-Small Cell Lung Cancer', 'interventions': 'savolitinib,tepotinib,capmatinib', 'terms': 'osimertinib combination, MET inhibitor', 'required\_mutations': 'EGFR', 'age\_group': 'ADULT', 'recruiting\_status': 'OPEN', 'page\_size': 100}

Tool call: clinical\_trial\_search

Tool call input: {'conditions': 'Non-Small Cell Lung Cancer', 'interventions': 'BLU-945,BLU-701,BBT-176', 'required\_mutations': 'EGFR', 'age\_group': 'ADULT', 'recruiting\_status': 'OPEN', 'page\_size': 100}

## Step 3: TOOL

# Clinical Trial Search Results

\*\*Total trials found:\*\* 10

\*\*Returned in this batch:\*\* 10

## Trial List:

### 1. NCT07310589

\*\*Title:\*\* Effects of a Visual Interactive LINE Chatbot on Self-Management of EGFR-TKI Related Side Effects in Patients With Lung Cancer

\*\*Status:\*\* NOT\_YET\_RECRUITING

\*\*Phase:\*\* NA

\*\*Conditions:\*\* Non-Small Cell Lung Cancer

**\*\*Interventions:\*\*** Visual-Interactive LINE Chatbot  
**\*\*URL:\*\*** <https://clinicaltrials.gov/ct2/show/NCT07310589>  
**###** 2. NCT03260491  
**\*\*Title:\*\*** U3-1402 in Metastatic or Unresectable Non-Small Cell Lung Cancer  
**\*\*Status:\*\*** RECRUITING  
**\*\*Phase:\*\*** PHASE1  
**\*\*Conditions:\*\*** Non-Small Cell Lung Cancer (NSCLC)  
**\*\*Interventions:\*\*** HER3-DXd (FL-DP)|HER3-DXd (CTM-1 Lyo-DP)|HER3-DXd (CTM-3 Lyo-DP)

## Step 4: TOOL

# Clinical Trial Search Results

**\*\*Total trials found:\*\*** 90

**\*\*Returned in this batch:\*\*** 90

## Trial List:

**###** 1. NCT07315113

**\*\*Title:\*\*** Study of NXP900 With Osimertinib in Subjects With Advanced, EGFR-Mutated Non-Small Cell Lung Cancer

**\*\*Status:\*\*** RECRUITING

**\*\*Phase:\*\*** PHASE1

**\*\*Conditions:\*\*** EGFR Mutation Positive Non-small Cell Lung Cancer|EGFR Mutated Non-small Cell Lung Cancer Patients

**\*\*Interventions:\*\*** NXP900|Osimertinib

**\*\*URL:\*\*** <https://clinicaltrials.gov/ct2/show/NCT07315113>

**###** 2. NCT04401059

**\*\*Title:\*\*** Synergistic Effect of Elemene Plus TKIs Compared With TKIs in EGFR-mutated Advanced NSCLC■Prospective Study

**\*\*Status:\*\*** RECRUITING

**\*\*Phase:\*\*** PHASE4

**\*\*Conditions:\*\*** Carcinoma|Non-Small-Cell Lung Cancer|Adenocarcinoma

**\*\*Interventions:\*\*** Elemene plus first or third generation EGFR-TKIs|First or third generation EGFR-TKIs

## Step 5: TOOL

# Clinical Trial Search Results

**\*\*Total trials found:\*\*** 12

**\*\*Returned in this batch:\*\*** 12

## Trial List:

**###** 1. NCT05469022

**\*\*Title:\*\*** Neoadjuvant Lazertinib Therapy in EGFR-Mutation Positive Lung Adenocarcinoma Detected by BALF Liquid Biopsy

**\*\*Status:\*\*** RECRUITING

**\*\*Phase:\*\*** PHASE2

**\*\*Conditions:\*\*** Non Small Cell Lung Cancer

**\*\*Interventions:\*\*** Neoadjuvant lazertinib

**\*\*URL:\*\*** <https://clinicaltrials.gov/ct2/show/NCT05469022>

### 2. NCT07227025

**\*\*Title:\*\*** A Study of Amivantamab and Olomorasib Combination Therapy in Participants With Metastatic Non-Small Cell Lung Cancer

**\*\*Status:\*\*** RECRUITING

**\*\*Phase:\*\*** PHASE1|PHASE2

**\*\*Conditions:\*\*** Carcinoma, Non-Small-Cell Lung

**\*\*Interventions:\*\*** Amivantamab|Olomorasib

## Step 6: TOOL

# Clinical Trial Search Results

**\*\*Total trials found:\*\*** 4

**\*\*Returned in this batch:\*\*** 4

## Trial List:

### 1. NCT03260491

**\*\*Title:\*\*** U3-1402 in Metastatic or Unresectable Non-Small Cell Lung Cancer

**\*\*Status:\*\*** RECRUITING

**\*\*Phase:\*\*** PHASE1

**\*\*Conditions:\*\*** Non-Small Cell Lung Cancer (NSCLC)

**\*\*Interventions:\*\*** HER3-DXd (FL-DP)|HER3-DXd (CTM-1 Lyo-DP)|HER3-DXd (CTM-3 Lyo-DP)

**\*\*URL:\*\*** <https://clinicaltrials.gov/ct2/show/NCT03260491>

### 2. NCT06172478

**\*\*Title:\*\*** A Study of HER3-DXd in Subjects With Locally Advanced or Metastatic Solid Tumors

**\*\*Status:\*\*** RECRUITING

**\*\*Phase:\*\*** PHASE2

**\*\*Conditions:\*\*** Advanced Solid Tumor|Melanoma|Head and Neck Cancer|Gastric Cancer|Ovarian Carcinoma|Cervical Cancer|Endometrial Cancer|Bladder Cancer|Esophageal Cancer|Pancreatic Carcinoma|Prostate Cancer|Non-small Cell Lung Cancer (NSCLC)|Lung Cancer|Breast Cancer

**\*\*Interventions:\*\*** HER3-DXd

## Step 7: TOOL

# Clinical Trial Search Results

**\*\*Total trials found:\*\* 5**

**\*\*Returned in this batch:\*\* 5**

**## Trial List:**

**### 1. NCT04322578**

**\*\*Title:\*\* Crizotinib or Standard Chemotherapy in Met Exon 14 Skipping Advanced NSCLC**

**\*\*Status:\*\* RECRUITING**

**\*\*Phase:\*\* PHASE2**

**\*\*Conditions:\*\* Non-small Cell Lung Cancer**

**\*\*Interventions:\*\* Crizotinib|Pemetrexed**

**\*\*URL:\*\* <https://clinicaltrials.gov/ct2/show/NCT04322578>**

**### 2. NCT05261399**

**\*\*Title:\*\* Savolitinib Plus Osimertinib Versus Platinum-based Doublet Chemotherapy in Participants With Non-Small Cell Lung Cancer Who Have Progressed on Osimertinib Treatment**

**\*\*Status:\*\* RECRUITING**

**\*\*Phase:\*\* PHASE3**

**\*\*Conditions:\*\* Carcinoma|Non-Small-Cell Lung**

**\*\*Interventions:\*\* Savolitinib|Osimertinib|Pemetrexed|Cisplatin|Carboplatin**

## Step 8: TOOL

Error searching clinical trials: 'str' object has no attribute 'columns'

## Step 9: AI

Tool call: clinical\_trial\_search

Tool call input: {'terms': 'BLU-945', 'recruiting\_status': 'OPEN', 'page\_size': 100}

## Step 10: TOOL

Error searching clinical trials: 'str' object has no attribute 'columns'

## Step 11: AI

1) Extracted patient information

- Demographics: 58-year-old female
- Primary diagnosis: Metastatic non-small cell lung cancer (NSCLC), adenocarcinoma
- Biomarker/genetics: EGFR mutation positive, exon 19 deletion
- Prior treatment: Erlotinib (first-generation EGFR TKI); disease progression after 14 months
- Disease status: Metastatic; no brain metastases reported
- Performance status: ECOG 1

- Comorbidities: Not reported
- Current medications: Not reported
- Key lab values: Not reported

Clinical context notes:

- The patient is EGFR-mutant (exon 19 del) and has progressed on a prior EGFR TKI (erlotinib). She has not received osimertinib per the note.
- Many contemporary trials in EGFR-mutant NSCLC include agents such as osimertinib (alone or in combination), amivantamab ± lazertinib, patritumab deruxtecan (HER3-DXd), various next-generation EGFR TKIs, and MET-directed combinations. Basket/umbrella trials may enroll biomarker-defined subgroups (e.g., HER3, MET amplification).

2) Search queries used

- Conditions: "Non-Small Cell Lung Cancer"

## Step 12: AI

Tool call: get\_trial\_details

Tool call input: {'trial\_ids': 'NCT03260491,NCT06172478,NCT05498428,NCT04762199,NCT04772235,NCT06417814,NCT04410796,NCT05642572,NCT03586453'}

Tool call: get\_trial\_details

Tool call input: {'trial\_ids': 'NCT06116682,NCT07058519,NCT04181060'}

## Step 13: TOOL

# Detailed Trial Information

**\*\*Trials retrieved:\*\* 9**

**## NCT06417814: A Study to Investigate the Efficacy and Safety of Dato-DXd With or Without Osimertinib Compared With Platinum Based Doublet Chemotherapy in Participants With EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer**

**\*\*Status:\*\* RECRUITING**

**\*\*Phase:\*\* PHASE3**

**\*\*Study Type:\*\* INTERVENTIONAL**

**\*\*Enrollment:\*\* 744**

**\*\*Conditions:\*\* Metastatic Non-small Cell Lung Cancer**

**\*\*Interventions:\*\* Dato-DXd|Osimertinib|Pemetrexed|Carboplatin|Cisplatin**

**### Brief Summary:**

This study will assess the effect of Dato-DXd in combination with osimertinib or Dato-DXd monotherapy versus platinum-based doublet chemotherapy in terms of progression-free survival (PFS).

**### Eligibility Criteria:**

**Inclusion Criteria:**

- \* Histologically or cytologically confirmed non-squamous NSCLC.

## Step 14: TOOL

# Detailed Trial Information

\*\*Trials retrieved:\*\* 3

## NCT07058519: A Study of Osimertinib-based Adaptive Treatment Guided by ctDNA EGFRm+ Monitoring in NSCLC

\*\*Status:\*\* RECRUITING

\*\*Phase:\*\* PHASE2

\*\*Study Type:\*\* INTERVENTIONAL

\*\*Enrollment:\*\* 250

\*\*Conditions:\*\* Locally Advanced or Metastatic EGFRm Non-small Cell Lung Cancer (NSCLC)

\*\*Interventions:\*\* Osimertinib-based adaptive treatment|Osimertinib 80 MG

### Brief Summary:

The goal of this adaptive, interventional study is to assess the efficacy and safety of osimertinib-based adaptive treatment based on ctDNA dynamic monitoring in locally advanced or metastatic EGFRm NSCLC participants with ctDNA EGFRm clearance after osimertinib plus chemotherapy. The main questions it aims to answer are: 1) PFS during adaptive treatment period in Cohort 1 defined as from initiation of Osimertinib in adaptive period to progression per investigator assessment; 2) Time from initiation of osimertinib in adaptive period to first ctDNA EGFRm relapse or death

### Eligibility Criteria:

Inclusion Criteria:

1. Provision of signed and dated, written informed consent form (ICF) prior to any study specific procedures.

## Step 15: AI

Tool call: evaluate\_eligibility

Tool call input: {'patient\_summary': '58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases; organ function/labs not reported; no known interstitial lung disease; no known cardiovascular contraindications.', 'eligibility\_criteria': 'Inclusion Criteria for both Dose Escalation and Dose Expansion:\n1. Has locally advanced or metastatic NSCLC, not amenable to curative surgery or radiation\n2. Has at least one measurable lesion per RECIST version 1.1\n3. Has Eastern Cooperative Oncology Group performance status of 0 or 1 at Screening\n\nInclusion Criteria for Dose Escalation only:\n1. Has histologically or cytologically documented adenocarcinoma NSCLC\n2. Has acquired resistance to EGFR TKI according to the Jackman criteria\n3. Is currently receiving and able to discontinue erlotinib, gefitinib, afatinib, or osimertinib\n4. Has been receiving erlotinib, gefitinib, afatinib, or osimertinib for at least 6 weeks with well-controlled related toxicities less than Grade 3 in severity at the time of Screening\n5. Has radiological documentation of disease progression while receiving continuous treatment with erlotinib, gefitinib, afatinib, or osimertinib\n6. Is willing to provide archival tumor tissue from a biopsy performed within 6 months of progression during treatment with erlotinib, gefitinib, afatinib, or osimertinib OR has at least one lesion, not previously irradiated, amenable to core biopsy and is willing to undergo screening tumor biopsy\n7. Demonstrates absence of EGFR T790M mutation if treated with erlotinib, gefitinib, or afatinib. No EGFR mutation testing is required if treated with osimertinib.\n\nInclusion Criteria for all cohorts of Dose Expansion only:\n1. Has received systemic therapy for locally advanced or metastatic disease including at least 1 platinum-based chemotherapy regimen\n2. Has documented radiological disease progression during/after most recent treatment regimen for locally-advanced or metastatic disease\n3. For Cohorts 1, 2, 3a, and 3b: Is willing to provide archival tumor tissue from a biopsy performed within 6 months of consent and performed after progression during/after treatment with most recent cancer therapy regimen OR has at least 1 lesion, not previously irradiated, amenable to core biopsy and is

willing to undergo tumor biopsy.\n\nInclusion Criteria specific to Cohorts 1, 3a, 3b, and 4 of Dose Expansion:\n2. Has documentation of radiological disease progression following one or more lines of EGFR TKI treatment. Participants with EGFR T790M mutation following treatment with erlotinib, gefitinib afatinib, or dacomitinib must have received and have documentation of radiological disease progression following treatment with osimertinib unless unable or unwilling.\n3. Has documentation of EGFR-activating mutation(s) detected from tumor tissue: G719X, exon deletion 19, L858R, or L861Q.\n\nKey Exclusion:\n- Clinically active CNS metastases; history of ILD/pneumonitis; significant cardiac issues; QTcF >470 ms females/>450 ms males; corneal disease.\n- For Cohort 2, EGFR-activating mutations are excluded.\n', 'trial\_id': 'NCT03260491'}

Tool call: evaluate\_eligibility

Tool call input: {'patient\_summary': '58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases; organ function/labs not reported; no known interstitial lung disease; no known cardiovascular contraindications.', 'eligibility\_criteria': 'Inclusion Criteria (excerpt):\n- Age  $\geq 18$ ; metastatic non-squamous NSCLC not amenable to curative treatment.\n- EGFR activating mutation (including exon 18, 19, 21, and T790M) locally diagnosed; central confirmation performed.\n- ECOG PS 0-1.\n- Measurable disease (RECIST 1.1).\n- Part B expansion cohorts include:\n \* Progression following first/second generation EGFR TKI regardless of T790M status.\n \* Progression following osimertinib with no evidence of C797S or MET amplification.\n- Adequate organ function; ability to provide recent tumor tissue (within 60 days prior to start).\n- Asymptomatic CNS metastases allowed.\n\nKey Exclusion:\n- Prior repotrectinib; other lung histologies; EGFR exon 20 insertion; significant cardiovascular disease; QTc >470 msec; active infections; ILD/pneumonitis; strong CYP3A inhibitors/inducers.\n', 'trial\_id': 'NCT04772235'}

Tool call: evaluate\_eligibility

Tool call input: {'patient\_summary': '58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases; organ function/labs not reported; no known interstitial lung disease; no known cardiovascular contraindications.', 'eligibility\_criteria': 'Inclusion:\n- Metastatic NSCLC with activating EGFR mutation (including exon 19 and 21).\n- ECOG 0-2.\n- Measurable disease for expansion cohort.\n- Dose Expansion Cohort B (EGFR TKI resistant): Have progression of disease on osimertinib, erlotinib, gefitinib or afatinib as last previous systemic treatment; if not previously treated with osimertinib, must be EGFR-T790M negative prior to study treatment.\n\nExclusion:\n- Chemo/radiotherapy within 4 weeks; unresolved  $\geq$  grade 2 toxicities; symptomatic untreated brain mets; history of ILD/pneumonitis; QTc >500 msec; keratitis; significant cardiac disease; inhibitors/inducers of CYP enzymes; pregnancy; HIV on ART; retinitis pigmentosa; specific T1D risk criteria.\n', 'trial\_id': 'NCT04762199'}

Tool call: evaluate\_eligibility

Tool call input: {'patient\_summary': '58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.', 'eligibility\_criteria': 'Inclusion (cohort-based):\n- Advanced/metastatic NSCLC; various cohorts.\n- Cohorts 1/5/6: no prior systemic therapy (first-line) with EGFR Ex19del/L858R; Cohort 2: EGFR Ex20ins; Cohorts 3/3b: must have progressed on or after osimertinib monotherapy as most recent line; Cohort 7: progressed on amivantamab+lazertinib.\n- ECOG 0-1; measurable disease.\n\nExclusion:\n- ILD/pneumonitis; significant cardiovascular disease; QTcF >480 msec; symptomatic brain metastases; strong CYP3A inducers for lazertinib-containing cohorts; hypersensitivity to product excipients.\n', 'trial\_id': 'NCT05498428'}

Tool call: evaluate\_eligibility

Tool call input: {'patient\_summary': '58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.', 'eligibility\_criteria': 'Inclusion:\n- Metastatic NSCLC with EGFR sensitizing mutation.\n- Documented extracranial progression on prior osimertinib monotherapy as most recent line.\n-  $\leq 2$  prior lines of EGFR TKIs; osimertinib is only permitted prior third-generation TKI.\n- ECOG 0-1; measurable disease; adequate organ function.\n\nExclusion:\n- Prior anti-cancer therapy in metastatic setting (other than osimertinib); ILD/pneumonitis; symptomatic brain mets; significant corneal disease; uncontrolled infection.\n', 'trial\_id': 'NCT06417814'}



Tool call: evaluate\_eligibility

Tool call input: {'patient\_summary': '58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.', 'eligibility\_criteria': 'Inclusion:\n- Metastatic NSCLC EGFR-mutant; first-line treatment setting. Either untreated or started osimertinib within a short window.\n- No prior systemic therapy for metastatic disease; no prior EGFR TKI except first-line osimertinib within defined window.\n- ECOG/KPS  $\geq 70\%$ ; measurable disease; adequate organ function.\n\nExclusion:\n- Prior EGFR targeted therapy (except first-line osimertinib in specific timing); prior systemic metastatic therapy; ILD/pneumonitis; significant cardiac/QTc issues.\n', 'trial\_id': 'NCT04410796'}

## Step 16: TOOL

# Eligibility Evaluation for NCT03260491

## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases; organ function/labs not reported; no known interstitial lung disease; no known cardiovascular contraindications.

## Trial Eligibility Criteria:

Inclusion Criteria for both Dose Escalation and Dose Expansion:

1. Has locally advanced or metastatic NSCLC, not amenable to curative surgery or radiation
2. Has at least one measurable lesion per RECIST version 1.1
3. Has Eastern Cooperative Oncology Group performance status of 0 or 1 at Screening

Inclusion Criteria for Dose Escalation only:

1. Has histologically or cytologically documented adenocarcinoma NSCLC
2. Has acquired resistance to EGFR TKI according to the Jackman criteria
3. Is currently receiving and able to discontinue erlotinib, gefitinib, afatinib, or osimertinib
4. Has been receiving erlotinib, gefitinib, afatinib, or osimertinib for at least 6 weeks with well-controlled related toxicities less than Grade 3 in severity at the time of Screening
5. Has radiological documentation of disease progression while receiving continuous treatment with erlotinib, gefitinib, afatinib, or osimertinib
6. Is willing to provide archival tumor tissue from a biopsy performed within 6 months of progression during treatment with erlotinib, gefitinib, afatinib, or osimertinib OR has at least one lesion, not previously irradiated, amenable to core biopsy and is willing to undergo screening tumor biopsy
7. Demonstrates absence of EGFR T790M mutation if treated with erlotinib, gefitinib, or afatinib. No EGFR mutation testing is required if treated with osimertinib.

## Step 17: TOOL

# Eligibility Evaluation for NCT04772235

## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases; organ function/labs not reported; no known interstitial lung disease; no known cardiovascular contraindications.

## Trial Eligibility Criteria:

#### Inclusion Criteria (excerpt):

- Age  $\geq 18$ ; metastatic non-squamous NSCLC not amenable to curative treatment.
- EGFR activating mutation (including exon 18, 19, 21, and T790M) locally diagnosed; central confirmation performed.
- ECOG PS 0-1.
- Measurable disease (RECIST 1.1).
- Part B expansion cohorts include:
  - \* Progression following first/second generation EGFR TKI regardless of T790M status.
  - \* Progression following osimertinib with no evidence of C797S or MET amplification.
- Adequate organ function; ability to provide recent tumor tissue (within 60 days prior to start).
- Asymptomatic CNS metastases allowed.

#### Key Exclusion:

- Prior repotrectinib; other lung histologies; EGFR exon 20 insertion; significant cardiovascular disease; QTc  $> 470$  msec; active infections; ILD/pneumonitis; strong CYP3A inhibitors/inducers.

### Step 18: TOOL

# Eligibility Evaluation for NCT04762199

#### ## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases; organ function/labs not reported; no known interstitial lung disease; no known cardiovascular contraindications.

#### ## Trial Eligibility Criteria:

##### Inclusion:

- Metastatic NSCLC with activating EGFR mutation (including exon 19 and 21).
- ECOG 0-2.
- Measurable disease for expansion cohort.
- Dose Expansion Cohort B (EGFR TKI resistant): Have progression of disease on osimertinib, erlotinib, gefitinib or afatinib as last previous systemic treatment; if not previously treated with osimertinib, must be EGFR-T790M negative prior to study treatment.

##### Exclusion:

- Chemo/radiotherapy within 4 weeks; unresolved  $\geq$  grade 2 toxicities; symptomatic untreated brain mets; history of ILD/pneumonitis; QTc  $> 500$  msec; keratitis; significant cardiac disease; inhibitors/inducers of CYP enzymes; pregnancy; HIV on ART; retinitis pigmentosa; specific T1D risk criteria.

#### ## Evaluation Framework:

##### ### Step 1: Inclusion Criteria Checklist

### Step 19: TOOL

# Eligibility Evaluation for NCT05498428

#### ## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.

#### ## Trial Eligibility Criteria:

##### Inclusion (cohort-based):

- Advanced/metastatic NSCLC; various cohorts.
- Cohorts 1/5/6: no prior systemic therapy (first-line) with EGFR Ex19del/L858R; Cohort 2: EGFR Ex20ins; Cohorts 3/3b: must have progressed on or after osimertinib monotherapy as most recent line; Cohort 7: progressed on amivantamab+lazertinib.
- ECOG 0-1; measurable disease.

##### Exclusion:

- ILD/pneumonitis; significant cardiovascular disease; QTcF >480 msec; symptomatic brain metastases; strong CYP3A inducers for lazertinib-containing cohorts; hypersensitivity to product excipients.

#### ## Evaluation Framework:

##### ### Step 1: Inclusion Criteria Checklist

For each inclusion criterion, assess:

## Step 20: TOOL

### # Eligibility Evaluation for NCT06417814

#### ## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.

#### ## Trial Eligibility Criteria:

##### Inclusion:

- Metastatic NSCLC with EGFR sensitizing mutation.
- Documented extracranial progression on prior osimertinib monotherapy as most recent line.
- ≤2 prior lines of EGFR TKIs; osimertinib is only permitted prior third-generation TKI.
- ECOG 0-1; measurable disease; adequate organ function.

##### Exclusion:

- Prior anti-cancer therapy in metastatic setting (other than osimertinib); ILD/pneumonitis; symptomatic brain mets; significant corneal disease; uncontrolled infection.

#### ## Evaluation Framework:

##### ### Step 1: Inclusion Criteria Checklist

## Step 21: TOOL

### # Eligibility Evaluation for NCT04410796

#### ## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.

#### ## Trial Eligibility Criteria:

Inclusion:

- Metastatic NSCLC EGFR-mutant; first-line treatment setting. Either untreated or started osimertinib within a short window.
- No prior systemic therapy for metastatic disease; no prior EGFR TKI except first-line osimertinib within defined window.
- ECOG/KPS  $\geq 70\%$ ; measurable disease; adequate organ function.

Exclusion:

- Prior EGFR targeted therapy (except first-line osimertinib in specific timing); prior systemic metastatic therapy; ILD/pneumonitis; significant cardiac/QTc issues.

## Evaluation Framework:

### Step 1: Inclusion Criteria Checklist

For each inclusion criterion, assess:

## Step 22: TOOL

# Eligibility Evaluation for NCT03586453

## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.

## Trial Eligibility Criteria:

Inclusion:

- Stage IV EGFR-mutant NSCLC (Ex19del or L858R).
- ECOG 0-1.
- Measurable disease.
- Intended as first-line osimertinib study; allows entry within first 3 months of commercial osimertinib.

Exclusion:

- Prior EGFR targeted therapy (other than first-line osimertinib within 3 months), prior systemic therapy for metastatic disease.

## Evaluation Framework:

### Step 1: Inclusion Criteria Checklist

## Step 23: TOOL

# Eligibility Evaluation for NCT05642572

## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.

## Trial Eligibility Criteria:

Inclusion:

- NSCLC with sensitizing EGFR mutation; progressed on osimertinib as most recent line.

- MET amplification (tissue or blood-based), post-osimertinib.
- ECOG 0-1; measurable or non-measurable disease; organ function; brain imaging.

Exclusion:

- Prior anti-VEGF/VEGFR or MET inhibitor; recent systemic therapy/radiation; uncontrolled comorbidities.

## Evaluation Framework:

### Step 1: Inclusion Criteria Checklist

For each inclusion criterion, assess:

## Step 24: TOOL

# Eligibility Evaluation for NCT06116682

## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.

## Trial Eligibility Criteria:

Inclusion:

- Advanced NSCLC with MET amplification confirmed by FMI tissue NGS.
- Measurable disease; brain imaging; ECOG Zubrod 0-2.
- Must not have other actionable alterations (e.g., EGFR sensitizing mutations).

Exclusion:

- Prior MET TKI; recent systemic therapy/radiation; other comorbidities.

## Evaluation Framework:

### Step 1: Inclusion Criteria Checklist

For each inclusion criterion, assess:

## Step 25: TOOL

# Eligibility Evaluation for NCT07058519

## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.

## Trial Eligibility Criteria:

Inclusion:

- First-line untreated advanced EGFRm NSCLC; intends to receive osimertinib + chemotherapy.
- Detectable plasma EGFRm at screening; ECOG 0-1.

Exclusion:

- Prior EGFR-TKI; prior systemic therapy for advanced disease; ILD/pneumonitis; significant cardiac/QTc issues.

## Evaluation Framework:

### ### Step 1: Inclusion Criteria Checklist

For each inclusion criterion, assess:

- [ ] Criterion 1: [MEETS/DOES NOT MEET/UNCLEAR]

## Step 26: TOOL

# Eligibility Evaluation for NCT04181060

## Patient Summary:

58-year-old female; metastatic non-squamous NSCLC adenocarcinoma; EGFR exon 19 deletion; progressed on erlotinib after 14 months; no prior osimertinib; ECOG PS 1; no brain metastases.

## Trial Eligibility Criteria:

Inclusion:

- Advanced EGFR-mutant NSCLC first-line; pathologically confirmed; ECOG 0-2.
- No prior EGFR TKI; no prior systemic therapy for metastatic disease.
- Allows if already started osimertinib within 21 days before randomization with baseline imaging.

Exclusion:

- Prior anti-VEGF; risk factors for anti-VEGF; prior systemic metastatic therapy; prior EGFR TKI except first-line osimertinib within 21 days window.

## Evaluation Framework:

### ### Step 1: Inclusion Criteria Checklist

For each inclusion criterion, assess:

## Step 27: AI

Below is a ranked list of the most suitable actively recruiting trials based on the patient's profile, with detailed eligibility assessments and rationales.

1) NCT04772235

- Trial title: Phase I Study of Repotrectinib and Osimertinib in NSCLC Patients
- Eligibility assessment: LIKELY\_ELIGIBLE
- Eligibility score: 0.85
- Key matching points:
  - Metastatic non-squamous NSCLC with EGFR exon 19 deletion
  - Progressed on a first-generation EGFR TKI (erlotinib); Part B includes patients who have progressed after first/second-generation EGFR TKI regardless of T790M status
  - ECOG PS 0–1 (patient ECOG 1)
  - No brain metastases (asymptomatic CNS disease allowed)
- Key concerns:
  - Requires recent tumor tissue (biopsy or resection) within 60 days prior to start; biopsy feasibility and willingness required
  - Must meet organ function criteria and avoid strong CYP3A inhibitors/inducers

- Cardiac/QTc and ILD/pneumonitis exclusions need to be checked

- Brief rationale:

- This study adds repotrectinib (a next-generation tyrosine kinase inhibitor targeting bypass resistance pathways) to osimertinib, aiming to overcome resistance after earlier EGFR TKI exposure. It is specifically designed to enroll patients like this after progression on erlotinib/gefitinib/afatinib (without requiring prior osimertinib). High relevance and a favorable inclusion fit.

2) NCT04762199

- Trial title: MRX-2843 and Osimertinib for the Treatment of Advanced EGFR Mutant NSCLC

# Results and Analysis

## Summary

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### 2) NCT04762199

- Trial title: MRX-2843 and Osimertinib for the Treatment of Advanced EGFR Mutant NSCLC
- Eligibility assessment: UNCERTAIN (depends on T790M status)
- Eligibility score: 0.55
- Key matching points:
  - Metastatic EGFR-mutant NSCLC; progression after erlotinib fits the “EGFR TKI-resistant” expansion cohort
  - ECOG PS 0–2 allowed (patient ECOG 1)
- Key concerns:
  - If the patient has NOT previously received osimertinib, the protocol requires EGFR T790M negativity to enroll in the resistant cohort; current T790M status is unknown and must be tested
  - Requires adequate labs and cardiac/QTc (<500 ms) and excludes ILD/pneumonitis
  - Single-site or limited sites may impact logistics (e.g., Emory University, Atlanta, GA)
- Brief rationale:



- MRX-2843 (MerTK/FLT3 inhibitor) plus osimertinib is a rational combination to address resistance mechanisms. If T790M is negative (a common scenario in ~40–50% post–first-gen EGFR TKI progressors), this becomes a strong option. If T790M positive, standard-of-care osimertinib is preferred first; trial may then be considered after osimertinib resistance.

### 3) NCT03260491

- Trial title: U3-1402 (Patritumab deruxtecan, HER3-DXd) in Metastatic or Unresectable NSCLC
- Eligibility assessment: UNCERTAIN (dose-escalation cohort criteria)
- Eligibility score: 0.50
- Key matching points:
- Designed for EGFR-mutant NSCLC after progression on EGFR TKI
- ECOG 0–1
- HER3 is commonly upregulated in EGFR-mutant, TKI-resistant disease; HER3-DXd has shown activity across resistance mechanisms
- Key concerns:
- Dose-escalation cohort requires the patient to be currently receiving erlotinib/gefitinib/afatinib/osimertinib with radiologic progression while on therapy and able to discontinue; if erlotinib has already been stopped, eligibility may be uncertain
- If treated with a first- or second-generation TKI (erlotinib), the study requires absence of T790M for enrollment in certain cohorts; T790M status is unknown and must be tested
- Expansion cohorts generally require prior chemotherapy; the patient has not had platinum chemotherapy, so expansion cohorts are likely not applicable
- Excludes ILD/pneumonitis and significant cardiac/QTc issues; corneal disease exclusion applies
- Brief rationale:
- HER3-DXd is a promising ADC for EGFR-mutant NSCLC after EGFR TKI resistance. If she qualifies for the dose-escalation cohort (e.g., if still on erlotinib at screening with documented progression and T790M negative), this could offer targeted benefit irrespective of specific resistance pathways.

### 4) NCT05498428

- Trial title: A Study of Amivantamab in Advanced/Metastatic Solid Tumors Including EGFR-Mutated NSCLC
- Eligibility assessment: LIKELY\_INELIGIBLE (current line-of-therapy constraints)
- Eligibility score: 0.20
- Key matching points:
- EGFR exon 19 deletion NSCLC included across cohorts; ECOG 0–1
- Key concerns:
- Relevant cohorts for EGFR-mutant NSCLC either require no prior systemic therapy (first-line) or progression on osimertinib as the most recent line; the patient has prior erlotinib in the metastatic setting and has not received osimertinib, so she does not fit the key cohorts
- ILD/pneumonitis, cardiovascular, and QTc exclusions require screening
- Brief rationale:
- Amivantamab (EGFR/MET bispecific) is important in EGFR-mutant disease. However, without prior osimertinib and with prior erlotinib, current cohorts likely do not fit. Could be reconsidered if she receives osimertinib and later progresses.

### 5) NCT06417814

- Trial title: Dato-DXd With or Without Osimertinib vs Platinum-Based Chemotherapy in EGFR-Mutated Locally Advanced/Metastatic NSCLC
- Eligibility assessment: INELIGIBLE (requires progression on prior osimertinib)
- Eligibility score: 0.10
- Key matching points:
- EGFR-mutant NSCLC; ECOG 0–1; strong relevance once patients have progressed on osimertinib
- Key concerns:
- Requires documented extracranial progression on prior osimertinib monotherapy as the most recent line; patient has not received osimertinib
- Brief rationale:
- High potential utility after osimertinib resistance; not applicable now but could be valuable if she later receives osimertinib and progresses.

Summary of top recommendations and caveats:

- Top trials to discuss now:
  - 1) NCT04772235 (Repotrectinib + Osimertinib): Best immediate fit after progression on erlotinib, without requiring prior osimertinib; high relevance and strong likelihood of eligibility if organ function and cardiac/ILD criteria are met and tissue biopsy is feasible.
  - 2) NCT04762199 (MRX-2843 + Osimertinib): Very relevant; eligibility hinges on EGFR T790M being negative if she has not received osimertinib. Order EGFR resistance testing (tissue or plasma) to determine T790M status.
  - 3) NCT03260491 (HER3-DXd/Patritumab deruxtecan): Promising option in EGFR-mutant NSCLC post-TKI; eligibility depends on enrollment to a dose-escalation cohort (often requires being on a TKI with progression and T790M negative in some settings). Clarify current erlotinib status and T790M result.
- Immediate next steps:
  - Obtain resistance testing (plasma ctDNA and/or tissue) to determine EGFR T790M status and check for other resistance mechanisms (e.g., MET amplification). T790M positivity would support starting standard-of-care osimertinib promptly; T790M negativity would strengthen eligibility for NCT04762199 and NCT04772235.
  - Confirm measurable disease per RECIST v1.1 and ensure recent imaging.
  - Review cardiac (ECG/QTc) and pulmonary history to exclude ILD/pneumonitis; verify organ function labs.
  - Confirm willingness and feasibility of a fresh biopsy if required (particularly for NCT04772235).
  - Future options if she receives osimertinib and later progresses:
    - NCT06417814 (Dato-DXd ± Osimertinib vs chemo)
    - Amivantamab-based trials post-osimertinib (e.g., NCT05498428 relevant cohorts)
    - MET-directed combinations if resistance testing reveals MET amplification (e.g., Lung-MAP S1900G, NCT05642572; or amivantamab-SC in MET amplification, NCT06116682 but note exclusions for concurrent actionable EGFR).
- Important caveats:
  - Many first-line osimertinib trials (e.g., NCT04410796; NCT03586453; NCT04181060; NCT07058519) exclude patients with prior EGFR TKI therapy in the metastatic setting. Given her prior erlotinib, these are likely ineligible now.
  - The best therapeutic course outside trials remains guided by resistance testing:
  - If T790M positive: initiate osimertinib as standard-of-care and consider trials after progression.

- If T790M negative: clinical trial participation is attractive; otherwise, platinum-pemetrexed chemotherapy is standard.

Please discuss the top 3 trials (NCT04772235, NCT04762199, NCT03260491) with your oncologist, alongside prompt resistance testing to clarify EGFR T790M status and any other resistance alterations (e.g., MET amplification) which can further tailor trial selection.

## Supplementary Materials

This section contains detailed code implementations and execution results.