# ACTIN Report (research use only)

PATIENT
**EXAMPLE-LUNG-01**

REPORT DATE
**17-Sep-2025**

Gender: **Female** | Birth year: **1975** | WHO: **1**

Tumor: **Lung adenocarcinoma** | Lesions: **Liver, Lung** | Stage: **IV**

## Clinical summary

| | | |
|---|---|---|
| Relevant systemic treatment history | **6/2023-1/2025** | **Osimertinib** |

## Recent molecular results

### Hartwig WGS (22-Feb-2025)

| | |
|---|---|
| Biopsy location | **Lung (purity 50%)** |
| Molecular tissue of origin prediction | **Lung: Non-small cell: LUAD (98%)** |
| Tumor mutational load / burden | **TML 160 / TMB 14 mut/Mb** |
| Microsatellite (in)stability | **Stable** |
| HR status | **Proficient (0)** |
| Driver mutations | **EGFR C797S, EGFR L858R, KRAS G12C, KRAS G12D** |
| Amplified genes | **None** |
| Deleted genes | **TP53** |
| Homozygously disrupted genes | **None** |
| Gene fusions | **MET(exon13)::MET(exon15) fusion** |
| Virus | **None** |

### Trial-relevant IHC results

| | |
|---|---|
| PD-L1 | **Score > 50%** |

## Trials in NL that are open and potentially eligible (5 cohorts from 5 trials)

| Trial | Cohort | Molecular | Sites | Warnings |
|---|---|---|---|---|
| METC 04 TEDR1 | Lung cancer C797S cohort | EGFR C797S | NKI-AvL | None |
| METC 02 KAYRAS | Dose expansion - monotherapy - NSCLC | KRAS G12D, PD-L1 >= 50.0 | Erasmus MC | Variant(s) G12D in KRAS but subclonal likelihood of > 50% |
| **METC 01** IEMOEN | Dose escalation - monotherapy *(no slots)* | None | | Has not exhausted SOC (at least platinum doublet remaining) |
| *EGFR-C797S-TRIAL* | *EGFR C797S* | *EGFR C797S* | *Elisabeth-TweeSteden Ziekenhuis* | |
| *EGFR-L858R-TRIAL* | *EGFR L858R* | *EGFR L858R* | *Elisabeth-TweeSteden Ziekenhuis* | |

Trials matched solely on molecular event and tumor type (no clinical data used) are shown in italicized, smaller font.

## International trials that are open and potentially eligible (2 cohorts from 2 trials)

| Trial | Cohort | Molecular | Sites |
|---|---|---|---|
| *EGFR-BE* | *EGFR L858R* | *EGFR L858R* | *Belgium: Brussels* |
| *KRAS-G12C-TRIAL-DE* | *KRAS G12C* | *KRAS G12C* | *Germany: Stuttgart* |

International trials are matched solely on molecular event and tumor type (clinical data excluded).

# Molecular Details

## Hartwig WGS (EXAMPLE-LUNG-01-T, 22-Feb-2025)

### General

| Purity | Ploidy | TML Status | TMB Status | MS Stability | HR Status | DPYD | UGT1A1 |
|---|---|---|---|---|---|---|---|
| 50% | 2.3 | **High (160)** | **High (14)** | Stable | Proficient (0) | *1_HOM (Normal function) | *1_HOM (Normal function) |

### Predicted tumor origin

| | 1. Lung: Non-small cell: LUAD |
|---|---|
| **Combined prediction score** | **98%** |
| This score is calculated by combining information on: | |
| (1) SNV types | 60% |
| (2) SNV genomic localisation distribution | 70% |
| (3) Driver genes and passenger characteristics | 80% |

Other cohorts have a combined prediction of 2% or lower

### Key drivers

| Type | Driver | Trials (Locations) | Trials in Hartwig | Best evidence in External | Resistance in External |
|---|---|---|---|---|---|
| Mutation (gain of function) | EGFR L858R (2/4 copies) | | NCT00000006, NCT00000007 | Approved | |
| Mutation (gain of function) | EGFR C797S (1/4 copies) | TEDR1 (NKI-AvL) | NCT00000008 | Pre-clinical | |
| Mutation (gain of function) | KRAS G12D (0.3/2 copies)* | KAYRAS (Erasmus MC) | | | |
| Mutation (gain of function) | KRAS G12C (0.3/2 copies)* | | NCT00000009 | | |
| Deletion | TP53 del, 0 copies | | | | |

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| Type | Driver | Trials (Locations) | Trials in Hartwig | Best evidence in External | Resistance in External |
|---|---|---|---|---|---|
| Known fusion | MET(exon13)::MET(exon15) fusion | | | | |

* Variant has > 50% likelihood of being sub-clonal

## Other drivers or relevant events

| Type | Driver | Trials (Locations) | Trials in Hartwig | Best evidence in External | Resistance in External |
|---|---|---|---|---|---|
| None | | | | | |

## IHC results

| | |
|---|---|
| PD-L1 | **Score > 50%** |

# Clinical Details

## Clinical summary

| | | |
|---|---|---|
| Relevant systemic treatment history | **6/2023-1/2025** | **Osimertinib** |
| Relevant other oncological history | **None** | |
| Previous primary tumor | **None** | |
| Relevant non-oncological history | **2023** | **Rheumatoid arthritis** |

## Patient current details (20-Feb-2025)

| | |
|---|---|
| Unresolved toxicities grade => 2 | **None** |
| LVEF | **50%** |
| Cancer-related complications | **None** |
| Known allergies | **None** |
| Recent surgeries | **01-Aug-2024 Cholecystectomy** |

## Tumor details (20-Feb-2025)

| | |
|---|---|
| Measurable disease | **Yes** |
| Known lesions | **Liver, Lung** |
| Unknown lesions | **None** |
| No lesions present | **CNS, Brain, Bone, Lymph node** |

## Active medication details

| Medication | Administration route | Start date | Stop date | Dosage | Frequency |
|---|---|---|---|---|---|
| St. John's Wort | Oral | 01-Feb-2023 | | 300 MILLIGRAMS | 1 / 2 DAYS |

## Blood transfusions

| Product | Date |
|---|---|
| ERTHROCYTES_FILTERED | 20-Sep-2024 |

## Other Trial Matching Results

### Trials and cohorts that are potentially eligible, but are closed (1)

| Trial | Cohort | Molecular | Sites | Warnings |
|---|---|---|---|---|
| **METC 01**<br>IEMOEN | Dose expansion - monotherapy | None | | Has not exhausted SOC (at least platinum doublet remaining) |

### Trials and cohorts that are considered ineligible (4)

| Trial | Cohort | Molecular | Ineligibility reasons |
|---|---|---|---|
| **METC 03**<br>NO-SEE797ES | Dose escalation - monotherapy | EGFR C797S | C797S in EGFR in canonical transcript |
| METC 02<br>KAYRAS | Dose expansion - monotherapy - Colorectum | KRAS G12D,<br>PD-L1 >= 50.0 | No colorectal cancer |
| **METC 05**<br>PICKME3CA | *Applies to all cohorts below* | None | No PIK3CA activating mutation(s) |
| | Dose expansion - monotherapy - NSCLC *(closed)* | | |
| | Dose expansion - monotherapy - Other cancer types *(closed)* | | Tumor belongs to DOID term(s) lung non-small cell carcinoma |

### Trials and cohorts that are not evaluable or ignored (0)

| Trial | Cohort | Molecular | Sites | Configuration |
|---|---|---|---|---|

None

## Trial Matching Details

### Potentially eligible open trials & cohorts

#### METC 01

| | |
|---|---|
| Potentially eligible | **Yes** |
| Acronym | **IEMOEN** |
| Title | **Phase I first-in-human study to evaluate safety of IEMOEN, a new PD-L1 inhibitor in advanced solid tumors** |

| Reference | Evaluation |
|---|---|
| I-03 | WARN<br>Has not exhausted SOC (at least platinum doublet remaining) |
| E-02 | UNDETERMINED<br>No measurement found for hemoglobin |
| E-03 | UNDETERMINED<br>No measurement found for absolute neutrophil count |
| E-01 | PASS<br>Has no other condition belonging to category autoimmune disease |
| I-01 | PASS<br>Patient is at least 18 years old |
| I-02 | PASS<br>Has solid primary tumor<br>Stage IV is considered metastatic |

#### METC 01 - Dose escalation - monotherapy

| | |
|---|---|
| Cohort ID | **A** |
| Potentially eligible? | **Yes** |
| Open for inclusion? | **Yes** |
| Has slots available? | **No** |

#### METC 01 - Dose expansion - monotherapy

| | |
|---|---|
| Cohort ID | **B** |
| Potentially eligible? | **Yes** |
| Open for inclusion? | **No** |
| Has slots available? | **No** |

## METC 02

| | |
|---|---|
| Potentially eligible | **Yes** |
| Acronym | **KAYRAS** |
| Title | **A phase 1/2 trial for first in-human usage of KAYRAS, a new specific KRAS G12D inhibitor in NSCLC and colorectal cancer** |

| Reference | Evaluation |
|---|---|
| I-04 | WARN<br>Variant(s) G12D in KRAS but subclonal likelihood of > 50% |
| I-03 | UNDETERMINED<br>ASAT and ALAT are not present or cannot be evaluated |
| I-01 | PASS<br>Patient is at least 18 years old |
| I-02 | PASS<br>Stage IV is considered metastatic |
| I-05 | PASS<br>PD-L1 expression above minimum of 50.0 |

## METC 02 - Dose expansion - monotherapy - NSCLC

| | |
|---|---|
| Cohort ID | **A** |
| Potentially eligible? | **Yes** |
| Open for inclusion? | **Yes** |
| Has slots available? | **Yes** |

| Reference | Evaluation |
|---|---|
| I-02 | PASS<br>Tumor belongs to DOID term(s) lung non-small cell carcinoma |

## METC 02 - Dose expansion - monotherapy - Colorectum

| | |
|---|---|
| Cohort ID | **B** |
| Potentially eligible? | **No** |
| Open for inclusion? | **Yes** |
| Has slots available? | **Yes** |

| Reference | Evaluation |
|---|---|
| I-02 | FAIL<br>No colorectal cancer |

## METC 04

| | |
|---|---|
| Potentially eligible | **Yes** |
| Acronym | **TEDR1** |
| Title | **TEDR1 Trial: A phase II trial to evaluate efficacy of specific EGFR inhibitors in lung cancer** |

| Reference | Evaluation |
|---|---|
| I-1 | PASS<br>Patient is at least 18 years old |
| I-2 | PASS<br>Stage IV is considered metastatic<br>Tumor belongs to DOID term(s) lung cancer |
| I-3 | PASS<br>C797S in EGFR in canonical transcript |

## METC 04 - Lung cancer C797S cohort

| | |
|---|---|
| Cohort ID | **A** |
| Potentially eligible? | **Yes** |
| Open for inclusion? | **Yes** |
| Has slots available? | **Yes** |

## Other trials & cohorts

### METC 03

| | |
|---|---|
| Potentially eligible | No |
| Acronym | **NO-SEE797ES** |
| Title | **Phase I trial for development of NO-SEE797ES, a specific inhibitor for EGFR with C797 mutations but not C797S in solid tumors** |

| Reference | Evaluation |
|---|---|
| I-03 | FAIL<br>C797S in EGFR in canonical transcript |

### METC 03 - Dose escalation - monotherapy

| | |
|---|---|
| Cohort ID | **A** |
| Potentially eligible? | No |
| Open for inclusion? | **Yes** |
| Has slots available? | **Yes** |

### METC 05

| | |
|---|---|
| Potentially eligible | No |
| Acronym | **PICKME3CA** |
| Title | **A phase 1/2 trial of ABC123 +/- platinum doublet in PIK3CA-mutated solid cancer** |

| Reference | Evaluation |
|---|---|
| I-04 | FAIL<br>No PIK3CA activating mutation(s) |

### METC 05 - Dose expansion - monotherapy - NSCLC

| | |
|---|---|
| Cohort ID | **A** |
| Potentially eligible? | No |
| Open for inclusion? | **No** |
| Has slots available? | **Yes** |

### METC 05 - Dose expansion - monotherapy - Other cancer types

| | |
|---|---|
| Cohort ID | **B** |
| Potentially eligible? | No |
| Open for inclusion? | **No** |
| Has slots available? | **Yes** |

| Reference | Evaluation |
|---|---|
| I-03 | FAIL<br>Tumor belongs to DOID term(s) lung non-small cell carcinoma |