# ACTIN Report (research use only)

PATIENT
EXAMPLE-LUNG-01

REPORT DATE
05-Nov-2024

Gender: Male | Birth year: 1950 | WHO: 0

Tumor: Lung - Adenocarcinoma | Lesions: Liver | Stage: IV

## Summary

### Clinical summary

| | | | |
|---|---|---|---|
| Gender | **Male** | Birth year | **1950** |
| WHO | **0** | Tumor | **Lung - Adenocarcinoma** |
| Lesions | **Liver** | Stage | **IV** |
| Measurable disease (RECIST) | **NA** | DPYD | ***1_HOM (Normal function)** |
| UGT1A1 | ***1_HOM (Normal function)** | | |

| | | |
|---|---|---|
| Relevant systemic treatment history | **1/2023-9/2024** | **Osimertinib** |
| Relevant other oncological history | **None** | |
| Previous primary tumor | **None** | |
| Relevant non-oncological history | **2022** | **Rheumatoid arthritis** |
| Recent molecular results | **KRAS G12D (0.3/2 copies)*, NRAS: No reportable events, BRAF: No reportable events, HER2: No reportable events, MSS** | |

### Recent molecular results

#### Hartwig WGS (20-Aug-2024)

| | |
|---|---|
| Biopsy location | **Liver (purity 50%)** |
| Molecular tissue of origin prediction | **Lung: Non-small cell (98%)** |
| Tumor mutational load / burden | **TML low (40) / TMB low (2)** |
| Microsatellite (in)stability | **Stable** |
| HR status | **Proficient (0)** |
| High driver mutations | **EGFR L858R, EGFR C797S, KRAS G12D** |
| Amplified genes | **None** |
| Deleted genes | **TP53** |
| Homozygously disrupted genes | **None** |
| Gene fusions | **None** |
| Virus detection | **None** |
| Potentially actionable events with medium/low driver: | **None** |

#### IHC results

**PD-L1: Score 1%**

### Standard of care options considered potentially eligible

There are no standard of care treatment options for this patient

### Approved treatments considered eligible

| Treatment |
|---|
| Not yet determined |

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

| Trial | Cohort | Molecular | Warnings |
|---|---|---|---|
| **METC 04** TEDR1 | Lung cancer C797S cohort | EGFR C797S | None |
| **METC 02** KAYRAS | Dose expansion - monotherapy - NSCLC | KRAS G12D | Variant(s) KRAS G12D in KRAS but subclonal likelihood of > 50% |

## Example trials that are open and potentially eligible but currently have no slots available (1 cohort from 1 trial)

| Trial | Cohort | Molecular | Warnings |
|---|---|---|---|
| **METC 01** IEMOEN | Dose escalation - monotherapy | | Hemoglobin 5.6 mmol/L below min of 6.0 mmol/L, History of rheumatoid arthritis, SOC not exhausted: at least platinum doublet remaining |

## External trials potentially eligible based on molecular results which are potentially recruiting locally in Netherlands (1)

| Event | Source Event | Cancer Type | Trial title | Hospitals |
|---|---|---|---|---|
| EGFR L858R | EGFR L858R | Lung non-small cell carcinoma | EGFR-NEW | Elisabeth-TweeSteden Ziekenhuis |

## Example trials and cohorts that are open but considered ineligible (2)

| Trial | Cohort | Molecular | Ineligibility reasons |
|---|---|---|---|
| **METC 02** KAYRAS | Dose expansion - monotherapy - Colorectum | KRAS G12D | No colorectal cancer |
| **METC 03** NO-SEE797ES | Dose escalation - monotherapy | | C797S detected in EGFR |

Open cohorts with no slots available are shown in grey.

## Resistance evidence

There are no standard of care treatment options for this patient

## Molecular Details

**IHC results** **PD-L1: Score 1%**

### Hartwig WGS (EXAMPLE-LUNG-01-T, 20-Aug-2024)

#### General

| Purity | TML Status | TMB Status | MS Stability | HR Status | DPYD | UGT1A1 |
|---|---|---|---|---|---|---|
| 50% | low (40) | low (2) | Stable | Proficient (0) | *1_HOM (Normal function) | *1_HOM (Normal function) |

#### Predicted tumor origin

| | 1. Lung: Non-small cell |
|---|---|
| **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

#### Drivers

| Type | Driver | Driver likelihood | Trials in Example | Trials in Hartwig | Best evidence in External | Resistance in External |
|---|---|---|---|---|---|---|
| Mutation (Hotspot) | EGFR C797S (1/4 copies) | High | TEDR1 | | | |
| Mutation (Hotspot) | EGFR L858R (2/4 copies) | High | | NCT00000006 | | |
| Mutation (Hotspot) | KRAS G12D (0.3/2 copies)* | High | KAYRAS | | | |
| Loss | TP53 del, 0 copies | High | | | | |

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

## Molecular History

### Molecular history

| Event | Description | Driver likelihood | 2024-08-20<br>Hartwig WGS |
|---|---|---|---|
| EGFR C797S<br>(Tier III) | Missense<br>Gain of function<br>Hotspot | High | VAF 0.25% |
| EGFR L858R<br>(Tier III) | Missense<br>Gain of function<br>Hotspot | High | VAF 0.5% |
| KRAS G12D<br>(Tier III) | Missense<br>Gain of function<br>Hotspot | High | VAF 0.15% |
| TP53 del<br>(Tier III) | Deletion<br>Unknown protein effect | High | Detected |
| TMB | | | 2.0 |
| MSI | | | Stable |

## SOC literature efficacy evidence

### Standard of care options considered potentially eligible

The following standard of care treatment(s) could be an option for this patient. For further details per study see 'SOC literature details' section in extended report.

There are no standard of care treatment options for this patient

# Clinical Details

## Clinical summary

| | | |
|---|---|---|
| Relevant systemic treatment history | **1/2023-9/2024** | **Osimertinib** |
| Relevant other oncological history | **None** | |
| Previous primary tumor | **None** | |
| Relevant non-oncological history | **2022** | **Rheumatoid arthritis** |

## Patient current details (01-Oct-2024)

| | |
|---|---|
| Unresolved toxicities grade => 2 | **None** |
| Cancer-related complications | **None** |
| Known allergies | **None** |

## Tumor details (01-Oct-2024)

| | |
|---|---|
| Measurable disease | **Unknown** |
| CNS lesion status | **No known CNS lesions** |
| Brain lesion status | **No known brain lesions** |

## Active medication details

| Medication | Administration route | Start date | Stop date | Dosage | Frequency |
|---|---|---|---|---|---|
| None | | | | | |

## SOC literature details

There are no standard of care treatment options for this patient

## Molecular Evidence

### On label clinical evidence

| Event | CKB Event | Level A | Level B | Level C | Level D |
|---|---|---|---|---|---|

### Off label clinical evidence

| Event | CKB Event | Level A | Level B | Level C | Level D |
|---|---|---|---|---|---|

### Efficacy evidence description

## Trial Matching Summary

### External trials potentially eligible based on molecular results which are potentially recruiting locally in Netherlands (1)

| Event | Source Event | Cancer Type | Trial title | Hospitals |
|---|---|---|---|---|
| EGFR L858R | EGFR L858R | Lung non-small cell carcinoma | EGFR-NEW | Elisabeth-TweeSteden Ziekenhuis |