

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

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

Summary

Clinical summary

|                                     |   |                      |                          |
|-------------------------------------|---|----------------------|--------------------------|
| Gender                              | Female  | Birth year           | 1975                     |
| WHO                                 | 1   | Tumor                | Lung - Adenocarcinoma    |
| Lesions                             | Liver, Lung   | Stage                | IV                       |
| Measurable disease (RECIST)         | Yes   | DPYD                 | *1_HOM (Normal function) |
| UGT1A1                              | *1_HOM (Normal function)  |                      |                          |
| 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 |                          |
| Recent molecular results            | KRAS G12C (0.3/2 copies)*, KRAS G12D (0.3/2 copies)*, NRAS: No reportable events, BRAF: No reportable events, HER2: No reportable events, MSS |                      |                          |

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 High (160) / TMB High (14)               |
| Microsatellite (in)stability                         | Stable                                       |
| HR status  | Proficient (0)                               |
| High driver mutations                                | EGFR L858R, EGFR C797S, KRAS G12D, KRAS G12C |
| Amplified genes                                      | None   |
| Deleted genes  | TP53   |
| Homozygously disrupted genes                         | None   |
| Gene fusions   | MET_MET                                      |
| Virus detection                                      | None   |
| Trial-relevant events, considered medium/low driver: | None   |
| IHC results  | PD-L1: Score > 50%                           |

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

Trials in The Netherlands that are open and potentially eligible (4 cohorts from 4 trials)

| Trial                            | Cohort                               | Molecular         | Sites                                  | Warnings  |
|----------------------------------|--------------------------------------|-------------------|--|---|
| <a href="#">METC 04 TEDR1</a>    | Lung cancer C797S cohort             | EGFR C797S        | NKI-AvL                                | None  |
| <a href="#">METC 02 KAYRAS</a>   | Dose expansion - monotherapy - NSCLC | KRAS G12D         | Erasmus MC                             | Variant(s) G12D in KRAS but subclonal likelihood of > 50% |
| <a href="#">EGFR-C797S-TRIAL</a> | <i>EGFR C797S</i>                    | <i>EGFR C797S</i> | <i>Elisabeth-TweeSteden Ziekenhuis</i> |   |
| <a href="#">EGFR-L858R-TRIAL</a> | <i>EGFR L858R</i>                    | <i>EGFR L858R</i> | <i>Elisabeth-TweeSteden Ziekenhuis</i> |   |

Open cohorts with no slots available are shown in grey.  
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 (3 cohorts from 3 trials)

| Trial                         | Cohort                    | Molecular  | Sites               |
|-------------------------------|---------------------------|------------|---------------------|
| <a href="#">EGFR-BE</a>       | EGFR L858R                | EGFR L858R | Belgium (Brussels)  |
| <a href="#">NCT00000019</a>   | KRAS G12                  | KRAS G12C  | Belgium (Antwerpen) |
| <a href="#">KRAS-TRIAL-DE</a> | KRAS activating mutations | KRAS G12C  | Germany (Stuttgart) |

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

Trials and cohorts that are considered ineligible (2)

| Trial                          | Cohort                                    | Molecular  | Sites      | Ineligibility reasons                 |
|--------------------------------|---|------------|------------|---------------------------------------|
| <b>METC 03 NO-SEE797ES</b>     | Dose escalation - monotherapy             | EGFR C797S |            | C797S in EGFR in canonical transcript |
| <a href="#">METC 02 KAYRAS</a> | Dose expansion - monotherapy - Colorectum | KRAS G12D  | Erasmus MC | No colorectal cancer                  |

Resistance evidence

There are no standard of care treatment options for this patient

Molecular Details

IHC results

PD-L1: Score > 50%

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 |     |

Drivers

| Type               | Driver                    | Driver likelihood | Trials (Locations)  | Trials in Hartwig        | Best evidence in External | Resistance in External |
|--------------------|---------------------------|-------------------|---------------------|--------------------------|---------------------------|------------------------|
| Mutation (Hotspot) | EGFR C797S (1/4 copies)   | High              | TEDR1 (NKI-AvL)     | NCT00000008              | Pre-clinical              |                        |
| Mutation (Hotspot) | EGFR L858R (2/4 copies)   | High              |                     | NCT00000006, NCT00000007 | Approved                  |                        |
| Mutation (Hotspot) | KRAS G12C (0.3/2 copies)* | High              |                     | NCT00000019, NCT00000009 |                           |                        |
| Mutation (Hotspot) | KRAS G12D (0.3/2 copies)* | High              | KAYRAS (Erasmus MC) |                          |                           |                        |
| Loss               | TP53 del, 0 copies        | High              |                     |                          |                           |                        |

The table continues on the next page

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Gene and variant annotations and related content are powered by Genomenon Cancer Knowledgebase (CKB).

ACTIN Report (research use only)

PATIENT  
EXAMPLE-LUNG-01  
  
REPORT DATE  
07-Nov-2024

Continued from the previous page

| Type   | Driver                     | Driver likelihood | Trials (Locations) | Trials in Hartwig | Best evidence in External | Resistance in External |
|--|----------------------------|-------------------|--------------------|-------------------|---------------------------|------------------------|
| Known fusion                                       | MET_MET, exon 14 - exon 14 | High              |                    |                   |                           |                        |
| * Variant has > 50% likelihood of being sub-clonal |                            |                   |                    |                   |                           |                        |

Molecular History

Molecular history

| Event                   | Description                            | Driver likelihood | 2025-02-22<br>Hartwig WGS |
|-------------------------|--|-------------------|---------------------------|
| EGFR L858R<br>(Tier I)  | Mutation (Hotspot)<br>Gain of function | High              | VOAF 0.5%                 |
| EGFR C797S<br>(Tier II) | Mutation (Hotspot)<br>Gain of function | High              | VOAF 0.25%                |
| KRAS G12C<br>(Tier III) | Mutation (Hotspot)<br>Gain of function | High              | VOAF 0.15%                |
| KRAS G12D<br>(Tier III) | Mutation (Hotspot)<br>Gain of function | High              | VOAF 0.15%                |
| MET_MET<br>(Tier III)   | Known fusion<br>Gain of function       | High              | Detected                  |
| TP53 del<br>(Tier III)  | Loss<br>Unknown protein effect         | High              | Detected                  |
| TMB                     |  |                   | 14.0                      |
| 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 | 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                    |
| 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  |
|-----------------|----------------------|-------------|-----------|----------------|------------|
| St. John's Wort | Oral                 | 01-Feb-2023 |           | 300 MILLIGRAMS | 1 / 2 DAYS |

Blood transfusions

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



**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   |
|------------|------------|---|---------|---------|---|
| EGFR C797S | EGFR C797S |   |         |         | AFATINIB<br><i>Lung non-small cell carcinoma (2015)</i> |
| EGFR L858R | EGFR L858R | OSIMERTINIB<br><i>Lung non-small cell carcinoma (2016)</i><br><br>AFATINIB<br><i>Lung non-small cell carcinoma (2013)</i> |         |         |   |

Off label clinical evidence

| Event                         | CKB Event      | Level A                       | Level B   | Level C | Level D |
|-------------------------------|----------------|-------------------------------|---|---------|---------|
| Efficacy evidence description |                |                               |   |         |         |
| EGFR L858R                    |                |                               |   |         |         |
| OSIMERTINIB:                  | Level A (2016) | Lung non-small cell carcinoma | Osimertinib is effective in patients with EGFR L858R mutations                          |         |         |
| AFATINIB:                     | Level A (2013) | Lung non-small cell carcinoma | Afatinib is effective in patients with EGFR L858R mutations                             |         |         |
| EGFR C797S                    |                |                               |   |         |         |
| AFATINIB:                     | Level D (2015) | Lung non-small cell carcinoma | In a case-report, afatinib was effective against EGFR L858R/C797S positive lung cancer. |         |         |

Trial Matching Overview

Trials in The Netherlands that are open and potentially eligible (2 cohorts from 2 trials)

| Trial                            | Cohort     | Molecular  | Sites                           |
|----------------------------------|------------|------------|---------------------------------|
| <a href="#">EGFR-C797S-TRIAL</a> | EGFR C797S | EGFR C797S | Elisabeth-TweeSteden Ziekenhuis |
| <a href="#">EGFR-L858R-TRIAL</a> | EGFR L858R | EGFR L858R | Elisabeth-TweeSteden Ziekenhuis |

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International trials that are open and potentially eligible (3 cohorts from 3 trials)

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| <a href="#">NCT00000019</a>   | KRAS G12                  | KRAS G12C  | Belgium (Antwerpen) |
| <a href="#">KRAS-TRIAL-DE</a> | KRAS activating mutations | KRAS G12C  | Germany (Stuttgart) |

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

Filtered trials potentially eligible based on molecular results which are potentially recruiting (0)

None