

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 | 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 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 (01-Sep-2024)

|  |  |
|--|--|
| 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

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

| Trial             | Cohort                               | Molecular  | Warnings   |
|-------------------|--------------------------------------|------------|--|
| METC 04<br>TEDR1  | Lung cancer C797S cohort             | EGFR C797S | None   |
| METC 02<br>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<br>IEMOEN | Dose escalation - monotherapy |           | 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 (2)

| Trial title                      | Events     | Source Events | Cancer Types                  | Hospitals                       |
|----------------------------------|------------|---------------|-------------------------------|---------------------------------|
| <a href="#">EGFR-C797S-TRIAL</a> | EGFR C797S | EGFR C797S    | Lung non-small cell carcinoma | Elisabeth-TweeSteden Ziekenhuis |
| <a href="#">EGFR-L858R-TRIAL</a> | EGFR L858R | EGFR L858R    | Lung non-small cell carcinoma | Elisabeth-TweeSteden Ziekenhuis |

External trials potentially eligible based on molecular results which are potentially recruiting internationally (2)

| Trial title                        | Events     | Source Events | Cancer Types                  | Country (cities)    |
|------------------------------------|------------|---------------|-------------------------------|---------------------|
| <a href="#">EGFR-BE</a>            | EGFR L858R | EGFR L858R    | Lung non-small cell carcinoma | Belgium (Brussels)  |
| <a href="#">KRAS-G12C-TRIAL-DE</a> | KRAS G12C  | KRAS G12C     | Lung non-small cell carcinoma | Germany (Stuttgart) |

Example trials and cohorts that are considered ineligible (4)

| Trial                  | Cohort  | Molecular | Ineligibility reasons   |
|------------------------|---|-----------|---|
| METC 02<br>KAYRAS      | Dose expansion - monotherapy - Colorectum   | KRAS G12D | No colorectal cancer  |
| METC 03<br>NO-SEE797ES | Dose escalation - monotherapy   |           | C797S detected in EGFR  |
| METC 05<br>PICKME3CA   | Applies to all cohorts below<br>Dose expansion - monotherapy - NSCLC<br>Dose expansion - monotherapy - Other cancer types | None      | No PIK3CA activating mutation(s)<br><br>Has tumor belonging to DOID term(s) lung non-small cell carcinoma |

Open cohorts with no slots available are shown in grey.

Resistance evidence

There are no standard of care treatment options for this patient

ACTIN Report (research use only)

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

Molecular Details

IHC results PD-L1: Score > 50%

Hartwig WGS (EXAMPLE-LUNG-01-T, 01-Sep-2024)

General

| Purity | TML Status | TMB Status | MS Stability | HR Status      | DPYD                     | UGT1A1                   |
|--------|------------|------------|--------------|----------------|--------------------------|--------------------------|
| 50%    | 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 in Example | Trials in Hartwig        | Best evidence in External | Resistance in External |
|--------------------|----------------------------|-------------------|-------------------|--------------------------|---------------------------|------------------------|
| Mutation (Hotspot) | EGFR C797S (1/4 copies)    | High              | TEDR1             | NCT00000008              | Pre-clinical              |                        |
| Mutation (Hotspot) | EGFR L858R (2/4 copies)    | High              |                   | NCT00000006, NCT00000007 | Approved                  |                        |
| Mutation (Hotspot) | KRAS G12C (0.3/2 copies)*  | High              | KAYRAS            | NCT00000009              |                           |                        |
| Mutation (Hotspot) | KRAS G12D (0.3/2 copies)*  | High              |                   |                          |                           |                        |
| Loss               | TP53 del, 0 copies         | High              |                   |                          |                           |                        |
| 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 | 2024-09-01<br>Hartwig WGS |
|-------------------------|--|-------------------|---------------------------|
| EGFR L858R<br>(Tier I)  | Missense<br>Gain of function<br>Hotspot    | High              | VAF 0.5%                  |
| EGFR C797S<br>(Tier II) | Missense<br>Gain of function<br>Hotspot    | High              | VAF 0.25%                 |
| KRAS G12C<br>(Tier III) | Missense<br>Gain of function<br>Hotspot    | High              | VAF 0.15%                 |
| KRAS G12D<br>(Tier III) | Missense<br>Gain of function<br>Hotspot    | High              | VAF 0.15%                 |
| MET_MET<br>(Tier III)   | Fusion<br>Known fusion<br>Gain of function | High              | Detected                  |
| TP53 del<br>(Tier III)  | Deletion<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 | 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                        |
| LVEF                             | 50%                         |
| Cancer-related complications     | None                        |
| Known allergies                  | None                        |
| Recent surgeries                 | 01-Aug-2024 Cholecystectomy |

Tumor details (01-Oct-2024)

|                     |                        |
|---------------------|------------------------|
| 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 Summary

External trials potentially eligible based on molecular results which are potentially recruiting locally in Netherlands (2)

| Trial title                      | Events     | Source Events | Cancer Types                  | Hospitals                       |
|----------------------------------|------------|---------------|-------------------------------|---------------------------------|
| <a href="#">EGFR-C797S-TRIAL</a> | EGFR C797S | EGFR C797S    | Lung non-small cell carcinoma | Elisabeth-TweeSteden Ziekenhuis |
| <a href="#">EGFR-L858R-TRIAL</a> | EGFR L858R | EGFR L858R    | Lung non-small cell carcinoma | Elisabeth-TweeSteden Ziekenhuis |

External trials potentially eligible based on molecular results which are potentially recruiting internationally (2)

| Trial title                        | Events     | Source Events | Cancer Types                  | Country (cities)    |
|------------------------------------|------------|---------------|-------------------------------|---------------------|
| <a href="#">EGFR-BE</a>            | EGFR L858R | EGFR L858R    | Lung non-small cell carcinoma | Belgium (Brussels)  |
| <a href="#">KRAS-G12C-TRIAL-DE</a> | KRAS G12C  | KRAS G12C     | Lung non-small cell carcinoma | Germany (Stuttgart) |