

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          |
| Relevant other oncological history  | None          |                      |
| Previous primary tumor              | None          |                      |
| Relevant non-oncological history    | 2023          | Rheumatoid arthritis |

Recent molecular results

Hartwig WGS (22-Feb-2025)

|                                       |  |
|---------------------------------------|--|
| 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 del                                     |
| Homozygously disrupted genes          | None   |
| Gene fusions                          | MET(exon13)::MET(exon15) fusion              |
| Driver virus                          | None   |

Trial-relevant IHC results

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

Standard-of-care options considered potentially eligible

There are no standard of care treatment options for this patient

Phase 2/3+ trials in NL that are open and potentially eligible (2 trials)

| Trial   | Cohort                   | Molecular  | Sites                           | Warnings |
|---|--------------------------|------------|---------------------------------|----------|
| <a href="#">METC 04</a><br><a href="#">TEDR1</a><br><a href="#">(Phase 2)</a> | Lung cancer C797S cohort | EGFR C797S | NKI-AvL                         | None     |
| <a href="#">EGFR-C797S-TRIAL</a><br><a href="#">(Phase 2)</a>                 | EGFR C797S               | EGFR C797S | Elisabeth-TweeSteden Ziekenhuis |          |

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

Phase 1/2 (or unknown phase) trials in NL that are open and potentially eligible (3 trials)

| Trial  | Cohort                               | Molecular                | Sites      | Warnings  |
|--|--------------------------------------|--------------------------|------------|---|
| <a href="#">METC 02</a><br><a href="#">KAYRAS</a><br><a href="#">(Phase 1/2)</a> | Dose expansion - monotherapy - NSCLC | KRAS G12D, PD-L1 >= 50.0 | Erasmus MC | Variant(s) G12D in KRAS but subclonal likelihood of > 50% |

| Trial   | Cohort                                      | Molecular         | Sites                                  | Warnings  |
|---|---|-------------------|--|---|
| <b>METC 01</b><br>IEMOEN<br>(Phase 1)                       | Dose escalation - monotherapy<br>(no slots) | None              |  | Has not exhausted SOC (at least platinum doublet remaining) |
| <i><a href="#">EGFR-L858R-TRIAL</a></i><br><i>(Phase 1)</i> | <i>EGFR L858R</i>                           | <i>EGFR L858R</i> | <i>Elisabeth-TweeSteden Ziekenhuis</i> |   |

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 trials)

| Trial   | Cohort            | Molecular         | Sites                     |
|---|-------------------|-------------------|---------------------------|
| <i><a href="#">EGFR-BE</a></i><br><i>(Phase 1)</i>            | <i>EGFR L858R</i> | <i>EGFR L858R</i> | <i>Belgium: Brussels</i>  |
| <i><a href="#">KRAS-G12C-TRIAL-DE</a></i><br><i>(Phase 1)</i> | <i>KRAS G12C</i>  | <i>KRAS G12C</i>  | <i>Germany: Stuttgart</i> |

Trials in this table 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                  |                     |                          |                           |                        |

The table continues on the next page

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PATIENT  
EXAMPLE-LUNG-01  
REPORT DATE  
17-Sep-2025

| Type         | Driver  | Trials (Locations) | Trials in Hartwig | Best evidence in External | Resistance in External |
|--------------|---|--------------------|-------------------|---------------------------|------------------------|
| Known fusion | MET(exon13)::MET(exon15) fusion<br>Domain(s) kept: Tyrosine Kinase<br>Domain(s) lost: Juxtamembrane |                    |                   |                           |                        |

### Other drivers or relevant events

## IHC results

## Molecular history

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| Event      | Description            | 2025-02-22<br>Hartwig WGS |
|------------|------------------------|---------------------------|
| (Tier III) | Unknown protein effect |                           |
| TMB        |                        | 14.0                      |
| MSI        |                        | Stable                    |

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

There are no standard of care treatment options for this patient

Resistance evidence

There are no standard of care treatment options for this patient

Treatment ranking

| Event                    | Treatment   | Score |
|--------------------------|-------------|-------|
| EGFR L858R<br>EGFR C797S | AFATINIB    | 2,400 |
| EGFR L858R               | OSIMERTINIB | 1,900 |

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> | AFATINIB<br><i>Lung non-small cell carcinoma (2013)</i> |         |   |

Off label clinical evidence

None

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%                         |
| Known allergies                  | None                        |
| Recent surgeries                 | 01-Aug-2024 Cholecystectomy |

Tumor details (20-Feb-2025)

|                    |                              |
|--------------------|------------------------------|
| Measurable disease | Yes                          |
| Known lesions      | Liver, Lung                  |
| 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 |



Trial Matching Details

National trials that are open and potentially eligible (2 trials)

| Trial   | Cohort     | Molecular  | Sites                           |
|---|------------|------------|---------------------------------|
| <a href="#">EGFR-C797S-TRIAL</a><br>(Phase 2) | EGFR C797S | EGFR C797S | NL: Tilburg, Germany: Stuttgart |
| <a href="#">EGFR-L858R-TRIAL</a><br>(Phase 1) | EGFR L858R | EGFR L858R | NL: Tilburg, Germany: Stuttgart |

Trials in this table are matched solely on molecular event and tumor type (clinical data excluded).

International trials that are open and potentially eligible (2 trials)

| Trial   | Cohort     | Molecular  | Sites              |
|---|------------|------------|--------------------|
| <a href="#">EGFR-BE</a><br>(Phase 1)            | EGFR L858R | EGFR L858R | Belgium: Brussels  |
| <a href="#">KRAS-G12C-TRIAL-DE</a><br>(Phase 1) | KRAS G12C  | KRAS G12C  | Germany: Stuttgart |

Trials in this table are matched solely on molecular event and tumor type (clinical data excluded).

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

| Trial                                 | Cohort                       | Molecular | Sites | Warnings  |
|---------------------------------------|------------------------------|-----------|-------|---|
| <b>METC 01</b><br>IEMOEN<br>(Phase 1) | Dose expansion - monotherapy | None      |       | Has not exhausted SOC (at least platinum doublet remaining) |

Trials and cohorts that are considered ineligible (4 cohorts from 3 trials)

| Trial  | Cohort   | Molecular                   | Ineligibility reasons                 |
|--|--|-----------------------------|---------------------------------------|
| <a href="#">METC 02</a><br><a href="#">KAYRAS</a><br>(Phase 1/2) | Dose expansion - monotherapy - Colorectum              | KRAS G12D,<br>PD-L1 >= 50.0 | No colorectal cancer                  |
| <b>METC 03</b><br>NO-SEE797ES                                    | Dose escalation - monotherapy                          | EGFR C797S                  | C797S in EGFR in canonical transcript |
| <b>METC 05</b><br>PICKME3CA                                      | <i>Applies to all cohorts below</i>                    | None                        | No PIK3CA activating mutation(s)      |
|  | Dose expansion - monotherapy - NSCLC ( <i>closed</i> ) |                             |                                       |

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ACTIN Report (research use only)

| Trial | Cohort  | Molecular | Ineligibility reasons                                       |
|-------|---|-----------|---|
|       | Dose expansion - monotherapy - Other cancer types <i>(closed)</i> |           | Tumor belongs to DOID term(s) lung non-small cell carcinoma |

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

None

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

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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  |

ACTIN Report (research use only)

PATIENT  
EXAMPLE-LUNG-01

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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      | <b>WARN</b><br>Variant(s) G12D in KRAS but subclonal likelihood of > 50%    |
| I-03      | <b>UNDETERMINED</b><br>ASAT and ALAT are not present or cannot be evaluated |
| I-01      | <b>PASS</b><br>Patient is at least 18 years old                             |
| I-02      | <b>PASS</b><br>Stage IV is considered metastatic                            |
| I-05      | <b>PASS</b><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      | <b>PASS</b><br>Tumor belongs to DOID term(s) lung non-small cell carcinoma |

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METC 02 - Dose expansion - monotherapy - Colorectum

Cohort ID

Potentially eligible?

Open for inclusion?

Has slots available?

B

No

Yes

Yes

| Reference | Evaluation           |
|-----------|----------------------|
| I-02      | FAIL                 |
|           | 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       | <b>PASS</b><br>Patient is at least 18 years old   |
| I-2       | <b>PASS</b><br>Stage IV is considered metastatic<br>Tumor belongs to DOID term(s) lung cancer |
| I-3       | <b>PASS</b><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><br>Tumor belongs to DOID term(s) lung non-small cell carcinoma |