

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%

Phase 2/3+ trials in NL that are open and potentially eligible (1 trial)

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

Phase 1/2 (or unknown phase) trials in NL that are open and potentially eligible (4 trials)

| Trial  | Cohort                                   | Molecular                | Sites                                  | Warnings  |
|--|--|--------------------------|--|---|
| <a href="#">METC 02</a><br><a href="#">KAYRAS</a><br>(Phase 1/2) | Dose expansion - monotherapy - NSCLC     | KRAS G12D, PD-L1 >= 50.0 | Erasmus MC                             | Variant(s) G12D in KRAS but subclonal likelihood of > 50%   |
| <b>METC 01</b><br>IEMOEN<br>(Phase 1)                            | Dose escalation - monotherapy (no slots) | None                     |  | Has not exhausted SOC (at least platinum doublet remaining) |
| <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> |   |

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 (1 trial)

| Trial                              | Cohort    | Molecular | Sites              |
|------------------------------------|-----------|-----------|--------------------|
| <a href="#">KRAS-G12C-TRIAL-DE</a> | KRAS G12C | KRAS G12C | Germany: Stuttgart |

Trials in this table are matched solely on molecular event and tumor type (clinical data excluded).  
1 trial filtered due to trials recruiting nationally for the same molecular target. See Other Trial Matching Results for filtered matches.

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       | 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              |                     |                   |                           |                        |
| 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%                         |
| 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 |

Trial Matching Details

Filtered trials potentially eligible based on molecular results which are potentially recruiting (1 trial)

| Trial                   | Cohort     | Molecular  | Sites             |
|-------------------------|------------|------------|-------------------|
| <a href="#">EGFR-BE</a> | EGFR L858R | EGFR L858R | Belgium: Brussels |

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> )              |                             |   |
|  | 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)

| Trial | Cohort | Molecular | Sites | Configuration |
|-------|--------|-----------|-------|---------------|
| None  |        |           |       |               |