

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

Trial-relevant IHC results

PD-L1 Score > 50%

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

| Trial | Cohort | Molecular | Sites | Warnings |
|---|--------------------------|------------|---------------------------------|----------|
| METC 04 TEDR1 (Phase 2) | Lung cancer C797S cohort | EGFR C797S | NKI-AvL | None |
| EGFR-C797S-TRIAL (Phase 2) | 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 |
|--|--|--------------------------|---------------------------------|---|
| METC 02 KAYRAS (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% |
| METC 01 IEMOEN (Phase 1) | Dose escalation - monotherapy (no slots) | None | | Has not exhausted SOC (at least platinum doublet remaining) |
| EGFR-L858R-TRIAL (Phase 1) | EGFR L858R | EGFR L858R | Elisabeth-TweeSteden Ziekenhuis | |

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 |
|--|-----------|-----------|--------------------|
| KRAS-G12C-TRIAL-DE (Phase 1) | 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 | | | | |

The table continues on the next page

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 Domain(s) kept: Tyrosine Kinase Domain(s) lost: Juxtamembrane | | | | |

Other drivers or relevant events

IHC results

4/6

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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

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

| Trial | Cohort | Molecular | Sites |
|--|------------|------------|-------------------|
| EGFR-BE (Phase 1) | EGFR L858R | EGFR L858R | Belgium: Brussels |

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

| Trial | Cohort | Molecular | Sites | Warnings |
|---------------------------------------|------------------------------|-----------|-------|---|
| METC 01 IEMOEN (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 |
|--|---|-----------------------------|---|
| METC 02 KAYBAS (Phase 1/2) | Dose expansion - monotherapy - Colorectum | KRAS G12D, PD-L1 >= 50.0 | No colorectal cancer |
| METC 03 NO-SEE797ES | Dose escalation - monotherapy | EGFR C797S | C797S in EGFR in canonical transcript |
| METC 05 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)

None