

ACTIN Report (research use only)

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

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)

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%
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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
<u>METC 04</u> <u>TEDR1</u> <u>(Phase 2)</u>	Lung cancer C797S cohort	EGFR C797S	NKI-AvL	None
<u>EGFR-C797S-TRIAL</u> <u>(Phase 2)</u>	<i>EGFR C797S</i>	<i>EGFR C797S</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.

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

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

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Trial	Cohort	Molecular	Sites	Warnings
METC 01 IEMOEN (Phase 1)	Dose escalation - monotherapy <i>(no slots)</i>	None		Has not exhausted SOC (at least platinum doublet remaining)
<i>EGFR-L858R-TRIAL</i> <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>EGFR-BE</i> <i>(Phase 1)</i>	<i>EGFR L858R</i>	<i>EGFR L858R</i>	<i>Belgium: Brussels</i>
<i>KRAS-G12C-TRIAL-DE</i> <i>(Phase 1)</i>	<i>KRAS G12C</i>	<i>KRAS G12C</i>	<i>Germany: Stuttgart</i>

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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%
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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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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				

* Variant has > 50% likelihood of being sub-clonal

Other drivers or relevant events

None

IHC results

PD-L1

Score > 50%

Molecular history

Event	Description	2025-02-22 Hartwig WGS
EGFR L858R (Tier I)	Mutation (gain of function)	VAF 0.5%
EGFR C797S (Tier II)	Mutation (gain of function)	VAF 0.25%
KRAS G12C (Tier III)	Mutation (gain of function)	VAF 0.15%
KRAS G12D (Tier III)	Mutation (gain of function)	VAF 0.15%
MET(exon13)::MET(exon15) fusion (Tier III)	Known fusion Gain of function	Detected
TP53 del	Deletion	Detected

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Event	Description	Date	Method
(Tier III)	Unknown protein effect	2025-02-22	Hartwig WGS
TMB		14.0	
MSI		Stable	

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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		
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 <small>Lung non-small cell carcinoma (2015)</small>
EGFR L858R	EGFR L858R	OSIMERTINIB <small>Lung non-small cell carcinoma (2016)</small>			
		AFATINIB <small>Lung non-small cell carcinoma (2013)</small>			

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Off label clinical evidence

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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

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

Trial	Cohort	Molecular	Sites
EGFR-C797S-TRIAL (Phase 2)	EGFR C797S	EGFR C797S	NL: Tilburg, Germany: Stuttgart
EGFR-L858R-TRIAL (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
EGFR-BE (Phase 1)	EGFR L858R	EGFR L858R	Belgium: Brussels
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).

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 KAYRAS (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	Applies to all cohorts below	None	No PIK3CA activating mutation(s)
	Dose expansion - monotherapy - NSCLC (closed)		

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Trial	Cohort	Molecular	Ineligibility reasons
	Dose expansion - monotherapy - Other cancer types (closed)		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 WARN

Has not exhausted SOC (at least platinum doublet remaining)

E-02 UNDETERMINED

No measurement found for hemoglobin

E-03 UNDETERMINED

No measurement found for absolute neutrophil count

E-01 PASS

Has no other condition belonging to category autoimmune disease

I-01 PASS

Patient is at least 18 years old

I-02 PASS

Has solid primary tumor

Stage IV is considered metastatic

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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**

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

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METC 02 - Dose expansion - monotherapy - Colorectum

Cohort ID **B**

Potentially eligible? **No**

Open for inclusion? **Yes**

Has slots available? **Yes**

Reference	Evaluation
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I-02	FAIL
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No colorectal cancer

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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	PASS Patient is at least 18 years old
I-2	PASS Stage IV is considered metastatic Tumor belongs to DOID term(s) lung cancer
I-3	PASS 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

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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 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 No PIK3CA activating mutation(s)

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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
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I-03	FAIL
Tumor belongs to DOID term(s) lung non-small cell carcinoma	