

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
Homozygously disrupted genes	None
Gene fusions	MET(exon13)::MET(exon15) fusion
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

Trials in Other that are open and potentially eligible (3 cohorts from 3 trials)

Trial	Cohort	Molecular	Sites	Warnings
<a href="#">METC 04 TEDR1</a>	Lung cancer C797S cohort	EGFR C797S	NKI-AvL	None
<a href="#">METC 02 KAYRAS</a>	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 IEMOEN</b>	Dose escalation - monotherapy (no slots)	None		Has not exhausted SOC (at least platinum doublet remaining)

International trials that are open and potentially eligible (4 cohorts from 4 trials)

Trial	Cohort	Molecular	Sites
<a href="#">EGFR-C797S-TRIAL</a>	EGFR C797S	EGFR C797S	NL: Tilburg, Germany: Stuttgart
<a href="#">EGFR-L858R-TRIAL</a>	EGFR L858R	EGFR L858R	NL: Tilburg, Germany: Stuttgart
<a href="#">EGFR-BE</a>	EGFR L858R	EGFR L858R	Belgium: Brussels

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

International trials 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				

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

Type	Driver	Trials (Locations)	Trials in Hartwig	Best evidence in External	Resistance in External
None					

PD-L1 **Score > 50%**

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	2025-02-22 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

On label clinical evidence

Event	CKB Event	Level A	Level B	Level C	Level D
EGFR C797S	EGFR C797S				AFATINIB <i>Lung non-small cell carcinoma (2015)</i>
EGFR L858R	EGFR L858R	OSIMERTINIB <i>Lung non-small cell carcinoma (2016)</i>  AFATINIB <i>Lung non-small cell carcinoma (2013)</i>			

Off label clinical evidence

Event	CKB Event	Level A	Level B	Level C	Level D
None					

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				

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AFATINIB:

Level D (2015)

Lung non-small cell carcinoma

In a case-report, afatinib was effective against EGFR L858R/C797S positive lung cancer.

Treatment ranking

Treatment	Events	Score
AFATINIB	EGFR L858R	2,150
	EGFR C797S	
OSIMERTINIB	EGFR L858R	1,900

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

Trials in Other that are open and potentially eligible (0)

Trial	Cohort	Molecular	Sites	Warnings
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International trials that are open and potentially eligible (4 cohorts from 4 trials)

Trial	Cohort	Molecular	Sites
<a href="#">EGFR-C797S-TRIAL</a>	EGFR C797S	EGFR C797S	NL: Tilburg, Germany: Stuttgart
<a href="#">EGFR-L858R-TRIAL</a>	EGFR L858R	EGFR L858R	NL: Tilburg, Germany: Stuttgart
<a href="#">EGFR-BE</a>	EGFR L858R	EGFR L858R	Belgium: Brussels
<a href="#">KRAS-G12C-TRIAL-DE</a>	KRAS G12C	KRAS G12C	Germany: Stuttgart

International trials are matched solely on molecular event and tumor type (clinical data excluded).

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

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

Trials and cohorts that are considered ineligible (4)

Trial	Cohort	Molecular	Ineligibility reasons
<b>METC 03</b> NO-SEE797ES	Dose escalation - monotherapy	EGFR C797S	C797S in EGFR in canonical transcript
<a href="#">METC 02</a> <a href="#">KAYRAS</a>	Dose expansion - monotherapy - Colorectum	KRAS G12D, PD-L1 >= 50.0	No colorectal cancer
<b>METC 05</b> 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)

Trial	Cohort	Molecular	Sites	Configuration
None				

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Potentially eligible open trials & cohorts

METC 01

Potentially eligibleYes

AcronymIEMOEN

TitlePhase 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>

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	<b>WARN</b> Variant(s) G12D in KRAS but subclonal likelihood of > 50%
I-03	<b>UNDETERMINED</b> ASAT and ALAT are not present or cannot be evaluated
I-01	<b>PASS</b> Patient is at least 18 years old
I-02	<b>PASS</b> Stage IV is considered metastatic
I-05	<b>PASS</b> 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> 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

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

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