

Gender: Female | Birth year: 1975 | WHO: 1

Tumor: Lung - Adenocarcinoma | Lesions: Liver, Lung | Stage: IV

Summary

Clinical summary

Gender	Female	Birth year	1975
WHO	1	Tumor	Lung - Adenocarcinoma
Lesions	Liver, Lung	Stage	IV
Measurable disease (RECIST)	Yes	DPYD	*1_HOM (Normal function)
		UGT1A1	*1_HOM (Normal function)
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	KRAS G12C (0.3/2 copies)*, KRAS G12D (0.3/2 copies)*, NRAS: No reportable events, BRAF: No reportable events, HER2: No reportable events, MSS		

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 detection	None
Potential trial events, considered no high driver	None

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

Trial	Cohort	Molecular	Sites	Warnings
METC 04 TEDR1	Lung cancer C797S cohort	EGFR C797S	NKI-AvL	None
METC 02 KAYRAS	Dose expansion - monotherapy - NSCLC	KRAS G12D	Erasmus MC	Variant(s) G12D in KRAS but subclonal likelihood of > 50%
EGFR-C797S-TRIAL	<i>EGFR C797S</i>	<i>EGFR C797S</i>	<i>Elisabeth-TweeSteden Ziekenhuis</i>	
EGFR-L858R-TRIAL	<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 cohorts from 2 trials)

Trial	Cohort	Molecular	Sites
EGFR-BE	EGFR L858R	EGFR L858R	Belgium: Brussels
KRAS-G12C-TRIAL-DE	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 considered ineligible (2)

Trial	Cohort	Molecular	Ineligibility reasons
METC 03 NO-SEE797ES	Dose escalation - monotherapy	EGFR C797S	C797S in EGFR in canonical transcript
METC 02 KAYRAS	Dose expansion - monotherapy - Colorectum	KRAS G12D	No colorectal cancer

Resistance evidence

Resistance evidence

There are no standard of care treatment options for this patient

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	

Drivers

Type	Driver	Driver likelihood	Trials (Locations)	Trials in Hartwig	Best evidence in External	Resistance in External
Mutation (Gain of function)	EGFR C797S (1/4 copies)		TEDR1 (NKI-AvL)	NCT00000008	Pre-clinical	
Mutation (Gain of function)	EGFR L858R (2/4 copies)			NCT00000006, NCT00000007	Approved	
Mutation (Gain of function)	KRAS G12C (0.3/2 copies)*			NCT00000009		
Mutation (Gain of function)	KRAS G12D (0.3/2 copies)*		KAYRAS (Erasmus MC)			

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Type	Driver	Driver likelihood	Trials (Locations)	Trials in Hartwig	Best evidence in External	Resistance in External
Deletion	TP53 del, 0 copies	High				
Known fusion	MET(exon13)::MET(exon15) fusion	High				

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

IHC results

PD-L1

Score > 50%

Molecular History

Molecular history

Event	Description	Driver likelihood	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	High	Detected
TP53 del (Tier III)	Deletion Unknown protein effect	High	Detected
TMB			14.0
MSI			Stable

SOC literature 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

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%
Cancer-related complications	None
Known allergies	None
Recent surgeries	01-Aug-2024 Cholecystectomy

Tumor details (20-Feb-2025)

Measurable disease	Yes
CNS lesion status	No known CNS lesions
Brain lesion status	No known brain lesions

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

SOC literature details

There are no standard of care treatment options for this patient

Molecular Evidence

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			
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 EGFR C797S	2,150
OSIMERTINIB	EGFR L858R	1,900

Other Trial Matching Results

Trials in NL that are open and potentially eligible (2 cohorts from 2 trials)

Trial	Cohort	Molecular	Sites	Warnings
EGFR-C797S-TRIAL	EGFR C797S	EGFR C797S	Elisabeth-TweeSteden Ziekenhuis	
EGFR-L858R-TRIAL	EGFR L858R	EGFR L858R	Elisabeth-TweeSteden Ziekenhuis	

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

Trial Matching Details

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>

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

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

METC 02 - Dose expansion - monotherapy - NSCLC

Cohort ID	A
Potentially eligible?	Yes
Open for inclusion?	Yes
Has slots available?	Yes
Reference	Evaluation
I-02	<div>PASS</div> <div>Tumor belongs to DOID term(s) lung non-small cell carcinoma</div>

METC 02 - Dose expansion - monotherapy - Colorectum

Cohort ID	B
Potentially eligible?	No
Open for inclusion?	Yes
Has slots available?	Yes
Reference	Evaluation
I-02	<div>FAIL</div> <div>No colorectal cancer</div>

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

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