PATIENT **EXAMPLE-LUNG-01**

REPORT DATE 17-Apr-2025

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 Yes DPYD *1_HOM (Normal function)

(RECIST)

UGT1A1 *1_HOM (Normal function)

Relevant systemic treatment history 6/2023-1/2025 Osimertinib

Relevant other oncological history

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 High (160) / TMB High (14)

Microsatellite (in)stability Stable

HR status Proficient (0)

High driver mutations EGFR L858R, EGFR C797S, KRAS G12D, KRAS G12C

Amplified genes

Deleted genes

TP53

Homozygously disrupted genes

Gene fusions

Virus detection

Trial-relevant events, considered medium/low driver:

None

IHC results PD-L1: Score > 50%

Standard of care options considered potentially eligible

There are no standard of care treatment options for this patient

Approved treatments considered eligible

Treatment

Not yet determined

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

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Trial	Cohort	Molecular	Sites	Warnings
METC 04	Lung cancer C797S cohort	EGFR C797S	NKI-AvL	None
TEDR1				
METC 02	Dose expansion - monotherapy -	KRAS G12D	Erasmus MC	Variant(s) G12D in KRAS but subclonal likelihood of >
KAYRAS	NSCLC			50%
EGFR-L858R-	EGFR L858R	EGFR L858R	Elisabeth-	
<u>TRIAL</u>			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 cohort from 1 trial)

Trial	Cohort	Molecular	Sites
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	Sites	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	Erasmus MC	No colorectal cancer

¹ trial filtered due to eligible local trials for the same molecular target or because the trial is for young adult patients only. See Trial Matching Overview for filtered matches.

¹ trial filtered due to trials recruiting nationally for the same molecular target. See Trial Matching Overview for filtered matches.

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Resistance evidence

Resistance evidence

There are no standard of care treatment options for this patient

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Molecular Details

IHC results PD-L1: Score > 50%

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

Туре	Driver	Driver likelihood	Trials (Locations)	Trials in Hartwig	Best evidence in External	Resistance in External
Mutation (Hotspot)	EGFR C797S (1/4 copies)	High	TEDR1 (NKI-AvL)		Pre-clinical	
Mutation (Hotspot)	EGFR L858R (2/4 copies)	High		NCT0000006	Approved	
Mutation (Hotspot)	KRAS G12C (0.3/2 copies)*	High		NCT00000009		
Mutation (Hotspot)	KRAS G12D (0.3/2 copies)*	High	KAYRAS (Erasmus Mo	C)		
Loss	TP53 del, 0 copies	High				
Known fusion	MET::MET, exon 13 - exon 15	High				

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

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Molecular History

Molecular history

Event	Description	Driver likelihood	2025-02-22 Hartwig WGS	
EGFR L858R (Tier I)	Mutation (Hotspot) Gain of function	High	VAF 0.5%	
EGFR C797S (Tier II)	Mutation (Hotspot) Gain of function	High	VAF 0.25%	
KRAS G12C (Tier III)	Mutation (Hotspot) Gain of function	High	VAF 0.15%	
KRAS G12D (Tier III)	Mutation (Hotspot) Gain of function	High	VAF 0.15%	
MET::MET (Tier III)	Known fusion Gain of function	High	Detected	
TP53 del (Tier III)	Loss Unknown protein effect	High	Detected	
TMB			14.0	
MSI			Stable	

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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

None

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Clinical Details

Clinical summary

6/2023-1/2025 Relevant systemic treatment history Osimertinib

Relevant other oncological history None

Previous primary tumor 2023 Rheumatoid arthritis Relevant non-oncological history

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 No known brain lesions Brain lesion status

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
Discourse for the con-					

Blood transfusions

Product	Date
ERTHROCYTES_FILTERED	20-Sep-2024

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Molecular Evidence

On I	abel	clini	cal	evid	lence
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Event	CKB Event	Level A	Level B	Level C	Level D
EGFR C797S	EGFR C797S				AFATINIB
					Lung non-small cell carcinoma (2015)
EGFR L858R	EGFR L858R	OSIMERTINIB			
		Lung non-small cell carcinoma (2016)			
		AFATINIB			
		Lung non-small cell carcinoma (2013)			
Off label clinic	al evidence				
Event	CKB Event	Level A	Level B	Level C	Level D
None					
Efficacy evide	nce 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.

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Trial Matching Overview

Trials in NL that are open and potentially eligible (1 cohort from 1 trial)

Trial	Cohort	Molecular	Sites	Warnings
EGFR-L858R-	EGFR L858R	EGFR L858R	Elisabeth-	
<u>TRIAL</u>			TweeSteden	
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International trials that are open and potentially eligible (1 cohort from 1 trial)

Trial	Cohort	Molecular	Sites
KRAS-G12C-TRIAL-DE	KRAS G12C	KRAS G12C	Germany (Stuttgart)

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

Filtered trials potentially eligible based on molecular results which are potentially recruiting (2)

Trial	Cohort	Molecular	Sites
EGFR-C797S-TRIAL	EGFR C797S	EGFR C797S	Elisabeth-TweeSteden Ziekenhuis
EGFR-BE	EGFR L858R	EGFR L858R	Belgium (Brussels)

¹ trial filtered due to trials recruiting nationally for the same molecular target. See Trial Matching Overview for filtered matches.