PATIENT
EXAMPLE-LUNG-01

REPORT DATE 06-Nov-2024

Gender: Male | Birth year: 1950 | WHO: 0

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

Summary

Clinical summary

Gender Male Birth year 1950

WHO 0 Tumor Lung - Adenocarcinoma

Lesions Liver Stage IV

Measurable disease NA DPYD *1_HOM (Normal function)

(RECIST)

UGT1A1 *1_HOM (Normal function)

Relevant systemic treatment history 1/2023-9/2024 Osimertinib

Relevant other oncological history

Previous primary tumor

None

Relevant non-oncological history 2022 Rheumatoid arthritis

Recent molecular results KRAS G12D (0.3/2 copies)*, NRAS: No reportable events, BRAF: No reportable

events, HER2: No reportable events, MSS

Recent molecular results

Hartwig WGS (20-Aug-2024)

Biopsy location Liver (purity 50%)

Molecular tissue of origin prediction

Lung: Non-small cell (98%)

Tumor mutational load / burden

TML Low (40) / TMB Low (2)

Microsatellite (in)stability Stable

HR status Proficient (0)

High driver mutations EGFR L858R, EGFR C797S, KRAS G12D

Amplified genes

Deleted genes

TP53

Homozygously disrupted genes

Gene fusions

Virus detection

Potentially actionable events with medium/low driver:

None

IHC results PD-L1: Score 1%

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

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Example trials that are open and potentially eligible (2 cohorts from 2 trials)

Trial	Cohort	Molecular	Warnings
METC 04 TEDR1	Lung cancer C797S cohort	EGFR C797S	None
METC 02 KAYRAS	Dose expansion - monotherapy - NSCLC	KRAS G12D	Variant(s) KRAS G12D in KRAS but subclonal likelihood of > 50%

Example trials that are open and potentially eligible but currently have no slots available (1 cohort from 1 trial)

Trial	Cohort	Molecular	Warnings
METC 01	Dose escalation - monotherapy		Hemoglobin 5.6 mmol/L below min of 6.0 mmol/L, History of rheumatoid
IEMOEN			arthritis, SOC not exhausted: at least platinum doublet remaining

External trials potentially eligible based on molecular results which are potentially recruiting locally in Netherlands (1)

Trial title	Events	Source Events	Cancer Types	Hospitals
EGFR-NEW	EGFR L858R	EGFR L858R	Lung non-small cell	Tilburg
			carcinoma	

Example trials and cohorts that are open but considered ineligible (2)

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

Open cohorts with no slots available are shown in grey.

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Resistance evidence

There are no standard of care treatment options for this patient

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Molecular Details

IHC results PD-L1: Score 1%

Hartwig WGS (EXAMPLE-LUNG-01-T, 20-Aug-2024)

General

Purity	TML Status	TMB Status	MS Stability	HR Status	DPYD	UGT1A1
50%	Low (40)	Low (2)	Stable	Proficient (0)	*1_HOM (Normal function)	*1_HOM (Normal function)

Predicted tumor origin

1. Lung: Non-small cell

	_			
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 in Example	Trials in Hartwig	Best evidence in External	Resistance in External
Mutation (Hotspot)	EGFR C797S (1/4 copies)	High	TEDR1			
Mutation (Hotspot)	EGFR L858R (2/4 copies)	High				
Mutation (Hotspot)	KRAS G12D (0.3/2 copies)*	High	KAYRAS			
Loss	TP53 del, 0 copies	High				

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

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Molecular History

Molecular history

Event	Description	Driver likelihood	2024-08-20
			Hartwig WGS
EGFR C797S	Mutation (Hotspot)	High	VAF 0.25%
(Tier III)	Gain of function		
EGFR L858R	Mutation (Hotspot)	High	VAF 0.5%
(Tier III)	Gain of function		
KRAS G12D	Mutation (Hotspot)	High	VAF 0.15%
(Tier III)	Gain of function		
TP53 del	Loss	High	Detected
(Tier III)	Unknown protein effect		
TMB			2.0
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

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Clinical Details

Clinical summary

Relevant systemic treatment history 1/2023-9/2024 Osimertinib

Relevant other oncological history None

Previous primary tumor None

Relevant non-oncological history 2022 Rheumatoid arthritis

Patient current details (01-Oct-2024)

Tumor details (01-Oct-2024)

Measurable disease Unknown

CNS lesion status

Brain lesion status

No known CNS lesions

No known brain lesions

Active medication details

Medication Administration route Start date Stop date Dosage Frequency

None

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Molecular Evidence

On label clinical evidence

Event CKB Event Level A Level B Level C Level D

Off label clinical evidence

Event CKB Event Level A Level B Level C Level D

Efficacy evidence description

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Trial Matching Summary

External trials potentially eligible based on molecular results which are potentially recruiting locally in Netherlands (1)

Trial title	Events	Source Events	Cancer Types	Hospitals
EGFR-NEW	EGFR L858R	FR L858R EGFR L858R		Tilburg
			carcinoma	