ACTIN Report (research use only)

PATIENT
EXAMPLE-LUNG-01

REPORT DATE
07-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 (RECIST)	**NA**	DPYD	***1_HOM (Normal function)**
UGT1A1	***1_HOM (Normal function)**		

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**
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	**None**
Deleted genes	**TP53**
Homozygously disrupted genes	**None**
Gene fusions	**None**
Virus detection	**None**
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

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 IEMOEN	Dose escalation - monotherapy		Hemoglobin 5.6 mmol/L below min of 6.0 mmol/L, History of rheumatoid 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 carcinoma	Tilburg

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 NO-SEE797ES	Dose escalation - monotherapy		C797S detected in EGFR

Open cohorts with no slots available are shown in grey.

Resistance evidence

There are no standard of care treatment options for this patient

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

Type	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

Molecular History

Molecular history

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

Unresolved toxicities grade => 2	**None**
Cancer-related complications	**None**
Known allergies	**None**

Tumor details (01-Oct-2024)

Measurable disease	**Unknown**
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
None					

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

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
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