ACTIN Report (research use only)

PATIENT
EXAMPLE-LUNG-01

REPORT DATE
07-Nov-2024

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 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	**None**
Deleted genes	**TP53**
Homozygously disrupted genes	**None**
Gene fusions	**MET_MET**
Virus detection	**None**
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 The Netherlands 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	*EGFR C797S*	*EGFR C797S*	*Elisabeth-TweeSteden Ziekenhuis*	
EGFR-L858R-TRIAL	*EGFR L858R*	*EGFR L858R*	*Elisabeth-TweeSteden Ziekenhuis*	

Open cohorts with no slots available are shown in grey.
Trials matched on molecular event and tumor type only (i.e. no clinical data used) are displayed in italic and small font.

International trials that are open and potentially eligible (3 cohorts from 3 trials)

Trial	Cohort	Molecular	Sites	Warnings
EGFR-BE	*EGFR L858R*	*EGFR L858R*	*Belgium (Brussels)*	
NCT00000019	*KRAS G12*	*KRAS G12C*	*Belgium (Antwerpen)*	
KRAS-TRIAL-DE	*KRAS activating mutations*	*KRAS G12C*	*Germany (Stuttgart)*	

Open cohorts with no slots available are shown in grey.
Trials matched on molecular event and tumor type only (i.e. no clinical data used) are displayed in italic and small font.

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

Resistance evidence

There are no standard of care treatment options for this patient

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

Type	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)	NCT00000008	Pre-clinical	
Mutation (Hotspot)	EGFR L858R (2/4 copies)	High		NCT00000006, NCT00000007	Approved	
Mutation (Hotspot)	KRAS G12C (0.3/2 copies)*	High		NCT00000019, NCT00000009		
Mutation (Hotspot)	KRAS G12D (0.3/2 copies)*	High	KAYRAS (Erasmus MC)			
Loss	TP53 del, 0 copies	High				
Known fusion	MET_MET, exon 14 - exon 14	High				

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

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

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 *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 clinical evidence

Event	CKB Event	Level A	Level B	Level C	Level D

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.

Trial Matching Chapter

Trials in The Netherlands 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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