

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	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 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 (01-Sep-2024)

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

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

Trial	Cohort	Molecular	Warnings
NCT00000004 TEDR1	Lung cancer C797S cohort	EGFR C797S	None
NCT00000002 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
NCT00000001 IEMOEN	Dose escalation - monotherapy		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 (2)

Trial title	Events	Source Events	Cancer Types	Hospitals
<a href="#">EGFR-C797S-TRIAL</a>	EGFR C797S	EGFR C797S	Lung non-small cell carcinoma	Elisabeth-TweeSteden Ziekenhuis
<a href="#">EGFR-L858R-TRIAL</a>	EGFR L858R	EGFR L858R	Lung non-small cell carcinoma	Elisabeth-TweeSteden Ziekenhuis

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

Trial title	Events	Source Events	Cancer Types	Country (cities)
<a href="#">EGFR-BE</a>	EGFR L858R	EGFR L858R	Lung non-small cell carcinoma	Belgium (Brussels)
<a href="#">KRAS-G12C-TRIAL-DE</a>	KRAS G12C	KRAS G12C	Lung non-small cell carcinoma	Germany (Stuttgart)

Example trials and cohorts that are considered ineligible (4)

Trial	Cohort	Molecular	Ineligibility reasons
NCT00000002 KAYRAS	Dose expansion - monotherapy - Colorectum	KRAS G12D	No colorectal cancer
NCT00000003 NO-SEE797ES	Dose escalation - monotherapy		C797S detected in EGFR
NCT00000020 PICKME3CA	Applies to all cohorts below Dose expansion - monotherapy - NSCLC Dose expansion - monotherapy - Other cancer types	None	No PIK3CA activating mutation(s)  Has tumor belonging to DOID term(s) lung non-small cell carcinoma

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 > 50%

Hartwig WGS (EXAMPLE-LUNG-01-T, 01-Sep-2024)

General

Purity	TML Status	TMB Status	MS Stability	HR Status	DPYD	UGT1A1
50%	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 in Example	Trials in Hartwig	Best evidence in External	Resistance in External
Mutation (Hotspot)	EGFR C797S (1/4 copies)	High	TEDR1	NCT00000008	Pre-clinical	
Mutation (Hotspot)	EGFR L858R (2/4 copies)	High		NCT00000006, NCT00000007	Approved	
Mutation (Hotspot)	KRAS G12C (0.3/2 copies)*	High	KAYRAS	NCT00000009		
Mutation (Hotspot)	KRAS G12D (0.3/2 copies)*	High				
Loss	TP53 del, 0 copies	High				
Known fusion	MET_MET, exon 14 - exon 14	High				

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

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Gene and variant annotations and related content are powered by Genomenon Cancer Knowledgebase (CKB).

Molecular History

Molecular history

Event	Description	Driver likelihood	2024-09-01 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	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
LVEF	50%
Cancer-related complications	None
Known allergies	None
Recent surgeries	01-Aug-2024 Cholecystectomy

Tumor details (01-Oct-2024)

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
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 Summary

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

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<a href="#">KRAS-G12C-TRIAL-DE</a>	KRAS G12C	KRAS G12C	Lung non-small cell carcinoma	Germany (Stuttgart)