

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 NL 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	<i>EGFR C797S EGFR C797S Elisabeth-TweeSteden Ziekenhuis</i>			
EGFR-L858R-TRIAL	<i>EGFR L858R EGFR L858R Elisabeth-TweeSteden Ziekenhuis</i>			
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 (2 cohorts from 2 trials)

Trial	Cohort	Molecular	Sites
EGFR-BE	EGFR L858R	EGFR L858R	Belgium (Brussels)
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			

Resistance evidence

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)	NCT000000008	Pre-clinical		
Mutation (Hotspot)	EGFR L858R (2/4 copies)	High		NCT000000006, NCT000000007	Approved		
Mutation (Hotspot)	KRAS G12C (0.3/2 copies)*	High		NCT000000009			
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							

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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	2025-02-22 Hartwig WGS
EGFR L858R (Tier I)	Mutation (Hotspot) Gain of function	High	VOF 0.5%
EGFR C797S (Tier II)	Mutation (Hotspot) Gain of function	High	VOF 0.25%
KRAS G12C (Tier III)	Mutation (Hotspot) Gain of function	High	VOF 0.15%
KRAS G12D (Tier III)	Mutation (Hotspot) Gain of function	High	VOF 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 <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
None					

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 Overview

Trials in NL that are open and potentially eligible (2 cohorts from 2 trials)			
Trial	Cohort	Molecular	Sites
EGFR-C797S-TRIAL	EGFR C797S	EGFR C797S	<i>Elisabeth-TweeSteden Ziekenhuis</i>
EGFR-L858R-TRIAL	EGFR L858R	EGFR L858R	<i>Elisabeth-TweeSteden Ziekenhuis</i>
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 (2 cohorts from 2 trials)			
Trial	Cohort	Molecular	Sites
EGFR-BE	EGFR L858R	EGFR L858R	Belgium (Brussels)
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 (0)			
None			