ACTIN Report (research use only)

Gender: **Female** | Birth year: **1975** | WHO: **1**

Tumor: **Lung adenocarcinoma** | Lesions: **Liver, Lung** | Stage: **IV**

Clinical summary

Relevant systemic treatment history	**6/2023-1/2025**	**Osimertinib**

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 160 / TMB 14 mut/Mb**
Microsatellite (in)stability	**Stable**
HR status	**Proficient (0)**
Driver mutations	**EGFR C797S, EGFR L858R, KRAS G12C, KRAS G12D**
Amplified genes	**None**
Deleted genes	**TP53**
Homozygously disrupted genes	**None**
Gene fusions	**MET(exon13)::MET(exon15) fusion**
Virus	**None**

Trial-relevant IHC results

PD-L1	**Score > 50%**

Trials in NL that are open and potentially eligible (5 cohorts from 5 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, PD-L1 >= 50.0	Erasmus MC	Variant(s) G12D in KRAS but subclonal likelihood of > 50%
METC 01 IEMOEN	Dose escalation - monotherapy *(no slots)*	None		Has not exhausted SOC (at least platinum doublet remaining)
EGFR-C797S-TRIAL	*EGFR C797S*	*EGFR C797S*	*Elisabeth-TweeSteden Ziekenhuis*	
EGFR-L858R-TRIAL	*EGFR L858R*	*EGFR L858R*	*Elisabeth-TweeSteden Ziekenhuis*	

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).

Molecular Details

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

Key drivers

Type	Driver	Trials (Locations)	Trials in Hartwig	Best evidence in External	Resistance in External
Mutation (gain of function)	EGFR L858R (2/4 copies)		NCT00000006, NCT00000007	Approved	
Mutation (gain of function)	EGFR C797S (1/4 copies)	TEDR1 (NKI-AvL)	NCT00000008	Pre-clinical	
Mutation (gain of function)	KRAS G12D (0.3/2 copies)*	KAYRAS (Erasmus MC)			
Mutation (gain of function)	KRAS G12C (0.3/2 copies)*		NCT00000009		
Deletion	TP53 del, 0 copies				

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Type	Driver	Trials (Locations)	Trials in Hartwig	Best evidence in External	Resistance in External
Known fusion	MET(exon13)::MET(exon15) fusion				

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

Other drivers or relevant events

Type	Driver	Trials (Locations)	Trials in Hartwig	Best evidence in External	Resistance in External
None					

IHC results

PD-L1   **Score > 50%**

Molecular history

Event	Description	2025-02-22 Hartwig WGS
EGFR L858R (Tier I)	Mutation (gain of function)	VAF 0.5%
EGFR C797S (Tier II)	Mutation (gain of function)	VAF 0.25%
KRAS G12C (Tier III)	Mutation (gain of function)	VAF 0.15%
KRAS G12D (Tier III)	Mutation (gain of function)	VAF 0.15%
MET(exon13)::MET(exon15) fusion (Tier III)	Known fusion Gain of function	Detected
TP53 del	Deletion	Detected

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Event	Description	2025-02-22 Hartwig WGS
(Tier III)	Unknown protein effect	
TMB		14.0
MSI		Stable

Efficacy evidence

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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**
Known lesions	**Liver, Lung**
Unknown lesions	**None**
No lesions present	**CNS, Brain, Bone, Lymph node**

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

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Trial Matching Details

Trials and cohorts that are potentially eligible, but are closed (1)

Trial	Cohort	Molecular	Sites	Warnings
METC 01 IEMOEN	Dose expansion - monotherapy	None		Has not exhausted SOC (at least platinum doublet remaining)

Trials and cohorts that are considered ineligible (4)

Trial	Cohort	Molecular	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, PD-L1 >= 50.0	No colorectal cancer
METC 05 PICKME3CA	*Applies to all cohorts below*	None	No PIK3CA activating mutation(s)
	Dose expansion - monotherapy - NSCLC *(closed)*		
	Dose expansion - monotherapy - Other cancer types *(closed)*		Tumor belongs to DOID term(s) lung non-small cell carcinoma

Trials and cohorts that are not evaluable or ignored (0)

Trial	Cohort	Molecular	Sites	Configuration

None