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

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

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%

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

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

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					

Trial Matching Summary

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

Trial	Cohort	Molecular	Warnings
METC 01 IEMOEN	Dose expansion - 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

Example trials and cohorts that are 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.

Example trials and cohorts that are not evaluable or ignored (0)

None

Trial Matching Details

Potentially eligible open trials & cohorts

METC 01

Potentially eligible	**Yes**
Acronym	**IEMOEN**
Title	**Phase I first-in-human study to evaluate safety of IEMOEN, a new PD-L1 inhibitor in advanced solid tumors**

Rule	Reference	Evaluation
E-02	Has hemoglobin below 6 mmol/l	FAIL (potentially recoverable) Hemoglobin 5.6 mmol/L is below minimum of 6.0 mmol/L
I-03	Patient should have exhausted applicable available standard-of-care treatments.	WARN Patient has not exhausted SOC (at least platinum doublet remaining)
E-01	Has an active autoimmune disease that requires systemic treatment and poses a risk according to the investigator.	WARN Patient has history of condition(s) rheumatoid arthritis, which is indicative of autoimmune disease
E-03	Has absolute neutrophil count below 1.5 x 10^9/l	UNDETERMINED No measurement found for absolute neutrophil count
I-01	Patients must be ≥18 years old.	PASS Patient is at least 18 years old
I-02	IEMOEN monotherapy is indicated for the treatment of adults with advanced/metastatic solid tumors.	PASS Patient has solid primary tumor Tumor stage IV is considered metastatic

METC 01 - Dose escalation - monotherapy

Cohort ID	**A**
Potentially eligible?	**Yes**
Open for inclusion?	**Yes**
Has slots available?	**No**

METC 01 - Dose expansion - monotherapy

Cohort ID	**B**
Potentially eligible?	**Yes**
Open for inclusion?	**No**
Has slots available?	**No**

METC 02

Potentially eligible	**Yes**
Acronym	**KAYRAS**
Title	**A phase 1/2 trial for first in-human usage of KAYRAS, a new specific KRAS G12D inhibitor in NSCLC and colorectal cancer**

Rule	Reference	Evaluation
I-04	Patient has confirmed KRAS G12D mutation	WARN Variant(s) KRAS G12D in KRAS detected in canonical transcript but subclonal likelihood of > 50%
I-03	ALAT and ASAT should be at most 3*ULN, or at most 5*ULN in case of liver metastases.	UNDETERMINED ASAT and ALAT are not present or cannot be evaluated
I-01	Patient is ≥18 years old.	PASS Patient is at least 18 years old
I-02	KAYRAS monotherapy is indicated for the treatment of NSCLC or colorectal patients with metastatic cancer.	PASS Tumor stage IV is considered metastatic

METC 02 - Dose expansion - monotherapy - NSCLC

Cohort ID	**A**
Potentially eligible?	**Yes**
Open for inclusion?	**Yes**
Has slots available?	**Yes**

Rule	Reference	Evaluation
I-02	KAYRAS monotherapy is indicated for the treatment of NSCLC or colorectal patients with metastatic cancer.	PASS Patient has tumor belonging to DOID term(s) lung non-small cell carcinoma

METC 02 - Dose expansion - monotherapy - Colorectum

Cohort ID	**B**
Potentially eligible?	**No**
Open for inclusion?	**Yes**
Has slots available?	**Yes**

Rule	Reference	Evaluation
I-02	KAYRAS monotherapy is indicated for the treatment of NSCLC or colorectal patients with metastatic cancer.	FAIL Patient has no colorectal cancer

METC 04

Potentially eligible	**Yes**
Acronym	**TEDR1**
Title	**TEDR1 Trial: A phase II trial to evaluate efficacy of specific EGFR inhibitors in lung cancer**

Rule	Reference	Evaluation
I-1	Patient is ≥18 years of age.	PASS Patient is at least 18 years old
I-2	Drug 1 as monotherapy is indicated for the treatment of adults with advanced lung cancer.	PASS Patient has tumor belonging to DOID term(s) lung cancer Tumor stage IV is considered metastatic
I-3	Patient has a confirmed EGFR C797S mutation	PASS Variant(s) C797S in gene EGFR detected in canonical transcript

METC 04 - Lung cancer C797S cohort

Cohort ID	**A**
Potentially eligible?	**Yes**
Open for inclusion?	**Yes**
Has slots available?	**Yes**

Other trials & cohorts

METC 03

Potentially eligible	No
Acronym	**NO-SEE797ES**
Title	**Phase I trial for development of NO-SEE797ES, a specific inhibitor for EGFR with C797 mutations but not C797S in solid tumors**

Rule	Reference	Evaluation
I-03	Tumors should contain EGFR C797 but not EGFR C797S mutation.	FAIL Variant(s) C797S in gene EGFR detected in canonical transcript

METC 03 - Dose escalation - monotherapy

Cohort ID	**A**
Potentially eligible?	No
Open for inclusion?	**Yes**
Has slots available?	**Yes**