ACTN01029999

REPORT DATE 18-Jun-2024

Gender: Male | Birth year: 1950 | WHO: 1

Tumor: Skin - Melanoma | Lesions: Brain, CNS, Liver, Lung, Test Lesion, Lymph nodes (abdominal, cervical and

supraclavicular) | Stage: IV

## Summary

#### **Clinical summary**

Relevant systemic treatment history 2019 Therapy1

?-6/2020 Therapy2 8/2020-3/2021 Therapy3

2022 Clinical trial: Trial1

2022 Clinical trial: Trial1 (3 cycles, stop reason: toxicity)
2022 Clinical trial (tr2): Trial2 (3 cycles, stop reason: toxicity)
2022 Clinical trial: Trial4 (adjuvant, 1 cycle, stop reason: toxicity)
2022 Clinical trial: Trial5 (adjuvant and consolidation, stop reason:

toxicity)

**2023** Therapy4 Date unknown Therapy

Relevant other oncological history 2022 Clinical trial (details unknown)

Previous primary tumor Lung adenocarcinoma (diagnosed 6/2021, considered non-active)

Relevant non-oncological history Pancreatitis

Coronary artery bypass graft (CABG)

#### **Recent molecular results**

#### Hartwig WGS of ACTN01029999 (13-Jun-2024)

Biopsy location Liver (purity 98%)

Molecular tissue of origin prediction Melanoma (100%)

Tumor mutational load / burden TML high (185) / TMB high (13.7)

Microsatellite (in)stability Stable

HR status Proficient (0.45)

Genes with high driver mutation BRAF

Amplified genes MYC

Deleted genes PTEN

Homozygously disrupted genes PTEN

Gene fusions EML4 - ALK fusion

Virus detection HPV positive (3 int. detected)

Potentially actionable events with medium/low driver: PTEN disruption

#### Approved treatments considered eligible

**Treatment** 

Not yet determined

EMC trials that are open and considered eligible and currently have slots available (1 cohort from 1 trial)

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Trial	Cohort	Molecular	Warnings
Test Trial 1 TEST-1 (Phase 1)	Cohort B	None	Undetermined SOC exhaustion

## EMC trials that are open and considered eligible but currently have no slots available (2 cohorts from 2 trials)

Trial	Cohort	Molecular	Warnings
Test Trial 1 TEST-1 (Phase 1)	Cohort A	MSI	Undetermined SOC exhaustion
Test Trial 2 TEST-2	Cohort A	MSI	None

## trial kb trials potentially eligible based on molecular results which are potentially recruiting in The Netherlands (2)

Event	Trial title	NCT number
TMB High,	treatment	NCT00000001
TML High,		
PTEN hom disruption,		
PTEN disruption,		
EML4 - ALK fusion,		
HPV positive		
MYC amp	A Phase 1 Study of XYXYXY, a T-Cell-Redirecting Agent Targeting Z, for Advanced Prostate	NCT00000003
	Cancer	

## trial kb trials potentially eligible based on molecular results which are potentially recruiting outside the Netherlands (1)

Event	Trial title	NCT number	Country
PTEN del	A Phase 1/2 Randomized Study to Evaluate the Safety and Efficacy of treatment X Plus Y, as First-Line Treatment for Participants With Advanced Solid Tumor (acronym)	NCT00000020	Belgium, Germany

Currently only Belgian and German trials are supported

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## **Molecular Details**

## Hartwig WGS (ACTN01029999T, 13-Jun-2024)

#### General

Purity	TML Status	TMB Status	MS Stability	HR Status	DPYD	UGT1A1
98%	High (185)	High (13.7)	Stable	Proficient (0.45)	*1_HOM (Normal	*1_HET (Normal function), *28_HET
					function)	(Reduced function)

#### **Predicted tumor origin**

1. Melanoma

Combined prediction score 100%				
This score is calculated by combining information on:				
(1) SNV types	98%			
(2) SNV genomic localisation distribution	99%			
(3) Driver genes and passenger characteristics	97%			

Other cohorts have a combined prediction of 0% or lower

#### **Drivers**

Туре	Driver	Driver likelihood	Trials in EMC	Trials in trial kb	Best evidence in kb	Resistance in kb
Mutation (Hotspot)	BRAF V600E (4/6 copies)	High			Approved	
Amplification	MYC amp, 38 copies	High		NCT0000003		
Loss	PTEN del, 0 copies	High		NCT00000020		
Known fusion	EML4 - ALK fusion, exon 6 - exon 20	High		NCT0000001	Approved	Known resistance
Disruption (homozygous)	PTEN	High		NCT0000001	Approved	Known resistance
Virus	HPV positive, 3 integrations detected	High		NCT0000001	Approved	Known resistance
Disruption	PTEN, DEL (1.1 disr. / 1.8 undisr. copies)	Low		NCT0000001	Approved	Known resistance

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#### **Clinical Details**

### **Clinical summary**

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## Patient current details (08-Jun-2024)

Unresolved toxicities grade => 2 Fatigue (2)

Cancer-related complications Ascites

Known allergies Wasps (Environment)

Recent surgeries 19-May-2024

## Tumor details (08-Jun-2024)

Measurable disease Yes

CNS lesion status Present CNS lesions (active)

Brain lesion status Present brain lesions (not active)

## **Active medication details**

Medication Administration route Start date Stop date Dosage Frequency

None

## **Blood transfusions**

Product Date

Thrombocyte concentrate 03-Jun-2024

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## **Trial Matching Summary**

EMC trials and cohorts that meet molecular requirements and may be eligible, but are closed (0)

None

EMC trials and cohorts that are open but considered ineligible (1)

Trial	Cohort	Molecular	Ineligibility reasons
Test Trial 2	Cohort B	None	Pembrolizumab treatment
TEST-2			