

Gender: Female | Birth year: 1946 | WHO: 0

Tumor: Colorectum (cecum) carcinoma | Lesions: Lung, Peritoneal | Stage: IV

Clinical summary

Relevant systemic treatment history	None	
Relevant other oncological history	11/2021	Hemicolectomy right (Cecum)
Previous primary tumor	Skin squamous cell carcinoma (diagnosed 6/2016, last treatment 8/2016, considered non-active)	
Relevant non-oncological history	1/2019	Cerebrovascular accident

Recent molecular results

NGS & MSI Panel (15-Jan-2023)

Tumor mutational burden	TMB 8 mut/Mb
Microsatellite (in)stability	Stable
Driver mutations	KRAS G12D

Trial-relevant IHC results

PD-L1	Score < 50%
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Standard-of-care options considered potentially eligible

Treatment	Literature efficacy evidence	Real-world efficacy evidence	Warnings
FOLFIRI	PHASE-3-CRC		
	PFS: 10.0 months (95% CI: 10.0-12.0)	PFS: 13.3 months, IQR: 12.6	
	OS: 25.0 months (95% CI: 25.0-30.0)	OS: 22.2 months, IQR: 24.8	

Trials in Other that are open and potentially eligible (0)

Trial	Cohort	Molecular	Sites	Warnings
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International trials that are open and potentially eligible (1 cohort from 1 trial)

Trial	Cohort	Molecular	Sites
KRAS-G12D-TRIAL	KRAS G12D	KRAS G12D	NL: Utrecht, Germany: Stuttgart

International trials are matched solely on molecular event and tumor type (clinical data excluded).

Molecular Details

NGS & MSI Panel (15-Jan-2023)

Biopsy location	Lung
Tumor mutational burden	TMB 8 mut/Mb
Microsatellite (in)stability	Stable
Driver mutations	KRAS G12D

IHC results

Ki67	Positive, score 90%
PD-L1	Score < 50%

Molecular history

Event	Description	2023-01-15 NGS & MSI Panel
KRAS G12D (Tier III)	Mutation (cancer-associated variant) Loss of function	VAF 0.2232%
TMB		8.0
MSI		Stable

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.

Treatment	Literature efficacy evidence
FOLFIRI	PHASE-3-CRC
	Patient characteristics:
	WHO/ECOG0: 100, 1: 80, 2: 20, 3: 0, 4: 0
	Primary tumor locationLeft: 145, Both or unknown: 10, Right: 45
	MutationsKRAS exon 2 wild-type 200/200
	Metastatic sitesLiver only: 58 (32.0%), Lung only: 10 (6.0%)
	Previous systemic therapy35/200
	Prior therapiesAdjuvant chemotherapy
	Median PFS: 10.0 months (95% CI: 10.0-12.0)
	Median OS: 25.0 months (95% CI: 25.0-30.0)

PHASE-3-CRC

Study: PHASE-3-CRC, Phase III, Adjuvant

Molecular requirements: None

Therapies: FOLFIRI+Cetuximab, FOLFIRI

Patient characteristics:

	Cetuximab + FOLFIRI (n=100)	FOLFIRI (n=200)
Age (median [range])	65.0 [40-75]	65.0 [30-75]
Sex	Male: 50	Male: 120

	Female: 50	Female: 80
Race	NA	NA
Region	Europe: 100 patients	Europe: 200 patients
WHO/ECOG	0: 80, 1: 10, 2: 10, 3: 0, 4: 0	0: 100, 1: 80, 2: 20, 3: 0, 4: 0
Primary tumor location	Left: 78 Both or unknown: 3 Right: 19	Left: 145 Both or unknown: 10 Right: 45
Mutations	KRAS exon 2 wild-type 100/100	KRAS exon 2 wild-type 200/200
Metastatic sites	Liver only: 62 (62.0%), Lung only: 4 (4.0%)	Liver only: 58 (32.0%), Lung only: 10 (6.0%)
Time of metastases	Unknown	Unknown
Previous systemic therapy	30/100	35/200
Prior therapies	Adjuvant chemotherapy	Adjuvant chemotherapy

Primary endpoints:

	Cetuximab + FOLFIRI	FOLFIRI	Hazard ratio (HR) / Odds Ratio (OR)	P value
Median follow-up for PFS was 70 months				

Secondary endpoints:

	Cetuximab + FOLFIRI	FOLFIRI	Hazard ratio (HR) / Odds Ratio (OR)	P value
Median Overall Survival (95% CI)	35.0 (25.0 - 40.0)	25.0 months (25.0 - 30.0)	0.75 (0.6 - 0.95)	p = 0.011
Median Progression-Free Survival (95% CI)	10.0 (10.0 - 12.0)	10.0 months (10.0 - 12.0)	0.99 (0.8 - 1.25)	p = 1
Median follow-up for PFS was 70 months				

Treatment decisions (percentage of population assigned to systemic treatment) in NCR real-world data set

	All (n=9207)	Age 73-83y (n=2727)	WHO 1 (n=2828)	RAS positive (n=2760)	Liver only lesions (n=2715)
FOLFIRI	38.5%	23.8%	37.9%	44.6%	39.5%

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Median overall survival (OS) in months in NCR real-world data set

	All (n=9207)	Age 73-83y (n=2727)	WHO 1 (n=2828)	RAS positive (n=2760)	Liver only lesions (n=2715)
FOLFIRI	16.1, IQR: 18.2 (n=3543)	15.4, IQR: 18.2 (n=649)	14.8, IQR: 16.3 (n=1071)	15.8, IQR: 14.2 (n=1230)	16.5, IQR: 17.4 (n=1073)

Median progression-free survival (PFS) in months in NCR real-world data set

	All (n=5018)	Age 73-83y (n=1330)	WHO 1 (n=1623)	RAS positive (n=1822)	Liver only lesions (n=1534)
FOLFIRI	8.2, IQR: 5.5 (n=2106)	8, IQR: 6.1 (n=340)	7.9, IQR: 5 (n=661)	8, IQR: 4.7 (n=836)	8.3, IQR: 5.3 (n=652)

Explanation:

These tables only show treatments that are considered standard of care (SOC) in colorectal cancer in the Netherlands.

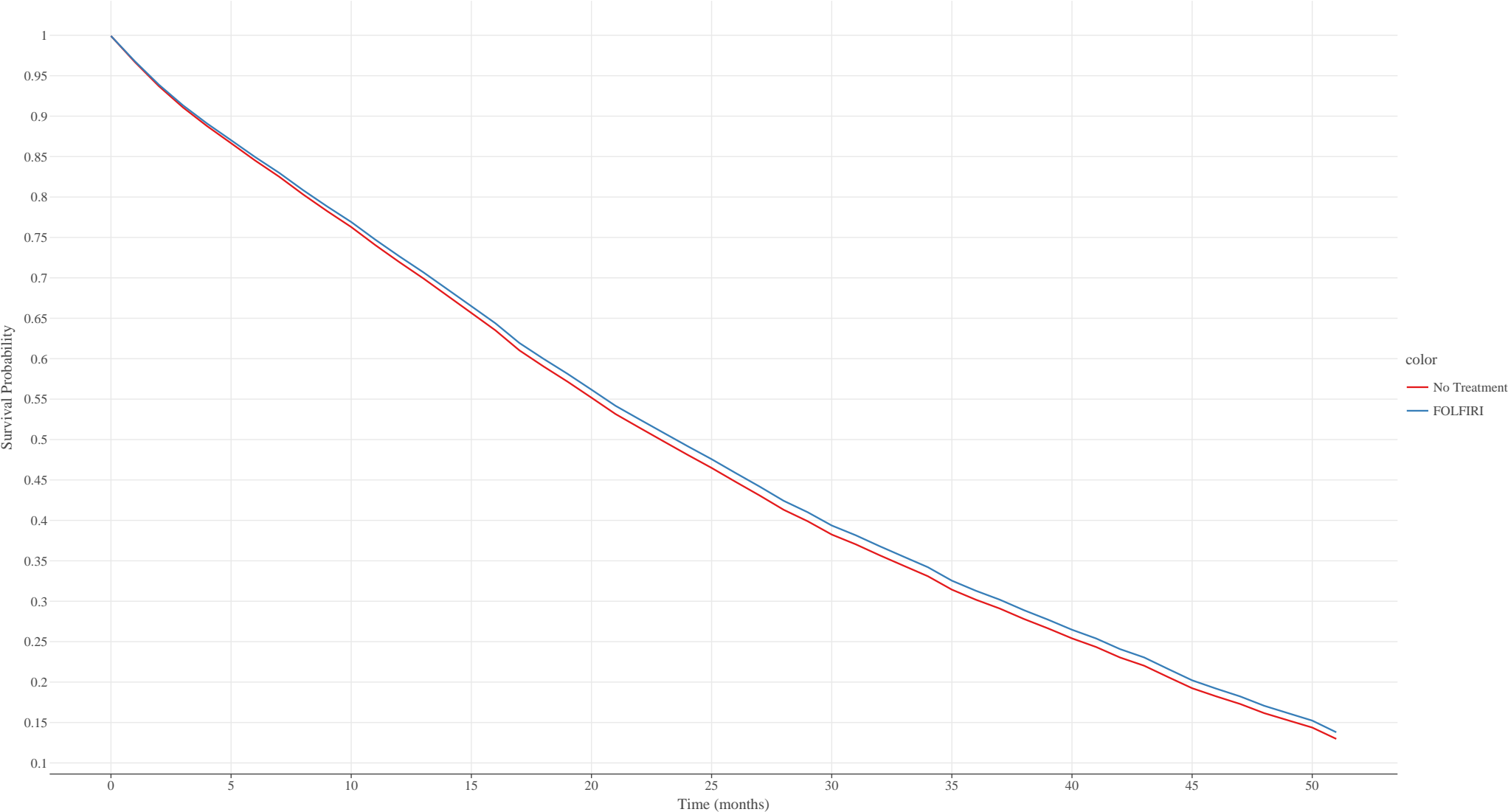
The 'All' column shows results in NCR patients who were previously untreated, diagnosed with colorectal cancer with distant metastases and treated systemically without surgery, for whom the treatment could be categorized in SOC treatments.

The 'Age', 'WHO', 'RAS' and 'Lesions' columns show results based on patients from the 'All' population, filtered for equal WHO, similar age, equal RAS status or equal lesion localization, respectively.

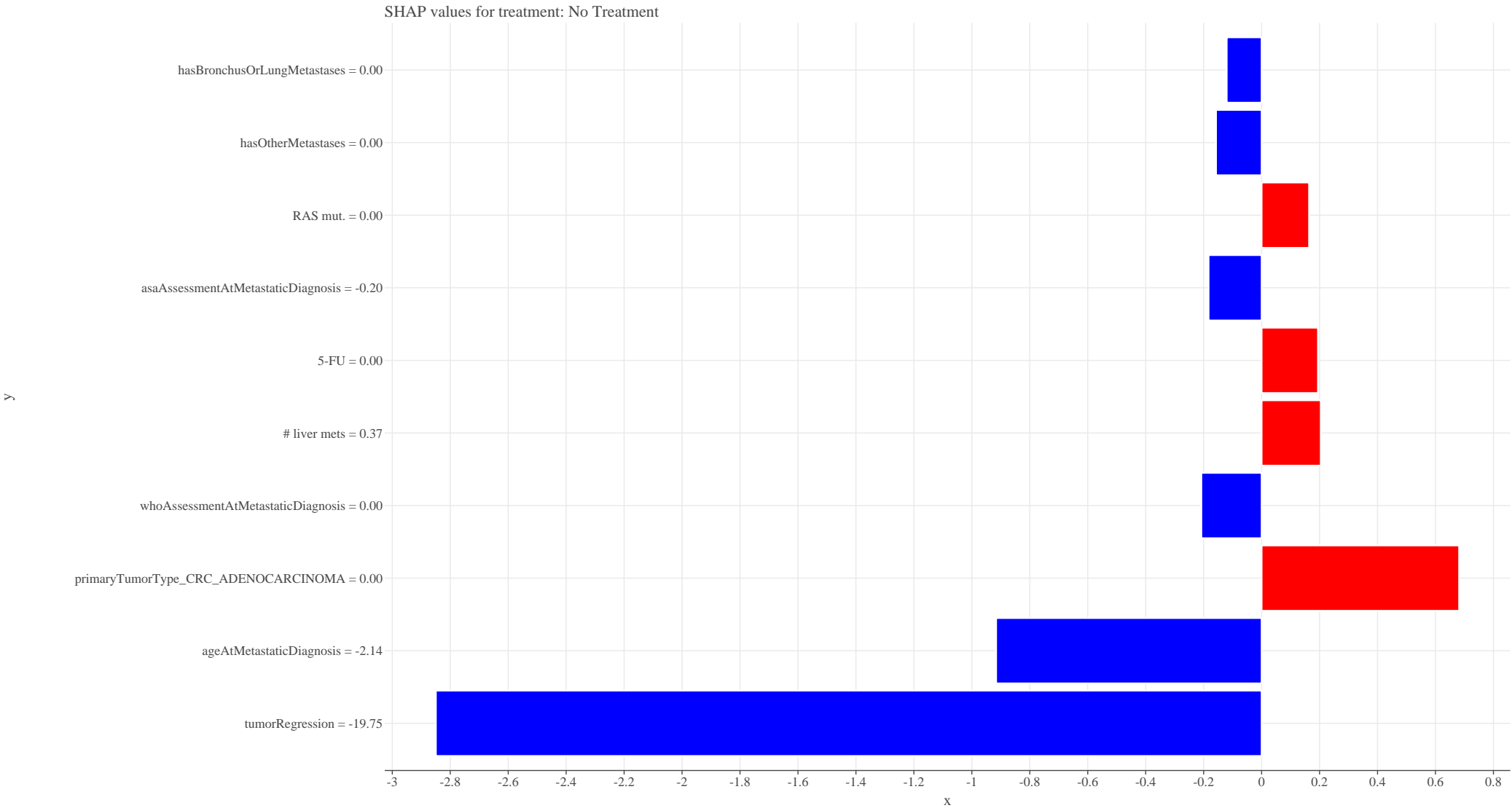
'PFS' is calculated as the duration from the date on which the first compound of the treatment was administered, until first progression.

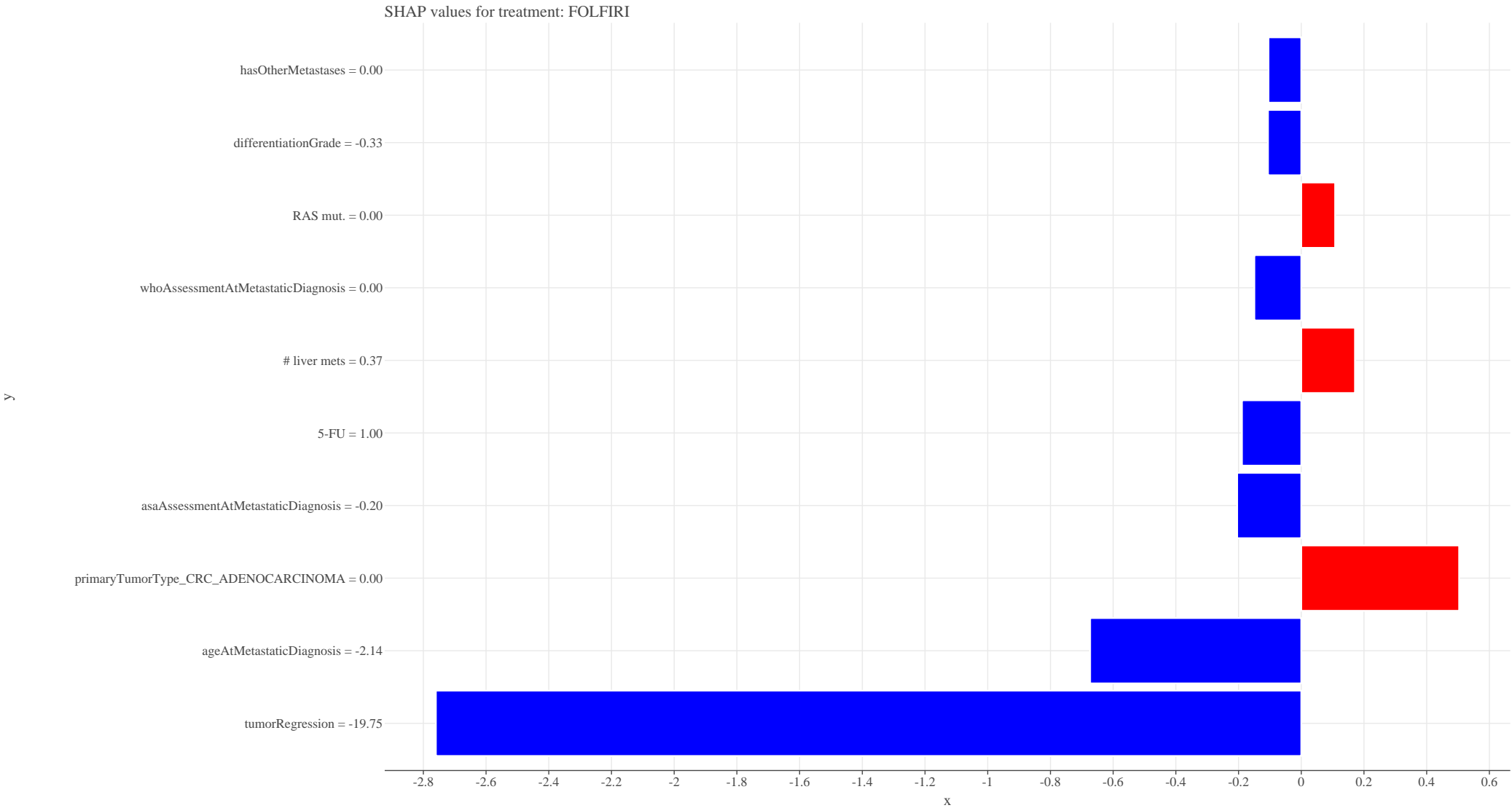
'OS' is calculated as the duration from the date on which the first compound of the treatment was administered, until death from any cause.

When patient number is too low (n <= 20) to predict PFS or OS, "NA" is shown.

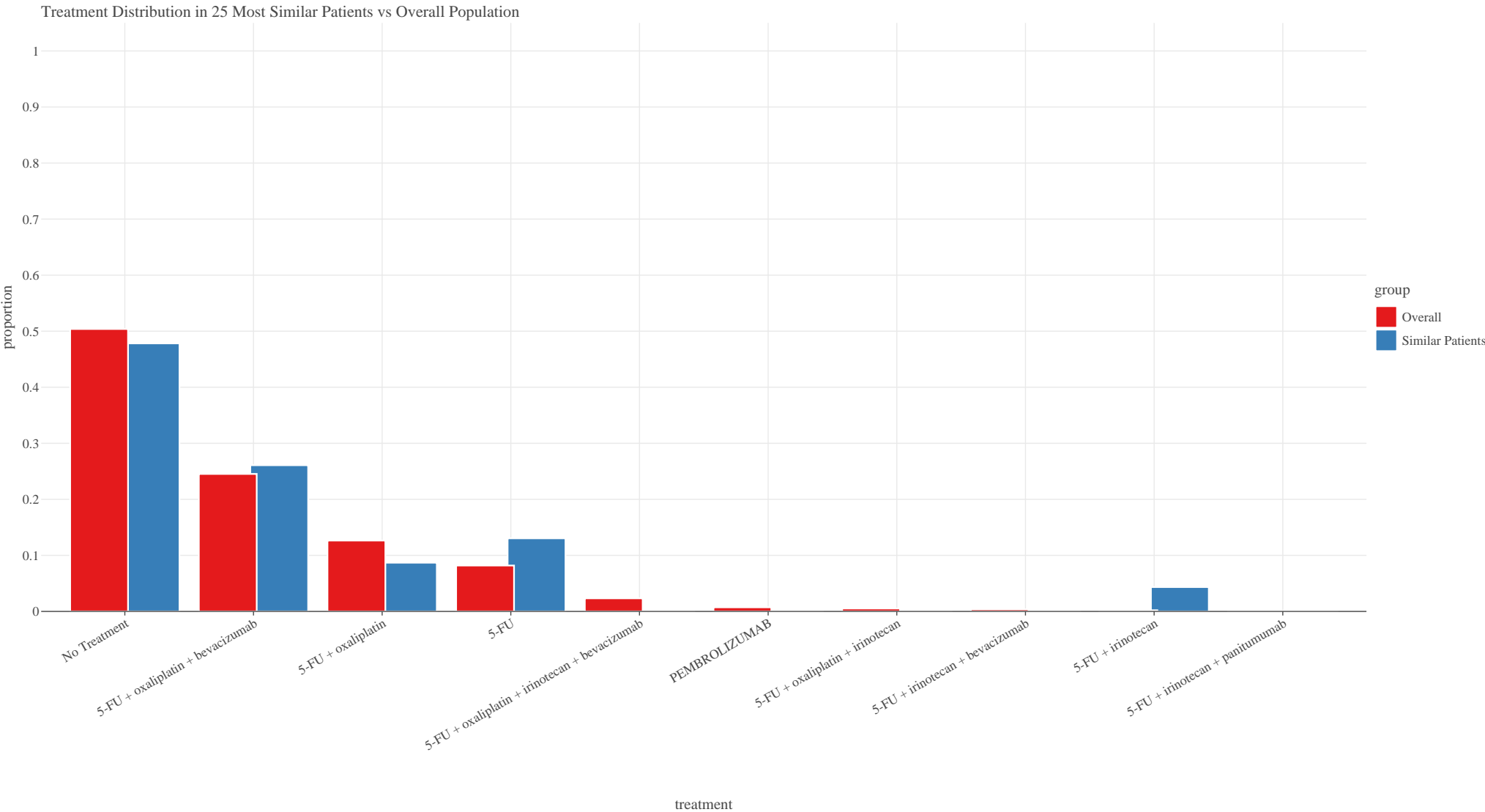


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Resistance evidence

Treatment	Mutation	Evidence source	Evidence level	Found in molecular analysis
FOLFIRI	GENE S11C	[1]	D	Yes

On label clinical evidence

Event	CKB Event	Level A	Level B	Level C	Level D
None					

Off label clinical evidence

Event	CKB Event	Level A	Level B	Level C	Level D
None					

Efficacy evidence description

None

Treatment ranking

Treatment	Events	Score
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Clinical Details

Clinical summary

Relevant systemic treatment history	None	
Relevant other oncological history	11/2021	Hemicolectomy right (Cecum)
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Relevant non-oncological history	1/2019	Cerebrovascular accident

Patient current details (05-Mar-2023)

Unresolved toxicities grade => 2	None
Cancer-related complications	Unknown
Known allergies	Morphine
Recent surgeries	12-Nov-2021 Hemicolectomy right

Tumor details (05-Mar-2023)

Measurable disease	Yes
Known lesions	Lung, Peritoneal
Unknown lesions	Lymph node
No lesions present	CNS, Brain, Liver, Bone

Active medication details

Medication	Administration route	Start date	Stop date	Dosage	Frequency
None					

Blood transfusions

Product	Date
ERTHROCYTES_FILTERED	10-Jan-2023

Trial Matching Details

Trials in Other that are open and potentially eligible (0)

Trial	Cohort	Molecular	Sites	Warnings
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International trials that are open and potentially eligible (1 cohort from 1 trial)

Trial	Cohort	Molecular	Sites
KRAS-G12D-TRIAL	KRAS G12D	KRAS G12D	NL: Utrecht, Germany: Stuttgart

International trials are matched solely on molecular event and tumor type (clinical data excluded).

Trials and cohorts that are potentially eligible, but are closed (2)

Trial	Cohort	Molecular	Sites	Warnings
METC 01 IEMOEN	Applies to all cohorts below	None		Has not exhausted SOC
	Dose escalation - monotherapy			
	Dose expansion - monotherapy			

Trials and cohorts that are considered ineligible (2)

Trial	Cohort	Molecular	Ineligibility reasons
METC 02 KAYRAS	Applies to all cohorts below	KRAS G12D	PD-L1 expression below minimum of 50.0
	Dose expansion - monotherapy - Colorectum		
	Dose expansion - monotherapy - NSCLC		No lung non-small cell carcinoma

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

Trial	Cohort	Molecular	Sites	Configuration
None				

Other trials & cohorts

METC 02

Potentially eligible	No
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
Reference	Evaluation
I-05	FAIL
	PD-L1 expression below minimum of 50.0

METC 02 - Dose expansion - monotherapy - NSCLC

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

Reference	Evaluation
I-02	FAIL No 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

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

Reference	Evaluation
I-03	WARN Has not exhausted SOC
E-01	PASS Has no other condition belonging to category autoimmune disease
E-02	PASS Hemoglobin above 6 mmol/L
E-03	PASS Neutrophils above 1.5
I-01	PASS Patient is at least 18 years old
I-02	PASS Has solid primary tumor Stage IV is considered metastatic

METC 01 - Dose escalation - monotherapy

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

METC 01 - Dose expansion - monotherapy

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