

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    |

Standard-of-care options considered potentially eligible

| Treatment | Literature efficacy evidence         | Real-world efficacy evidence | Warnings |
|-----------|--------------------------------------|------------------------------|----------|
| FOLFIRI   | <a href="#">PHASE-3-CRC</a>          |                              |          |
|           | 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 NL that are open and potentially eligible (1 cohort from 1 trial)

| Trial                           | Cohort    | Molecular | Sites       | Warnings |
|---------------------------------|-----------|-----------|-------------|----------|
| <a href="#">KRAS-G12D-TRIAL</a> | KRAS G12D | KRAS G12D | UMC Utrecht |          |

Trials matched solely on molecular event and tumor type (no clinical data used) are shown in italicized, smaller font.

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%         |

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                   | <div><a href="#">PHASE-3-CRC</a><br/><b>Patient characteristics:</b><table><tr><td>WHO/ECOG</td><td>0: 100, 1: 80, 2: 20, 3: 0, 4: 0</td></tr><tr><td>Primary tumor location</td><td>Left: 145, Both or unknown: 10, Right: 45</td></tr><tr><td>Mutations</td><td>KRAS exon 2 wild-type 200/200</td></tr><tr><td>Metastatic sites</td><td>Liver only: 58 (32.0%), Lung only: 10 (6.0%)</td></tr><tr><td>Previous systemic therapy</td><td>35/200</td></tr><tr><td>Prior therapies</td><td>Adjuvant chemotherapy</td></tr></table><br/><b>Median PFS:</b> 10.0 months (95% CI: 10.0-12.0)<br/><b>Median OS:</b> 25.0 months (95% CI: 25.0-30.0)</div> | WHO/ECOG | 0: 100, 1: 80, 2: 20, 3: 0, 4: 0 | Primary tumor location | Left: 145, Both or unknown: 10, Right: 45 | Mutations | KRAS exon 2 wild-type 200/200 | Metastatic sites | Liver only: 58 (32.0%), Lung only: 10 (6.0%) | Previous systemic therapy | 35/200 | Prior therapies | Adjuvant chemotherapy |
| WHO/ECOG                  | 0: 100, 1: 80, 2: 20, 3: 0, 4: 0   |          |                                  |                        |   |           |                               |                  |  |                           |        |                 |                       |
| Primary tumor location    | Left: 145, Both or unknown: 10, Right: 45  |          |                                  |                        |   |           |                               |                  |  |                           |        |                 |                       |
| Mutations                 | KRAS exon 2 wild-type 200/200  |          |                                  |                        |   |           |                               |                  |  |                           |        |                 |                       |
| Metastatic sites          | Liver only: 58 (32.0%), Lung only: 10 (6.0%)   |          |                                  |                        |   |           |                               |                  |  |                           |        |                 |                       |
| Previous systemic therapy | 35/200   |          |                                  |                        |   |           |                               |                  |  |                           |        |                 |                       |
| Prior therapies           | Adjuvant chemotherapy  |          |                                  |                        |   |           |                               |                  |  |                           |        |                 |                       |

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%                       |

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<br>(n=3543) | 15.4, IQR: 18.2<br>(n=649) | 14.8, IQR: 16.3<br>(n=1071) | 15.8, IQR: 14.2<br>(n=1230) | 16.5, IQR: 17.4<br>(n=1073) |

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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<br>(n=2106) | 8, IQR: 6.1<br>(n=340) | 7.9, IQR: 5<br>(n=661) | 8, IQR: 4.7<br>(n=836) | 8.3, IQR: 5.3<br>(n=652)    |

Explanation:

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

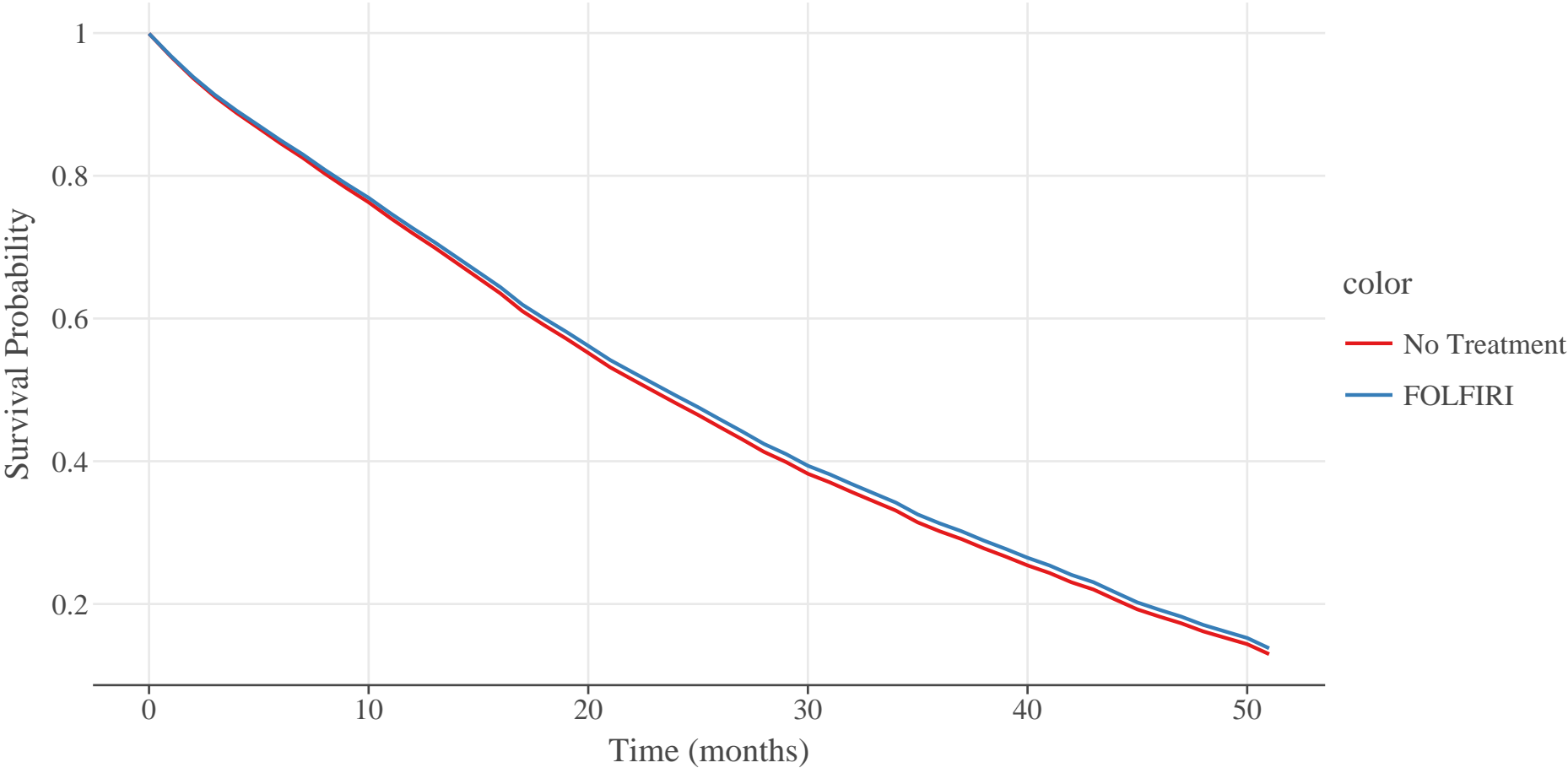
The 'All' column shows results in NCR patients who were previously untreated, diagnosed with colorectal cancer with distant metastases and treated systemically without surgery, for whom the treatment could be categorized in SOC treatments.

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.

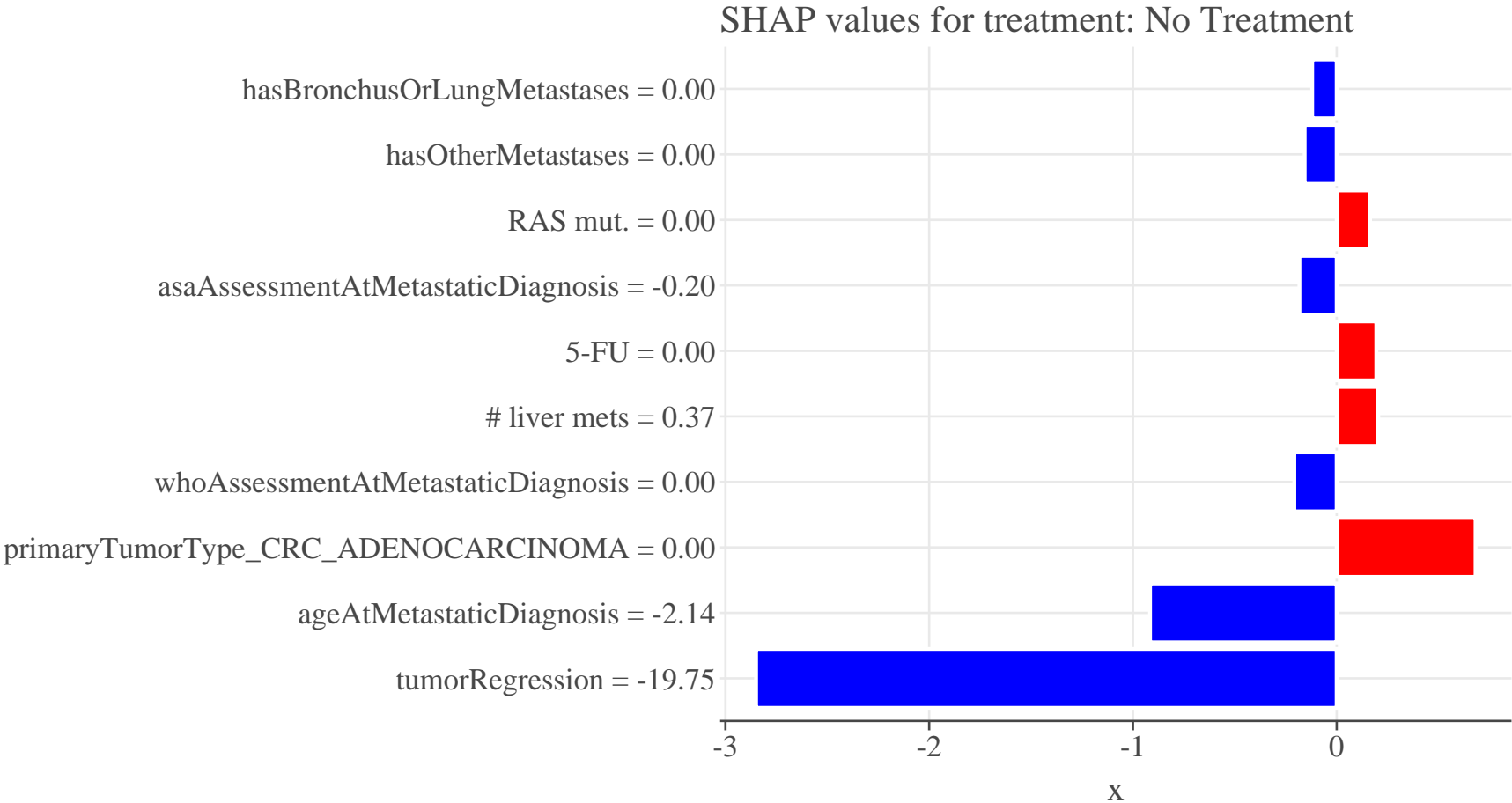
'PFS' is calculated as the duration from the date on which the first compound of the treatment was administered, until first progression.

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

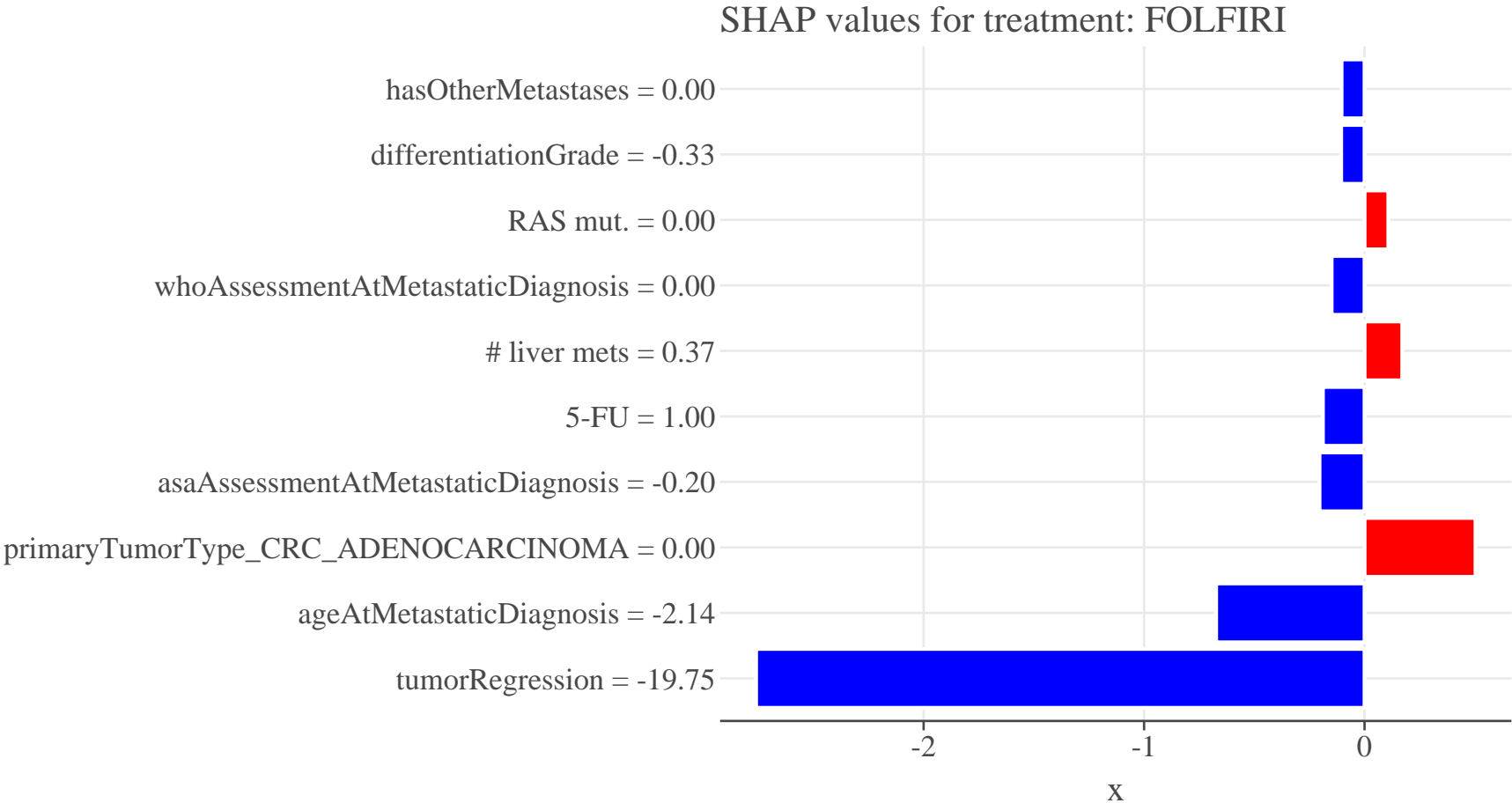
When patient number is too low (n <= 20) to predict PFS or OS, "NA" is shown.

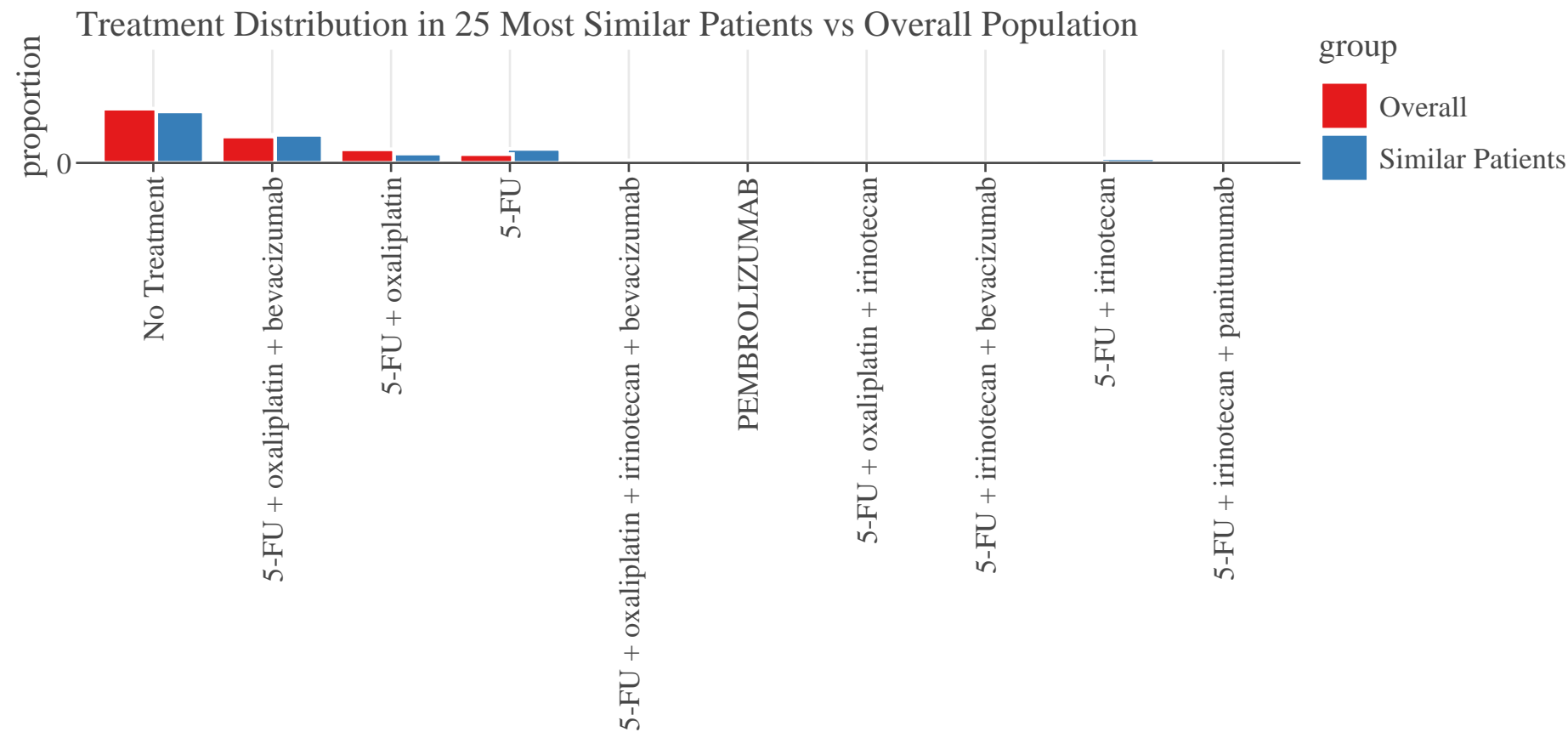


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Resistance evidence

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



Clinical Details

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    |

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

| Trial             | Cohort                        | Molecular | Sites | Warnings              |
|-------------------|-------------------------------|-----------|-------|-----------------------|
| METC 01<br>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                  |
|---|---|-----------|--|
| <a href="#">METC 02</a><br><a href="#">KAYRAS</a> | Applies to all cohorts below              | KRAS G12D | PD-L1 expression below minimum of 50.0 |
|   | Dose expansion - monotherapy - Colorectum |           | No lung non-small cell carcinoma       |
|   | Dose expansion - monotherapy - NSCLC      |           |  |

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

| Trial | Cohort | Molecular | Sites | Configuration |
|-------|--------|-----------|-------|---------------|
| None  |        |           |       |               |