

Supplementary Table 1 Unconditional univariate logistic analysis of factors associated with FOLFOXIRI in first-line chemotherapy

| Characteristics | Patients (<i>n</i>) | Patients treated with FOLFOXIRI (<i>n</i>) | OR (95%CI) | <i>P</i> value |
|--------------------------------|--------------------------|--|----------------------|----------------|
| Demographic parameters | | | | |
| Age, years | 288 | 165 | 1.014 (0.991-1.039) | 0.236 |
| Missing | 1 | 0 | | |
| Gender | | | | |
| Male | 170 | 97 | 1.00 (Reference) | |
| Female | 119 | 68 | 1.003 (0.625-1.611) | 0.989 |
| Familial history of cancer | | | | |
| No | 121 | 89 | 1.00 (Reference) | |
| Yes | 114 | 75 | 0.691 (0.395-1.210) | 0.196 |
| Missing | 54 | 1 | | |
| Personal history of cancer | | | | |
| No | 249 | 139 | 1.00 (Reference) | |
| Yes | 36 | 24 | 1.583 (0.758-3.306) | 0.222 |
| Missing | 4 | 2 | | |
| Pathological parameters | | | | |
| Stage at diagnosis | | | | |
| Localized | 33 | 13 | 1.00 (Reference) | |
| Locally advanced | 78 | 60 | 5.128 (2.139-12.298) | |
| Metastatic | 178 | 92 | 1.646 (0.772-3.511) | < 0.001 |
| Primary tumor site | | | | |
| Head | 146 | 93 | 1.00 (Reference) | |
| Body and/or tail | 141 | 71 | 0.578 (0.361-0.927) | 0.023 |
| Missing | 2 | 1 | | |
| Histological grade | | | | |

| | | | |
|---|-----|----|----------------------------|
| Well or Moderately differentiated | 84 | 39 | 1.00 (Reference) |
| Poorly differentiated or Undifferentiated | 32 | 23 | 2.949 (1.221- 0.016 7.122) |
| Missing | 173 | 10 | |

Tumor extension

Stage at chemotherapy initiation

| | | | |
|------------------|-----|-----|------------------------------|
| Locally advanced | 74 | 60 | 1.00 (Reference) |
| Metastatic | 215 | 105 | 0.223 (0.117- < 0.001 0.423) |

Number of metastatic sites

| | | | |
|-----|-----|----|------------------------------|
| 0 | 74 | 60 | 1.00 (Reference) |
| 1 | 143 | 74 | 0.250 (0.128- 1.488) |
| ≥ 2 | 72 | 31 | 0.176 (0.084- < 0.001 0.372) |

Lymph node metastases

| | | | |
|-----|-----|-----|------------------------------|
| No | 248 | 153 | 1.00 (Reference) |
| Yes | 41 | 12 | 0.257 (0.125- < 0.001 0.528) |

Liver metastases

| | | | |
|-----|-----|----|------------------------------|
| No | 121 | 84 | 1.00 (Reference) |
| Yes | 168 | 81 | 0.410 (0.251- < 0.001 0.670) |

Peritoneal metastases

| | | | |
|-----|-----|-----|----------------------------|
| No | 243 | 134 | 1.00 (Reference) |
| Yes | 46 | 31 | 1.681 (0.863- 0.127 3.273) |

Lung metastases

| | | | |
|-----|-----|-----|----------------------------|
| No | 248 | 146 | 1.00 (Reference) |
| Yes | 41 | 19 | 0.603 (0.311- 0.136 1.172) |

Other metastases

| | | | |
|-----|-----|-----|----------------------------|
| No | 278 | 162 | 1.00 (Reference) |
| Yes | 11 | 3 | 0.269 (0.070- 0.056 1.034) |

Clinical parameters

| | | | |
|------------------------------------|-----|-----|-----------------------------|
| Performance status (WHO) | | | |
| 0 | 96 | 54 | 1.00 (Reference) |
| 1 | 169 | 103 | 1.214 (0.730-2.017) |
| ≥ 2 | 20 | 8 | 0.519 (0.194-1.383) 0.195 |
| Missing | 4 | 0 | |
| Body mass index, kg/m ² | | | |
| | 280 | 165 | 0.967 (0.920-1.016) 0.182 |
| Missing | 9 | 0 | |
| Pain | | | |
| No | 173 | 83 | 1.00 (Reference) |
| Yes | 112 | 80 | 2.711 (1.633-4.501) < 0.001 |
| Missing | 4 | 2 | |
| Jaundice | | | |
| No | 262 | 148 | 1.00 (Reference) |
| Yes | 25 | 17 | 1.637 (0.682-3.927) 0.270 |
| Missing | 2 | 0 | |
| Ascites | | | |
| No | 274 | 157 | 1.00 (Reference) |
| Yes | 11 | 6 | 0.894 (0.266-2.999) 0.856 |
| Missing | 4 | 2 | |
| Biological parameters | | | |
| Albumin, g/L | | | |
| | 161 | 85 | 0.881 (0.832-0.933) < 0.001 |
| Missing | 128 | 80 | |
| Lymphocytes, mm ³ | | | |
| < 1000 | 22 | 10 | 1.462 (0.592-3.613) 0.410 |
| ≥ 1000 | 146 | 53 | 1.00 (Reference) |
| Missing | 121 | 102 | |
| Neutrophil-to-lymphocyte ratio | | | |
| < 5 | 124 | 42 | 1.00 (Reference) |

| | | | | |
|---------------------------|-----|-----|------------------|---------------|
| ≥ 5 | 44 | 21 | 1.783 3.585) | (0.886- 0.105 |
| Missing | 121 | 102 | | |
| CA19-9, UI/mL | 252 | 131 | 1.000 1.000) | (1.000- 0.452 |
| Missing | 37 | 34 | | |
| Previous treatment | | | | |
| Primary tumor resection | | | | |
| Yes | 35 | 17 | 1.00 (Reference) | |
| No | 254 | 148 | 1.478 3.002) | (0.728- 0.279 |
| Adjuvant chemotherapy | | | | |
| Yes | 27 | 15 | 1.00 (Reference) | |
| No | 262 | 150 | 1.072 2.379) | (0.483- 0.865 |

Logistic regression models used to estimate association of the parameters with FOLFOXIRI regimen. Values of $P < 0.05$ were considered statistically significant and all tests were two-sided. OR: Odds ratio; CI: Confidence interval; WHO: World Health Organization; CA19-9: Carbohydrate antigen 19-9.

Supplementary Table 2 Unconditional multivariate logistic analysis of factors associated with FOLFOXIRI in first-line chemotherapy for the construction of the propensity score ($n = 283$)

| Characteristics | Patients (n) | Patients treated with FOLFOXIRI (n) | OR (95%CI) | P value |
|----------------------------------|---------------------|---|-------------------------|-----------|
| Primary tumor site | | | | |
| Head | 143 | 91 | 1.00 (Reference) | |
| Body and/or tail | 140 | 71 | 0.669 (0.383- 1.170) | 0.159 |
| Stage at diagnosis | | | | |
| Localized | 32 | 13 | 1.00 (Reference) | |
| Locally advanced | 75 | 57 | 0.663 (0.113- 3.869) | |
| Metastatic | 176 | 92 | 2.120 (0.891- 5.047) | 0.143 |
| Stage at chemotherapy initiation | | | | |
| Locally advanced | 71 | 57 | 1.00 (Reference) | |
| Metastatic | 212 | 105 | 0.179 (0.025- 1.262) | 0.084 |
| Number of metastatic sites | | | | |
| 0 | 71 | 57 | 1.00 (Reference) | |
| 1 | 142 | 74 | 0.944 (0.460- 1.937) | |
| ≥ 2 | 70 | 31 | NA | 0.876 |
| Lymph node metastases | | | | |
| No | 244 | 150 | 1.00 (Reference) | |
| Yes | 39 | 12 | 0.325 (0.132- 0.799) | 0.014 |
| Liver metastases | | | | |
| No | 117 | 81 | 1.00 (Reference) | |
| Yes | 166 | 81 | 0.639 (0.304- 1.345) | 0.239 |
| Pain | | | | |
| No | 172 | 83 | 1.00 (Reference) | |

| | | | | |
|-----|-----|----|-----------------|-----------------|
| Yes | 111 | 79 | 2.937 5.089) | (1.695- < 0.001 |
|-----|-----|----|-----------------|-----------------|

Logistic regression models used to estimate association of the parameters with FOLFOXIRI regimen. Values of $P < 0.05$ were considered statistically significant and all tests were two-sided. OR: Odds ratio; CI: Confidence interval.

Supplementary Table 3 Patient characteristics of the entire metastatic population according to first-line chemotherapy, *n* (%)

| Characteristics | FOLFIRINOX (<i>n</i> = 110) | FOLFOXIRI (<i>n</i> = 105) | <i>P</i> value |
|---|------------------------------|-----------------------------|----------------|
| Demographic parameters | | | |
| Age, median [IQR], yr | 60.0 [53.0-65.2] | 62.0 [53.4-67.0] | 0.147 |
| Missing | 1 | 0 | |
| Gender | | | 0.386 |
| Male | 66 (60.0) | 69 (65.7) | |
| Female | 44 (40.0) | 36 (34.3) | |
| Familial history of cancer | | | 0.131 |
| No | 26 (42.6) | 57 (54.8) | |
| Yes | 35 (57.4) | 47 (45.2) | |
| Missing | 49 | 1 | |
| Personal history of cancer | | | 0.056 |
| No | 98 (90.7) | 85 (81.7) | |
| Yes | 10 (9.3) | 19 (18.3) | |
| Missing | 2 | 1 | |
| Pathological parameters | | | |
| Stage at diagnosis | | | 0.406 |
| Localized | 18 (16.4) | 13 (12.4) | |
| Advanced | 92 (83.6) | 92 (87.6) | |
| Primary tumor site | | | 0.520 |
| Head | 42 (38.5) | 45 (42.9) | |
| Body and/or tail | 67 (61.5) | 60 (57.1) | |
| Missing | 1 | 0 | |
| Histological grade | | | 0.014 |
| Well or Moderately differentiated | 40 (81.6) | 27 (58.7) | |
| Poorly differentiated or Undifferentiated | 9 (18.4) | 19 (41.3) | |
| Missing | 61 | 59 | |
| Tumor extension | | | |
| Number of metastatic sites | | | 0.229 |
| 1 | 69 (62.7) | 74 (70.5) | |
| ≥ 2 | 41 (37.3) | 31 (29.5) | |
| Lymph node metastases | | | 0.005 |
| No | 81 (73.6) | 93 (88.6) | |

| | | | |
|------------------------------------|------------------|------------------|--------|
| Yes | 29 (26.4) | 12 (11.4) | |
| Liver metastases | | | 0.730 |
| No | 23 (20.9) | 24 (22.9) | |
| Yes | 87 (79.1) | 81 (77.1) | |
| Peritoneal metastases | | | 0.005 |
| No | 95 (86.4) | 74 (70.5) | |
| Yes | 15 (13.6) | 31 (29.5) | |
| Lung metastases | | | 0.722 |
| No | 88 (80.0) | 86 (81.9) | |
| Yes | 22 (20.0) | 19 (18.1) | |
| Other metastases | | | 0.142 |
| No | 102 (92.7) | 102 (97.1) | |
| Yes | 8 (7.3) | 3 (2.9) | |
| <hr/> | | | |
| Clinical parameters | | | |
| Performance status (WHO) | | | 0.086 |
| 0 | 36 (34.0) | 30 (28.6) | |
| 1 | 59 (55.7) | 71 (67.6) | |
| ≥ 2 | 11 (10.4) | 4 (3.8) | |
| Missing | 4 | 0 | |
| Body mass index, kg/m ² | 23.9 [21.2-27.8] | 23.1 [20.8-26.1] | 0.167 |
| Missing | 9 | 0 | |
| Pain | | | 0.005 |
| No | 77 (71.3) | 55 (52.4) | |
| Yes | 31 (28.7) | 50 (47.6) | |
| Missing | 2 | 0 | |
| Jaundice | | | 0.272 |
| No | 102 (94.4) | 95 (90.5) | |
| Yes | 6 (5.6) | 10 (9.5) | |
| Missing | 2 | 0 | |
| Ascites | | | 0.721 |
| No | 103 (95.4) | 99 (94.3) | |
| Yes | 5 (4.6) | 6 (5.7) | |
| Missing | 2 | 0 | |
| <hr/> | | | |
| Biological parameters | | | |
| Albumin, median [IQR], g/L | 39.0 [37.0-42.6] | 34.6 [29.0-39.0] | <0.001 |
| Missing | 41 | 52 | |

| | | | | |
|--|----------------------|------------------------|--|-------|
| Lymphocytes, median [IQR], mm ³ | | | | 0.066 |
| < 1000 | 10 (10.7) | 9 (23.1) | | |
| ≥ 1000 | 83 (89.3) | 30 (76.9) | | |
| Missing | 17 | 66 | | |
| Neutrophil-to-lymphocyte ratio, median [IQR] | | | | 0.010 |
| < 5 | 71 (76.3) | 21 (53.9) | | |
| ≥ 5 | 22 (23.7) | 18 (46.1) | | |
| Missing | 17 | 66 | | |
| CA19-9, median [IQR], UI/mL | 1077.0 [76.7-7400.0] | 1333.0 [208.7-12956.0] | | 0.184 |
| Missing | 3 | 23 | | |
| <hr/> | | | | |
| Previous treatment | | | | |
| Primary tumor resection | | | | 0.642 |
| Yes | 16 (14.5) | 13 (12.4) | | |
| No | 94 (85.5) | 92 (87.6) | | |
| Adjuvant chemotherapy | | | | 0.904 |
| Yes | 12 (10.9) | 12 (11.4) | | |
| No | 98 (89.1) | 93 (88.6) | | |

χ^2 tests or Fisher's exact tests used to compare proportions, and Wilcoxon tests used to compare continuous variables between FOLFIRINOX and FOLFOXIRI groups. All statistical tests were two-sided. CA19-9: Carbohydrate antigen 19-9; IQR: Interquartile range; WHO: World Health Organization.

Supplementary Table 4 Outcomes of the entire metastatic population according to first-line chemotherapy, *n* (%)

| Outcomes | FOLFIRINOX (<i>n</i> = 110) | FOLFOXIRI (<i>n</i> = 105) | <i>P</i> value |
|---|--|---------------------------------------|---------------------------|
| Number of cycles, median [IQR] | 11.0 [6.0-13.0] | 7.0 [4.0-14.0] | 0.110 |
| Missing | 1 | 0 | |
| RECIST best response | | | 0.096 |
| Complete or partial response | 47 (48.0) | 31 (38.3) | |
| Stability | 26 (26.5) | 17 (21.0) | |
| Progression | 25 (25.5) | 33 (40.7) | |
| Missing | 12 | 24 | |
| Toxicity of grade 3 or 4 | | | 0.201 |
| No | 83 (79.1) | 75 (71.4) | |
| Yes | 22 (20.9) | 30 (28.6) | |
| Digestive | 5 (4.8) | 10 (9.5) | |
| Hematology | 1 (0.9) | 5 (4.8) | |
| Neurology | 9 (8.5) | 10 (9.5) | |
| Other | 7 (6.7) | 5 (4.8) | |
| Missing | 5 | 0 | |
| Reason for discontinuation | | | 0.731 |
| Progression | 78 (71.6) | 80 (76.2) | |
| Toxicity | 8 (7.3) | 7 (6.7) | |
| Other | 23 (21.1) | 18 (17.1) | |
| Missing | 1 | 0 | |
| Maintenance | | | 0.055 |
| Yes | 53 (48.2) | 37 (35.2) | |
| No | 57 (51.8) | 68 (64.8) | |
| Second-line chemotherapy administration | | | 0.504 |
| Yes | 82 (74.6) | 74 (70.5) | |
| No | 28 (25.4) | 31 (29.5) | |

χ^2 tests or Fisher's exact tests used to compare proportions, and Wilcoxon tests used to compare continuous variables between FOLFIRINOX and FOLFOXIRI groups. All statistical tests were two-sided. IQR: Interquartile range.

Supplementary Table 5 Unconditional univariate logistic analysis of factors associated with FOLFOXIRI in first-line chemotherapy in patients with metastatic disease

| Characteristics | Patients (<i>n</i>) | Patients treated with FOLFOXIRI (<i>n</i>) | OR (95%CI) | <i>P</i> value |
|-----------------------------------|--------------------------|--|----------------------------|----------------|
| Demographical parameters | | | | |
| Age, years | 214 | 105 | 1.020 (0.992- 1.049) | 0.159 |
| Missing | 1 | 0 | | |
| Gender | | | | |
| Male | 135 | 69 | 1.00 (Reference) | |
| Female | 80 | 36 | 0.783 (0.449- 1.363) | 0.387 |
| Familial history of cancer | | | | |
| No | 83 | 57 | 1.00 (Reference) | |
| Yes | 82 | 47 | 0.613 (0.324- 1.159) | 0.132 |
| Missing | 50 | 1 | | |
| Personal history of cancer | | | | |
| No | 183 | 85 | 1.00 (Reference) | |
| Yes | 29 | 19 | 2.190 (0.966- 4.968) | 0.061 |
| Missing | 3 | 1 | | |
| Pathological parameters | | | | |
| Stage at diagnosis | | | | |
| Localized | 31 | 13 | 1.00 (Reference) | |
| Advanced | 184 | 92 | 1.385 (0.641- 2.990) | 0.407 |
| Primary tumor site | | | | |
| Head | 87 | 45 | 1.00 (Reference) | |
| Body and/or tail | 127 | 60 | 0.836 (0.484- 1.443) | 0.520 |
| Missing | 1 | 0 | | |
| Histological grade | | | | |
| Well or Moderately differentiated | 67 | 27 | 1.00 (Reference) | |

| | | | | | |
|----------------------------|----|-----|-----|------------------|---------------|
| Poorly differentiated | or | 28 | 19 | 3.127 | (1.232- 0.016 |
| Undifferentiated | | | | 7.936) | |
| Missing | | 120 | 59 | | |
| Tumor extension | | | | | |
| Number of metastatic sites | | | | | |
| 1 | | 143 | 74 | 1.00 (Reference) | |
| ≥ 2 | | 72 | 31 | 0.705 | (0.399- 0.230 |
| | | | | 1.247) | |
| Lymph node metastases | | | | | |
| No | | 174 | 93 | 1.00 (Reference) | |
| Yes | | 41 | 12 | 0.360 | (0.173- 0.007 |
| | | | | 0.752) | |
| Liver metastases | | | | | |
| No | | 47 | 24 | 1.00 (Reference) | |
| Yes | | 168 | 81 | 0.892 | (0.467- 0.730 |
| | | | | 1.704) | |
| Peritoneal metastases | | | | | |
| No | | 169 | 74 | 1.00 (Reference) | |
| Yes | | 46 | 31 | 2.653 | (1.334- 0.005 |
| | | | | 5.274) | |
| Lung metastases | | | | | |
| No | | 174 | 86 | 1.00 (Reference) | |
| Yes | | 41 | 19 | 0.884 | (0.447- 0.723 |
| | | | | 1.748) | |
| Other metastases | | | | | |
| No | | 204 | 102 | 1.00 (Reference) | |
| Yes | | 11 | 3 | 0.375 | (0.097- 0.156 |
| | | | | 1.454) | |
| Clinical parameters | | | | | |
| Performance status (WHO) | | | | | |
| 0 | | 66 | 30 | 1.00 (Reference) | |
| 1 | | 130 | 71 | 1.444 | (0.797- |
| | | | | 2.618) | |
| ≥ 2 | | 15 | 4 | 0.436 | (0.126- 0.098 |
| | | | | 1.512) | |
| Missing | | 4 | 0 | | |

| | | | | | |
|------------------------------------|-----|-----|------------------|----------------|--|
| Body mass index, kg/m ² | 206 | 105 | 0.967 1.022) | (0.915- 0.239 | |
| Missing | 9 | 0 | | | |
| Pain | | | | | |
| No | 132 | 55 | 1.00 (Reference) | | |
| Yes | 81 | 50 | 2.258 3.977) | (1.282- 0.005 | |
| Missing | 2 | 0 | | | |
| Jaundice | | | | | |
| No | 197 | 95 | 1.00 (Reference) | | |
| Yes | 16 | 10 | 1.789 5.114) | (0.626- 0.277 | |
| Missing | 2 | 0 | | | |
| Ascites | | | | | |
| No | 202 | 99 | 1.00 (Reference) | | |
| Yes | 11 | 6 | 1.248 4.220) | (0.369- 0.722 | |
| Missing | 2 | 0 | | | |
| Clinical parameters | | | | | |
| Albumin, g/L | 122 | 53 | 0.891 0.948) | (0.838- <0.001 | |
| Missing | 93 | 52 | | | |
| Lymphocytes, mm ³ | | | | | |
| < 1000 | 19 | 9 | 2.490 6.719) | (0.923- | |
| ≥ 1000 | 113 | 30 | 1.00 (Reference) | 0.072 | |
| Missing | 83 | 66 | | | |
| Neutrophil-to-lymphocyte ratio | | | | | |
| < 5 | 92 | 21 | 1.00 (Reference) | | |
| ≥ 5 | 40 | 18 | 2.766 6.099) | (1.255- 0.012 | |
| Missing | 83 | 66 | | | |
| CA19-9, UI/mL | 189 | 82 | 1.000 1.000) | (1.000- 0.155 | |
| Missing | 26 | 23 | | | |
| Previous treatment | | | | | |

| | | | | |
|-------------------------|-----|----|------------------|-------------------------|
| Primary tumor resection | | | | |
| Yes | 29 | 13 | 1.00 (Reference) | |
| No | 186 | 92 | 1.205 | (0.549- 0.643 2.644) |
| Adjuvant chemotherapy | | | | |
| Yes | 24 | 12 | 1.00 (Reference) | |
| No | 191 | 93 | 0.949 | (0.406- 0.904 2.218) |

Logistic regression models used to estimate association of the parameters with FOLFOXIRI regimen. Values of $P < 0.05$ were considered statistically significant and all tests were two-sided. OR: Odds ratio; CI: Confidence interval; WHO: World Health Organization; CA19-9: Carbohydrate antigen 19-9.

Supplementary Table 6 Unconditional multivariate logistic analysis of factors associated with FOLFOXIRI in first-line chemotherapy for the construction of the propensity score in patients with metastatic disease ($n = 122$).

| Characteristics | Patients (n) | Patients treated with FOLFOXIRI (n) | OR (95%CI) | <i>P</i> value |
|-----------------------|---------------------|---|---------------------|-------------------|
| Lymph node metastases | | | | |
| No | 94 | 49 | 1.00 (Reference) | |
| Yes | 28 | 4 | 0.165 (0.049-0.562) | 0.004 |
| Peritoneal metastases | | | | |
| No | 96 | 38 | 1.00 (Reference) | |
| Yes | 26 | 15 | 2.243 (0.793-6.344) | 0.128 |
| Pain† | | | | |
| No | 75 | 24 | 1.00 (Reference) | |
| Yes | 47 | 29 | 3.124 (1.321-7.390) | 0.010 |
| Albumin, g/L | 122 | 53 | 0.896 (0.839-0.956) | 0.001 |

A propensity score was performed by an unconditional multivariable logistic regression model including lymph node and peritoneal metastases, pain and albumin level. Neutrophil-to-lymphocyte ratio was not selected in the propensity score process due to a high rate of missing data. Logistic regression models used to estimate association of the parameters with FOLFOXIRI regimen. Values of $P < 0.05$ were considered statistically significant and all tests were two-sided. OR: Odds ratio; CI: Confidence interval.

Supplementary Table 7 Patient characteristics of the propensity score - matched metastatic population according to first-line chemotherapy, *n* (%)

| Characteristics | FOLFIRINOX (<i>n</i> = 32) | FOLFOXIRI (<i>n</i> = 32) | <i>P</i> value |
|---|-----------------------------|----------------------------|----------------|
| Demographic parameters | | | |
| Age, median [IQR], years | 59.8 [54.5-67.9] | 60.4 [51.7-66.3] | 0.669 |
| Missing | 0 | 0 | |
| Gender | | | 0.599 |
| Male | 20 (62.5) | 22 (68.8) | |
| Female | 12 (37.5) | 10 (31.2) | |
| Familial history of cancer | | | |
| No | 9 (56.3) | 18 (56.3) | 1.000 |
| Yes | 7 (43.7) | 14 (43.7) | |
| Missing | 16 | 0 | |
| Personal history of cancer | | | |
| No | 27 (87.1) | 27 (84.4) | 1.000 |
| Yes | 4 (12.9) | 5 (15.6) | |
| Missing | 1 | 0 | |
| Pathologic parameters | | | |
| Stage at diagnosis | | | |
| Localized | 5 (15.6) | 4 (12.5) | 1.000 |
| Advanced | 27 (84.4) | 28 (87.5) | |
| Primary tumor site | | | |
| Head | 14 (45.2) | 16 (50.0) | 0.701 |
| Body and/or tail | 17 (54.8) | 16 (50.0) | |
| Histological grade | | | |
| Well or Moderately differentiated | 11 (68.8) | 8 (66.7) | 1.000 |
| Poorly differentiated or Undifferentiated | 5 (31.2) | 4 (33.3) | |
| Missing | 16 | 20 | |
| Tumor extension | | | |
| Number of metastatic sites | | | |
| 1 | 21 (65.6) | 26 (81.3) | 0.157 |
| ≥ 2 | 11 (34.4) | 6 (18.7) | |
| Lymph node metastases | | | |
| No | 28 (87.5) | 28 (87.5) | 1.000 |

| | | | |
|--|-------------------|------------------|-------|
| Yes | 4 (12.5) | 4 (12.5) | |
| Liver metastases | | | 1.000 |
| No | 7 (21.9) | 7 (21.9) | |
| Yes | 25 (78.1) | 25 (78.1) | |
| Peritoneal metastases | | | 0.756 |
| No | 26 (81.3) | 25 (78.1) | |
| Yes | 6 (18.7) | 7 (21.9) | |
| Lung metastases | | | 0.740 |
| No | 26 (81.3) | 27 (84.4) | |
| Yes | 6 (18.7) | 5 (15.6) | |
| Other metastases | | | 0.238 |
| No | 29 (90.6) | 32 (100.0) | |
| Yes | 3 (9.4) | 0 (0.0) | |
| Clinical parameters | | | |
| Performance status (WHO) | | | 0.719 |
| 0 | 9 (29.0) | 8 (25.0) | |
| ≥ 1 | 22 (71.0) | 24 (75.0) | |
| Missing | 1 | 0 | |
| Body mass index, kg/m ² | 24.5 [21.3 -26.6] | 23.9 [21.6-26.7] | 0.537 |
| Missing | 3 | 0 | |
| Pain | | | 0.611 |
| No | 20 (62.5) | 18 (56.3) | |
| Yes | 12 (37.5) | 14 (43.7) | |
| Jaundice | | | 0.426 |
| No | 30 (93.8) | 27 (84.4) | |
| Yes | 2 (6.2) | 5 (15.6) | |
| Missing | 0 | 0 | |
| Ascites | | | 0.113 |
| No | 32 (100.0) | 28 (87.5) | |
| Yes | 0 (0.0) | 4 (12.5) | |
| Biological parameters | | | |
| Albumin, median [IQR], g/L | 38.1 [33.3-41.5] | 38.0 [32.1-42.1] | 0.899 |
| Lymphocytes, median [IQR], mm ³ | | | 0.702 |
| < 1000 | 5 (16.1) | 4 (23.5) | |
| ≥ 1000 | 26 (83.9) | 13 (76.5) | |
| Missing | 1 | 15 | |

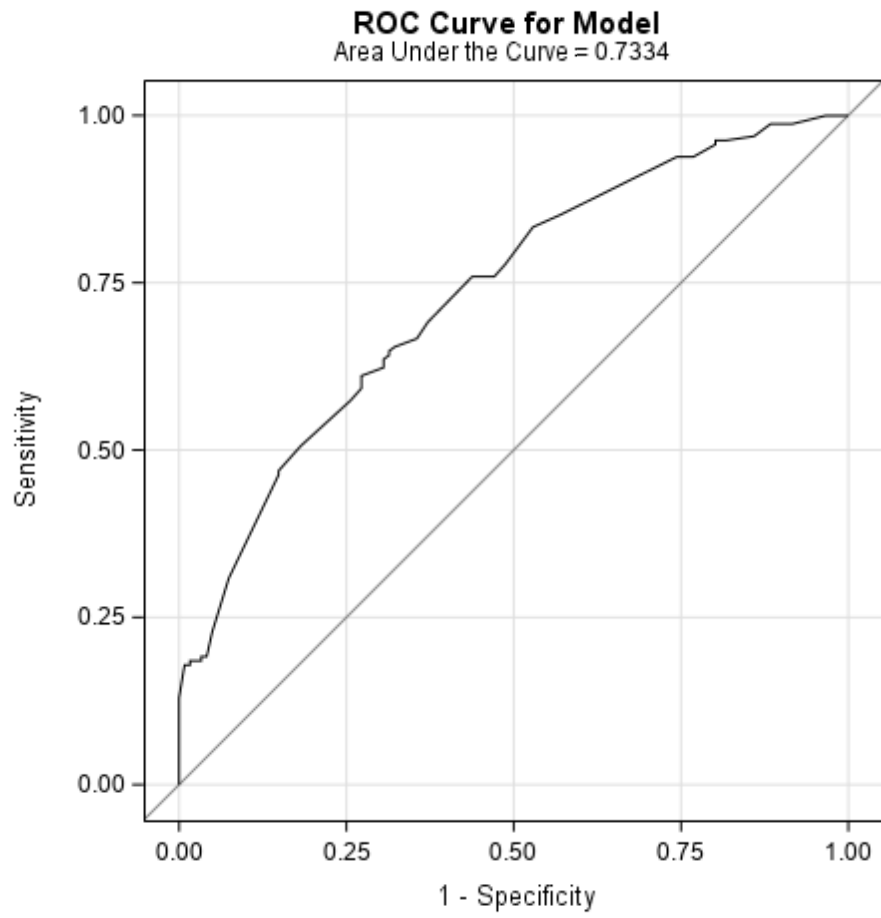
| | | | |
|--|---------------------|-----------------------|-------|
| Neutrophil-to-lymphocyte ratio, median [IQR] | | | 0.393 |
| < 5 | 22 (71.0) | 10 (58.8) | |
| ≥ 5 | 9 (29.0) | 7 (41.2) | |
| Missing | 1 | 15 | |
| CA19-9, median [IQR], UI/mL | 150.0 [32.1-8700.0] | 1307.0 [108.0-8608.0] | 0.439 |
| Missing | 0 | 3 | |
| Previous treatment | | | |
| Primary tumor resection | | | 1.000 |
| Yes | 3 (9.4) | 4 (12.5) | |
| No | 29 (90.6) | 28 (87.5) | |
| Adjuvant chemotherapy | | | 1.000 |
| Yes | 3 (9.4) | 3 (9.4) | |
| No | 29 (90.6) | 29 (90.6) | |

After propensity score matching, 32 patients each group (29.0% and 30.5% in the FOLFIRINOX and FOLFOXIRI groups, respectively) have been matched successfully. Baseline characteristics were no statistically different between the two matched groups. χ^2 tests or Fisher's exact tests used to compare proportions, and Wilcoxon tests used to compare continuous variables between FOLFIRINOX and FOLFOXIRI groups. All statistical tests were two-sided. CA19-9: Carbohydrate antigen 19-9; IQR: Interquartile range; WHO: World Health Organization.

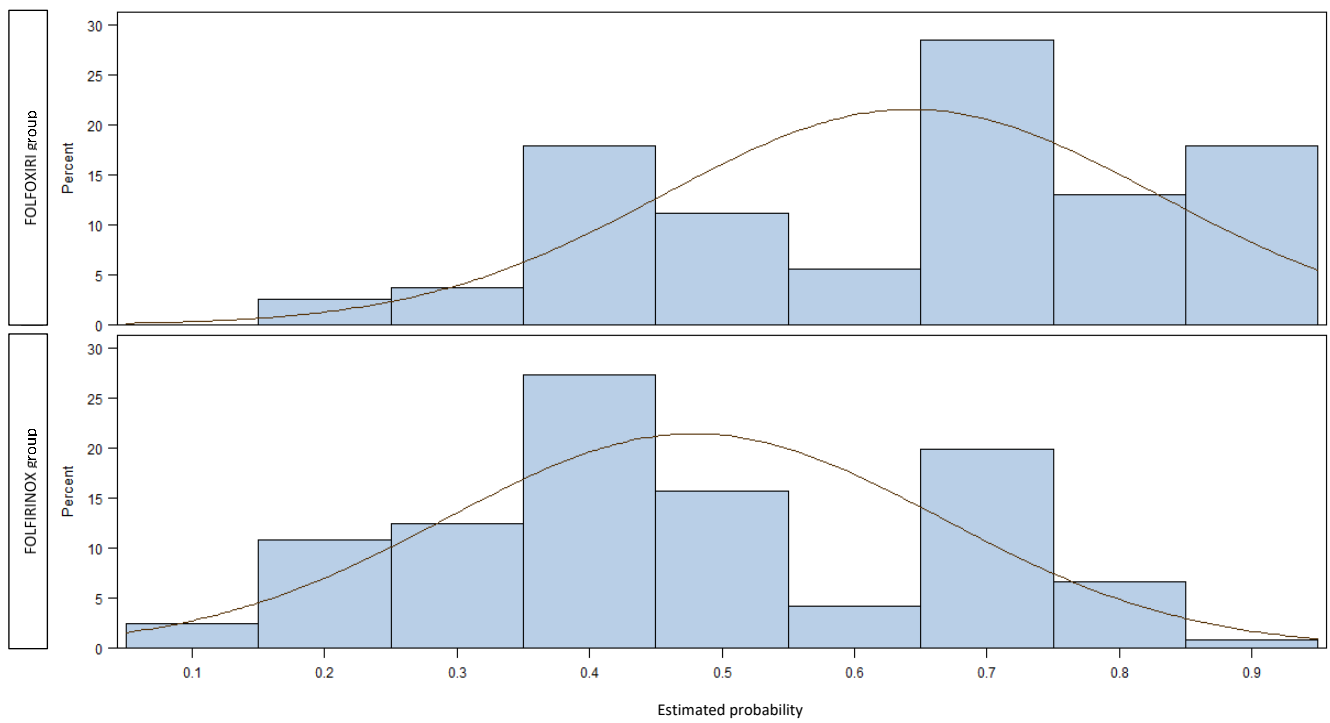
Supplementary Table 8 Outcomes of the propensity score - matched metastatic population according to first-line chemotherapy, *n* (%)

| Outcomes | FOLFIRINOX (<i>n</i> = 32) | FOLFOXIRI (<i>n</i> = 32) | <i>P</i> value |
|---|---------------------------------------|----------------------------------|---------------------------|
| Number of cycles, median [IQR] | 10.0 [4.0-12.0] | 12.0 [4.0-17.0] | 0.213 |
| Missing | 0 | 0 | |
| RECIST best response | | | 0.317 |
| Complete or partial response | 11 (40.8) | 15 (60.0) | |
| Stability | 10 (37.0) | 5 (20.0) | |
| Progression | 6 (22.2) | 5 (20.0) | |
| Missing | 5 | 7 | |
| Toxicity of grade 3 or 4 | | | 0.362 |
| No | 22 (73.3) | 20 (62.5) | |
| Yes | 8 (26.7) | 12 (37.5) | |
| Digestive | 4 (1.3) | 3 (0.9) | |
| Hematology | 1 (0.3) | 1 (0.3) | |
| Neurology | 2 (0.6) | 6 (1.8) | |
| Other | 1 (0.3) | 3 (0.3) | |
| Missing | 2 | 0 | |
| Reason for discontinuation | | | 1.000 |
| Progression | 20 (62.5) | 20 (62.5) | |
| Toxicity | 4 (12.5) | 5 (15.6) | |
| Other | 8 (25.0) | 7 (21.9) | |
| Maintenance | | | 1.000 |
| Yes | 12 (37.5) | 12 (37.5) | |
| No | 20 (62.5) | 20 (62.5) | |
| Second-line chemotherapy administration | | | 1.000 |
| Yes | 22 (68.8) | 22 (68.8) | |
| No | 10 (31.2) | 10 (31.2) | |

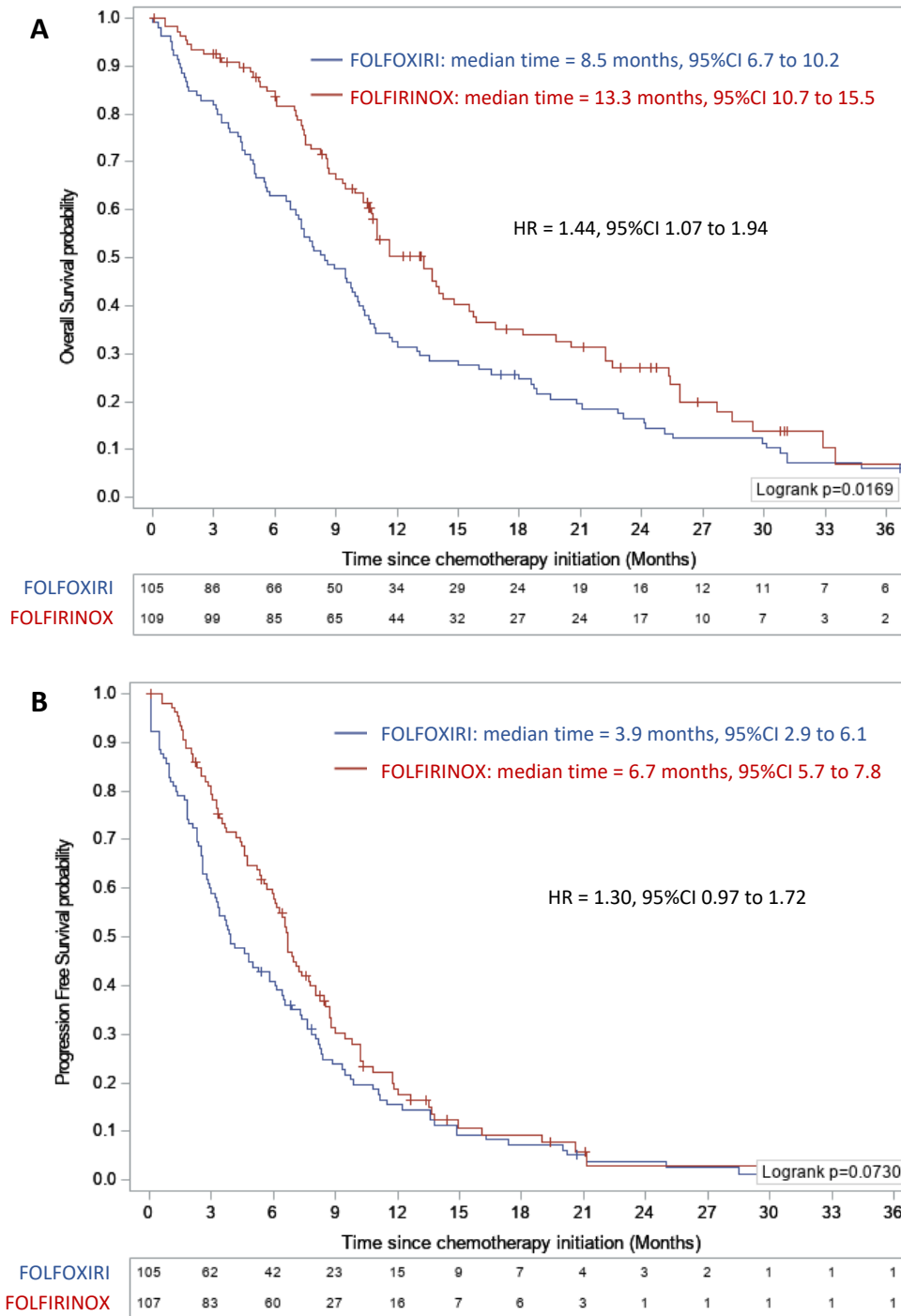
χ^2 tests or Fisher's exact tests used to compare proportions, and Wilcoxon tests used to compare continuous variables between FOLFIRINOX and FOLFOXIRI groups. All statistical tests were two-sided. IQR: Interquartile range.



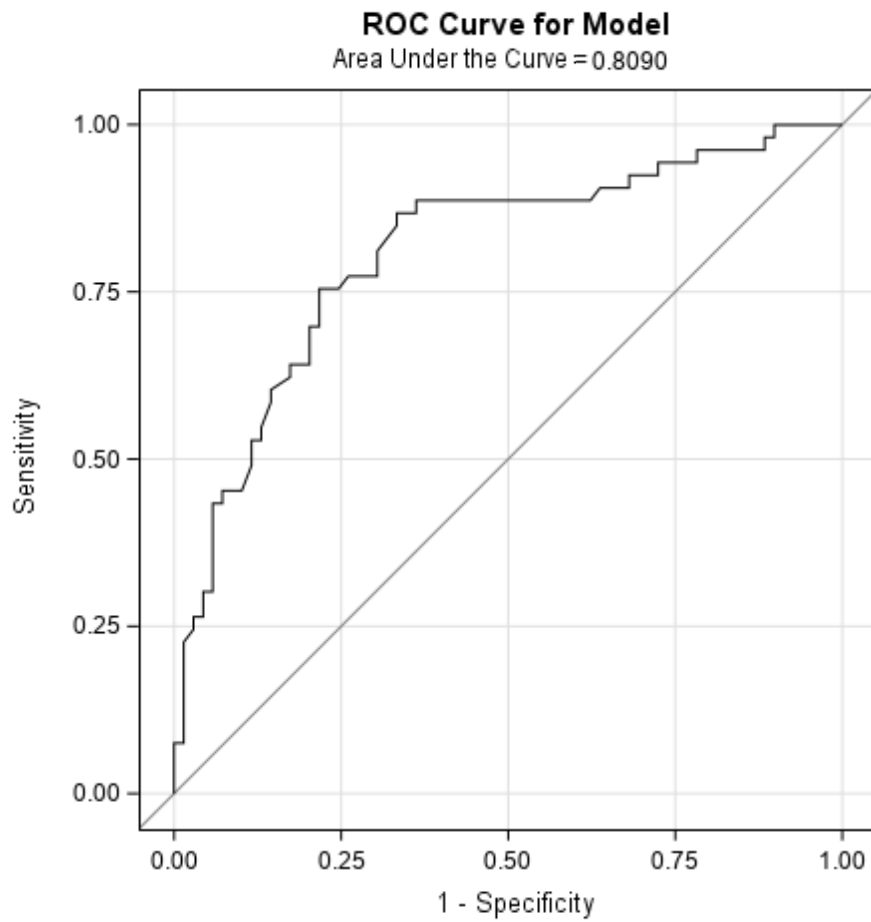
Supplementary Figure 1 Unconditional multivariable logistic regression ROC Curve analysis.



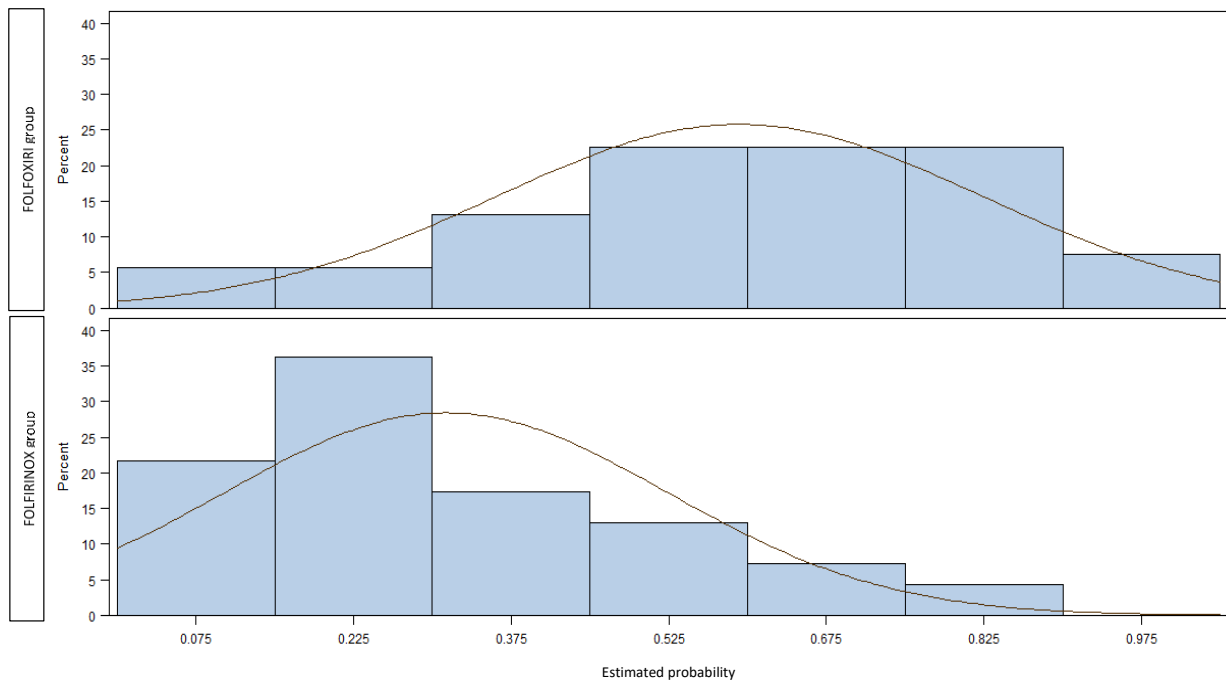
Supplementary Figure 2 Distribution of the probability estimated of the propensity score by the logistic multivariable model in FOLFIRINOX and FOLFOXIRI groups.



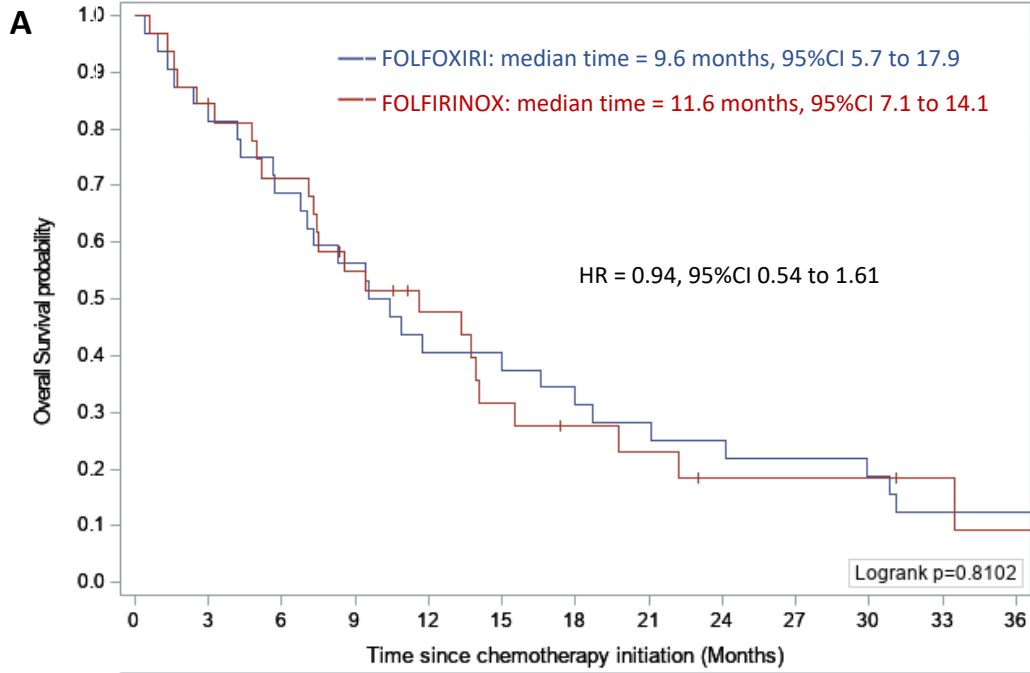
Supplementary Figure 3 Kaplan-Meier curves of (A) overall survival and (B) progression free survival for the FOLFIRINOX and FOLFOXIRI groups in the entire metastatic population. Values of the log-rank test $P < 0.05$ were considered statistically significant, and all tests were two-sided. CI: confidence interval; HR: hazard ratio.



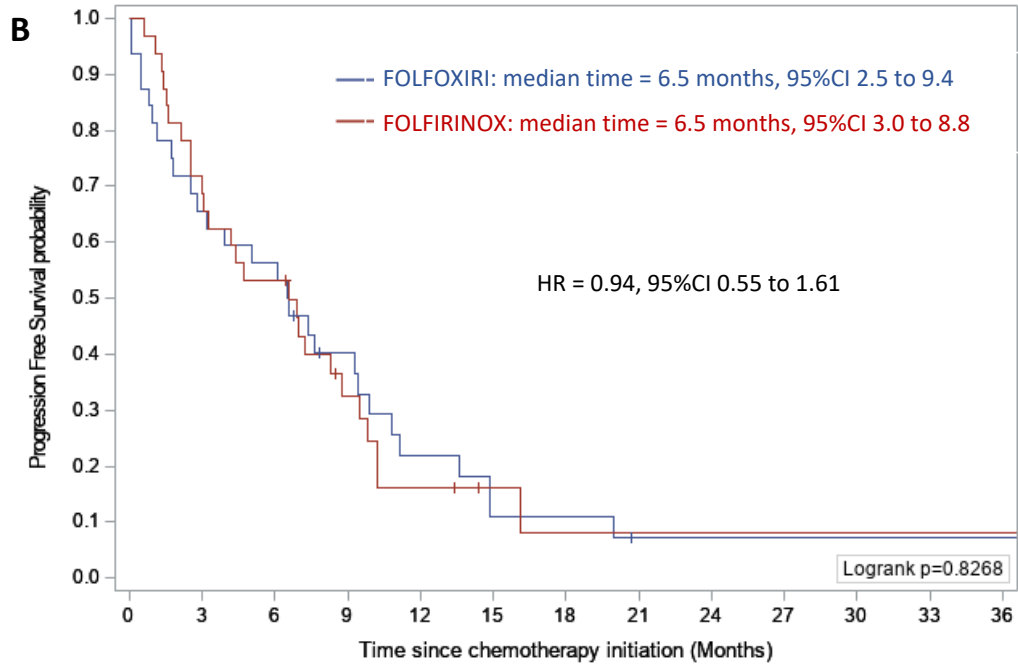
Supplementary Figure 4 Unconditional multivariable logistic regression receiver operating characteristic curve analysis in patients with metastatic disease.



Supplementary Figure 5 Distribution of the probability estimated of the propensity score by the logistic multivariable model in FOLFIRINOX and FOLFOXIRI groups in patients with metastatic disease. After a propensity score value calculated for each patient, patients treated with FOLFOXIRI regimen were matched, with a caliper of 0.10 and ratio of 1:1, with patients in the FOLFIRINOX group.



| | | | | | | | | | | | | | |
|------------|----|----|----|----|----|----|----|---|---|---|---|---|---|
| FOLFOXIRI | 32 | 26 | 22 | 18 | 13 | 12 | 10 | 9 | 8 | 7 | 6 | 4 | 4 |
| FOLFIRINOX | 32 | 26 | 22 | 16 | 12 | 8 | 6 | 5 | 3 | 3 | 3 | 2 | 1 |



| | | | | | | | | | | | | | |
|------------|----|----|----|----|---|---|---|---|---|---|---|---|---|
| FOLFOXIRI | 32 | 21 | 18 | 11 | 6 | 3 | 3 | 1 | 1 | 1 | 1 | 1 | 1 |
| FOLFIRINOX | 32 | 22 | 17 | 8 | 4 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

Supplementary Figure 6 Kaplan-Meier curves of (A) overall survival and (B) progression free survival for the FOLFIRINOX and FOLFOXIRI groups in the propensity score-matched metastatic population. Values of the log-rank test $P < 0.05$ were considered statistically significant, and all tests were two-sided. CI: confidence interval; HR: hazard ratio.