| Table S1  | List of the 19 institutions participating in SCRUM-Japan GI-SCREEN during the study period |
|-----------|-----------------------------------------------------------------------------------------|
| Aichi Cancer Center Hospital |                                           |
| Cancer Institute Hospital of JFCR |                                           |
| Chiba Cancer Center |                                           |
| Hokkaido University Hospital |                                           |
| Kanagawa Cancer Center |                                           |
| Kanazawa University Hospital |                                           |
| Kansai Rosai Hospital |                                           |
| Keio University Hospital |                                           |
| Kindai University Hospital |                                           |
| Kyorin University Hospital |                                           |
| Kyushu Cancer Center |                                           |
| Kyushu University Hospital |                                           |
| National Cancer Center Hospital |                                           |
| National Cancer Center Hospital East |                                           |
| Osaka University Hospital |                                           |
| Saitama Cancer Center, Chiba Cancer Center |                                           |
| Shikoku Cancer Center |                                           |
| St. Marianna University School of Medicine Hospital |                                           |
| Tsukuba University Hospital |                                           |
Table S2  QC-metrics established in the central laboratory for OCP/CE-IVD tests

| Metric          | Criteria                                                                 |
|-----------------|--------------------------------------------------------------------------|
| **Run QC**      |                                                                          |
| DNA NTC         | Read length histogram evaluated to ensure no contamination in the run and IR review of variant level data |
| RNA NTC         | Read length histogram evaluated to ensure no contamination in the run and IR review of variant level data |
| Mappable Fusion Reads | >20,000                                                                 |
| **Sample QC - DNA Only** |                                                                          |
| Uniformity      | 85%                                                                      |
| Mean Depth      | >1000                                                                    |
| **DNA Control** |                                                                          |
| BRAF p.Val600Glu | Present in IR and >5% AF                                                 |
| EGFR p.Glu746_Ala750del | Present in IR and >5% AF                       |
| KRAS p.Gly12Phe  | Present in IR and >5% AF                                                 |
| **RNA Control** |                                                                          |
| EML4/ALK        | Present in IR                                                            |
| Clinicopathological factors                              | Univariable (n=2573) | Multivariable (n=2572) |
|--------------------------------------------------------|----------------------|------------------------|
|                                                         | Odds (95% CI)        | P-value                | Odds (95% CI)        | P-value                |
| DNA integrity (intermediate/high)                       | 0.206 (0.137–0.309)  | <0.0001                | 0.211 (0.140–0.319)  | <0.0001                |
| DNA integrity (low/high)                               | 0.009 (0.006–0.013)  | <0.0001                | 0.010 (0.007–0.015)  | <0.0001                |
| Sex (female/male)                                      | 1.246 (1.000–1.552)  | 0.0495                 | 1.164 (0.858–1.578)  | 0.3301                 |
| Age (>50 years/≤50 years)                              | 0.961 (0.703–1.313)  | 0.8014                 | 1.397 (0.914–2.136)  | 0.1220                 |
| Specimen type (surgical/biopsy)                        | 1.667 (1.356–2.049)  | <0.0001                | 1.386 (1.015–1.894)  | 0.0402                 |
| Site of obtained specimen (metastatic/primary)         | 0.954 (0.717–1.268)  | 0.7433                 | 0.850 (0.562–1.288)  | 0.4439                 |
| Histology (non-adenocarcinoma/adenocarcinoma)          | 0.709 (0.543–0.925)  | 0.0114                 | 1.076 (0.724–1.600)  | 0.7171                 |
| Primary tumor site (non-colorectal/colorectal)         | 0.495 (0.393–0.623)  | <0.0001                | 0.615 (0.441–0.858)  | 0.0042                 |
| FFPE-sample storage period (>4 years/<4 years)†        | 0.241 (0.178–0.325)  | <0.0001                | 0.510 (0.329–0.790)  | 0.0025                 |
| Previous chemotherapy (received/not received)          | 1.439 (1.099–1.884)  | 0.0082                 | 1.244 (0.836–1.851)  | 0.2822                 |
| Previous radiotherapy (received/not received)          | 1.099 (0.572–2.112)  | 0.7762                 | 0.924 (0.368–2.322)  | 0.8665                 |

†One case with no records was excluded from univariable analysis.
| Institution ID | n  | %OCP-success (95% CI) | Univariable (n=2573) | Multivariable (n=2572) |
|----------------|----|-----------------------|----------------------|------------------------|
|                |    |                       | Odds (95% CI) P-value | Odds (95% CI) P-value  |
| 01             | 718| 73.8% (70.4–77.0%)    | ref. (0.1374) <0.0001 | ref. (0.543 0.366–0.805) 0.0024 |
| 02             | 282| 69.2% (63.4–74.5%)    | 0.795 (0.587–1.076) 0.1374 | 0.543 (0.366–0.805) 0.0024 |
| 03             | 185| 81.1% (74.7–86.5%)    | 1.520 (1.015–2.277) 0.0420 | 1.156 (0.664–2.014) 0.6080 |
| 04             | 178| 83.2% (76.8–88.3%)    | 1.750 (1.143–2.680) 0.0101 | 0.740 (0.436–1.254) 0.2628 |
| 05             | 177| 60.5% (52.8–67.7%)    | 0.542 (0.384–0.765) 0.0005 | 0.351 (0.225–0.547) 0.0001 |
| 06             | 174| 74.1% (67.0–80.5%)    | 1.017 (0.697–1.484) 0.9309 | 0.562 (0.340–0.930) 0.0249 |
| 07             | 160| 71.9% (64.2–78.7%)    | 0.906 (0.618–1.329) 0.6151 | 0.562 (0.340–0.930) 0.0249 |
| 08             | 117| 54.7% (45.2–63.9%)    | 0.428 (0.287–0.639) <0.0001 | 0.208 (0.122–0.357) <0.0001 |
| 09             | 107| 51.4% (41.5–61.2%)    | 0.375 (0.248–0.568) <0.0001 | 0.284 (0.164–0.492) <0.0001 |
| 10             | 86 | 81.4% (71.6–89.0%)    | 1.552 (0.879–2.739) 0.1294 | 1.454 (0.671–3.151) 0.3429 |
| 11             | 76 | 50.0% (38.3–61.7%)    | 0.355 (0.220–0.573) <0.0001 | 0.430 (0.233–0.792) 0.0068 |
| 12             | 66 | 22.7% (13.3–34.7%)    | 0.104 (0.057–0.190) <0.0001 | 0.116 (0.053–0.258) <0.0001 |
| 13             | 60 | 60.0% (46.5–72.4%)    | 0.532 (0.309–0.915) 0.0227 | 0.228 (0.115–0.452) <0.0001 |
| 14             | 54 | 55.6% (41.4–69.1%)    | 0.443 (0.253–0.778) 0.0046 | 0.237 (0.111–0.502) 0.0002 |
| 15             | 52 | 48.1% (34.0–62.4%)    | 0.328 (0.186–0.580) 0.0001 | 0.367 (0.159–0.845) 0.0184 |
| 16             | 43 | 72.1% (56.3–84.7%)    | 0.916 (0.461–1.821) 0.8031 | 0.599 (0.244–1.472) 0.2641 |
| 17             | 18 | 66.7% (41.0–86.7%)    | 0.709 (0.263–1.917) 0.4985 | 1.178 (0.238–5.830) 0.8413 |
| 18             | 13 | 15.4% (1.9–45.5%)     | 0.064 (0.014–0.294) 0.0004 | 0.058 (0.009–0.349) 0.0019 |
| 19             | 7  | 14.3% (0.4–57.9%)     | 0.059 (0.007–0.494) 0.0090 | 0.016 (0.001–0.175) 0.0007 |
| Institution ID | n  | %OCP-success (95% CI) | Univariable (n=2573) | Multivariable (n=2572) |
|---------------|----|-----------------------|----------------------|------------------------|
|               |    |                       | Odds (95% CI)        | P-value                |
|               |    |                       | Odds (95% CI)        | P-value                |
| 01            | 718| 85.5% (82.7–88.0%)    | ref                  | (<0.0001)              |
| 02            | 282| 86.2% (81.6–90.0%)    | 1.055 (0.710–1.570)  | 0.7901                 |
| 03            | 185| 89.7% (84.4–93.7%)    | 1.480 (0.881–2.485)  | 0.1382                 |
| 04            | 178| 94.9% (90.6–97.7%)    | 3.181 (1.576–6.417)  | 0.0012                 |
| 05            | 177| 80.8% (74.2–86.3%)    | 0.712 (0.464–1.093)  | 0.1203                 |
| 06            | 174| 85.6% (79.5–90.5%)    | 1.010 (0.630–1.618)  | 0.9686                 |
| 07            | 160| 85.0% (78.5–90.2%)    | 0.960 (0.593–1.553)  | 0.8673                 |
| 08            | 117| 76.1% (67.3–83.5%)    | 0.538 (0.336–0.864)  | 0.0103                 |
| 09            | 107| 71.0% (61.5–79.4%)    | 0.415 (0.260–0.662)  | 0.0002                 |
| 10            | 86 | 87.2% (78.3–93.4%)    | 1.155 (0.593–2.248)  | 0.6718                 |
| 11            | 76 | 69.7% (58.1–79.8%)    | 0.390 (0.229–0.664)  | 0.0005                 |
| 12            | 66 | 40.9% (29.0–53.7%)    | 0.117 (0.069–0.200)  | <0.0001                |
| 13            | 60 | 81.7% (69.6–90.5%)    | 0.755 (0.380–1.499)  | 0.4211                 |
| 14            | 54 | 81.5% (68.6–90.8%)    | 0.745 (0.364–1.527)  | 0.4218                 |
| 15            | 52 | 67.3% (52.9–79.7%)    | 0.349 (0.188–0.645)  | 0.0008                 |
| 16            | 43 | 90.7% (77.9–97.4%)    | 1.651 (0.578–4.718)  | 0.3490                 |
| 17            | 18 | 83.3% (58.6–96.4%)    | 0.847 (0.241–2.976)  | 0.7955                 |
| 18            | 13 | 38.5% (13.9–68.4%)    | 0.106 (0.034–0.330)  | 0.0001                 |
| 19            | 7  | 42.9% (9.9–81.6%)     | 0.127 (0.028–0.576)  | 0.0075                 |
| Clinicopathological factors                        | Univariable (n=2573) |                      | Multivariable (n=2572) |                      |
|--------------------------------------------------|----------------------|----------------------|------------------------|----------------------|
|                                                  | Odds (95% CI)        | P-value              | Odds (95% CI)          | P-value              |
| DNA integrity (intermediate/high)                | 0.210 (0.167–0.265)  | <0.0001              | 0.195 (0.151–0.251)    | <0.0001              |
| DNA integrity (low/high)                         | 0.006 (0.004–0.010)  | <0.0001              | 0.007 (0.004–0.012)    | <0.0001              |
| Sample-submitted institution (ID02-19/ID01)†     | (provided in Table S4) | <0.0001             | (provided in Table S4) | <0.0001             |
| Sex (female/male)                                | 1.198 (1.005–1.427)  | 0.0441               | 1.053 (0.827–1.341)    | 0.6765               |
| Age (>50 years/≤50 years)                        | 0.906 (0.703–1.168)  | 0.4484               | 1.256 (0.894–1.764)    | 0.1892               |
| Specimen type (surgical/biopsy)                  | 1.542 (1.305–1.821)  | <0.0001              | 1.796 (1.392–2.319)    | <0.0001              |
| Site of obtained specimen (metastatic/primary)   | 1.054 (0.834–1.334)  | 0.6584               | 1.002 (0.713–1.408)    | 0.9906               |
| Histology (non-adenocarcinoma/adenocarcinoma)    | 0.663 (0.530–0.829)  | 0.0003               | 0.777 (0.555–1.088)    | 0.1425               |
| Primary tumor site (non-colorectal/colorectal)   | 0.580 (0.486–0.692)  | <0.0001              | 0.674 (0.517–0.878)    | 0.0035               |
| FFPE-sample storage period (>4 years/<4 years)‡   | 0.215 (0.158–0.290)  | <0.0001              | 0.376 (0.249–0.568)    | <0.0001              |
| Previous chemotherapy (received/not received)    | 1.252 (1.017–1.541)  | 0.0338               | 1.061 (0.785–1.434)    | 0.6988               |
| Previous radiotherapy (received/not received)    | 0.933 (0.562–1.550)  | 0.789                | 0.774 (0.385–1.553)    | 0.4706               |

†Details are listed in Table S4.
‡One case with no records was excluded from univariable analysis.
**Table S7 Clinicopathological factors associated with %combined-success (with the institution factor included in multivariate analysis)**

|                                | Univariable (n=2573) |         | Multivariable (n=2572) |         |
|--------------------------------|----------------------|---------|-------------------------|---------|
|                                | Odds (95% CI)        | P-value | Odds (95% CI)           | P-value |
| DNA integrity (intermediate/high) | 0.206 (0.137–0.309)  | <0.0001 | 0.214 (0.141–0.326)     | <0.0001 |
| DNA integrity (low/high)        | 0.009 (0.006–0.013)  | <0.0001 | 0.011 (0.007–0.017)     | <0.0001 |
| Sample-submitted institution (ID02-19/ID01)† | (provided in Table S5) | <0.0001 | (provided in Table S5)  | 0.0002  |
| Sex (female/male)               | 1.246 (1.000–1.552)  | 0.0495  | 1.144 (0.837–1.565)     | 0.3983  |
| Age (>50 years/≤50 years)       | 0.961 (0.703–1.313)  | 0.8014  | 1.451 (0.938–2.243)     | 0.0941  |
| Specimen type (surgical/biopsy) | 1.667 (1.356–2.049)  | <0.0001 | 1.482 (1.064–2.065)     | 0.0200  |
| Site of obtained specimen (metastatic/primary) | 0.954 (0.717–1.268) | 0.7433  | 0.802 (0.524–1.230)     | 0.3120  |
| Histology (non-adenocarcinoma/adenocarcinoma) | 0.709 (0.543–0.925) | 0.0114  | 1.107 (0.727–1.685)     | 0.6365  |
| Primary tumor site (non-colorectal/colorectal) | 0.495 (0.393–0.623) | <0.0001 | 0.606 (0.429–0.856)     | 0.0044  |
| FFPE-sample storage period (>4 years/<4 years)‡ | 0.241 (0.178–0.325) | <0.0001 | 0.444 (0.284–0.695)     | 0.0004  |
| Previous chemotherapy (received/not received) | 1.439 (1.099–1.884) | 0.0082  | 1.264 (0.841–1.898)     | 0.2594  |
| Previous radiotherapy (received/not received) | 1.099 (0.572–2.112) | 0.7762  | 0.849 (0.342–2.104)     | 0.7232  |

†Details are listed in Table S5.
‡One case with no records was excluded from univariable analysis.
Figure S1  OCP and CE-IVD success rates in biopsy and surgical samples

Proportion of final NGS results

Proportion of DNA integrity category

Bx  Surgical
OCP  CEIVD  No Results
High  Intermediate  Low