

Table SI. Baseline value of patients' biochemistry.

| Blood and chemistry                     | Patients | Percentage of patients (%) |
|---|----------|----------------------------|
| Hb (g/dl)                               |          |                            |
| <10                                     | 10       | 7.75                       |
| ≥10                                     | 119      | 92.25                      |
| N/L ratio                               |          |                            |
| <5                                      | 118      | 91.47                      |
| ≥5                                      | 11       | 8.53                       |
| PLT (10 <sup>3</sup> /mm <sup>3</sup> ) |          |                            |
| ≥400.000                                | 15       | 11.63                      |
| <400.000                                | 114      | 88.37                      |
| Fibrinogen (mg/dl)                      |          |                            |
| ≥400                                    | 43       | 33.33                      |
| <400                                    | 77       | 59.69                      |
| NA                                      | 9        | 6.98                       |
| HbA1c (mmol/mol)                        |          |                            |
| ≥42                                     | 23       | 17.83                      |
| <42                                     | 80       | 62.02                      |
| NA                                      | 26       | 20.16                      |
| Dysthyroidism                           |          |                            |
| Yes                                     | 13       | 10.08                      |
| No                                      | 98       | 75.97                      |

|                       |    |       |
|-----------------------|----|-------|
| NA                    | 18 | 13.95 |
| Cholesterol (mg/dl)   |    |       |
| ≥200                  | 40 | 31.01 |
| <200                  | 72 | 55.81 |
| NA                    | 17 | 13.18 |
| HDL (mg/dl)           |    |       |
| <50                   | 49 | 37.98 |
| ≥50                   | 63 | 48.84 |
| NA                    | 17 | 13.18 |
| Triglycerides (mg/dl) |    |       |
| ≥150                  | 20 | 15.50 |
| <150                  | 90 | 69.77 |
| NA                    | 19 | 14.73 |

Hb, haemoglobin; HDL, high-density lipoprotein; N/L ratio, neutrophils/Lymphocytes ratio; NA, not available; PLT, platelets.

Table SII. Clinical manifestations of FIC in the patients' cohort.

| Patients | High CV risk | Symptoms           |                    |                    |         | TnI         | ECG modification | Changing in CV therapy | FP stop     |
|----------|--------------|--------------------|--------------------|--------------------|---------|-------------|------------------|------------------------|-------------|
|          |              | Dyspnoea           | Palpitations       | Chest pain         | Syncope |             |                  |                        |             |
| 1        | -            | -                  | -                  | -                  | Yes     | -           | -                | -                      | -           |
| 2        | Yes          | -                  | -                  | -                  | Yes     | -           | -                | -                      | -           |
| 3        | Yes          | Yes                | Yes                | Yes                | -       | -           | -                | -                      | -           |
| 4        | -            | Yes                | Yes                | -                  | -       | -           | -                | -                      | -           |
| 5        | -            | Yes                | Yes                | -                  | -       | -           | -                | -                      | -           |
| 6        | -            | -                  | -                  | Yes                | -       | -           | -                | -                      | -           |
| 7        | -            | -                  | -                  | Yes                | -       | -           | -                | -                      | -           |
| 8        | Yes          | -                  | -                  | Yes                | -       | -           | -                | Yes                    | -           |
| 9        | Yes          | Yes                | Yes                | Yes                | -       | -           | -                | -                      | -           |
| 10       | Yes          | Yes                | Yes                | -                  | -       | -           | Yes              | -                      | Yes         |
| 11       | Yes          | -                  | Yes                | -                  | -       | -           | -                | -                      | -           |
| 12       | -            | -                  | -                  | Yes                |         |             | -                | Yes                    | -           |
| 13       | Yes          | Yes (at C2 and C6) | Yes (at C2 and C6) | Yes (at C2 and C6) |         | Yes (at C6) | Yes (at C6)      | Yes (at C6)            | Yes (at C6) |
| 14       | -            | Yes                | -                  | -                  | -       | -           | -                | -                      | -           |
| 15       | -            | Yes                | -                  | -                  | -       | -           | -                | -                      | -           |
| 16       | -            | Yes                | -                  | Yes                | -       | -           | -                | -                      | -           |

|    |     |     |     |   |     |   |     |     |     |
|----|-----|-----|-----|---|-----|---|-----|-----|-----|
| 17 | Yes | Yes | Yes | - | -   | - | Yes | -   | Yes |
| 18 | Yes | Yes | -   | - | -   | - | -   | -   | -   |
| 19 | -   | Yes | -   | - | -   | - | -   | -   | -   |
| 20 | -   | -   | -   | - | Yes | - | -   | Yes | -   |

CV, Cardiovascular; TnI, Troponin I; ECG, Electrocardiography; FP, Fluoropyrimidine; C2, Cycle 2; C6, Cycle 6.

Table SIII. Unpaired t-test applied to proBNP values variations among FIC vs. no FIC patients (comparisons for each time point).

| FIC vs. no FIC patients | P-value |
|-------------------------|---------|
| C1D1                    | 0.82    |
| C1D3                    | 0.18    |
| C2D1                    | 0.24    |
| C2D3                    | 0.15    |
| C3D1                    | 0.54    |
| C3D3                    | 0.57    |

FIC, Fluoropyrimidine-induced cardiotoxicity.

Table SIV. Paired t-test applied on proBNP values variation after administration of FP-based chemotherapy.

| Patients without FIC 5-FU/capecitabine | P-value               | Patients with FIC 5-FU/capecitabine | P-value |
|--|-----------------------|-------------------------------------|---------|
| C1D1 vs. C1D3                          | 0.0001                | C1D1 vs. C1D3                       | 0.52    |
| C2D1 vs. C2D3                          | 0.0001                | C2D1 vs. C2D3                       | 0.26    |
| C3D1 vs. C3D3                          | 0.0004                | C3D1 vs. C3D3                       | 0.21    |
| Patients without FIC 5-FU              | P-value               | Patients with FIC 5-FU              | P-value |
| C1D1 vs. C1D3                          | $9.4 \times 10^{-5}$  | C1D1 vs. C1D3                       | 0.04    |
| C2D1 vs. C2D3                          | $5.7 \times 10^{-5}$  | C2D1 vs. C2D3                       | 0.36    |
| C3D1 vs. C3D3                          | $1.22 \times 10^{-5}$ | C3D1 vs. C3D3                       | 0.22    |
| Patients without FIC capecitabine      | P-value               | Patients with FIC capecitabine      | P-value |
| C1D1 vs. C1D3                          | 0.26                  | C1D1 vs. C1D3                       | 0.31    |
| C2D1 vs. C2D3                          | 0.63                  | C2D1 vs. C2D3                       | 0.47    |
| C3D1 vs. C3D3                          | 0.25                  | C3D1 vs. C3D3                       | 0.82    |

5-FU, 5-fluorouracil; FIC, Fluoropyrimidine-induced cardiotoxicity; FP, fluoropyrimidines.

Table SV. Baseline characteristics of patients selected for microRNA analysis.

| Characteristics of patients | Number of patients |
|-----------------------------|--------------------|
| Sex                         | (n=24)             |
| Male                        | 12                 |
| Female                      | 12                 |
| Median age, years(range)    | 68 (52-80)         |
| Tumor site                  |                    |
| Colon                       | 22                 |
| Rectum                      | 2                  |
| Therapy                     |                    |
| 5-FU                        | 6                  |
| Capecitabine                | 18                 |
| Setting                     |                    |
| Adjuvant                    | 18                 |
| Metastatic                  | 6                  |
| CV event                    |                    |
| Yes                         | 8                  |
| No                          | 16                 |
| CV risk                     |                    |
| High                        | 12                 |
| Low                         | 12                 |

5-FU, 5-fluorouracil; CV, cardiovascular.