

Table S1: Comparison of clinical factors at the start of irinotecan plus fluorouracil/folinic acid (nal-IRI/FF) between the patients with and without discontinuation due to adverse event

|                                                           | With discontinuation<br>(n=10) |             |  | Without discontinuation<br>(n=30) |              |               |
|-----------------------------------------------------------|--------------------------------|-------------|--|-----------------------------------|--------------|---------------|
|                                                           | n/median                       | (%) / [IQR] |  | n/median                          | (%) / [IQR]  | p-value       |
| Age                                                       | 71.5                           | [69.5-72]   |  | 69.1                              | [60.8-72]    | 0.27          |
| Sex- male                                                 | 7                              | (70)        |  | 12                                | (40)         | 0.14          |
| ECOG PS $\geq$ 1                                          | 9                              | (90)        |  | 10                                | (33)         | <b>0.002*</b> |
| Presence of liver metastases                              | 4                              | (40)        |  | 12                                | (40)         | 1.00          |
| Presence of carcinomatosis                                | 5                              | (50)        |  | 14                                | (47)         | 0.85          |
| The interval from the diagnosis* to initiation of nal-IRI | 9.9                            | [3.2-24.8]  |  | 6.5                               | [2-20.3]     | <b>0.08</b>   |
| CA19-9 (U/mL)                                             | 873                            | [34-9594]   |  | 1200                              | [34-1100000] | 0.97          |
| GPS $\geq$ 2                                              | 5                              | (50)        |  | 6                                 | (20)         | <b>0.07</b>   |
| Alb (g/dL)                                                | 3.70                           | [2.75-4.0]  |  | 3.55                              | [3.2-3.7]    | 0.79          |
| CRP (mg/dL)                                               | 1.09                           | [0.35-2.73] |  | 0.50                              | [0.05-1.36]  | <b>0.08</b>   |
| The initial dose of nal-IRI (%)                           | 100                            | [75-100]    |  | 95                                | [73-100]     | 0.86          |
| Dose reduction within the first four cycles               | 4                              | (40)        |  | 10                                | (33)         | 0.72          |

CRP, C-reactive protein; Carcinomatosis, presence of multi-metastatic sites; GPS: Glasgow prognostic score; \* diagnosis, defined as diagnosis with unresectable status

Table S2: Univariate analysis of the clinical factors at the start of irinotecan plus fluorouracil/folinic acid (nal-IRI/FF) for progression-free survival

| Variables                         | n  |  | HR   | (95% CI)  | p-value |
|-----------------------------------|----|--|------|-----------|---------|
| Age                               |    |  |      |           |         |
| ≥ 70 y.o.                         | 20 |  | 1.20 | 5.56-2.57 | 0.65    |
| < 70 y.o.                         | 20 |  |      |           |         |
| Sex                               |    |  |      |           |         |
| male                              | 19 |  | 0.82 | 0.38-1.77 | 0.62    |
| female                            | 21 |  |      |           |         |
| ECOG PS                           |    |  |      |           |         |
| =1 or 2                           | 19 |  | 1.34 | 0.61-2.94 | 0.61    |
| =0                                | 21 |  |      |           |         |
| Presence of liver metastasis      |    |  |      |           |         |
| present                           | 19 |  | 1.19 | 0.53-2.64 | 0.67    |
| absent                            | 21 |  |      |           |         |
| Presence of peritoneal metastasis |    |  |      |           |         |
| present                           | 14 |  | 1.97 | 0.83-4.69 | 0.12    |
| absent                            | 26 |  |      |           |         |
| Carcinomatosis                    |    |  |      |           |         |
| present                           | 19 |  | 0.82 | 0.39-1.76 | 0.62    |
| absent                            | 21 |  |      |           |         |
| NLR                               |    |  |      |           |         |
| > 4                               | 10 |  | 1.66 | 0.56-4.90 | 0.36    |
| ≤ 4                               | 30 |  |      |           |         |
| CA19-9                            |    |  |      |           |         |
| >1000 U/dL                        | 20 |  | 0.82 | 0.38-1.76 | 0.61    |
| ≤ 1000 U/dL                       | 16 |  |      |           |         |
| GPS                               |    |  |      |           |         |
| =2                                | 11 |  | 1.58 | 0.58-4.25 | 0.36    |
| =0,1                              | 29 |  |      |           |         |
| LMR                               |    |  |      |           |         |
| < 3                               | 27 |  | 0.70 | 0.32-1.59 | 0.37    |
| ≥ 3                               | 13 |  |      |           |         |
| PLR                               |    |  |      |           |         |
| >150                              | 32 |  | 1.67 | 0.57-4.88 | 0.35    |

|                                                                   |    |  |      |           |      |
|-------------------------------------------------------------------|----|--|------|-----------|------|
| ≤150                                                              | 8  |  |      |           |      |
| PNI                                                               |    |  |      |           |      |
| < 45                                                              |    |  | 0.57 | 0.24-1.31 | 0.19 |
| ≥45                                                               |    |  |      |           |      |
| BW decrease compared with diagnosis                               |    |  |      |           |      |
| >5%                                                               | 14 |  | 1.78 | 0.74-4.29 | 0.20 |
| ≤5%                                                               | 23 |  |      |           |      |
| The interval from the diagnosis* to the administration of nal-IRI |    |  |      |           |      |
| > 6.6months                                                       | 20 |  | 0.74 | 0.36-1.51 | 0.40 |
| ≤ 6.6months                                                       | 20 |  |      |           |      |

Carcinomatosis, presence of multi-metastatic sites; GPS: Glasgow prognostic score

NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; LMR, lymphocyte-monocyte ratio;

PNI, prognostic-nutritional index;