

Supplemental Tables for:  
 Efficacy and Safety of Folfiri Regimen in Elderly Versus non-elderly Patients with Metastatic Colorectal or Gastric Cancer  
 Jee Hyun Kim et al.

**Table S1.** Dose modification guideline

(A) Hematologic toxicities

ANC(/mm <sup>3</sup> ) Platelet(/mm <sup>3</sup> )	Irinotecan/5-FU																
≥ 1,500 and ≥ 100,000	100% of the previous dose																
	1 week delay and CBC recheck ⇒ 1 week later																
	<table border="1"> <thead> <tr> <th>ANC</th> <th></th> <th>Platelet</th> <th></th> </tr> </thead> <tbody> <tr> <td>≥ 1,500</td> <td>and</td> <td>≥ 100,000</td> <td>100% of the previous dose</td> </tr> <tr> <td>&lt; 1,500</td> <td>or</td> <td>&lt; 100,000</td> <td>1 week delay and CBC recheck</td> </tr> </tbody> </table>	ANC		Platelet		≥ 1,500	and	≥ 100,000	100% of the previous dose	< 1,500	or	< 100,000	1 week delay and CBC recheck				
ANC		Platelet															
≥ 1,500	and	≥ 100,000	100% of the previous dose														
< 1,500	or	< 100,000	1 week delay and CBC recheck														
< 1,500 or <100,000	⇒ 2 weeks later																
	<table border="1"> <thead> <tr> <th>ANC</th> <th></th> <th>Platelet</th> <th></th> </tr> </thead> <tbody> <tr> <td>≥ 1,500</td> <td>and</td> <td>≥ 100,000</td> <td>100% of the previous dose</td> </tr> <tr> <td>1,000 – 1,500</td> <td>or</td> <td>75,000 – 100,000</td> <td>-1 dose level</td> </tr> <tr> <td>&lt; 1,000</td> <td>or</td> <td>&lt; 75,000</td> <td>Stop the chemotherapy</td> </tr> </tbody> </table>	ANC		Platelet		≥ 1,500	and	≥ 100,000	100% of the previous dose	1,000 – 1,500	or	75,000 – 100,000	-1 dose level	< 1,000	or	< 75,000	Stop the chemotherapy
ANC		Platelet															
≥ 1,500	and	≥ 100,000	100% of the previous dose														
1,000 – 1,500	or	75,000 – 100,000	-1 dose level														
< 1,000	or	< 75,000	Stop the chemotherapy														
< 500 or < 25,000	-1 dose level																

(B) Non-hematologic toxicities

Toxicities	Irinotecan	5-FU
Nausea/vomiting (Grade 4)	-1 dose level	
Diarrhea (Grade 3 or 4)	-1 dose level	
Stomatitis (Grade 3 or 4)	-1 dose level	
Dermatologic toxicity (Grade 3 or 4)	100% of the previous dose	Based on the physician's discretion
Neurologic toxicity (Grade 2, 3, or 4)	100% of the previous dose	
Other toxicities	Based on the physician's discretion	Based on the physician's discretion

Abbreviations: ANC, absolute neutrophil count; 5-FU, 5-fluorouracil; CBC, complete blood count

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**Table S2.** Relative dose intensity of FOLFIRI chemotherapy.

(A) CRC cohort

Variables		< 70 years (%)	70–74 years (%)	≥ 75 years (%)	P-value
<b>Irinotecan</b> <b>(180 mg/m<sup>2</sup>)</b>	Mean ± SD	80.9 ± 14.5	74.5 ± 15.4	75.4 ± 16.3	< 0.001
<b>5-FU bolus</b> <b>(400 mg/m<sup>2</sup>)</b>	Mean ± SD	84.6 ± 28.9	83.8 ± 31.1	84.1 ± 37.4	0.959
<b>5-FU infusion</b> <b>(2400 mg/m<sup>2</sup>)</b>	Mean ± SD	71.8 ± 24.8	66.6 ± 26.0	50.3 ± 25.2	< 0.001

(B) GC cohort

Variables		< 70 years (%)	70–74 years (%)	≥ 75 years (%)	P-value
<b>Irinotecan</b> <b>(180 mg/m<sup>2</sup>)</b>	Mean ± SD	76.2 ± 14.3	72.3 ± 12.8	72.7 ± 15.4	0.060
<b>5-FU bolus</b> <b>(400 mg/m<sup>2</sup>)</b>	Mean ± SD	72.1 ± 54.0	76.2 ± 50.3	80.2 ± 31.7	0.647
<b>5-FU infusion</b> <b>(2400 mg/m<sup>2</sup>)</b>	Mean ± SD	55.8 ± 27.1	43.5 ± 22.8	56.0 ± 27.2	0.002

Abbreviations: CRC, colorectal cancer; SD, standard deviation; 5-FU, 5-fluorouracil; GC, gastric cancer

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**Table S3.** Treatment response to FOLFIRI chemotherapy

(A) CRC cohort

<b>Response (%)</b>	<b>&lt; 70 years (N = 687)</b>	<b>≥ 70 years (N=128)</b>	<b>P-value</b>
CR	13 (1.9)	1 (0.8)	
PR	156 (22.7)	28 (21.9)	
SD	376 (54.7)	74 (57.8)	
PD	142 (20.7)	25 (19.5)	
RR	169 (24.6)	29 (22.7)	0.720

(B) GC cohort

<b>Response (%)</b>	<b>&lt; 70 years (N = 438)</b>	<b>≥ 70 years (N = 70)</b>	<b>P-value</b>
CR	11 (2.5)	1 (1.43)	
PR	54 (12.3)	11 (15.7)	
SD	234 (53.4)	35 (50.0)	
PD	139 (31.7)	23 (32.9)	
RR	65 (14.8)	12 (17.1)	0.749

Abbreviations: CRC, colorectal cancer; CR, complete remission; PR, partial response; SD, stable disease; PD, progressive disease; RR, response rate; GC, gastric cancer

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**Table S4.** Multivariable analysis of PFS in the CRC and GC cohorts

(A) Multivariable analysis of PFS in the CRC cohort

Characteristics		HR (95% CI)	P-value
<i>UGT1A1</i> genotype	0DA	1	0.229
	1DA	1.095 (0.945–1.268)	
	2DA	1.200 (0.953–1.511)	
Liver metastasis	No	1	< 0.001
	Yes	1.414 (1.215–1.647)	
Lung metastasis	No	1	0.152
	Yes	1.119 (0.959–1.306)	
Lymph node metastasis	No	1	0.006
	Yes	1.243 (1.064–1.453)	
Peritoneal metastasis	No	1	0.066
	Yes	1.206 (0.988–1.472)	
Previous adjuvant chemotherapy	No	1	0.010
	Yes	0.811 (0.691–0.952)	
Treatment line	1st-line	1	< 0.001
	2nd-line	1.354 (1.168–1.569)	
Age	< 70 years	1	0.244
	≥ 70 years	1.117 (0.927–1.345)	

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(B) Multivariable analysis of OS in the CRC cohort

Characteristics		HR (95% CI)	P-value
<i>UGT1A1</i> genotype	0DA	1	0.662
	1DA	0.922 (0.764–1.112)	
	2DA	1.007 (0.750–1.352)	
Liver metastasis	No	1	< 0.001
	Yes	1.540 (1.264–1.877)	
Lung metastasis	No	1	0.982
	Yes	1.002 (0.821–1.223)	
Lymph node metastasis	No	1	< 0.001
	Yes	1.582 (1.301–1.923)	
Peritoneal metastasis	No	1	0.015
	Yes	1.373 (1.064–1.773)	
Previous adjuvant chemotherapy	No	1	< 0.001
	Yes	0.679 (0.551–0.839)	
Treatment line	1st-line	1	< 0.001
	2nd-line	1.440 (1.196–1.733)	
Age	< 70 years	1	0.931
	≥ 70 years	0.989 (0.774–1.264)	

(C) Multivariable analysis of PFS in the GC cohort

Characteristics		HR (95% CI)	P-value
<i>UGT1A1</i> genotype	0DA	1	0.099
	1DA	1.101(0.917–1.322)	
	2DA	0.791(0.587–1.067)	
Liver metastasis	No	1	0.005
	Yes	1.336(1.090–1.638)	
Lung metastasis	No	1	0.054
	Yes	1.382(0.995–1.920)	
Lymph node metastasis	No	1	0.520
	Yes	0.942(0.784–1.131)	
Peritoneal metastasis	No	1	0.001
	Yes	1.377(1.131–1.676)	
Previous adjuvant chemotherapy	No	1	0.016
	Yes	0.788(0.650–0.956)	
Treatment line	1st-line	1	< 0.001
	2nd-line	1.549(1.287–1.865)	
Age	< 70 years	1	0.479
	≥ 70 years	1.093(0.854–1.400)	

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(D) Multivariable analysis of OS in the GC cohort

Characteristics		HR (95% CI)	P-value
<i>UGT1A1</i> genotype	0DA	1	0.323
	1DA	1.107 (0.894–1.370)	
	2DA	0.839 (0.572–1.230)	
Liver metastasis	No	1	0.036
	Yes	1.293 (1.017–1.645)	
Lung metastasis	No	1	0.118
	Yes	1.351 (0.927–1.969)	
Lymph node metastasis	No	1	0.281
	Yes	1.126 (0.908–1.395)	
Peritoneal metastasis	No	1	0.003
	Yes	1.429 (1.131–1.805)	
Previous adjuvant chemotherapy	No	1	< 0.001
	Yes	0.625 (0.493–0.794)	
Treatment line	1st-line	1	0.026
	2nd-line	1.284 (1.030–1.600)	
Age	< 70 years	1	0.241
	≥ 70 years	1.188 (0.891–1.585)	

Abbreviations: PFS, progression-free survival; CRC, colorectal cancer; GC, gastric cancer; HR, hazard ratio; CI, confidence interval; DA, defective allele; OS, overall survival

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**Table S5.** Treatment-related toxicity per treatment cycle

(A) CRC cohort

Variables		< 70 years (N = 6,057)	70–74 years (N = 779)	≥ 75 years (N = 291)	P-value
Neutropenia (%)	All grades	3,195 (52.7)	411 (52.7)	159 (54.6)	0.819
	Grade ≥ 2	2,018 (33.3)	268 (34.4)	113 (38.8)	0.136
	Grade ≥ 3	922 (15.2)	124 (15.9)	64 (22.0)	0.007
Febrile neutropenia (%)	Grade ≥ 3	22 (0.4)	5 (0.6)	2 (0.6)	0.385
Asthenia (%)	All grades	1,028 (17.0)	153 (19.6)	53 (18.2)	0.165
	Grade ≥ 2	128 (2.1)	22 (2.8)	16 (5.5)	0.001
	Grade ≥ 3	13 (0.2)	11 (1.4)	3 (1.0)	< 0.001
Mucositis (%)	All grades	565 (9.3)	95 (12.1)	31 (10.7)	0.033
	Grade ≥ 2	75 (1.2)	21 (2.7)	14 (4.8)	< 0.001
	Grade ≥ 3	4 (0.1)	2 (0.3)	2 (0.7)	0.010
Anorexia (%)	All grades	930 (15.4)	144 (18.5)	85 (29.2)	< 0.001
	Grade ≥ 2	135 (2.2)	39 (5.0)	29 (10.0)	< 0.001
	Grade ≥ 3	15 (0.2)	7 (0.9)	2 (0.7)	0.010
Nausea (%)	All grades	977 (16.1)	90 (11.6)	47 (16.2)	0.004
	Grade ≥ 2	149 (2.5)	26 (3.3)	9 (3.1)	0.297
	Grade ≥ 3	31 (0.5)	4 (0.5)	0 (0)	0.641
Vomiting (%)	All grades	265 (4.4)	10 (1.3)	16 (5.5)	< 0.001
	Grade ≥ 2	88 (1.5)	5 (0.6)	2 (0.6)	0.136
	Grade ≥ 3	26 (0.4)	3 (0.4)	0 (0)	0.765
Diarrhea (%)	All grades	575 (9.5)	84 (10.8)	28 (9.6)	0.517
	Grade ≥ 2	169 (2.8)	36 (4.6)	8 (2.7)	0.018
	Grade ≥ 3	51 (0.8)	8 (1.0)	3 (1.0)	0.683
Constipation (%)	All grades	429 (7.1)	40 (5.1)	28 (9.6)	0.026
	Grade ≥ 2	66 (1.1)	5 (0.6)	2 (0.7)	0.522
	Grade ≥ 3	6 (0.1)	0 (0)	0 (0)	1.000

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(B) GC cohort

Variables		< 70 years (N = 3,147)	70–74 years (N = 345)	≥ 75 years (N = 111)	P-value
Neutropenia (%)	All grades	1,592 (50.6)	176 (51.0)	54 (48.6)	0.909
	Grade ≥ 2	1,000 (31.8)	114 (33.0)	35 (31.5)	0.888
	Grade ≥ 3	545 (17.3)	70 (20.3)	16(14.4)	0.264
Febrile neutropenia (%)	Grade ≥ 3	21 (0.7)	4 (1.2)	1 (0.9)	0.576
Asthenia (%)	All grades	701 (22.3)	72 (20.9)	39 (35.1)	0.005
	Grade ≥ 2	153 (4.9)	23 (6.7)	13 (11.7)	0.003
	Grade ≥ 3	18 (0.6)	2 (0.6)	3 (2.7)	< 0.001
Mucositis (%)	All grades	484 (15.4)	48 (13.9)	13 (11.7)	0.458
	Grade ≥ 2	64 (2.0)	6 (1.7)	3 (2.7)	0.819
	Grade ≥ 3	7 (0.2)	0 (0)	1 (1.0)	0.250
Anorexia (%)	All grades	911 (28.9)	84 (24.3)	34 (30.6)	0.177
	Grade ≥ 2	306 (9.7)	33 (9.6)	9 (8.1)	0.850
	Grade ≥ 3	37 (1.2)	3 (0.9)	2 (1.8)	0.589
Nausea (%)	All grades	824 (26.2)	69 (20.0)	25 (22.5)	0.034
	Grade ≥ 2	245 (7.8)	13 (3.8)	2 (1.8)	0.002
	Grade ≥ 3	67 (2.1)	5 (1.4)	0 (0)	0.268
Vomiting (%)	All grades	334 (10.6)	22 (6.4)	7 (6.3)	0.019
	Grade ≥ 2	138 (4.4)	9 (2.6)	1 (1.0)	0.066
	Grade ≥ 3	31 (1.0)	3 (0.9)	0 (0)	0.913
Diarrhea (%)	All grades	343 (10.9)	34 (9.9)	9 (8.1)	0.558
	Grade ≥ 2	52 (1.7)	3 (0.9)	2 (1.8)	0.599
	Grade ≥ 3	14 (0.4)	0 (0)	0 (0)	< 0.001
Constipation (%)	All grades	157 (5.0)	18 (5.2)	7 (6.3)	0.815
	Grade ≥ 2	35 (1.1)	4 (1.2)	0 (0)	0.784
	Grade ≥ 3	5 (0.2)	0 (0)	0 (0)	1.000

Abbreviations: CRC, colorectal cancer; GC, gastric cancer