

**Supplementary Table S1.** Dose intensity of gemcitabine and cisplatin

Mapatumumab dose level in mg/kg	No of patients	Median no. of cycles (range)		No. of patients with delay (both gem and cis)	No. of administrations with delay (due to hematologic recovery)		Relative dose intensity (%) <sup>*</sup>	
		gem	Cis		Gem	cis	gem	cis
1	4	6 (4-6)	6 (3-6)	1	3 ( 1)	3 (1)	87.2	94.8
3	7	6 (3-6)	6 (3-6)	4	7 (3)	6 (3)	77.1	86.9
10	12	6 (1-6)	4.5 (1-6)	9	17 (15)	16 (14)	71.4	82.7
20	13	4 (1-6)	4 (1-6)	6	12 (10)	12 (10)	68.4	92.3
30	13	5 (1-6)	4 (1-6)	4	8 (7)	8 (7)	82.1	92.5
All	49	5 (1-6)	4 (1-6)	24	47 (36)	45 (35)	75.5	89.4

Abbreviations: gem, gemcitabine; cis, cisplatin.

\*Relative dose intensity= dose intensity in mg/m<sup>2</sup> / planned dose intensity in mg/m<sup>2</sup> x 100%

**Supplementary Table S2.** Gemcitabine, dFdU and unbound platinum AUCs in the absence (cycle 1) and presence (cycle 2) of mapatumumab

	Gemcitabine AUC <sub>0-∞</sub> (µg·hour/mL)		dFdU AUC <sub>last</sub> (µg·hour/mL)		Cisplatin-derived Unbound Platinum AUC <sub>0-6h</sub> (µg·hour/mL) <sup>a</sup>		Cisplatin-derived Unbound Platinum AUC <sub>last</sub> (µg·hour/mL) <sup>b</sup>	
	Cycle 1 Without mapatumumab	Cycle 2 With mapatumumab	Cycle 1 Without mapatumumab	Cycle 2 With mapatumumab	Cycle 1 Without mapatumumab	Cycle 2 With mapatumumab	Cycle 1 Without mapatumumab	Cycle 2 With mapatumumab
	1 mg/kg							
N	4	4	4	4	4	4	4	4
Mean	12.3	12.9	211	237	3.62	3.40	4.28	4.28
95% CI	9.80-14.8	9.78-16.1	179-242	182-292	2.82-4.42	1.97-4.84	2.81-5.76	2.01-6.55
3 mg/kg								
N	7	7	7	7	7	7	7	7
Mean	11.4	11.8	206	199	3.28	3.02	3.84	3.54
95% CI	9.19-13.6	10.4-13.3	164-247	175-223	2.86-3.69	2.67-3.38	2.94-4.73	3.02-4.07
10 mg/kg								
N	12	9	12	9	11	8	11	8
Mean	11.7	10.8	199	207	3.67	3.55	4.36	4.83
95% CI	10.4-13.1	8.2-13.3	177-220	189-225	3.23-4.11	2.97-4.13	3.61-5.11	3.89-5.77
20 mg/kg								
N	13	9	13	9	13	9	13	9
Mean	11.4	10.7	194	194	3.71	3.69	4.59	4.76
95% CI	9.91-13.0	9.4-12.0	169-220	172-217	3.35-4.07	3.27-4.12	3.98-5.20	4.05-5.46
30 mg/kg								
N	13	11	13	11	13	11	13	11
Mean	11.3	11.3	187	187	3.52	3.54	4.25	4.42
95% CI	9.82-12.7	10.2-12.4	168-206	170-205	3.34-3.70	3.21-3.87	3.89-4.61	3.85-4.99
In Cycle 1, gemcitabine was administered immediately prior to cisplatin and 24 hours prior to the 1st mapatumumab dose. In the 2nd cycle (21 days later), gemcitabine, cisplatin, and mapatumumab were administered on the same day in immediate succession.								

**Supplementary Table S3.** Staining intensity in number of patients (n=35) in relation to tumor response

Staining intensity	Tumor response according to RECIST <sup>11</sup>			
	PR	SD	PD	NA
No	0	0	0	0
Low	5	6	0	1
Moderate	1	4	0	3
Strong	3	7	4	1

Abbreviations: RECIST, Response Evaluation Criteria in Solid Tumors; PR, partial response; SD, stable disease; PD, progressive disease; NA, not available