A new concept of chemotherapy for major solid tumors- A study of low dose, divided MTD

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We attempted a new regimen with frequent administration of low dose, divided MTD (maximum tolerated dose) of CPT-11 to reduce its toxicities without any impairment of its efficacy. Twenty-five mg/m^2 of CPT-11, which was determined by dividing the MTD dose per month by 12, was administered on days 1, 2 and 3 of every week (Fig 1), to 21 consecutive patients of metastatic colon cancers (n=12) and metastatic gastric cancers (n=9). The total delivered dose of CPT-11 per patient in this study was more than 1,000 mg in 17 (80.1%) of 21 cases. Grade-3 marrow depression occurred in 3 (14.3%) patients, but rapidly improved during the washout period. Nausea, vomiting, alopecia, and diarrhea were observed in some cases, but were all categorized as grade 2 or milder(table 2). The antitumor effect was evaluated in 18 patients who had measurable lesions and received CPT-11 according to our regimen for at least 3 weeks. Of these 18 patients, 10, 7 and 1 patients were found to have PR (partial response), SD (stable disease) or PD (progressive disease), respectively, showing a 55.6% efficacy rate [colon 6/10 (60.0%) and stomach 4/8 (50.0%)] (table 1). In addition, time to progression (TTP) was greater than 90 days in 12 (75.0%) of our 18 patients. From these results we suggest that our low-dose, divided MTD of CPT-11 regimen is a promising method with potential for the reduction of toxicities as well as for strengthening the antitumor effect, deserving large-scaled comparative clinical studies to verify such potential.

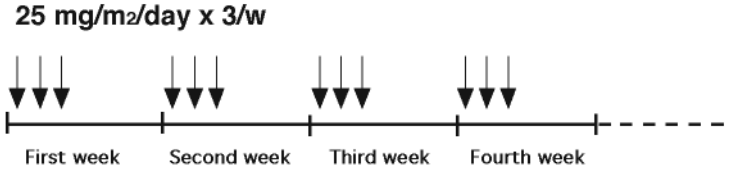

Fig 1. Method of MTD divided low dose CPT-11.

Table 1. Antitumor effects

	Total	Colon	Stomach
CR	0	0	0
PR	10	6	4
NC	7	4	3
PD	1	0	1

Table 2. Grading of toxicities

	Grade			
	0	1	2	3
Leukopenia	6	8	4	3
Diarrhea	8	7	6	0
Nausea/Vomiting	10	6	5	0
Alopecia	11	5	5	0