A pilot study of individualized maximum repeatable dose (iMRD), a new dose finding system, of weekly gemcitabine for patients with metastatic pancreas cancer

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We developed and established a new dose-finding system, the individualized maximum repeatable dose (iMRD), suitable to induce prolonged TTP rather than tumor shrinkage.

We applied this system in weekly gemcitabine therapy for 18 metastatic pancreas cancer patients. We determined the iMRD at the 5th week, after weekly dose adjustments. We started at 500 mg/m^2 (1/2 MTD (maximum tolerated dose)) of gemcitabine and repeated the treatment with an increase or a decrease of 100 mg/m^2 each week, if toxicity was 0 or more than grade 1, respectively (Figure 1).

The iMRD of weekly gemcitabine was 300 mg/m^2 in 2 patients, 400 mg/m^2 in 3 patients, 500 mg/m^2 in 5 patients, 600 mg/m^2 in 6 patients, and 700 mg/m^2 in 2 patients, demonstrating significant differences among individual patients. Grade 3 marrow depression occurred in only 1 patient (5.6%). Of these 18 patients, 3 (16.7%), 13 (72.2%) and 2 (11.1%) patients showed PR, SD and PD, respectively. The median of TTP and survival was 4.5 months and 9.5 months, respectively. There were no significant differences in 1 year survival time and more than 50 % reduction rate of serum CA19-9, a tumor marker for pancreatic cancer, between patients with lower (500 mg/m^2 or less) and higher (600 mg/m^2 or more) iMRD.

These results suggest that iMRD is a simple method to determine an individual's tailored dose for chemotherapy and could be the optimal dose for patients with non-curable cancers such as metastatic pancreas cancer.

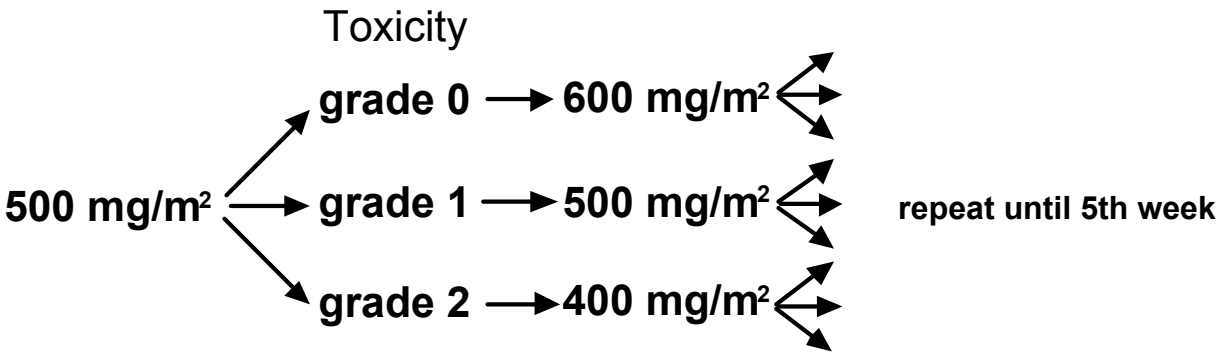

Figure 1. The method of determination of iMRD