

Safety and efficacy of platinum-based neoadjuvant chemotherapy with 800 mg/m² vs. 1000 mg/m² of gemcitabine in muscle-invasive bladder cancer

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Background:

• Platinum-based neoadjuvant chemotherapy (NAC) followed by radical cystectomy (RC) is the gold standard treatment for muscle-invasive bladder cancer (MIBC). Although gemcitabine plus platinum-based drugs have similar efficacy and less toxicity than MVAC, the optimal dose of gemcitabine for safety and efficacy remains unclear.

Methods:

- This multi-institutional retrospective study included 517 patients with MIBC who received 2–4 cycles of platinum-based NAC with gemcitabine followed by RC.
- Patients were divided into two groups: patients who received gemcitabine at a dose of 800 mg/m² (800 mg/m² group) and 1000 mg/m² (1000 mg/m² group). The rates of myelosuppressive hematological adverse events (AEs) were compared between the two groups.
- Multivariable Cox-proportional hazards regression analyses were performed to evaluate the impact of gemcitabine dose on cancer-specific survival (CSS) and overall survival (OS).

Results:

- The median age and follow-up period were 70 years and 55 months, respectively.
- Of the 517 patients, 348 (67%) and 169 (33%) received gemcitabine at a dose of 800 mg/m² and 1000 mg/m², respectively.
- The rates of grade ≥3 neutropenia and febrile neutropenia were not significantly different between the two groups (Fig. 1 and 2, respectively), whereas the rate of grade ≥3 thrombopenia in the 800 mg/m² group was significantly lower than that in the 1000 mg/m² group (Fig. 3).
- CSS and OS in the 800 mg/m² group were significantly shorter than those in the 1000 mg/m² group (Fig. 4 and 5, respectively).
- After adjustment for confounding variables, 800 mg/m² of gemcitabine was not significantly associated with shorter CSS and OS (Table).

Fig. 1

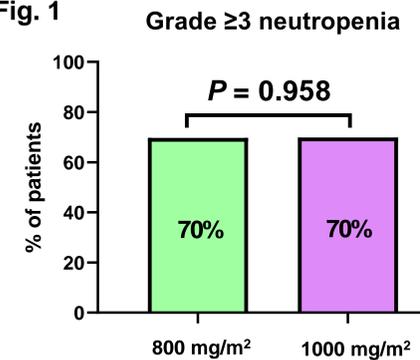


Fig. 2

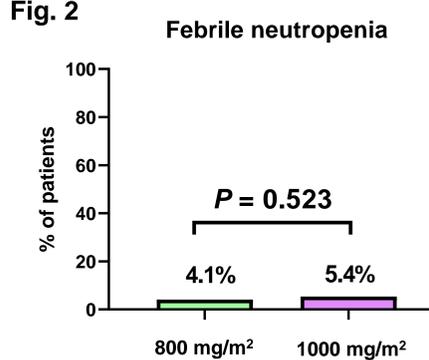


Fig. 3

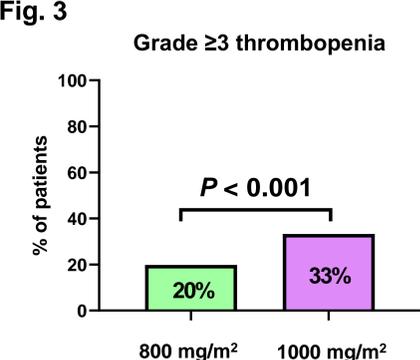


Fig. 4

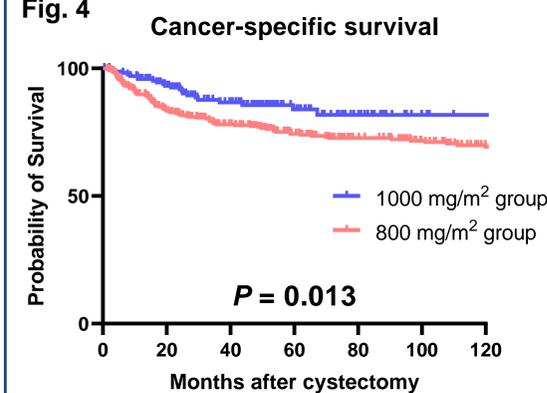
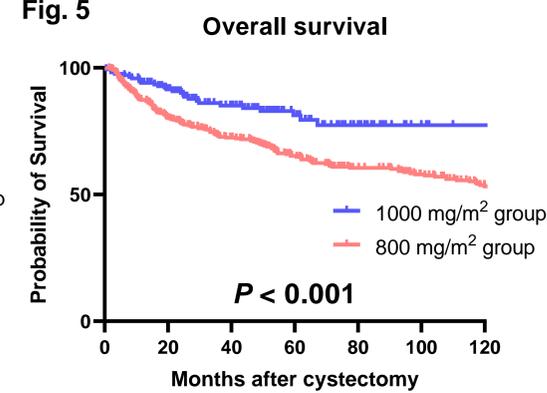


Fig. 5



Multivariable analysis for CSS

Factor	P value	HR	95% CI
Age	0.683	1.006	0.979–1.033
Sex	0.738	0.919	0.561–1.506
Performance status	0.569	1.154	0.705–1.889
Body mass index	0.853	1.005	0.950–1.065
Cisplatin-based regimens	0.215	0.665	0.348–1.268
Tumor grade	0.012	2.040	1.170–3.557
Pathological T stage	0.024	1.805	1.079–3.017
Pathological N stage	<0.001	2.742	1.663–4.522
Surgical margin	0.086	1.870	0.916–3.816
Urinary diversion	0.085	0.665	0.418–1.058
Gemcitabine	0.471	1.298	0.639–2.636

Multivariable analysis for OS

Factor	P value	HR	95% CI
Age	<0.001	1.038	1.015–1.060
Sex	0.341	1.214	0.814–1.809
Performance status	0.858	1.033	0.720–1.484
Body mass index	0.052	0.959	0.919–1.000
Cisplatin-based regimens	0.042	0.590	0.355–0.982
Tumor grade	0.037	1.492	1.025–2.172
Pathological T stage	0.058	1.499	0.986–2.279
Pathological N stage	<0.001	2.159	1.412–3.299
Surgical margin	0.207	1.529	0.790–2.959
Urinary diversion	0.037	1.492	1.025–0.866
Gemcitabine	0.308	1.351	0.758–2.410

Conclusion:

- The 800 mg/m² of gemcitabine might alleviate grade ≥3 thrombopenia without sacrificing oncological outcomes.