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Dose-dense chemotherapy in metastatic gastric cancer with a modified docetaxel-cisplatin-5-fluorouracil regimen

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ABSTRACT

Aims and background. Previous studies have reported that in early breast cancer, lymphomas and advanced bladder cancer, dose-dense chemotherapy may be more effective than conventional treatments. In metastatic gastric cancer, chemotherapy with docetaxel, cisplatin and 5-fluorouracil (TCF) q3w is very active, and, even though there is no international consensus on the subject, it is the regimen of choice of many European centers as first-line chemotherapy in this subset of patients. Based on these studies, we tested for the first time the feasibility and activity of an intensified dose-dense TCF regimen (q2w) modifying the 5-fluorouracil infusion with l-folinic acid/5-fluorouracil according to the "De Gramont regimen".

Methods and study design. Patients with histologically confirmed measurable metastatic gastric cancer, ECOG performance status ≤1, and not previously treated for advanced disease received docetaxel, 85 mg/m^2 (75 mg/m^2 after the first 6 patients, 70 mg/m^2 after the 19th patient) on day 1, cisplatin, 75 mg/m^2 on day 1 (60 mg/m^2 after the 19th patient), l-folinic acid, 100 mg/m^2 on days 1 and 2, followed by 5-fluorouracil, 400 mg/m^2 bolus on days 1 and 2 and then 600 mg/m^2 as a 22-h continuous infusion on days 1 and 2, every 14 days, plus pegfilgrastim, 6 mg on day 3. Patients aged ≥65 years received the same schedule with a dose reduction of 30%.

Results. Thirty-two consecutive patients were enrolled (63% male, 37% female); median age, 64 years (range, 40-81). A median of 4 cycles (range, 1-7) per patient was administered. Eleven of 32 patients (34%) required a dose reduction, mostly for hematological grade III-IV toxicity and severe asthenia. Twelve patients (38%) completed the first 4 cycles of therapy within 7 weeks, thereby finishing without delay the initially planned dose-density schedule. Twenty-eight patients were evaluated for response (1 early suspension after the first cycle because of toxicity, 3 deaths before response evaluation due to progression of disease). There were 3 complete responses (9%), 15 partial responses (47%), 7 stable disease (22%) and 3 progression of disease (9%), for an overall response rate, by intention to treat, of 56% (95% CI, 39-73). The most frequent grade 3-4 toxicities were: neutropenia (53%), thrombocytopenia (34%), anemia (16%) febrile neutropenia (22%), asthenia (38%) and diarrhea (19%). Median time to progression was 9.1 months (95% CI, 6.0-12.2); median overall survival was 10.1 months (95% CI, 8.8-12.2).

Conclusions. A dose-dense TCF regimen in metastatic gastric cancer is feasible, with activity comparable to previous results achieved with epirubicin-based chemotherapy and TCF q3wk in terms of overall survival and time to progression, and deserves to be further tested in randomized phase III studies. **Free full text available at www.tumorionline.it**

Key words: dose-dense chemotherapy, metastatic gastric cancer, TCF regimen.

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