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/m² (75 mg/m² after the first 6 patients, 70 mg/m² after the 19th patient) on day 1, cisplatin, 75 mg/m² on day 1 (60 mg/m² after the 19th patient), l-folinic acid, 100 mg/m² on days 1 and 2, followed by 5-fluorouracil, 400 mg/m² bolus on days 1 and 2 and then 600 mg/m² 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 q3w 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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