Incidence of febrile neutropenia during adjuvant chemotherapy for breast cancer: a prospective study

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1. INTRODUCTION

We read with great interest the recent article by Madernas et al. describing the clinical experience of four regional cancer centres in Ontario with rates of febrile neutropenia (FN) stemming from adjuvant FEC-D (5-fluorouracil–epirubicin–cyclophosphamide, then docetaxel) for early-stage breast cancer 1. Those authors retrospectively reviewed the electronic and paper records of 671 patients treated at the Ottawa Hospital Cancer Centre, the Cancer Centre of Eastern Ontario, the London Regional Cancer Program, and the Northeastern Ontario Regional Cancer Centre, who had completed adjuvant FEC-D chemotherapy between June 1, 2006, and December 31, 2008. They observed an overall FN event rate of 22.7% (152 in 671), which is considerably higher than that reported in the pivotal PACS 01 trial (11.2%) that led to the widespread adoption of adjuvant FEC-D for node-positive early-stage disease 2. Similar observations have been reported for TC (docetaxel–cyclophosphamide) chemotherapy, another recently introduced adjuvant regimen for early-stage breast cancer 3–5.

Clinical practice guidelines from the American Society of Clinical Oncology and the European Society for Medical Oncology both recommend that primary prophylaxis with granulocyte colony–stimulating factors (G-CSF) be considered for treatment regimens with the probability of a FN event rate of 20% or higher 6,7. With clinical experience suggesting that FN rates during FEC-D treatment are more common than reported in PACS 01, 35% of patients in the study by Madernas et al. did receive primary prophylaxis with G-CSF, leading to a statistically significant reduction in the observed FN rates for those who received primary prophylaxis compared with those who did not (6.4% vs. 31.4%; relative risk: 0.20; p < 0.001).

2. METHODS

Because of similar concerns, and in the context of a paucity of prospectively collected data about FN event rates among patients treated with either FEC-D or TC, we conducted a prospective, real-time assessment of a consecutive cohort of patients receiving standard adjuvant FEC-D, TC, or FEC 100 for early-stage breast cancer and beginning therapy between April 12 and October 20, 2010. Real-time prospective review of electronic records was conducted continuously, encompassing the entire duration of each patient’s treatment, with data abstracted at each treatment cycle for the entire cohort.

The Nova Scotia Cancer Centre, based in Halifax, is the largest tertiary cancer centre in Atlantic Canada, with a catchment area of roughly 700,000. Because of an excellent network of peripheral hospitals, a proportion of the patients seen in Halifax for their initial consultation receive their systemic therapy elsewhere, under the supervision of the consulting medical oncologist. The real-time electronic record review captured event rates regardless of where the patients actually received their systemic therapy.

3. RESULTS

All 79 patients who started adjuvant chemotherapy between the specified dates were included in the data capture process. Table 1 presents patient characteristics. Table II presents regimen-specific FN event rates, the rates of primary and secondary G-CSF prophylaxis, and the event rates after each type of prophylaxis. Figure 1 presents the distribution of the timing of FN events for FEC-D and TC. Of patients experiencing a FN event, 5 did not receive secondary prophylaxis: 3 because the FN episode occurred after the last planned cycle of chemotherapy, and 2, because of early treatment discontinuation. No treatment-related deaths occurred.

Previous work has suggested that certain patient subsets may be at higher risk of FN events and that primary prophylaxis might be considered at a lower regimen-specific FN probability (for example, 10%–20%) if certain demographic or clinical risk
factors are present. We assessed event rates as a function of two of the factors most commonly reported to increase risk; age and the presence of comorbidities. We observed no obvious differences in event rates according to age (<50 years: 9 in 27 (33.3%); 50–60 years: 7 in 31 (22.6%); >60 years: 7 in 21 (33.3%)) or number of comorbidities [0: 12 in 37 (32.4%); 1–2: 10 in 39 (25.6%); >2: 1 in 3 (33.3%)].

4. DISCUSSION

In our prospectively-assessed cohort receiving standard adjuvant chemotherapy for breast cancer, the event exceeded American Society of Clinical Oncology and European Society for Medical Oncology thresholds for consideration of primary G-CSF prophylaxis and was greater than the incidence reported in the relevant clinical trials (TC: 4% for <65 years of age and 8% for ≥65 years of age; FEC-D: 11.2%).

The event rates were similar across age groups and were not observed to vary by presence of 1 or more comorbidities, suggesting that elucidation of risk factors may not select patients preferentially at risk for because of adjuvant TC or FEC-D. In the context of data reported by Madernas et al. and others, our data suggest that event rates during adjuvant FEC-D and TC in clinical practice are substantially higher than those reported in the pivotal clinical trials and commonly exceed clinical guideline thresholds for consideration of primary prophylaxis with G-CSF for patients choosing to receive those adjuvant systemic regimens for moderate- to high-risk early-stage breast cancer.

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6. CONFLICT OF INTEREST DISCLOSURES

The authors have no relevant conflicts of interest to declare.
7. REFERENCES


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