

Real-world adjuvant TAC or FEC-D for HER2-negative node-positive breast cancer in women less than 50 years of age

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ABSTRACT

Purpose We compared the efficacy, toxicity, and use of granulocyte colony-stimulating factor (G-CSF) with TAC (docetaxel–doxorubicin–cyclophosphamide) and FEC-D (5-fluorouracil–epirubicin–cyclophosphamide followed by docetaxel) in women less than 50 years of age.

Methods The study included all women more than 18 years but less than 50 years of age with HER2-negative, node-positive, stage II or III breast cancer diagnosed in Alberta between 2008 and 2012 who received TAC ($n = 198$) or FEC-D ($n = 274$).

Results The patient groups were well-balanced, except that radiotherapy use was higher in the TAC group (91.9% vs. 79.9%, $p < 0.001$). At a median follow-up of 49.6 months, disease-free survival was 91.4% for TAC and 92.0% for FEC-D ($p = 0.76$). Overall survival (OS) was 96% with TAC and 95.3% with FEC-D ($p = 0.86$). The incidences of grades 3 and 4 toxicities were similar in the two groups (all $p > 0.05$). Overall, febrile neutropenia (FN) was reported in 11.6% of TAC patients and 15.7% of FEC-D patients ($p = 0.26$). However, use of G-CSF was higher in the TAC group than in the FEC-D group (96.4% vs. 71.5%, $p < 0.001$). Hospitalization for FN was required in 10.5% of TAC patients and 13.0% of FEC-D patients ($p = 0.41$). In G-CSF-supported and -unsupported patients receiving TAC, FN occurred at rates of 11.1% and 33.3% respectively ($p = 0.08$); in patients receiving the FEC portion of FEC-D, those proportions were 2.9% and 8.1% respectively ($p = 0.24$); and in patients receiving docetaxel after FEC, the proportions were 4.1% and 17.6% respectively ($p < 0.001$).

Conclusions In women less than 50 years of age receiving adjuvant TAC or FEC-D, we observed no differences in efficacy or other nonhematologic toxicities. Based on the timing and rates of FN, use of prophylactic G-CSF should be routine for the docetaxel-containing portion of treatment; however, prophylactic G-CSF could potentially be avoided during the FEC portion of FEC-D treatment.

Key Words Efficacy, toxicity, G-CSF, granulocyte colony-stimulating factor, febrile neutropenia, systemic therapy, hospitalization

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INTRODUCTION

Breast cancer remains the most commonly diagnosed cancer among women in North America, with an estimated 231,050 new diagnoses and 40,290 deaths having been expected in the United States in 2015¹. Women diagnosed with lymph node-positive disease will likely receive a strong clinical recommendation for adjuvant chemotherapy^{2,3}.

The introduction of CMF (cyclophosphamide–methotrexate–5-fluorouracil) chemotherapy⁴, and eventually anthracycline-containing⁵ and anthracycline–taxane^{6,7} regimens sequentially

improved disease-free (DFS) and overall (OS) survival for breast cancer patients^{6–9}. Strong evidence supports the use of concurrent^{6,7} or sequential^{8,9} anthracycline–taxane regimens for the treatment of node-positive breast cancer.

The phase III Breast Cancer International Research Group (BCIRG) 001 trial demonstrated the superiority of 6 cycles of adjuvant TAC (docetaxel–doxorubicin–cyclophosphamide) over FAC (5-fluorouracil–doxorubicin–cyclophosphamide), with an approximately 7% improvement in 10-year DFS and OS ($p = 0.004$ and $p = 0.002$ respectively)⁶. Similarly, the PACS-01 trial by the French Federation of Cancer Centers Sarcoma

Group demonstrated that, compared with FEC (5-fluorouracil–doxorubicin–cyclophosphamide every 3 weeks for 6 cycles), FEC-D (FEC every 3 weeks for 3 cycles, followed by docetaxel every 3 weeks for 3 cycles) improves the 5-year DFS by approximately 5.2% ($p = 0.011$) and the 5-year OS by approximately 4% ($p = 0.014$)⁸. However, subgroup analysis suggested that the benefit of FEC-D is confined to women 50 years of age and older.

No randomized controlled trials have directly compared TAC with FEC-D; adjuvant TAC and FEC-D are therefore both viable anthracycline–taxane chemotherapy options^{2,3}. A study of medical insurance claims patients in the United States found that, as of 2007, adjuvant TAC chemotherapy was used in approximately 20% of women less than 65 years of age and in nearly 10% of women more than 65 years of age¹⁰; however, FEC-D use was not reported. In contrast, a population-based cohort of Canadian women treated between 2003 and 2009 reported that 55.6% received FEC-D; TAC use was not reported, however¹¹.

The effectiveness of several anthracycline–taxane regimens has been demonstrated, but few direct comparisons have been made. Acute and late toxicities should, therefore, affect treatment decision-making. The BCIRG 001 study⁶ and retrospective analyses¹⁰ suggest that TAC is associated with a significant risk of febrile neutropenia (particularly in the absence of primary G-CSF support) and hospitalization. And although PACS-01 reported a relatively low incidence of febrile neutropenia⁸, retrospective studies have documented much higher rates of febrile neutropenia and hospitalization^{11,12}.

In Alberta, TAC and FEC-D were the most commonly prescribed adjuvant chemotherapy regimens for women less than 50 years of age with lymph node–positive, HER2-negative breast cancer. Here, we describe the effectiveness, toxicity, and G-CSF use in TAC and FEC-D patients treated in a single universally funded cancer care system.

METHODS

Data Source and Study Cohort

All patients were identified through the Alberta Cancer Registry, all were female, all were at least 18 but less than 50 years of age, and all had been diagnosed with stage II or III HER2-negative, node-positive breast cancer in Alberta. In total, 198 patients received TAC, and 274 received FEC-D. Figure 1 presents a complete accounting of the inclusion and exclusion criteria. All patients received publicly funded health care through a single provider. If used, G-CSF support was—almost exclusively—third-party funded.

Study Variables

We manually collected or confirmed patient demographics, tumour characteristics, treatment information, all grades 3 and 4 adverse events, hospitalizations required during or after treatment, pre- and post-chemotherapy treatments, relapse, and death. Patients were grouped by the type of adjuvant chemotherapy received and had to have received at least 1 cycle of chemotherapy to be included in the study.

Data Analysis

Proximity matching analysis was performed to detect whether comorbidities at diagnosis (1, 2, or >3), tobacco

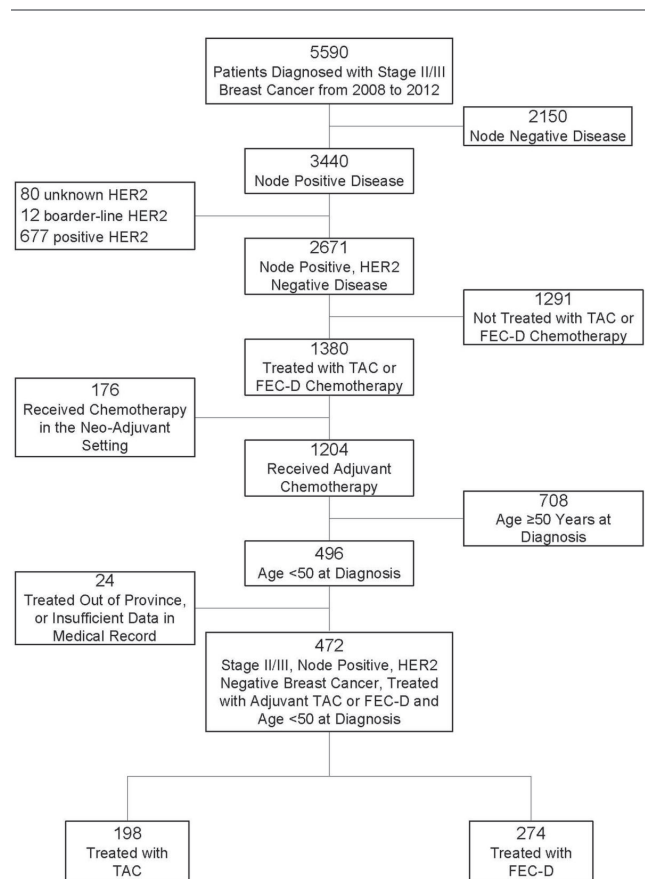


FIGURE 1 Patient selection flow chart. HER2 = human epidermal growth factor receptor 2; TAC = docetaxel–doxorubicin–cyclophosphamide; FEC-D = fluorouracil–epirubicin–cyclophosphamide, followed by docetaxel.

use, alcohol use, or illegal drug use had influenced whether the patient was given TAC or FEC-D.

Univariate analyses, with either the chi-square or Fisher exact test (for categorical variables) and the t-test or Mann–Whitney U-test (for continuous variables), were used to compare patient characteristics, general treatment characteristics, treatment support with G-CSF, and treatment complications.

The DFS and OS durations were calculated as the time from surgery to the time of relapse or death respectively; censoring was applied at the last entry in the patient's medical records. The DFS and OS rates were calculated by the Kaplan–Meier method. Treatment arms were compared using a log-rank test stratified for age and receipt of radiotherapy treatment and endocrine therapy. A supportive multivariate analysis using the Cox regression model was used, with adjustment for age, hormone receptor status, grade, and receipt of radiotherapy and endocrine therapy.

Time-to-event calculations were performed using the date of surgery as the starting point.

Proximity matching analysis was performed using the IBM SPSS Statistics software application (version 22: IBM, Armonk, NY, U.S.A.). All other statistical analyses were performed using the SigmaPlot software application (version 10: Systat Software, San Jose, CA, U.S.A.). For all

statistical analyses, a *p* value of 0.05 or less was considered significant.

Ethics were institutionally approved under the Alberta Research Ethics Community Consensus Initiative¹³.

RESULTS

Patient Characteristics

The 472 identified patients treated with FEC-D (*n* = 274) or TAC (*n* = 198) had a median follow-up of 49.6 months. Patient characteristics at diagnosis were balanced between the chemotherapy groups, with no significant differences in age, stage of disease, tumour grade, hormone receptor status, type of surgery performed, or comorbidities at baseline (Table I).

Proximity matching analysis did not indicate any relation between the number of comorbidities at diagnosis (1, 2, or >3), use of tobacco, use of alcohol, or use of illegal drugs and the prescription of TAC or FEC-D (all *p* > 0.05). A trend toward increased FEC-D use in the 14 patients with more than 3 comorbidities at diagnosis was observed, however (*p* = 0.08).

Treatment Characteristics

Treatment characteristics were balanced between the patient groups. We observed no significant differences in the time from surgery to the first cycle of chemotherapy, the frequency of chemotherapy dose reduction, the mean reduction in chemotherapy dose, or the number of chemotherapy cycles delivered (all *p* > 0.05). If treatment was halted before completion of the 6th cycle, the mean number of cycles delivered was also similar (3.4 for FEC-D and 3.6 for TAC, *p* > 0.05). If dose reduction was required, most patients in the TAC group (79.1%) and the FEC-D group (93.0%) had their dose reduced by 10%–25%. Compared with FEC-D patients, TAC patients were more likely to also receive radiotherapy (91.9% vs. 79.9%, *p* < 0.001, Table I). During the study period, the centre preferentially prescribing TAC was also more likely to offer postmastectomy radiation for pN1 disease.

Efficacy

We observed no significant differences in efficacy outcomes between the TAC and FEC-D groups. Overall, DFS at 1, 2, and 5 years was 98.4%, 95.4%, and 91.8% respectively in the TAC group and 98.5%, 96.7%, and 92.3% in the FEC-D group. Overall, OS at 1, 2, and 5 years was 99.5%, 98.5%, and 97.5% respectively in the TAC group, and 98.9%, 96.3%, and 95.6% in the FEC-D group.

At a median follow-up of 49.6 months, relapse rates were similar for the TAC (8.6%) and FEC-D (8.0%) patients [hazard ratio (HR): 1.11; 95% confidence interval (CI): 0.59 to 2.07; *p* = 0.76], with most relapses including disease at a distant site. Overall, 4.7% of the FEC-D patients and 4.0% of TAC patients died (HR: 0.923; 95% CI: 0.382 to 2.231; *p* = 0.86), with 1 treatment-associated death in each group (Table II). No significant differences in DFS (*p* = 0.99, Figure 2) or OS (*p* = 0.76, Figure 3) were detected after Kaplan–Meier modelling. In multivariate Cox regression analysis, a tumour grade of 3 (HR: 4.46; 95% CI: 1.01 to 19.66; *p* = 0.049) and more than 3 positive lymph nodes (HR: 3.40; 95% CI: 1.79 to

TABLE I Baseline patient and disease characteristics

Characteristic	Chemotherapy regimen			
	FEC-D		TAC	
Patients (<i>n</i>)	274		198	
Age at diagnosis (years)				
Median	45		45	
Range	24–49		23–49	
Surgery type [<i>n</i> (%)]				
Breast conservation	105	38.3	70	35.4
Mastectomy	169	61.7	128	64.6
Tumour size [<i>n</i> (%)]				
<2 cm	102	37.2	78	39.4
2–5 cm	145	52.9	104	52.5
>5 cm	27	9.9	16	8.1
Grade [<i>n</i> (%)]				
I	27	9.9	22	11.1
II	98	36.0	78	39.4
III	145	53.3	98	49.5
Unknown/not gradable	2		0	
Positive nodes [<i>n</i> (%)]				
1–3	197	72.2	148	75.5
>3	76	27.8	48	24.5
Missing	1		1	
Hormone receptors [<i>n</i> (%)]				
Positive (ER, PR, or both)	241	88.0	163	82.3
Negative (ER and PR)	33	12.0	35	17.7
ER				
Positive	240	87.6	162	81.8
Negative	34	12.4	36	18.2
PR				
Positive	227	82.8	153	77.3
Negative	47	17.2	45	22.7
Radiotherapy [<i>n</i> (%)] ^a				
Yes	218	79.9	181	91.9
No	55	20.1	16	8.1
Unknown	1	0.4	1	0.5

^a Differences between treatment groups were nonsignificant (all *p* > 0.05), except for radiotherapy (*p* < 0.001).

FEC-D = fluorouracil–epirubicin–cyclophosphamide, followed by docetaxel; TAC = docetaxel–doxorubicin–cyclophosphamide; ER = estrogen receptor; PR = progesterone receptor.

6.43; *p* < 0.001) were associated with a significantly elevated risk of relapse; chemotherapy type, histologic tumour size, hormone receptor status, endocrine therapy status, and radiotherapy status did not significantly affect DFS rates (Table III).

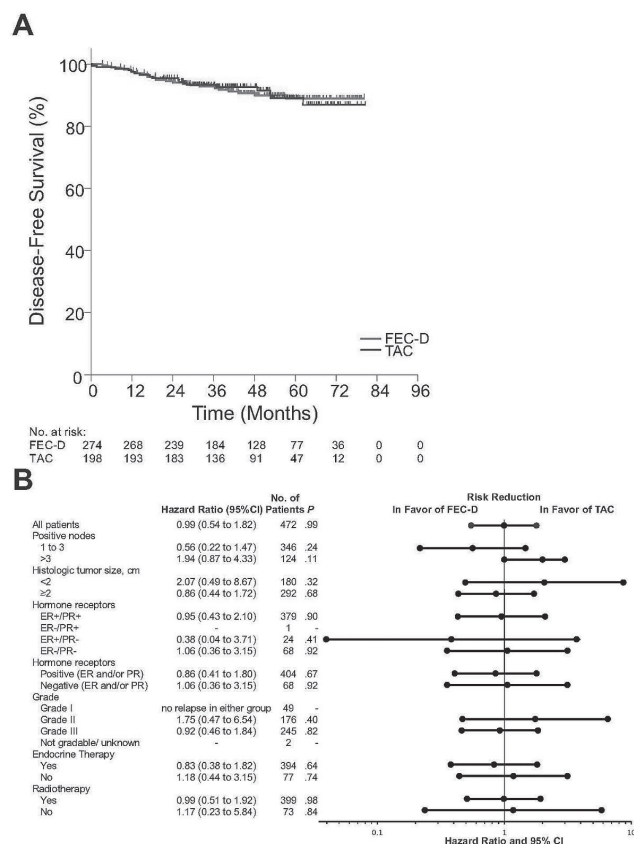
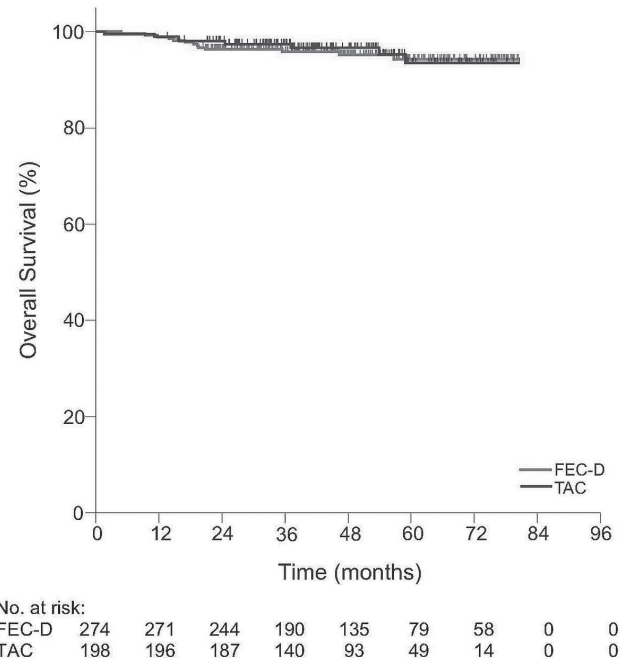
Subgroup analyses did not identify any significant tumour characteristics that would support one chemotherapy regimen over the other in terms of efficacy, and neither regimen was superior depending on whether the patient received or did not receive endocrine therapy or adjuvant radiotherapy. Numerically, the TAC regimen

TABLE II Analysis of events

Event	FEC-D (n=274)		TAC (n=198)		HR	95% CI	p Value ^a
	(n)	(%)	(n)	(%)			
First event ^b	25	9.1	19	9.6	1.072	0.58 to 1.97	0.82
Relapse of breast cancer	22	8.0	17	8.6	1.105	0.59 to 2.07	0.76
Local only	6	2.2	2	1.0			
Distant ^c	15	5.5	13	6.6			
Unknown	1	0.4	0	0.0			
Contralateral breast cancer	1	0.4	1	0.5			
Death	2	0.7	1	0.5			
Second cancer	1	0.4	1	0.5			
Any death	13	4.7	8	4.0	0.923	0.38 to 2.23	0.86
From breast cancer	11	4.0	7	3.5			
From a second cancer	1	0.4	0	0.0			
Because of toxicity	1	0.4	1	0.5			

^a Adjusted for nodal involvement.^b Defined using the disease-free survival criteria (that is, local relapse, distant relapse, contralateral breast cancer, and death from any cause).^c With or without local or regional relapse.

FEC-D = fluorouracil–epirubicin–cyclophosphamide, followed by docetaxel; TAC = docetaxel–doxorubicin–cyclophosphamide; HR = hazard ratio; CI = confidence interval.

**FIGURE 2** Disease-free survival. (A) Kaplan–Meier estimates. (B) Subgroup analysis, with hazard ratios, 95% confidence intervals (CIs), and forest plot analysis. FEC-D = fluorouracil–epirubicin–cyclophosphamide, followed by docetaxel; TAC = docetaxel–doxorubicin–cyclophosphamide; ER = estrogen receptor; PR = progesterone receptor.**FIGURE 3** Kaplan–Meier estimates of overall survival. FEC-D = fluorouracil–epirubicin–cyclophosphamide, followed by docetaxel; TAC = docetaxel–doxorubicin–cyclophosphamide.

appeared to perform better in patients with more than 3 positive nodes; however, that trend did not reach statistical significance ($p = 0.11$).

Adverse Events and G-CSF Use

No significant differences in nonhematologic grades 3 and 4 complications were noted between the TAC and FEC-D

TABLE III Cox regression analysis of disease-free survival

Factor	HR	95% CI	p Value
Regimen			
FEC-D		Reference	
TAC	1.14	0.60 to 2.15	0.69
Positive nodes			
1–3		Reference	
>3	3.40	1.79 to 6.43	<0.001
Tumour size			
<2		Reference	
≥2	2.01	0.95 to 4.26	0.07
Grade			
1		Reference	
2	2.90	0.56 to 14.88	0.21
3	4.46	1.01 to 19.66	0.049
Hormone receptor status			
ER+, PR+		Reference	
ER–, PR+	NA	NA	NA
ER+, PR–	3.9	0.922 to 16.56	0.06
ER–, PR–	1.96	0.571 to 6.71	0.29
Endocrine therapy			
Yes		Reference	
No	4.84	1.53 to 15.30	0.007
Radiotherapy			
Yes		Reference	
No	1.47	0.63 to 3.43	0.38

HR = hazard ratio; CI = confidence interval; FEC-D = fluorouracil–epirubicin–cyclophosphamide, followed by docetaxel; TAC = docetaxel–doxorubicin–cyclophosphamide; ER = estrogen receptor; PR = progesterone receptor.

groups. The rate of grades 3 and 4 non-febrile infections, thrombotic events, and hypersensitivities was also similar between the groups (Table iv).

The rate of febrile neutropenia was 15.7% in FEC-D patients and 11.6% in TAC patients ($p = 0.26$). In total, 13.0% of FEC-D patients and 10.5% of TAC patients required hospitalization for febrile neutropenia. Of those who experienced febrile neutropenia, most in the TAC group (52.2%) and the FEC-D group (43.6%) had an episode during cycle 1; the second most frequent cycle for febrile neutropenia was cycle 4 in FEC-D (25.6%) and cycle 2 in TAC (21.7%).

Use of G-CSF was dramatically different between groups, with 71.5% of FEC-D patients and 96.4% of TAC patients receiving G-CSF support for at least 1 cycle ($p < 0.001$). The mean number of cycles supported with G-CSF was 2.7 for FEC-D patients and 5.7 for TAC patients.

In total, 22.4% of FEC cycles and 71.3% of docetaxel cycles (in the FEC-D regimen) were delivered with prophylactic G-CSF support; 96.3% of TAC cycles were delivered with such support. Of the patients receiving prophylactic G-CSF during the FEC portion of the FEC-D regimen, 2.9% experienced an episode of febrile neutropenia; 8.1% of the

TABLE IV Grades 3 and 4 adverse events experienced per patient

Event type	Patient group (%)		<i>p</i> Value
	FEC-D (<i>n</i> =274)	TAC (<i>n</i> =198)	
Hematologic			
Febrile neutropenia			
Cycle 1	6.2	6.1	0.28
Cycle 2	1.1	2.5	
Cycle 3	0.0	0.5	
Cycle 4	3.6	2.0	
Cycle 5	2.2	0.5	
Cycle 6	1.1	0.0	
Unknown cycle ^a	1.5	0.0	
Cycles 1–6 (total)	15.7	11.6	
G-CSF support			
Yes	71.5	96.4	<0.001
No	28.5	3.6	
Unknown	(<i>n</i> =35)	(<i>n</i> =3)	
Infection	7.3	4.0	0.17
Thrombosis	1.5	0.5	0.41
Hypersensitivity	1.8	0.5	0.41
Nonhematologic			
Neuropathy	1.8	4.5	0.10
Diarrhea	1.8	2.0	0.99
Nausea or vomiting	1.8	0.0	0.08
Fatigue	0.7	2.0	0.24
GERD	0.4	1.0	0.58
Edema	0.4	0.5	0.99
Cardiac	0.0	0.0	0.99
Chest pain	1.5	0.0	0.14
Mucositis	0.7	0.0	0.51
Anuria	0.4	0.0	0.99
Other	2.9	0.5	

^a Documented in the medical record, but could not be attributed to any specific cycle.

FEC-D = fluorouracil–epirubicin–cyclophosphamide, followed by docetaxel; TAC = docetaxel–doxorubicin–cyclophosphamide; G-CSF = granulocyte colony-stimulating factor; GERD = gastroesophageal reflux disease.

patients not receiving prophylactic G-CSF for FEC experienced such an episode ($p = 0.235$). Of patients receiving prophylactic G-CSF during the docetaxel portion of FEC-D, 4.1% experienced an episode of febrile neutropenia; 17.6% of the patients not receiving prophylactic G-CSF support experienced such an episode ($p < 0.001$). In the TAC group, 11.1% of patients receiving prophylactic G-CSF support developed febrile neutropenia, compared with 33.3% of patients (3 of 9) not receiving prophylactic G-CSF ($p = 0.083$). Prophylactic G-CSF support therefore significantly lowered the rate of febrile neutropenia only in patients receiving the docetaxel portion of FEC-D.

DISCUSSION

As hypothesized, TAC and FEC-D showed no significant differences in 5-year DFS (91.8% vs. 92.3%) or 5-year OS (97.5% vs. 95.6%). Outcomes in our patients at 5 years appear better than those in the TAC arm of BCIRG 001⁶ and the FEC-D arm of PACS-01⁸, a result that likely can be attributed to our younger, purely HER2-negative cohort, with fewer patients having 4 or more positive axillary nodes. Both groups had similar treatment characteristics, although radiotherapy was given to significantly more patients who received TAC than to patients who received FEC-D (91.9% vs. 79.9%, $p < 0.001$). Despite differences in radiotherapy use, the local relapse rate was similar in the groups (1.0% for the TAC group vs. 2.2% for the FEC-D group); however, longer-term outcomes could be affected.

Nonhematologic grades 3 and 4 events were infrequent and appeared similar in the TAC and FEC-D groups. No grades 3 and 4 cardiac events were recorded during the follow-up period, which was unexpected, given that the BCIRG 001 TAC arm reported grade 3 or 4 congestive heart failure in 3% and serious cardiac events in another 3% of its enrollees⁶. In FEC-D arm of PACS-01, 0.4% of the enrollees experienced “any serious” adverse cardiac event over 5 years⁸. Our cohort was younger and had a shorter follow-up than the patients in the studies reporting cardiac toxicities. Longer follow-up will likely reveal cardiac events in our study population, given that anthracyclines are known to cause irreversible damage to the myocardium¹⁴.

Prophylactic use of G-CSF lowered the incidence of febrile neutropenia in both regimens; however, the only statistically significant decrease occurred in the docetaxel portion of FEC-D ($p < 0.001$), likely because of the low number of patients who did not receive prophylactic G-CSF during TAC (9 patients). In BCIRG 001 and PACS-01, primary prophylactic G-CSF use was prohibited, but in BCIRG 001, patients receiving TAC were prescribed prophylactic ciprofloxacin for days 5–14 of each cycle^{6,8}. The incidence of febrile neutropenia in the BCIRG 001 TAC arm was 24.7%⁶, which is similar to that in our small TAC group not receiving primary prophylaxis. The incidence of febrile neutropenia in the PACS-01 FEC-D arm for cycles 4–6 was 7.4%⁸, which was lower than that observed in our population (17.6%), and much lower than the 51.3% reported in a large retrospective study¹².

Torres *et al.*¹¹ confirmed a high rate of emergency room visits and hospitalizations for fever and neutropenia in their retrospective cohort study of patients receiving adjuvant FEC-D chemotherapy in Ontario; however, they did not report the incidence of febrile neutropenia by cycle. The incidence of febrile neutropenia with docetaxel in combination or as a single agent (100 mg/m²) is substantial. The current practice of primary G-CSF support for docetaxel-containing cycles in our province appears to be valid and consistent with the American Society of Clinical Oncology recommendation, which states that prophylactic G-CSF should be administered if the risk of febrile neutropenia is 20% or greater¹⁵.

Our study has important strengths that increase the validity of the results. We were able to capture data from 472 of 496 patients less than 50 years of age with

node-positive, HER2-negative breast cancer who were treated with TAC or FEC-D in Alberta during the study period; the 24 patients excluded had inaccessible or incomplete medical records. The accuracy of all data reported was manually confirmed using the province's electronic medical records for both cancer and comprehensive care.

Our study provides evidence that TAC and FEC-D are equivalent in terms of efficacy in young node-positive women, which allows for indirect comparisons of the 3rd-generation chemotherapy regimens used to treat operable breast cancer in the adjuvant setting. The National Surgical Adjuvant Breast and Bowel Project B30 and BCIRG 005 trials found no difference in OS between sequential (doxorubicin–cyclophosphamide followed by docetaxel) and concurrent TAC^{16,17}. Taken together, these data indicate that the efficacy differences between the regimens are minimal. Short- and long-term toxicities, together with pharmacoeconomic considerations, should therefore influence the choice of a “standard” adjuvant chemotherapy regimen for node-positive breast cancer.

In terms of limitations, our collection of non-laboratory-based adverse events was probably suboptimal given the retrospective nature of the study, which could explain the lower-than-expected values. We relied on toxicity descriptions in nursing and physician clinic visit notes, hospital encounters, and outside consultations submitted to the electronic medical record. Furthermore, although our study groups were similar in terms of age and tumour characteristics, any effect of selection bias for chemotherapy regimen will remain unknown, and other variables, such as socioeconomic status or race distribution were not controlled for. We have not evaluated women in the same age group with node-positive, HER2-negative breast cancer who received chemotherapy regimens other than TAC and FEC-D. Finally, if any differences in DFS or OS are detected with longer follow-up, we will have to account for non-significant imbalances in estrogen receptor status.

CONCLUSIONS

Our data suggest that, for women less than 50 years of age with node-positive, HER2-negative breast cancer, adjuvant TAC and FEC-D yield similar results in terms of 5-year DFS and OS. Furthermore, the toxicity of the two regimens is comparable. The frequency of febrile neutropenia during FEC cycles remained below 10% in patients of this cohort who did not receive primary prophylaxis with G-CSF. Therefore, if primary prophylaxis with G-CSF is restricted to cycles of chemotherapy containing docetaxel, then FEC-D could be associated with cost savings. Longer-term follow-up is warranted with respect to effectiveness and cardiac events.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

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