

# 677 The Role of Growth Factor Support Following Neutropenic Events in Early Stage Breast Cancer (BC) Patients Treated with Adjuvant Docetaxel, Doxorubicin, and Cyclophosphamide (TAC): A Subanalysis of BCIRG 001

Vogel CL,<sup>1</sup> Mackey JR,<sup>2</sup> Martin M,<sup>3</sup> on behalf of the BCIRG 001 Investigators

<sup>1</sup>Cancer Research Network, Plantation, FL, USA; <sup>2</sup>Cross Cancer Institute, Edmonton, AB, Canada; <sup>3</sup>Hospital Universitario San Carlos, Madrid, Spain

## ABSTRACT\*

**Background:** TAC significantly improves disease-free and overall survival over FAC (HR 0.72, 0.70, respectively) and is emerging as one of the most active adjuvant treatments in patients (pts) with node-positive early stage BC (Martin, SABCS 2003 #43). TAC is generally well tolerated but is associated with a higher incidence of febrile neutropenia (FN) vs FAC. ASCO clinical practice guidelines recommend secondary prophylaxis with G-CSF after FN in a prior cycle to maintain dose intensity.

**Methods:** Pts with node-positive BC were randomized to TAC (75/50/500 mg/m<sup>2</sup> q3wk x 6) or FAC (500/50/500 mg/m<sup>2</sup> q3wk x 6). Corticosteroid premedication and prophylactic ciprofloxacin were given with TAC, but not with FAC. In case of FN (≥ gr 2 fever with gr 4 neutropenia), infection, or prolonged neutropenia, pts were treated with G-CSF for all subsequent cycles. This retrospective subgroup analysis compares the incidence of FN for cycles treated without and with G-CSF.

**Results:** 1491 patients were accrued with 1480 evaluable for safety (TAC 744, FAC 736). A similar number of cycles were delivered and evaluable for febrile neutropenia in both arms (TAC 4278 delivered/4010 evaluable; FAC 4348 delivered/4007 evaluable). FN: TAC 183 pts (24.7% pts, 5.4% cycles), FAC 18 pts (2.5% pts, 0.5% cycles) with at least half the FN occurring in the first cycle (TAC: 97/183 pts; FAC 9/18 pts). Prophylactic G-CSF was administered to 250 TAC pts and 93 FAC pts. Among these, G-CSF was used as secondary prophylaxis for 87% (TAC) and 44% (FAC) of pts. The rate of FN (per cycle) without vs with G-CSF (+G) among all pts was: TAC 187/3114 (6.0%) vs TAC+G 28/896 (3.1%); FAC 19/3704 (0.5%) vs FAC+G 1/303 (0.3%). There were no septic deaths during treatment with either TAC or FAC, regardless of the use of G-CSF.

**Conclusions:** Among pts treated with TAC, the use of G-CSF decreased the incidence of neutropenic complications, although it remained higher than for pts treated with FAC. For pts experiencing a neutropenic event with TAC, secondary prophylaxis with G-CSF is appropriate. The impact of G-CSF on other clinical safety parameters will also be presented.

\*Updated data are presented in the abstract and poster.

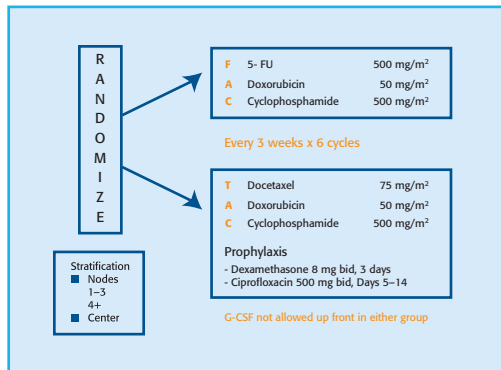


Figure 1. Study design.

## RESULTS

### Patient characteristics

	TAC (n=744)	FAC (n=736)
Median age, years [range]	49 [26-70]	49 [23-70]
Median Karnofsky performance status, %	100	100
Premenopausal, %	50	48
Mastectomy, %	60	59
Radiotherapy, %	69	72
Tamoxifen, %	68	69

Abbreviations: FAC = 5-fluorouracil-doxorubicin-cyclophosphamide; TAC = docetaxel-doxorubicin-cyclophosphamide.

Table 1. Baseline patient characteristics (all randomized patients, n=1491)

	TAC (n=744)	FAC (n=736)
Patients completing 6 cycles, n (%)	678 (91)	711 (97)
Relative dose intensity		
Median	0.99	0.98
>0.90, % of patients	90	85
Median total dose, mg/m <sup>2</sup>		
Docetaxel	449	-
Doxorubicin	299	300
Cyclophosphamide	2995	2998
5-Fluorouracil	-	2998

Abbreviations: FAC = 5-fluorouracil-doxorubicin-cyclophosphamide; TAC = docetaxel-doxorubicin-cyclophosphamide.

Table 2. Exposure to treatment

### Efficacy

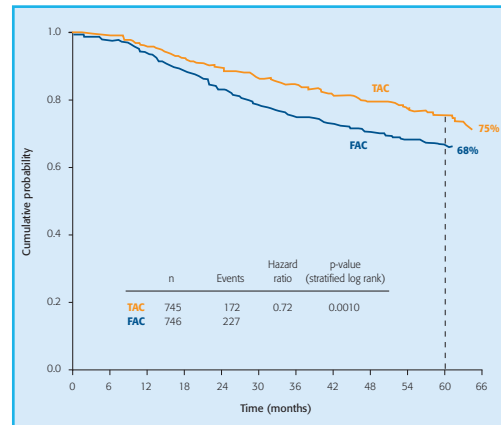


Figure 2. Disease-free survival at median 55 months' follow-up (intent to treat analysis).

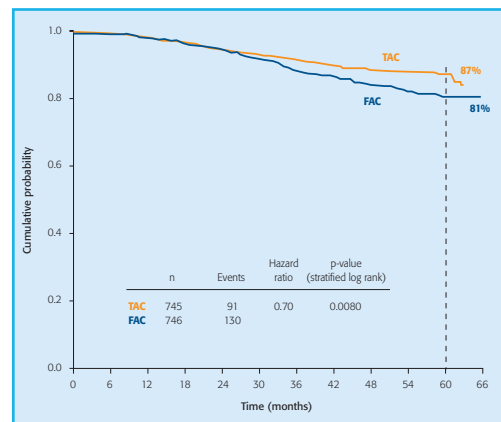


Figure 3. Overall survival at median 55 months' follow-up (intent to treat analysis).

### Toxicity

TOXICITY	% OF PATIENTS	
	TAC (n=744)	FAC (n=736)
Nausea	5.1	9.5
Vomiting	4.3	7.3
Diarrhea	3.8	1.8
Stomatitis	7.1	2.0
Asthenia	11.2	5.6
Congestive heart failure	1.6	0.5
Premenopausal patients		
On-treatment amenorrhea <sup>a</sup>	(n=420) 61.7	(n=403) 52.4

<sup>a</sup>Amenorrhea not graded.  
 Abbreviations: FAC = 5-fluorouracil-doxorubicin-cyclophosphamide; TAC = docetaxel-doxorubicin-cyclophosphamide.

Table 3. Selected grade 3-4 or severe nonhematologic toxicity

TOXICITY	% OF PATIENTS	
	TAC (n=744)	FAC (n=736)
Neutropenia (grade 3-4)	65.5	49.3
Febrile neutropenia	24.7	2.5
Neutropenic infection	12.1	6.3
Infection (grade 3-4)	3.9	2.2
Septic death	0	0

Abbreviations: FAC = 5-fluorouracil-doxorubicin-cyclophosphamide; TAC = docetaxel-doxorubicin-cyclophosphamide.

Table 4. Hematologic toxicity

### Use of G-CSF

TREATMENT	NO. OF PATIENTS (%)	
	TAC (n=744)	FAC (n=736)
Therapeutic G-CSF	162 (21.8)	90 (12.2)
Prophylactic G-CSF	250 (33.6)	93 (12.6)
Primary prophylaxis <sup>a</sup>	52 (7.0)	57 (7.7)
Secondary prophylaxis	217 (29.2)	41 (5.6)

<sup>a</sup>Protocol deviation.  
 Abbreviations: FAC = 5-fluorouracil-doxorubicin-cyclophosphamide; G-CSF = granulocyte colony-stimulating factor; TAC = docetaxel-doxorubicin-cyclophosphamide.

Table 5. Use of G-CSF by patient

CYCLES ADMINISTERED WITH	NO. OF CYCLES (%)	
	TAC (n=4278)	FAC (n=4348)
Therapeutic G-CSF	217 (5.1)	153 (3.5)
Prophylactic G-CSF	940 (22.0)	319 (7.3)
Primary prophylaxis <sup>a</sup>	141 (3.3)	193 (4.4)
Secondary prophylaxis	799 (18.7)	126 (2.9)

<sup>a</sup>Protocol deviation.  
 Abbreviations: FAC = 5-fluorouracil-doxorubicin-cyclophosphamide; G-CSF = granulocyte colony-stimulating factor; TAC = docetaxel-doxorubicin-cyclophosphamide.

Table 6. Use of G-CSF by cycle

EVALUABLE CYCLES	NO. OF CYCLES (%)			
	TAC		FAC	
	- G-CSF	+ G-CSF	- G-CSF	+ G-CSF
Neutropenic infection <sup>a</sup>	93 (3.0)	20 (2.2)	56 (1.5)	0 (0.0)

<sup>a</sup>Neutropenic infection defined as infection grade ≥2 concomitant with neutropenia grade ≥3 (NCI-CTC version 1.0).  
 Abbreviations: FAC = 5-fluorouracil-doxorubicin-cyclophosphamide; G-CSF = granulocyte colony-stimulating factor; NCI-CTC = National Cancer Institute Common Toxicity Criteria; TAC = docetaxel-doxorubicin-cyclophosphamide.

Table 7. Rates of neutropenic infection with and without prophylactic G-CSF

EVALUABLE CYCLES	NO. OF CYCLES (%)			
	TAC		FAC	
	- G-CSF	+ G-CSF	- G-CSF	+ G-CSF
Febrile neutropenia <sup>a</sup>	187 (6.0)	28 (3.1)	19 (0.5)	1 (0.3)

<sup>a</sup>Febrile neutropenia defined as a fever grade ≥2 in the absence of infection, concomitant with neutropenia grade 4 (NCI-CTC version 1.0) requiring intravenous antibiotics and/or hospitalization of the patient.  
 Abbreviations: FAC = 5-fluorouracil-doxorubicin-cyclophosphamide; G-CSF = granulocyte colony-stimulating factor; NCI-CTC = National Cancer Institute Common Toxicity Criteria; TAC = docetaxel-doxorubicin-cyclophosphamide.

Table 8. Rates of febrile neutropenia with and without prophylactic G-CSF

## CONCLUSIONS

- Neutropenic events were more frequent on TAC than FAC but no septic deaths were observed.
- Secondary prophylaxis with G-CSF resulted in reduction of febrile neutropenia.
- Primary prophylaxis with G-CSF might also be effective in reducing rates of febrile neutropenia. Data from trials with TAC as adjuvant treatment – both already completed (GEICAM 9805, BCIRG 005) and ongoing (NSABP B30) – are needed to confirm these results.

### Investigators

Canada: Mackay, Al Taweiri, Tomiak, Guevin, Tang, Colwell, Prady, Provencen, Walde, Gelmon, Sehdev, Drolet, Dufresne, Yelle, Zbdawa, Lesperance, Verma, Cantin, Holland, Trudeau, Chang, Rubin, Allan

USA: Vogel, Chap, Weaver, Hainsworth, Modiano, Erban, Czaibam, Harris, O'Rourke, Beck, Limentani, Robert, Tongol, Schnell, Beggs, Harif, Rosenberg, Campos, Foster, Beskes, Collin, George, Avery

Spain: Martin, Jimenez, Carrato, Mena, Pellegri, Saile, Alba, Consejo, Alvarez, Lopez, Aranda, Aguilera, Munariz, Gandia, Anton, Torres, Lobo, Samper, Lopez, Vega, Menendez, Prieto, Murias, Rosales, Cassinello, Espinosa, Garcia, Puche

Poland: Pienkowski, Pawlicki, Karnicka

UK: Howell, Coleman, Whipp, Le Vay

Hungary: Juhas, Pinter, Szanto

France: Guastalla

Brazil: Vinholes, Teixeira

Sweden: Fornander, Nylen

Israel: Luria, Meirinsky, Steiner

Argentina: Guika, Mickiewicz, Martinez

Uruguay: Viola, Garbino

Germany: Oberhoff

South Africa: Ruff

Egypt: Abd-El-Azim, Gad-El-Mawla

Austria: Schuller

Czech Rep.: Abrahamova, Finek

Portugal: Goncalves, Chumbo

Slovak Rep.: Kozar