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Patterns of granulocyte colony stimulating factor (G-CSF) use in elderly breast cancer patients receiving myelosuppressive chemotherapy

Introduction

- Febrile neutropenia (FN) is a potentially serious complication of myelosuppressive chemotherapy in breast cancer (BC) patients.
- Oncology guidelines recommend primary prophylaxis with G-CSF (PPG) in patients with a high risk of developing FN.
- High risk of FN (> 20%) is based on the following: myelotoxicity of the chemotherapy regimen, age of patient, associated comorbidities, disease characteristics (Lyman Cancer 2011).
- We report the use of G-CSF and incidence of FN in elderly breast cancer patients undergoing chemotherapy using the Medicare 5% database.

Methods

- Medicare 5% claims data set was used to identify BC patients age 65+ initiating chemotherapy between 7/1/2003 and 6/30/2009.
- Chemotherapy courses were identified for each patient, with the first course of chemotherapy being used for the analysis; courses that could not be classified into high (HR) or intermediate (IR) risk were excluded. Chemotherapy regimens are outlined in Table 1
- Duration of the first cycle was from the date of first chemotherapy claim to the chemotherapy claim at day 21 or later, which defined the first day of the second cycle, etc, to a maximum of 9 cycles.
- First administration of G-CSF [filgrastim (Neupogen©) or pegfilgrastim (Neulasta©)] was classified as either primary prophylaxis [(PPG) within first 5 days of the cycle], secondary prophylaxis (within first 5 days of second or subsequent cycles), or reactive (day 6 or later of first or subsequent cycles).
- FN assessed during the chemotherapy course was defined as hospitalization with a code for neutropenia in any position (ICD-9-CM 288.0x).

Results

- 885 courses with high FN risk and 1046 courses with intermediate FN risk were identified.
- The high FN risk cohort was younger (71.4 vs 74.5 years) and had fewer comorbidities than the intermediate FN risk group (Table 2).
- Among BC patients receiving HR regimens, 73.8% received G-CSF, but only 52.1% received it as PPG (Table 3).
- Secondary prophylaxis was received by 8.8%; 12.9% received G-CSF as reactive treatment (Table 3).
- Pegfilgrastim was received by 74.7% as PPG, and filgrastim was received by 64.0% as reactive treatment.
- Neutropenia-related hospitalization occurred in 11.8% of courses (ranges 5.0-13.9%), depending on chemotherapy regimen (Table 4).

Table 1: Description of high and intermediate risk chemotherapy regimes in patients with breast cancer

High risk	N
Dose dense AC+sequential T (doxorubicin/ cyclophosphamide, paclitaxel	345
TAC (docetaxel/doxorubicin/cyclophosphamide)	389
Docetaxel+trastuzumab	61
AT (doxorubicin/paclitaxel)	21
AT (doxorubicin/docetaxel)	50
Docetaxel every 14 days	19
Intermediate risk	**N**
CMF classic (cyclophosphamide/ methortexate/fluorouracil	481
Docetaxel every 21 days	94
Pacitaxel every 21 days	337
Pacitaxel + Trastuzumab	87
FEC (fluorouracit/epirubicin/cuclophosphamide	47

Table 2: Baseline characteristics and demographics in patients with breast cancer

Risk of febrile neutropenia (FN) by chemotherapy regimen: high(>20%) intermediate(10-20%)	High N courses=885 N percent	Intermediate N courses=1,046 N percent
Age		
65-69	417 (47.1)	281 (26.9)
70-74	265 (29.9)	303 (29.0)
75-80	148 (16.7)	278 (26.6)
80+	55 (6.2)	184 (17.6)
Race		
Caucasian	778 (87.9)	901 (86.1)
African American	73 (8.2)	112 (10.7)
Other	34 (3.8)	33 (3.2)
Sex		
Male	10 (1.1)	7 (0.7)
Female	875 (98.9)	1,039 (99.3)
Comorbidities*		
Atherosclerotic heart disease	112 (12.7)	178 (17.0)
Congestive heart failure	45 (5.1)	106 (10.1)
Cerebrovascular accident/ transient ischemic attacks	33 (3.7)	49 (4.7)
Peripheral vascular disease	56 (6.6)	99 (9.5)
Other cardiovascular disease	112 (12.7)	133 (12.7)
Chronic obstructive pulmonary disease	101 (11.4)	165 (15.8)
Gastrointestinal disorders	17 (1.9)	20 (1.9)
Liver disease	1 (0.1)	5 (0.5)
Dysrhythmia	79 (8.9)	149 (14.2)
Diabetes mellitus	185 (20.9)	257 (24.6)
Chronic kidney disease	31 (3.5)	76 (7.3)

Table 3: Patterns of G-CSF use in HR and IR chemotherapy regimes

	High N courses=885 N percent	Intermediate N courses=1,046 N percent
G-CSF use during the first course		
None	232 (26.2)	723 (69.1)
Either filgrastim or pegfilgrastim	653 (73.8)	323 (30.9)
Any filgrastim	178 (20.1)	144 (13.8)
Any pegfilgrastim	566 (64.0)	225 (21.5)
Both filgrastim and pegfilgrastim	91 (10.3)	46 (4.4)
First G-CSF use as		
None	232 (26.2)	723 (69.1)
Primary prophylaxis	461 (52.1)	102 (9.8)
Secondary prophylaxis	78 (8.8)	97 (9.3)
Reactive treatment	114 (12.9)	124 (11.9)

Table 4: Patterns of G-CSF use in patients with breast cancer, by chemotherapy regime

Chemotherapy regime G-CSF use during the first course	Dose dense AC + sequential T N course=345 N percent	TAC N course=389 N percent	CMF classic N course=481 N percent	TC N course=323 N percent	AC+ sequential T N course=256 N percent
Number of cycles median (10%, 90%)	7 (4, 9)	7 (4, 9)	5 (3, 8)	4 (3, 6)	6 (4, 8)
None	53 (15.4)	82 (21.1)	314 (65.3)	71 (22.0)	71 (27.7)
Either filgrastim or pegfilgrastim	292 (84.6)	307 (78.9)	167 (34.7)	252 (78.0)	185 (72.3)
Any filgrastim	62 (18.0)	94 (24.2)	79 (16.4)	55 (17.0)	53 (20.7)
Any pegfilgrastim	265 (76.8)	263 (67.6)	118 (24.5)	225 (69.7)	159 (62.1)
Both filgrastim and pegfilgrastim	35 (10.1)	50 (12.9)	30 (6.2)	26 (8.7)	27 (10.5)
First G-CSF use as:					
None	53 (15.4)	82 (21.1)	314 (65.3)	71 (22.0)	71 (27.7)
Primary prophylaxis	238 (69.0)	204 (52.4)	32 (6.7)	183 (56.7)	103 (64.8)
Secondary prophylaxis	19 (5.5)	44 (11.3)	67 (13.9)	27 (8.4)	36 (14.1)
Reactive treatment	35 (10.1)	59 (15.2)	68 (14.1)	42 (13.0)	33 (12.9)
Pegfilgrastim, first use as:					
Primary prophylaxis	222 (83.8)	186 (70.7)	29 (24.5)	174 (77.3)	103 (64.8)
Secondary prophylaxis	23 (8.7)	55 (20.9)	65 (55.1)	38 (16.9)	39 (24.5)
Reactive treatment	20 (7.5)	22 (8.4)	24 (20.3)	13 (5.8)	17 (10.7)
Filgrastim, first use as:					
Primary prophylaxis	16 (25.8)	19 (20.2)	3 (3.8)	9 (16.4)	13 (24.5)
Secondary prophylaxis	8 (12.9)	15 (16.0)	20 (25.3)	6 (10.9)	10 (18.9)
Reactive treatment	38 (61.3)	60 (63.8)	56 (70.9)	40 (72.7)	30 (56.6)
Day of filgrastim us in the first cycle among courses with filgrastim as primary prophylaxis					
Mean days (SD)	7.4 (3.4)	5.1 (2.7)	6.7 (2.9)	5.7 (1.2)	6.5 (3.1)
Median days (10%, 90%)	10 (2, 10)	5 (1, 10)	5 (5, 10)	6 (4, 7)	7 (2, 10)
Neutropenia-related hospitalization					
1+ hospitalization	42 (12.2)	54 (13.9)	24 (5.0)	27 (8.4)	26 (10.2)
Length of hospitalization median (10%, 90%)	4 (3, 6)	5 (3, 12)	5 (2, 14)	5 (2, 9)	5 (3, 12)

Conclusions

- NCCN recommends primary prophylaxis with G-CSF in patients with a high risk of developing FN, particularly in those with an older age (>65 years).
- However, in our study, only 52% of elderly breast cancer patients at high risk of FN and 10% of those with intermediate risk primary prophylaxis.
- Although there are currently no consensus nomograms for FN risk assessment, evaluation of risk factors for chemotherapy-induced FN prior to the first cycle, including disease type, chemotherapeutic regimen, patient risk factors and treatment intent should be considered for all oncology patients.
- Careful attention to FN risk factors, including regimen and patient age, is needed when planning treatment strategy.

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