Prophylaxis of chemotherapy-induced febrile neutropenia with biosimilar filgrastim: Description of patients, treatment patterns and outcomes in the MONITOR-GCSF Study in Romania

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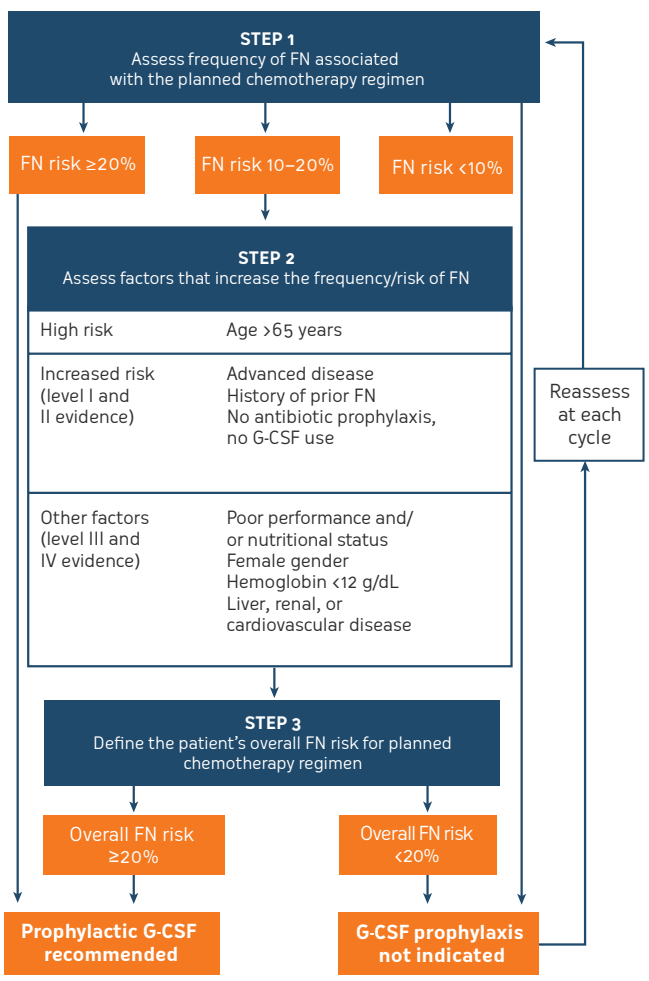
Introduction

- Chemotherapy-induced febrile neutropenia (CIN/FN) is a frequent and potentially life-threatening complication experienced in patients undergoing cancer treatment. FN can result in hospitalization and can jeopardize antineoplastic treatment through chemotherapy delay or dose reduction[1,2] as well as delays and cancellations of surgery. FN is also associated with increased morbidity, mortality, and health care costs.[3]
- The European Organization for Research and Treatment of Cancer (EORTC), among other clinical organizations, has established evidence-based guidelines for the use of granulocyte colony-stimulating factor (G-CSF) to reduce the incidence of CIN/FN.[4]
- The primary aims of the MONITOR-GCSF study are to[5]:
  - describe the patient population at risk for FN and treated prophylactically with biosimilar filgrastim (Zarzio®, Sandoz)
  - describe prophylaxis patterns involving Zarzio® and their congruence with the EORTC guidelines
  - identify the multi-level (patient- and centre-level) determinants of patient outcomes in terms of breakthrough episodes of CIN/FN and impact on chemotherapy delivery.
- This current analysis describes the patient characteristics, treatment patterns of Zarzio®, and outcomes in the Romanian sample.

Methods

- MONITOR-GCSF is an international, prospective, observational, open-label, pharmaco-epidemiologic study of cancer patients at risk of CIN/FN who received commercially available Zarzio® for prophylactic purposes.
- Treatment with Zarzio® was per the treating physician's best clinical judgment. Thus, there was no fixed protocol for treatment initiation, dose, or duration; data were collected on the actual real-world practice patterns for up to six chemotherapy cycles.
- Treatment with Zarzio® is described relative to the EORTC guideline recommendations.[4] The EORTC guideline algorithm is illustrated in Figure 1.
- 64 evaluable patients from 7 centers in Romania (from a total of 1447 patients from 140 centers from 12 European countries) participating in the MONITOR-GCSF study are presented in these analyses which include 300 cycles.

Figure 1. 2010 updated EORTC guideline algorithm



Primary prophylaxis: start G-CSF in first cycle 24–72 hours after end of the first chemotherapy and continue through all cycles (when appropriate as per cycle reassessment).

Secondary prophylaxis: start G-CSF if a neutropenic event was observed in the previous cycle.

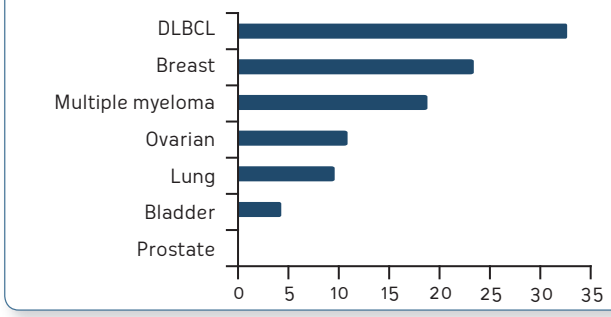
Results

- Table 1 lists patient demographic characteristics and Figure 2 presents cancer types. The most common cancers were diffuse large B-cell lymphoma (DLBCL) (33%), breast (23%), and multiple myeloma (19%) with a majority of patients (51.6%) having hematological cancers and 48.4% with solid tumors.

Table 1. Patient characteristics

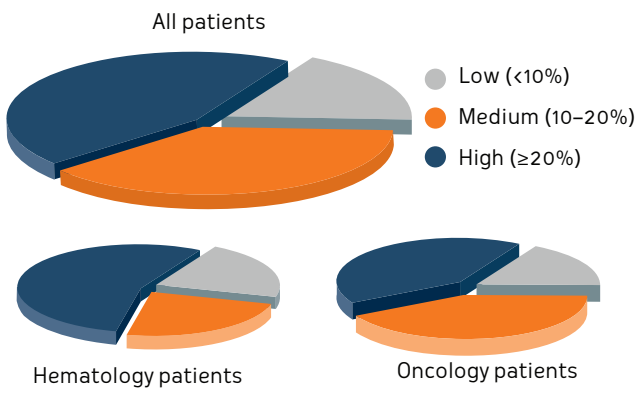
Gender	**Male**	**Female**
	39.1 %	60.9%
Age (years)	Mean ± SD (min, max) 58.0 ± 10.7 (32, 78)	

Figure 2. Cancer type



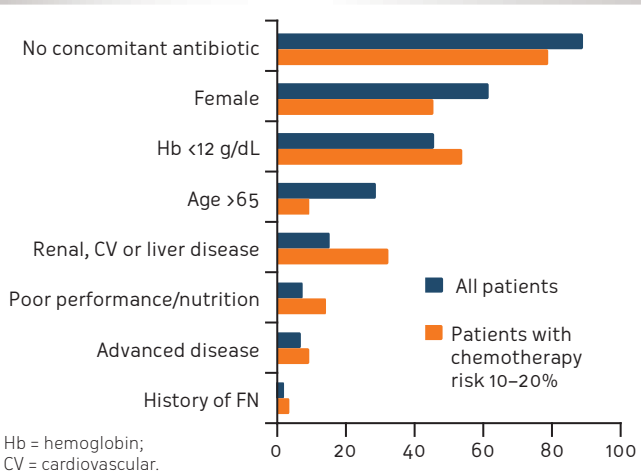
- Figure 3 shows chemotherapy-related risk of FN for all patients and for patients with hematological cancer (hematology) and solid tumors (oncology). A higher percentage of hematology patients (55%) were treated with chemotherapy regimens that have high risk (>20%) of associated FN compared with oncology patients (35%).

Figure 3. Chemotherapy-related risk for FN



- Figure 4 illustrates patient-related risk factors for FN for all patients and for those treated with chemotherapy regimens with medium risk (10–20%) of associated FN.
- Zarzio® prophylaxis initiation (primary vs. secondary) relative to the EORTC guideline recommendations is illustrated in Figure 5. Primary prophylaxis was initiated in 69% of all patients, with 71% of hematology patients and 67% of oncology patients receiving primary prophylaxis. Prophylaxis, either primary or secondary, was correctly initiated per EORTC guideline recommendations (considering CIN/FN risk and patient-related factors) in 34% of patients.

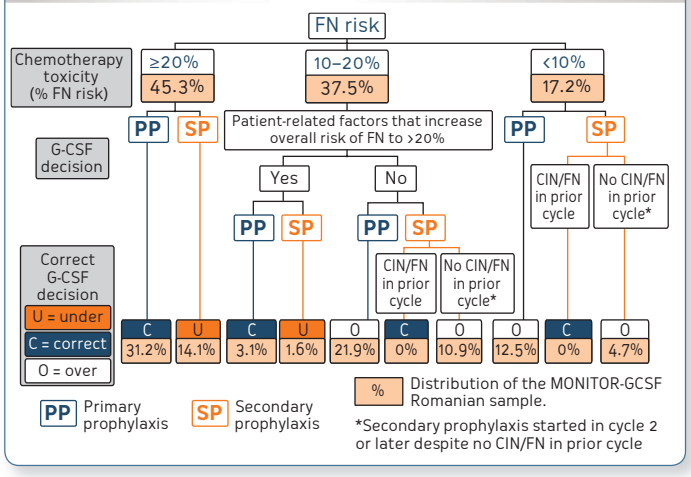
Figure 4. Patient-related risks of FN per EORTC guidelines



Hb = hemoglobin;
CV = cardiovascular.

- Table 2 presents Zarzio® treatment patterns. Zarzio® dose of 48 MIU/day was given in the majority (52.2%) of cycles and 30 MIU/day given in 47.8% of cycles. Zarzio® was started on average 1.0 ± 1.9 days after chemotherapy and given for 2.0 ± 1.0 days.

Figure 5. Zarzio® initiation relative to the EORTC guidelines



- CIN (any grade) occurred in 2.7% of all cycles and 9.4% of patients had one or more episodes of CIN (any grade); see Table 3. 6.3% of patients had at least one episode of Grade 3 or 4 CIN of which 1.6% were febrile. CIN/FN-related hospitalizations were experienced by 1.6% of patients. CIN/FN-related chemotherapy disturbances (dose reduction, delay or cancellation) occurred in 4.7%.

Table 2. Zarzio® treatment patterns

Prophylaxis type	Primary	68.8%
	Secondary	31.2%
Prophylaxis decision	Under treated	15.7%
	Correctly treated	34.3%
	Over treated	50.0%
Dose	30 MIU/day	47.8%
	48 MIU/day	52.2%
Day of initiation	During chemotherapy (day 0)	48.1%
	Per guidelines (day 1–3)	51.2%
	Late (day 4 or later)	0.7%
Duration	1–3 days	92.3%
	4–5 days	7.4%
	6 or more days	0.3%

Table 3. CIN/FN Outcomes

Outcome	Incidence (%)
CIN any Grade	9.4
CIN Grade 3 or 4	6.3
CIN Grade 4	1.6
FN	1.6
CIN/FN-related hospitalizations	1.6
CIN/FN-related chemotherapy disturbances (dose reduction, delay or cancellation)	4.7

Conclusions

- Real-world variations in practice patterns of biosimilar G-CSF (Zarzio®) are evident in the Romanian sample in terms of:
  - type of prophylaxis
  - prophylaxis decision (relative to guideline recommendations)
  - day of initiation.
- Clinician decision to 'over treat' in the low and moderate chemotherapy risk groups may be due to patient-related risk factors, safety profile of Zarzio®, and/or affordability of biosimilar G-CSF.
- Incidence of FN and CIN/FN-related hospitalizations is low.
- Zarzio® has similar real-world effectiveness as the originator and the G-CSF class in general.

References

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