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LETTER TO THE EDITOR

Pegfilgrastim in primary prophylaxis of febrile neutropenia during chemotherapy of relapsed and refractory multiple myeloma: a real-life experience

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Dear Editor,

Febrile neutropenia (FN) is a serious side effect of chemotherapy, and even when it does not result in significant morbidity, mortality and costs, it normally leads to a delay in subsequent chemotherapy treatments [1]. FN is also associated with suboptimal delivery of chemotherapy and reduced relative dose intensity (RDI), which adversely affects long-term cancer outcome and survival [2]. FN is a surrogate marker for infection during chemotherapy and is characterized by an absolute neutrophil count (ANC) <1000/mm^3 and a single temperature of >38.3 °C (101 °F) or a sustained temperature of ≥38 °C (100.4 °F) for more than 1 h [1, 3]. Risk of FN is dependent on both patient-specific factors (e.g. type of cancer, disease stage, co-morbid conditions and age) and the myelotoxicity of the chemotherapy regimen [1]. Once an episode of FN occurs, the risk of FN increases in subsequent chemotherapy cycles [4].

The American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) recommend the use of granulocyte colony-stimulating factors (G-CSFs) as primary prophylaxis (PP) when the overall FN risk is greater than 20 % following myelosuppressive chemotherapy, and secondary prophylaxis (SP) following FN or a dose-limiting neutropenic event [4, 5].

Recombinant granulocyte colony-stimulating factors (G-CSFs) have been developed to stimulate proliferation and differentiation of neutrophils in patients receiving chemotherapy. Pegfilgrastim is a pegylated long-acting recombinant form of G-CSF which extends the half-life, requiring less frequent dosing than non-pegylated G-CSF [6]. It is indicated to decrease the incidence of infection, as manifested by FN, in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy associated with a clinically significant incidence of FN [5]. Pegfilgrastim is cleared via a neutrophil-mediated system and requires only a single dose administered subcutaneously once per chemotherapy cycle [6–8].

Multiple myeloma (MM) in advanced phases of disease may be managed by regimens combining agents not frequently employed in early phases of treatment [9] (e.g. anthracyclines, alkylating agents, etc.), but myelotoxicity is the main expected side effect [10]. In this context, G-CSFs are often necessary to warrant an effective chemotherapy, counteracting the risks of febrile neutropenia: their use is bound to frequent evaluation of neutrophil counts which may not be frequently performed by patients in home-care. Avoiding severe neutropenia by prophylactic pegfilgrastim seems particularly useful in these cases, where treatment is performed with palliative intent and prolonging life in the best possible conditions is the aim.

The objective of this observational study was to evaluate the efficacy and safety of pegfilgrastim in patients affected by multiple myeloma in an advanced phase of disease, in order to determine whether a single subcutaneous injection of pegfilgrastim is as effective as daily injections of standard filgrastim, in terms of haematological toxicity, febrile neutropenic episodes, antibiotic usage and hospitalization duration.

We have considered 41 patients (22 male and 19 female) with a median age of 63.8 years (range 39–82) affected by multiple myeloma, all relapsed and refractory to a median of six lines of therapy (range 4–8), all previously exposed to bortezomib, lenalidomide and melphalan and all relapsed after auBMT, which have been treated with different chemotherapy regimens combining bortezomib, lenalidomide, bendamustine, melphalan and doxorubicin.

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Since first course, received in our outpatient unit, patients performed blood counts twice weekly and received, from day +8 to day +19 (considering "day +1" the day in which the chemotherapy protocol starts), prophylactic oral quinolones and anti-fungal drugs. During neutropenia after first cycle of chemotherapy, filgrastim (5 μg/kg/day for 3 days) was given if neutrophils count was $<1000\times 10^9$ cells/L. Median number of filgrastim administrations was 4.7 (r. 3–6); nadir neutropenia was registered after a median of 11.3 days (r. 8–14); median of nadir neutrophil count was 1.16×10^9 cells/L (range $0.4–1.8\times10^9$ cells/L), with maximum duration of 13 days.

From the second course of chemotherapy, all patients switched to prophylactic therapy with pegfilgrastim (6 mg), injected subcutaneously with a single administration on day + 3. Primary end point of this study was the duration of neutropenia (neutrophil count $<1.5\times10^9$ cells/L), comparing pegfilgrastim and filgrastim. During pegfilgrastim, neutropenia was never longer than 8 days, with a consequent reduction of neutropenia-related infections. Median nadir neutrophil count, evaluated for every patients for at least three courses of therapy (r. 3–6) registered at day +11, was 1.628 (range $0.93–2.25\times10^9$ cells/L); four patients (9.7 %) needed, after pegfilgrastim administration, a supplement of three administrations of filgrastim. During pegfilgrastim prophylaxis, neutropenia, when present, was shorter than during filgrastim treatment (median of 4 days, range 3–7). Apart from the advantage of the mono-administration, pegfilgrastim was well tolerated in all patients: main side effects in our patients were mild fever and bone pain (5/41 patients, 12 %). Moreover, no hospitalization was needed during pegfilgrastim treatment versus two hospitalizations for FN during filgrastim. During the observation period, no patient died during filgrastim or pegfilgrastim supportive treatment.

The reduction of the days of administration and of the days spent in the hospital make pegfilgrastim an advantageous option in most cases both in terms of quality of life and of cost-effectiveness.

In conclusions, in patients affected by MM exposed to myelosuppressive agents in advanced phases of myeloma disease, pegfilgrastim seems to reduce the incidence of neutropenia, is better tolerated and may increase the possibility to maintain the scheduled time of treatment.

Conflicts of interest No conflicts of interest.

References

1. Crawford J, Dale DC, Lyman GH (2004) Chemotherapy-induced neutropenia: risks, consequences, and new directions for its management. Cancer 100:228–237
2. Pettengell R, Schwenkglenks M, Leonard R et al (2008) Neutropenia occurrence and predictors of reduced chemotherapy delivery: results from the INC-EU prospective observational European neutropenia study. Support Care Cancer 16:1299–1309
3. United States Department of Health & Human Services, National Institutes of Health, National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE). Published: May 28, 2009 (v4.03: June 14, 2010)
4. Smith TJ, Khatcheressian J, Lyman GH et al (2006) 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. J Clin Oncol 24:3187–3205
5. National Comprehensive Cancer Network (NCCN), Inc. Clinical Practice Guidelines in Oncology: Myeloid Growth Factors Version 1.2012. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp#supportive. Accessed 1 Aug 2012
6. Amgen, Inc.(2011) Neulasta (pegfilgrastim) [prescribing information]. Thousand Oaks, CA: Amgen, Inc. http://pi.amgen.com/united_states/neulasta/neulasta_pi_hcp_english.pdf. Accessed Aug 28 2011
7. Green MD, Koelbl H, Baselga J et al (2003) A randomized double-blind multicenter phase III study of fixed-dose single-administration pegfilgrastim versus daily filgrastim in patients receiving myelosuppressive chemotherapy. Ann Oncol 14:29–35
8. Balducci L et al (2007) Elderly cancer patients receiving chemotherapy benefit from first-cycle pegfilgrastim. Oncologist 12:1416–1424
9. Ludwig H et al. (2014) European perspective on multiple myeloma treatment strategies in 2014. Oncol
10. Cömert M et al (2013) Quality of life and supportive care in multiple myeloma. Turk J Haematol 30(3):234–246