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LETTER TO THE EDITOR

Pegfilgrastim in primary prophylaxis of febrile neutropenia in elderly patients with hematological malignancies—bendamustine and G-CSF support

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Dear editor,

We would like to thank Osamu Imataki and his colleagues [1] for their comments on our recent original article about a real-life experience on the use of pegfilgrastim in primary prophylaxis of febrile neutropenia (FN) for patients with non-Hodgkin lymphoma (NHL) undergoing bendamustine plus rituximab (BR) treatment [2]. Their case report is an example of effectiveness of secondary prophylaxis with G-CSF in a setting of advanced mantle cell lymphoma of an elderly patient (82-year-old) who underwent BR [1]. The authors want to highlight how BR could cause prolonged neutropenia, especially during the following courses of therapy, rather than the initial; therefore, a secondary G-CSF prophylaxis is probably advocated as more properly indicated. There is still lack of data regarding the efficacy of a primary or secondary prophylaxis with G-CSF in BR for patients with NHL. However, our real-life experience suggests that, in a primary prophylactic setting, pegfilgrastim seems to give significant advantages in terms of reduction of FN-related chemotherapy disruption incidence, with subsequent overall improvement of treatment effectiveness. Moreover, it was observed that there is no significant G-CSF-related side effect with pegfilgrastim primary prophylaxis, compared with "on demand" secondary prophylaxis with filgrastim [2]. Considering the age of patients enrolled in our study, in the pegfilgrastim group, the median was 45.4 years (range, 33–77), with no patients > 80 years old.

Focusing on the aforementioned case report, the patient is an 82-year-old frail patient, with many comorbidities and diagnosis of mantle cell lymphoma, so, who does not fully match the overall elderly population risk, clinical course, and outcome in myelosuppressive therapy for an NHL. In fact, elderly patients could gain the same benefits from chemotherapy as young population, but, in most cases, the outcome is poorer due the higher susceptibility on myelosuppression, with the consequential use of reduced dose intensity regimen that leads to reduction of effectiveness of treatment [3]. Then, regardless of the treatment strategy, elderly patients are at high risk of severe infections during FN, since first cycle of chemotherapy potentially causes hospitalization, death, or sudden and prolonged delay of treatment administration [3]. Despite no specific data available on bendamustine-containing regimens, and no specific indication on preferred primary prophylaxis, recent retrospective evaluation of G-CSF support in elderly patients with cancer revealed that up to 61.5% of patients with NHL and high risk of FN receive growth factor support starting from the first cycle of chemotherapy [4].

Interestingly, our previous experience on primary prophylaxis with pegfilgrastim during bendamustine-based treatment, not only in follicular lymphomas [5] but particularly for another hematological malignancy, multiple myeloma, typical to elderly age, had also been given interests for this category of patients [6, 7]. In particular, patients treated with bendamustine and receiving primary prophylaxis had a median age of 62.1 years (range, 43–83) and showed a significant reduction in neutropenia-related infections and chemotherapy disruption due to FN compared to those who received secondary prophylaxis [7]. This evidence shows that effectiveness of primary prophylaxis with pegfilgrastim, during bendamustine-containing therapy, is probably more effective than secondary prophylaxis with non-pegylated G-CSF in

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elderly patients, regardless the type of lymphoproliferative disease, also when totally different in terms of biology and clinical behavior (lymphoma vs multiple myeloma). Other interesting data could be extracted from other two case reports by our Hematology Unit, where evaluation of supportive care with G-CSF was not the first objective of the study, but its effectiveness can be considered as part of the effectiveness of multiple salvage lines of therapy, in patients with relapsed/refractory multiple myeloma, including bendamustine-containing regimens [8, 9]. Seven and 11 lines of therapy were administered, respectively, to two old, frail, and heavily pretreated patients with a long clinical history of relapsed and refractory multiple myeloma: the support with pegylated G-CSF was the backbone for the pursuance of each subsequent line of potentially myelotoxic therapy.

The evaluations of specific comorbidities and individual risk factors for FN play also a key role on the decision of whether adopting a primary or secondary prophylaxis with G-CSF, but, in clinical practice, elderly age should be considered a strong parameter that drives to the choice of a primary prophylaxis. Our aim is also to highlight that, in an outpatient setting, using pegfilgrastim is very feasible and manageable, thanks also to its modality of administration that can reduce the necessity of caregivers' work.

In conclusion, we want to support the idea that a great advantage in terms of quality of life, effectiveness of therapy, and outcome could derive from a primary prophylaxis with easily manageable administration of pegfilgrastim, especially in advanced-age patients, such as the one described in the case report by Imataki et al., in which minimizing the risk of a FN since the first course can be the key for the best outcome.

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