Editorial

A new peg-filgrastim biosimilar, mecapegfilgrastim for primary prophylaxis of chemotherapy-related neutropenia is now available

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Chemotherapy is still one of the main tools for treatment of pediatric and adult blood and solid tumors and is capable of cure some acute leukemia, some advanced lymphomas, advanced testicular cancers among others (1). However, the main side effects and limiting factors for its use is myelotoxicity, in particular neutropenia and eventual life threatening febrile neutropenia. The recombinant human granulocyte colony stimulating factor, filgrastim, has been developed and employed in prevention of chemotherapy-related neutropenia but because of its relatively short half-life, daily filgrastim injections were required to stimulate neutrophil recovery (2). Evaluation of several PEG-related forms of filgrastim identified PEG-filgrastim as the construct with optimal balance of *in vitro* activity and *in vivo* resistance time, is capable of self regulating clearance, remains in circulation during chemotherapy-induced neutropenia and is not eliminated until neutrophils start to recover (3-6). Clinical efficacy of PEG-filgrastim is achieved with a single 6 mg dose once-per-chemotherapy cycle (7,8). Therefore PEG-filgrastim is more convenient and less expensive for patients and hospitals, but in China PEG-filgrastim is not available leaving filgrastim to be the only treatment option in this setting, but with the need of daily injections. Mecapegfilgrastim is a biosimilar of PEG-filgrastim and has been developed by Jiangsu Hengrui Medicine Co,. Ltd. (9,10) and has shown, in phase II studies in non small cell lung cancer (NSCLC) and in subsequent phase III study in the same tumors, to be effective as daily filgrastim prophylaxis of neutropenia-associated with chemotherapy and with comparable pharmacokinetics and safety profiles with PEG-filgrastim (9,10). Considering the deficiency in long-acting anti-neutropenia drugs in China, and the limited data of mecapegfilgrastim in breast cancer patients, being only one phase II trial of mecapegfilgrastim performed in breast cancer (11), a randomized phase III trial was needed. In this very well-done study in breast cancer, Xu and co-workers (12) showed that in a randomized comparison of two different doses of Mecapegfilgrastim or filgrastim given during the first cycle of chemotherapy, Mecapegfilgrastim, when administered in primary prophylaxis of chemotherapy-induced neutropenia, to be non inferior and even superior to filgrastim. The fixed 6 mg dose of Mecapegfilgrastim regimen showed similar efficacy and safety profile compared with the 100 μg/kg regimen of Meca and is preferable in clinical practice due to the convenient once per cycle administration and the high degree treatment compliance for the patient. This randomized study therefore provide new evidence for the novel long acting mecapegfilgrastim, to be a new safe and effective alternative for the prophylaxis of chemotherapy-induced neutropenia in comparison with filgrastim and can be used in a convenient one-per-cycle administration for breast cancer patients and possibly for other adult tumors. This new long acting PEG-filgrastim may be very useful also in some frail subgroups of patients like elderly patients (13,14) and HIV-related tumors (15-17), that fortunately

are less common in China than in Western countries, in that they are more sensible and prone to bone marrow toxicity after chemotherapy. In the Xu *et al.* randomized study, the mean age of the 3 groups of patients was around 48±8 years, therefore a quite young population, reflecting the epidemiology of breast cancer in China, in comparison with Western countries epidemiology. However, with the growing age in population occurring also in China, this long lasting PEG-filgrastim could be even more useful in elderly setting. The decreased cost due to the short period of hospitalization and the decreased risk of infection of mecapegfilgrastim with related limited costs, are both factors very important in the limited medical resources available now in all countries. It is also possible, but it is not yet known to us, also because mecapegfilgrastim it is not yet on the market, that this new mecapegfilgrastim by itself may cost less than filgrastim and other pegylated-filgrastim. Finally, for China but also for other countries, these results are very important in that allows the safe use with demonstrated activity of a new biosimilar of PEG-filgrastim, mecapegfilgrastim, developed in China. In addition, breast cancer is an ideal setting where this approach could be tested in that breast cancer is a very common malignancy and chemotherapy is still a very frequent and efficacious modality of treatment.

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Footnote

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