Pegfilgrastim for Chemotherapy-Induced Neutropenia

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Chemotherapy-induced neutropenia (CIN) is a frequent adverse event in patients treated with myelosuppressive chemotherapy. The depth and duration of the neutrophil nadir following chemotherapy correlates with the development of infectious complications. However, minimizing the duration and severity of neutropenia by stimulating the growth and development of neutrophils in the bone marrow is possible by using granulocyte-colony-stimulating factors, such as filgrastim (Welte, Gabrilove, Bronchud, Platzer, & Morstyn, 1996). The prophylactic administration of filgrastim can reduce the incidence of febrile neutropenia and decrease hospitalizations and IV antibiotic use, as well as facilitate the delivery of on-time chemotherapy doses (Crawford et al., 1991; Gabrilove, 1998; Morstyn et al., 1988; Trillet-Lenoir et al., 1993; Zinzani et al., 1997). Clinical data indicate that delivering the chemotherapy dose on time is important to treatment outcomes in certain tumor types (Bonadonna, Valagussa, Moliterni, Zambetti, & Brambilla, 1995; Kwak, Halpern, Olshen, & Horning, 1990).

One of the main drawbacks of filgrastim is that it is a small protein that is rapidly cleared from the body through the kidneys and requires daily injections. The need to administer daily injections can result in repeated visits to the clinic as well as decrease the number of trips that patients no longer have to rely on caregivers, healthcare providers, or themselves to administer their daily injections. The need to arrange for weekend administration and daily clinic visits is reduced because of the self-regulating nature of the drug.

The Science of Pegylation

The term pegylation refers to the process of attaching a polyethylene glycol (PEG) molecule to another molecule, such as a protein. PEG molecules are pH-neutral, nontoxic, water-soluble polymers that consist of repeating ethylene oxide subunits, each with a molecular weight of 44 daltons (d) and two terminal hydroxyl groups (Bailon & Berthold, 1998). They can be either linear (5–30 kd) or branched (40–60 kd) chain structures. A protein can be pegylated by attaching a single large PEG chain at one site or by attaching several smaller PEG chains at many sites. In the case of pegfilgrastim, a 20 kd PEG chain is covalently attached directly to the N-terminal amino acid of filgrastim. To increase the duration of action, pegfilgrastim, a pegylated form of filgrastim, has been developed and can be administered subcutaneously once per chemotherapy cycle. Once-per-cycle dosing with pegfilgrastim can reduce the number of trips that patients and their caregivers make to the clinic as well as decrease the number of injections that patients must endure as part of their treatment regimen.

Pegfilgrastim also may result in improvements with patient adherence because patients no longer have to rely on caregivers, healthcare providers, or themselves to administer their daily injections. The need to arrange for weekend administration and daily clinic visits is reduced because of the self-regulating nature of the drug.

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