Abstract Neutropenia induced by chemotherapy (CT) is an infection risk factor associated to greater morbidity/mortality and dose-limiting toxicity that on many occasions requires a reduction of the dose of cytostatics or a delay in the administration of treatment. This may have a negative effect on the patient’s quality of life and even diminish the efficacy of the treatment, especially when the intention is to cure or prolong survival. Management of treatment or prophylaxis of grade 3–4 neutropenia and febrile neutropenia with myeloid growth factors (CSF) varies very much in clinical practice, both in the time of starting treatment and the types of patients it is given to. The need to generalise and facilitate practice based on clinical evidence has led the Spanish Society of Medical Oncology (SEOM) to prepare clinical practice guidelines on the use of myeloid growth factors.

Keywords Neutropenia · Febrile neutropenia · Myeloid growth factors · G-CSF · Clinical practice guidelines · Filgrastim · Pegfilgrastim

Introduction

For years, myelosuppression associated to chemotherapy (CT) has been a major limitation of patient tolerance to antineoplastic treatment. Moreover, the clinical consequences of this myelosuppression (increased risk of infection leading to greater morbidity and mortality, rise in hospital admissions, reduction of cytostatics dose or delayed administration of CT) can have a negative effect on the quality of life of patients or even diminish treatment efficacy and patient survival.

At present, there are molecules capable of stimulating growth, survival and differentiation of the myeloid progenitor cells, as well as functional activation of their mature cells. This family of molecules is called haematopoietic growth factors (hGFs), colony-stimulating factors (CSFs) or haematopoietic cytokines. Table 1 shows all recombinant human myelopoietic growth factors approved by the Food and Drug Administration (FDA) and/or the European Medicines Agency (EMA) for clinical use.

Benefits of treatment with CSF

From the randomised clinical trials with CSFs and the various meta-analyses conducted, we can conclude the following about adjuvant therapy with CSF:

- It reduces the incidence, duration and severity of CT-induced neutropenia in solid and haematological tumours (small lung cancer, breast cancer, sarcomas and non-Hodgkin’s lymphomas) [1–4].
- It allows the administration of full doses of CT, the possibility of completing the number of cycles planned, and increasing the intensity or density of doses, improving therapeutic response, tumour control and survival of patients with breast cancer [5, 6], high-grade lymphomas [7], lung cancer [8] and ovarian cancer [9].
- It reduces the cost of febrile neutropenia (FN) by diminishing the number of hospitalisations and the...
Two meta-analyses [12, 13], of studies published up to 2007, confirmed the efficacy of prophylaxis with CSFs in diminishing the rate of infections and the risk of neutropenia and FN during CT, but no significant benefit was found in terms of tumour response and survival.

Another meta-analysis [14], of 17 randomised clinical trials and 3493 patients with solid tumours and lymphoma, shows that primary prophylaxis with G-CSF reduces the risk of FN (RR: 0.54; CI 95%: 0.43–0.67); increases the intensity of the CT dose administered (difference of 8.4%; p=0.001); and, for the first time, reduces the risk of death related to infection (RR=0.55; CI 95%: 0.33–0.90) and the risk of early death during CT (RR=0.60; CI 95%: 0.43–0.83).

The need for support with G-CSF must be evaluated individually before each cycle of CT in order to assess the overall risk of FN. This assessment must take into account not only the type of CT but also individual patient factors that may increase the risk of FN and the aim of the treatment to be administered. This assessment process can be conducted in four steps (Fig. 1):

**Use of CSFs to support conventional chemotherapy**

The use of CSFs to support CT may have a prophylactic purpose, to prevent the onset of FN, or a therapeutic one, to treat an episode of FN documented in a patient who has not received CSFs previously.

**Primary prophylaxis**

This is defined as the use of CSFs to prevent the onset of FN during the first cycle of CT, when no episode has yet occurred, based on the risk of suffering an episode of FN (see Table 2, Fig. 1).