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Duration of Therapy of Colony Stimulating Factors in Oncology

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Abstract

BACKGROUND: According to ASCO Guidelines, the optimal duration of administration for colony-stimulating factors (CSFs) has not been clearly established. Yet, long-acting forms are being developed with a suggested duration equivalent to 10 daily doses. Long-acting forms may result in unnecessary drug exposure and cost of therapy.

PURPOSE: To better understand how long-acting forms might fit into the current treatment paradigm, we studied the duration of administration of CSFs in patients receiving chemotherapy.

METHODS: We conducted a retrospective review of randomly selected medical records from 278 oncologists and hematologists. Data were analyzed to quantify the duration of CSF administration, stratified by CSF, cycle of chemotherapy, reason for administration (prophylaxis or treatment), cancer type, and treatment setting.

RESULTS: 1,112 patient records were reviewed (264 receiving GM-CSF and 848 receiving G-CSF). The most common cancer types were breast (20%), lymphoma (12%), non-Hodgkin's lymphoma (12%), and lung (11%). The CSFs were used either for prophylaxis (66%) or treatment (34%). The overall mean duration of CSF administration was 7.7-8.3 days, depending on the cycle when CSFs were used. Results are also presented for stratification by cycle, prophylaxis versus treatment, cancer type, and treatment setting.

CONCLUSION: The mean duration of CSF administration was generally in the range of 7-8 days, regardless of the stratification, with little variation between GM-CSF and G-CSF.

Purpose

The purpose of this study was to examine timing and duration of CSF treatment schedules of patients receiving chemotherapy and to compare G-CSF (filgrastim, Neupogen®) and GM-CSF (sargramostim, Leukine®) on mean days of administration by cycle of chemotherapy, purpose (prophylaxis versus treatment), cancer type (breast, lymphoma, lung) and site of CSF administration (inpatient or outpatient).

Background

- Granulocyte colony-stimulating factor (G-CSF - filgrastim or Neupogen®) and granulocyte macrophage colony-stimulating factor (GM-CSF - sargramostim or Leukine®) stimulate proliferation and differentiation of hematopoietic progenitor cells.
- A major use of these drugs is to treat neutropenia associated with cancer chemotherapy, and to promote hematopoietic recovery following high dose chemotherapy.
- Optimal timing and duration of CSF administrations is a vital component of the treatment process.
- The CSF Clinical Practice Guidelines, published by the American Society of Clinical Oncology¹, address the initiation, dose, and duration of administration. However, they also suggest that the optimal timing and duration need to be further investigated.

Methods

- Oncologists and hematologists randomly selected from a list provided by the American Medical Association were contacted during the Autumn of 2001 and asked to participate.
- Up to five follow-up contacts were made with initial non-responding physicians to enhance study participation.
- A total of 278 physicians agreed to participate (163 in national probability sample and 115 in quota sample).
- Physicians who agreed arranged for the retrospective review of the charts of a randomized selection of up to four of their CSF patients.
- Data were recorded on pre-approved case report forms and returned by fax or mail.

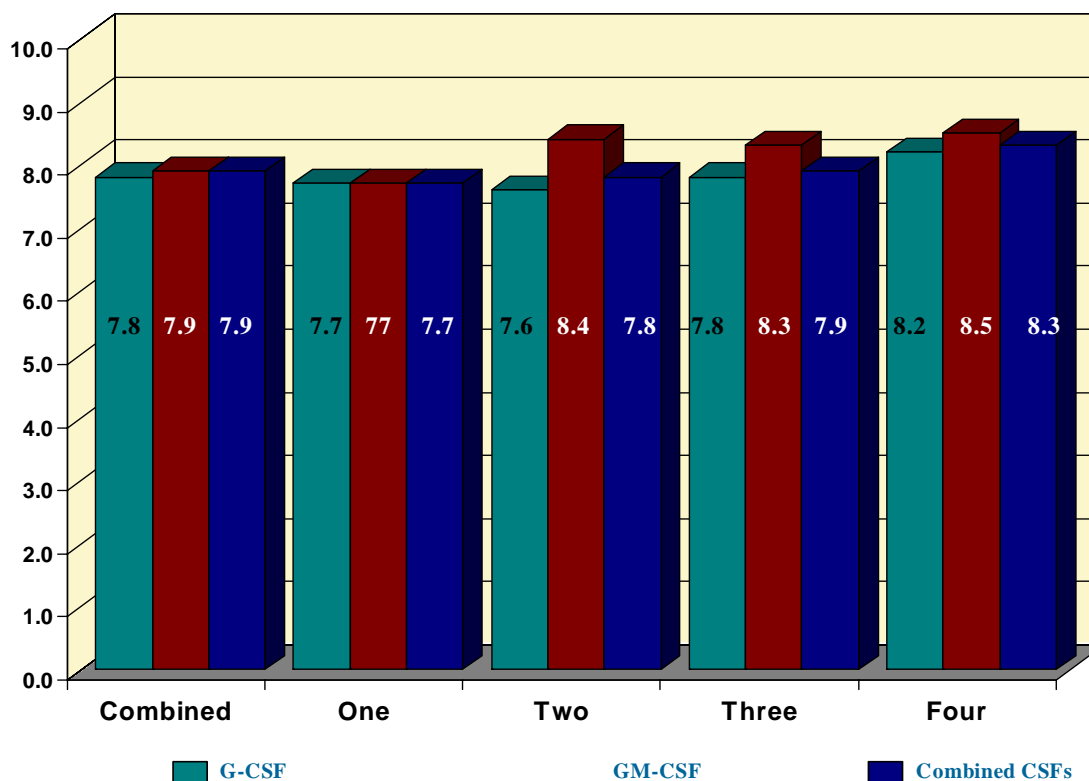
Methods (*cont.*)

- Data were collected on 1112 patients (264 receiving sargramostim and 848 receiving filgrastim).
- Data were analyzed to quantify the mean days of administration by CSF used, cycle of chemotherapy, cancer type, purpose for CSF administration (prophylaxis or treatment), and site of CSF administration (inpatient or outpatient).
- The t test for independent means and the one-way analysis of variance were used to make statistical comparisons (differences beyond the 0.05 level of confidence considered statistically significant).
- Definition of CSF prophylaxis and active CSF treatment as used in study:
- Over-sampling of some strata was required. Over-sampling cases were provided by physicians in the quota sample. Data were adjusted correspondingly (for example, data from the probability sample were used to determine mean duration).
 - CSF prophylaxis = administering CSF 24-48 hours after last chemotherapy drug administered but before nadir.
 - CSF treatment = administering CSF only after patient has developed neutropenia or to actively treat infection.
- Outpatients were characterized as patients in all settings of CSF administration other than a hospital inpatient setting.

Results

- The most common cancer types were breast (20%), lymphoma (12%), non-Hodgkin's lymphoma (12%), and lung (11%).
- Approximately 80% of patients in both groups received daily, flat doses.
- The mean daily dose for sargramostim was 421 mcg; for filgrastim it was 385 mcg.
- The overall mean duration of CSF administration ranged from 7.7-8.3 days, depending on cycle.

Mean CSF Duration (Days) Per Cycle



Mean and Median CSF Duration (Days) Per Cycle

Parameter	G-CSF		GM-CSF		Combined	
	Mean	Median	Mean	Median	Mean	Median
By Cycle						
Cycle 1	7.7	7	7.7	7	7.7	7
Cycle 2	7.6	7	8.4	7	7.8	7
Cycle 3	7.8	7	8.3	7	7.9	7
Cycle 4	8.2	7	8.5	7	8.3	7
All Cycles Combined	7.8	7	7.9	7	7.9	7
By Tumor Type						
Breast	8.0	7	7.6	7	8.0	7
Lymphoma	7.6	7	10.8	10	7.6	7
Lung	7.7	7	7.0	7	7.7	7
By Reason						
Prophylaxis	8.0	7	8.6	8	8.2	7
Treatment	6.9	6	6.6	5	6.9	6
By Site						
Inpatient	7.7	7	8.2	7	7.8	7
Outpatient	8.2	7	8.7	7	8.3	7

Conclusions

- The mean duration per cycle of CSF used with patients receiving chemotherapy was 7.9 days for all cycles combined. The median duration was 7 days.
- The mean and median duration per cycle was similar for both CSFs.
- Both the mean and median duration per cycle were significantly greater for CSF prophylaxis (8.2 days +/- 0.25 [n = 667]) compared to active CSF treatment (6.9 days +/- 0.42 [n = 347]) .
- Neither the mean nor the median duration per cycle for three selected cancer types (breast, lymphoma, and lung) were statistically different. However, the mean duration per cycle for sargramostim-treated lymphoma patients (10.8 days +/- 1.91 [n = 43]) days) was greater than for filgrastim-treated lymphoma patients (7.6 days +/- 0.52 [n = 215]). This could be due to the aggressiveness of either the tumor growth or the chemotherapy regimen.
- Neither the mean nor the median duration per CSF cycle differed significantly for inpatients versus outpatients.

References

1. Ozer H, Armitage JO, Bennett CL, et al. 2000 Update of recommendations for the use of hematopoietic colony- stimulating factors: evidence-based clinical practice guidelines. *Journal of Clinical Oncology* 2000 (October 15);18(20):3558-3585