EFFECT OF PREVENTIVE ADMINISTRATION OF GRANULOCYTE COLONY-STIMULATING FACTOR (FILGRASTIM) ON DOSE INTENSITY IN NEOADJUVANT CHEMOTHERAPY FOR HEAD AND NECK CANCERS.

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PURPOSE

In a pilot study among head and neck cancer patients receiving a neoadjuvant chemotherapy we tested the possible role of preventive administration of granulocyte colony-stimulating factor in the search of optimal dose intensity.

RATIONALE (1)

Effectiveness of cancer chemotherapy correlates to a large extent with dose intensity. A positive correlation with response rate and survival time has been demonstrated in breast cancer but also e. g. in lymphomas as well as in lung, colon, ovarian carcinomas

(Hryniuk, Levin, Bonadonna,...).

An influence on response rate was noticed in some series of neoadjuvant chemotherapy for head and neck cancers

(Greenberg, Deneufbourg).

RATIONALE (2)

In the treatment of head and neck cancer, neoadjuvant chemotherapy is used to select patients curable by exclusive radiotherapy rather than by mutilating surgery.

As part of such an organ preservation strategy, chemotherapy should meet several requirements :

-effectiveness to induce a major response of primary tumour and nodes,

- acceptable toxicity not to delay nor jeopardize the radical treatment,

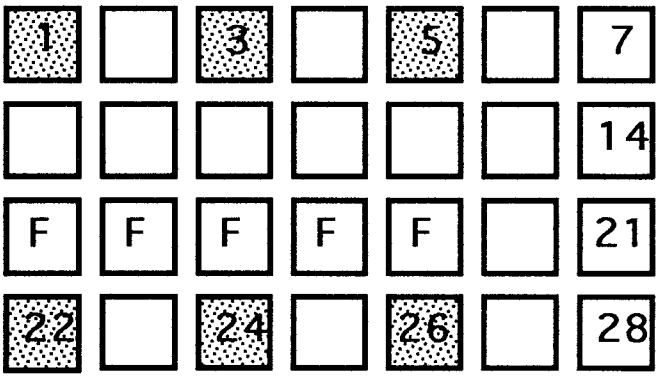
- optimal duration to prevent potential accelerated repopulation of tumour clonogens in responders and minimize disease progression in non responders.

PATIENTS

	Study group	Control group
cases	27	47
males/females	20/7	35/12
age mean	57	61
range	30-76	43-86
oropharynx	12	22
hypopharynx	6	9
oral cavity	6	11
other sites	3	5

METHODS

CHEMOTHERAPY



at each treatment day :

B	bleomycin (10 mg)
V	etoposide (100 mg/m^2)
P	cis-platinum (20 mg/m^2)
FU	fluorouracil (750 mg/m^2)

in a 3 hours perfusion
on ambulatory mode

GRANULOCYTE STIMULATING FACTOR

Filgrastim 5 microgm/kg/day
consecutively on days 15 to 19

RESULTS (1)

PROTRACTION OF CHEMOTHERAPY (per cent of cases)

Filgrastim group	Control group
11	63

$p < 0.001$
($X2 = 19.29$ for 1 degree of freedom)

PROTRACTION OF CHEMOTHERAPY (days)

	Filgrastim group	Control group
range	2-7	1-17
median	3	7
mean	4±3	9±4

$p < 0.05$
($t = 2$ for 31 degrees of freedom)

RESULTS (2)

DURATION OF CHEMOTHERAPY (days)

	Filgrastim group	Control group
range	23-33	24-43
median	26	33
mean	26±2	31±5

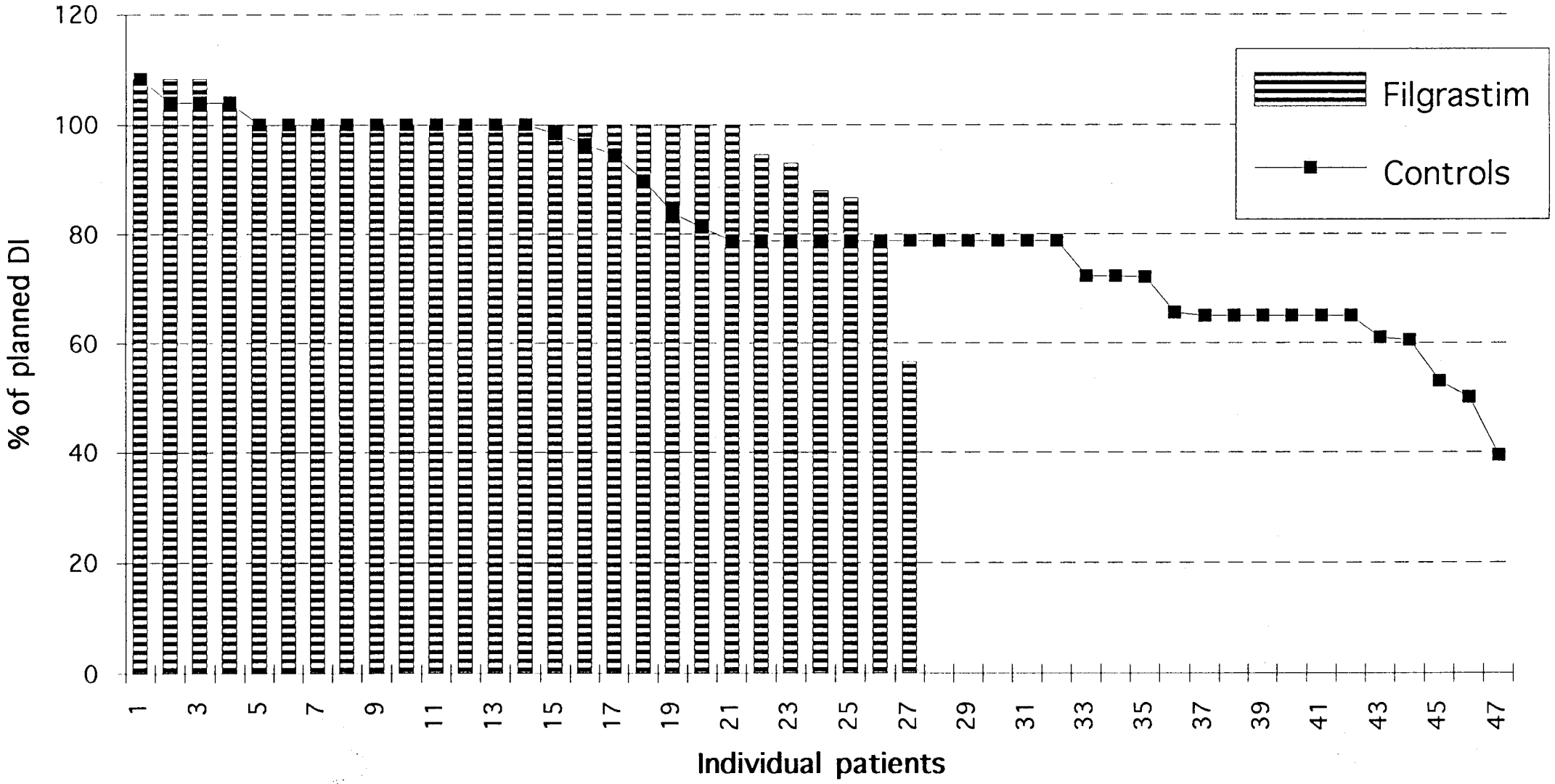
$p < 0.001$
($t = 4.99$ for 72 degrees of freedom)

DOSE INTENSITY (% of planned DI)

	Filgrastim group	Control group
range	56-108	39-108
median	100	79
mean	97±10	82±17

$p < 0.001$
($t = 4.31$ for 72 degrees of freedom)

DOSE INTENSITY PROFILE



SUMMARY AND CONCLUSIONS

In a pilot study among 27 head and neck cancer patients we tested the role of preventive administration of granulocyte colony-stimulating factor in the course of a neoadjuvant chemotherapy used in a strategy of organ preservation. Filgrastim at the dose of 5 mcg/kg/day was injected on days 15 to 19 of a single cycle chemotherapy administered on days 1,3,5 and 22,24,26 (bleomycin 10 mg, etoposide 100 mg/m^2, cis-platinum 20 mg/m^2 and fluorouracil 750 mg/m^2 at each injection). Parameters of dose intensity were compared with 47 cases having received the same treatment without growth factor support. 11% of Filgrastim treated patients required a protraction of chemotherapy as opposed to 63% of controls; mean extension 4 days instead of 9 days. The mean delivered dose intensity amounts to 97% of planned DI as compared to 82% in controls, the median delivered DI being equal to 100 instead of 79. Preventive administration of Filgrastim allows to reach an optimal dosing and timing of the neoadjuvant chemotherapy. This should normally correlate with a higher effectiveness to induce a major response at the lowest toxicity level and should prevent the radical treatment from undue delay. Discriminant analysis of hematological parameters will be performed to select cases needing growth factor support in order to optimize the organ preservation strategy at the best possible cost to benefit ratio.