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Letter to the editor

Upfront chemohormonal therapy for prostate cancer: Neutropenia and G-CSF Use

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Dear Editor,

a great interest has rightly been reserved to the article recently published by Sweeney et al in the New England Journal of Medicine (1) about the results of CHAARTED study. The potential introduction of a new standard, anticipating chemotherapy to the hormone-sensitive phase of metastatic prostate cancer, undoubtedly requires careful consideration of the treatment cost-effectiveness.

We noticed the toxic effects of docetaxel in combination with androgen-deprivation therapy (ADT), surprisingly observing an haematological toxicity much lower than expected. The reported rate of overall severe neutropenia of 18.2%, including both G3-4 neutropenia (12.1%) and febrile neutropenia (FN, 6.1%), result to be definitely lower when compared with those of similar studies and pivotal trials for docetaxel in castration-resistant prostate cancer (CRPC) (Table 1).

Table 1. Docetaxel in CRPC and Neutropenia

Study	Setting	Median Age	PS	Treatment Schedule	G3-G4 Neutropenia	Febrile Neutropenia	Overall Neutropenia	G-CSF Use
CHAARTED Sweeney et al, 2015 (1)	HSPC	64	70% PS=0 29% PS=1	ADT + Docetaxel 75 mg/m^2 every 3 weeks	12.1%	6.1%	18.2%	At the discretion of the investigator†
GETUG-AFU15 Gravis et al, 2013 (2)	HSPC	63	100% Karnofsky score 90-100	ADT + Docetaxel 75 mg/m^2 every 3 weeks	32%	7%	39%	recommended* use of G-CSF
Petrylak et al, 2004 (3)	CRPC	70	90% PS=0-1	Docetaxel 60-70 mg/m^2 + 280 mg Estramustine every 3 weeks	16%	5%	21%	NR
Tannock et al, 2004 (4)	CRPC	68	87% Karnofsky score >70%	Docetaxel 75 mg/m^2 every 3 weeks	32%	3%	35%	G-CSF allowed for

* monitoring committee recommended G-CSF while the study was still ongoing due to two neutropenia-related deaths in the ADT plus docetaxel group
†Not reported how many patient received G-CSF.
HSPC = hormone-sensible prostate cancer; CRPC = castration resistant prostate cancer;
G-CSF = granulocyte colony-stimulating factor; PS = performance status; NR = not reported; FN = febrile neutropenia

In the analogous study by Gravis et al, the rates of neutropenia had an overall incidence of 39% (32% G3-4 neutropenia and 7% FN) and two neutropenia-related deaths occurred in the ADT plus docetaxel group; noteworthy, these findings lead to the data monitoring committee recommendation for use of granulocyte colony-stimulating factor (G-CSF) (2).

Again, in the MINSAIL trial, Petrylak et al reported 16% of G3-5 neutropenia and 5% of FN (21% overall) in the treatment arm with docetaxel plus estramustine. Of note, the doses of docetaxel in this study were lower than those of the CHAARTED trial and no informations were provided about the possible use of G-CSF in the study population (3).

Similarly, in the study by Tannock et al, the same docetaxel schedule of the CHAARTED has resulted in a rate of 35% among G3-4 neutropenia (32%) and FN (3%); treatment with G-CSF was allowed for patients with FN (4).

Overall, in the current study the rates of neutropenia are about half of those expected: nevertheless, no comment in this regard was made by the authors and data about the prophylactic or therapeutic use of G-CSF in the experimental arm were not provided. Even assuming an influence of the younger median age (64 years), of the good performance status (70% ECOG PS = 0) respect to those usual for CRPC patients and of a limited number of administered chemotherapy cycles (a maximum of six), to justify such a better tolerability of treatment we wonder whether the use of prophylactic G-CSF may have had a decisive role in the low hematological toxicity.

Considering the CHAARTED as a landmark study, whose data are powerful enough to modify clinical practice in prostate cancer, we definitely need more detailed "instructions for use" to better apply these promising results to patient care in real life.

References

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