

## Impact of Chemotherapy Dose Intensity on Cancer Patient Outcomes

Lyman GH, *J Nat Compr Canc Netw*. 2009;**7**:99-108.

Relative dose intensity (RDI) is defined as the ratio of the actually delivered dose intensity (dose per body surface area per time) to a standard dose intensity, for example as determined in clinical trials. Reductions in chemotherapy dose intensity have been reported to compromise progression free and overall survival in early-stage and advanced cancer, both in prospective and retrospective studies. Data from early-stage breast cancer patients and a large study in unselected cancer patients identified the critical RDI as approximately 85%, with significantly worse survival in patients receiving a lower RDI. Attempts to increase RDI by using dose-dense regimens with a compressed chemotherapy cycle length have shown promising results in breast cancer and Non-Hodgkin lymphoma, further emphasising the importance of RDI.

In normal clinical practice, reductions in RDI are a major reason for treatment failure in patients with chemoresponsive cancer. A number of studies report up to 30% of patients having received planned RDIs  $\leq$  85%. This practice often occurs in obese patients, in whom dose calculations are often based on ideal rather than actual body surface area, and in the elderly, even though elderly patients have been shown to tolerate standard chemotherapy if appropriate support is given.

The most common dose-limiting toxicities causing unplanned reductions in RDI are febrile neutropenia (FN) and neutropenic complications following myelosuppressive chemotherapy. FN is considered a medical emergency usually requiring hospitalisation, with an inpatient mortality rate of about 10% and high associated costs for health care systems. For several types of cancer, a strong correlation between severe neutropenia and clinical efficacy of chemotherapy, in terms of improving progression-free and overall survival, has been observed. Myelosuppression can thus be considered a surrogate for chemotherapy dose intensity.

Chemotherapy dose delays are most commonly observed in patients with insufficient neutrophil recovery; dose reductions are normally the consequence of severe neutropenia or FN. This may be necessary in very vulnerable patients or in the palliative setting, where quality of life should be optimised; however, the strong evidence supporting the importance of full dose intensities for cancer patient outcomes should be considered.

Granulocyte colony-stimulating factor (G-CSF) has been shown to reduce the severity and duration of neutropenia following myelosuppression. Several clinical trials have demonstrated that patients receiving G-CSF experience significantly higher RDIs. Moreover, growth factor support has proven to be beneficial in dose-dense regimens and for elderly patients, by enabling administration of full chemotherapy as planned.

In all patients with potentially curable cancers, the delivery of full chemotherapy dose intensity should be a goal and can be considered an important process measure of quality cancer care.

<http://www.ncbi.nlm.nih.gov/pubmed/19176210>

You can contact the INC-EU co-ordinating centre at: [info@inceu.org](mailto:info@inceu.org)  
Telephone: +41 (0) 41 377 48 39 Fax: +41 (0) 41 377 48 35