



# Neutropenia Management with Neulasta®

Presented at the 2003 ASH Meeting

The 2003 ASH meeting contained several abstracts pertaining to growth colony stimulating factors, in particular pegfilgrastim. Results were presented on clinical trials with pegfilgrastim in chemotherapy regimens administered in less than 21-day regimens. Currently, pegfilgrastim is approved as a single subcutaneous injection of 6 mg once per chemotherapy cycle that is administered 24 hours following chemotherapy, but not within the 14 days prior to the next cycle.

Dose-dense regimens represent a newer approach to cancer treatment in which patients receive standard doses of chemotherapy on a condensed 14-day cycle, as opposed to traditional 21-day or 28-day regimens. Shortening the intervals between standard doses of chemotherapy limits the amount of time the tumor can re-grow between treatment cycles. However, colony-stimulating factors are typically needed to help protect patients from neutropenic complications, including neutropenia with

**In summary both these studies suggest that risk models can be useful to identify patients most likely to benefit from early use of colony-stimulating factors beginning within the first cycle of chemotherapy.**

fever and prolonged severe neutropenia, in these dose-dense regimens.

## Potential Safety Issues

The first study [Abstract #1918] addressing potential safety issues with more frequent administration of pegfilgrastim was a retrospective analysis evaluating the relationship between pegfilgrastim serum concentration and absolute neutrophil count (ANC) data from six clinical studies in patients with non-myeloid malignancies

receiving myelosuppressive chemotherapy. The analysis showed that pegfilgrastim serum concentrations decrease as the number of WBCs increase, which is consistent with the products self-regulating clearance. The study found that once the postnadir ANC recovers to  $\geq 1 \times 10^9/L$ , pegfilgrastim concentrations are negligible and pose a minimum risk of over-stimulating WBC production, potentially allowing the drug to be administered as early as the twelfth day after the previous dose. Further clinical studies are planned to confirm these pharmacokinetic findings.

## CHOP and pegfilgrastim in Patients Over Age 60

One Phase 2 study [Abstract # 2348] evaluated CHOP given every 14 days with pegfilgrastim support in previously untreated aggressive NHL patients over age 60. The interim analysis of the first 26 patients in this study showed that the full chemotherapy dose was delivered in 86 percent of chemotherapy cycles and treatment was delivered as scheduled on day 15 in 88 percent (97/110 occasions) of chemotherapy cycles. Responses to chemotherapy treatment were seen in 20 patients (77 percent), 10 with a complete response and 10 with a partial response. Patients received cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) every 14 days supported by a single 6 mg dose of pegfilgrastim on day two of each treatment cycle. A total of 136 cycles (110 cycles, 2-6) have been administered.

## Dose-Dense CHOP Plus Rituximab

A second Phase 2 study [Abstract # 2365] of 31 previously untreated intermediate grade NHL patients evaluated the use of dose-dense CHOP plus rituximab with a single dose of pegfilgrastim. A total of 194 cycles were administered. Ninety percent of NHL patients completed their dose-dense chemotherapy cycles on schedule. No unexpected toxicities were seen and no delays in neutrophil recovery were found in any of the patients treated with six to eight cycles to date.

## Summary and Findings

In summary these interim analyses suggest that pegfilgrastim, administered once-per-cycle, can safely and effectively facilitate full dose on-schedule of a dose-dense, or every-two-week, chemotherapy regimen in

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