The Effect of Pegylated Granulocyte-Colony Stimulating Factor administration timing after CHOP or CHOP-R regimen administration in Non-Hodgkin's Lymphoma patients on the development of neutropenia


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Introduction

- Granulocyte-Colony Stimulating Factor (G-CSF) or Filgrastim is a humanised cytokine which acts on
  mononuclear stem cells by binding to their specific surface receptors and regulating neutrophil
  production and their progenitors proliferation, and differentiation.
- The Pegylated form is a longer acting agent and is called Pegfilgrastim, that is produced by binding 20-
  kD of monomethyleneoxypolyethylene glycol molecule to the N-terminal methionyl residue of filgrastim.
- They both used to prevent or reduce the risk of development of neutropenia post myelosuppressive
  chemotherapy.
- Clearance of Pegfilgrastim is almost entirely via a saturable neutrophil receptor-mediated clearance
  (self-regulation).
- Pegfilgrastim serum clearance decreases with increasing doses, and it is directly related to the number
  of neutrophils (Product Info NEULASTA®).
- Furthermore, serum concentrations of the drug remain elevated during chemotherapy-related
  neutropenia, and it falls rapidly at the onset of neutrophil recovery.
- Pegfilgrastim is also thought to increase sensitivity of rapidly-dividing myeloid cells and might cause
  excessive cytopenias if administered concomitantly with chemotherapy.

Aim

The aim of this study is to assess the effect of administration timing of the Pegfilgrastim on the development of neutropenic episodes, infections and hospital admission in relation to CHOP or CHOP-R regimen administration timing in patients with NHL.

Treatment regimens

CHOP and CHOP-R
- CHOP is a standard regimen to treat aggressive NHL.
  This regimen, with the addition of Rituximab, is called CHOP-R and is the standard treatment to
  treat Diffuse Large B-Cell Lymphoma (DLBCL).
- Both regimens consist of Cyclophosphamide 750mg/m², Doxorubicin 50mg/m², Vincristine
  1.4mg/m² (maximum dose is 2mg) all given intravenously on Day 1 of the cycle and also
  Prednisolone 100mg orally given on Day 1 to Day 5.
- When Rituximab is added in CHOP-R, its dose is
  375mg/m² either on D1 or D2 of the cycle
- The original regimen is repeated every 21 days (CHOP 21 or CHOP-R 21) for 6-8 cycles.
- It can also be repeated every 14 days (CHOP 14 or CHOP-R 14) known as “intensified
  regimen”.
- It is worth noting that intensified regimen is only made possible with the introduction of
  Pegfilgrastim into the treatment cycle traditionally on the following Day (D2).

Method

- The study is a retrospective analysis to patients’ records who were admitted to Hollywood Private
  Hospital during January 2010 to March 2011.
- Twenty four patients aged between 40-80 years with NHL received Pegfilgrastim immediately after
  CHOP or CHOP-R chemotherapy (D1, Group A) or ≥ 24 hours post treatment (D2, Group B)
  were included in the study.
- Those patients received a total of 117 cycles of CHOP-like regimen followed by Pegfilgrastim.
- Group A had 60 pt-cycles and Group B had 57 pt-cycles with similar demographics.
- Any neutropenia (ANC<1.5x10⁹/Cell/cc), febrile neutropenia (ANC<0.5x10⁹/Cell/cc with temperature
  38°C or above), infection episodes and related hospital admissions were documented.
- The frequency of these episodes between the two groups was then analysed.

Neutropenia
- Neutropenia is one of the main adverse
  reaction to CHOP and CHOP-R regimens.
- It has a significant morbidity and mortality on patients with NHL (Grade V).
- Febrile neutropenia is a life threatening condition that usually affect patients on
  myelosuppressive chemotherapy (CHOP or CHOP-R).

Results and discussion

- Evidences have proven the importance of the use of GCSF (Pegfilgrastim) primary prophylaxis for
  patients treated with myelosuppressive regimen (i.e. CHOP or CHOP-R).
- The Pegfilgrastim use has shown to reduce the duration and extent of neutropenia and febrile neutropenia with those
  regimens.
- This study has confirmed the need to space the dosing of Pegfilgrastim to at least 24 hours post chemotherapy to
  reduce adverse events; as proven by the significant increase of those events of total neutropenia (mild or grade V (i.e. FN)),
  hospital admissions due to infections and the total events (neutropenia and infections) in the immediate administration
  group (Group A <24 hours post chemotherapy).

Conclusion

In association with other evidences, Pegfilgrastim, should be administered at least 24 hours post CHOP or CHOP-R regimen for patient with NHL to reduce episodes of the neutropenia (Grade II-V) hospital admissions (due to neutropenia and infections) and all adverse events (infection and neutropenia) and NOT immediately post chemotherapy.

Data

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<tr>
<td>Admission</td>
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Summary

International Guidelines recommend the administration of Pegfilgrastim as follows

- CHOP regimen: 1.4mg/m² was administered 24 hours before the beginning of chemotherapy.
- CHOP-R regimen: 1.4mg/m² was administered 24 hours prior to the start of chemotherapy.
- CHOP: 1.4mg/m² was administered on Day 1 of the cycle.
- CHOP-R: 1.4mg/m² was administered on Day 2 of the cycle.

Tables Provided

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References