Government of **Western Australia**
Department of **Health**
South Metropolitan Area Health Service

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 marrow hematopoietic cells by binding to their specific surface receptors and regulating neutrophils 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 monomethoxypolyethylene 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/m^2 , Doxorubicin 50mg/m^2, Vincristine 1.4mg/m^2 (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/m^2 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).

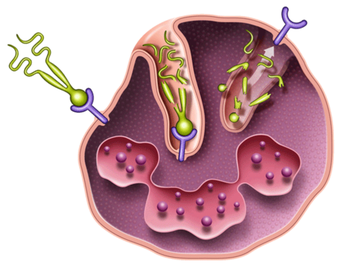
Neutropenia

- 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).

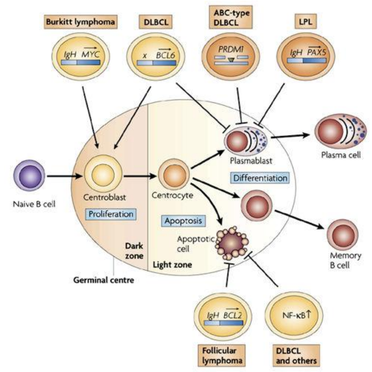
Method

- 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<1.5x 10^9 Cell/cc), febrile neutropenia (ANC <0.5x 10^9 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.

Neulasta MOA



Molecular mechanisms promoting B-cell lymphomagenesis



Data

Summary

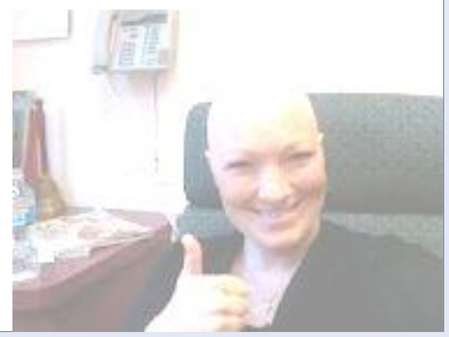
Item	Group A (D1)	Group B (D2)	Total
Women-cycles	13 cycles	13 cycles	26 cycles (6 women)
Men-cycles	47 cycles	44 cycles	91 cycles (18 men)
Pt-cycles	60	57	117 with peg
Neutropenia	8	4	12
Febrile neutropenia	8	2	10
Infection	4	1	5
Admission	12	3	15

Analysis

Item	Group A	%age	Group B	%age	P value (Two tailed paired test)
Neutropenia	8	13.33	4	7.02	0.364 (NS)
Febrile neutropenia	8	13.33	2	3.51	0.095 (trend)
Total neutropenia	16	26.67	6	10.53	0.033 (significant)
Infection	4	6.6	1	1.75	0.365 (NS)
Admission	12	20	3	5.26	0.025 (significant)
All events	20	33.33	7	12.28	0.008 (significant)

Results and discussion

- Evidences have proven the importance of the use of GCSF (Pegfilgrastim) primary prophylaxis for patients treated with myelosupprive 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 24hours 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.

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