Supportive Care in Cancer

Efficacy and safety of lipegfilgrastim versus pegfilgrastim in elderly patients with aggressive B-cell non-Hodgkin lymphoma (B-NHL): Results of the randomized, open label, non-inferiority AVOID neutropenia study neutropenia study

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Supplementary Table S1. Overview of key study inclusion and exclusion criteria

Inclusion criteria	Age 65–85 years
	Histological documentation of aggressive B-cell NHL
	Planned to receive systemic anticancer therapy with at least 6 cycles of R-CHOP21, according to local standards
	Eastern Cooperative Oncology Group [ECOG] performance status ≤2
	Life expectancy ≥3 months
	Adequate bone marrow, renal, and hepatic function as evidenced by the following within 14 days before start of chemotherapy: • Absolute neutrophil count ≥1.5 x 10^9/L • Platelets ≥100 x 10^9/L • Hemoglobin ≥9.0 g/dL • Serum creatinine ≤1.5 x upper limit of the normal range (ULN) OR glomerular filtration rate ≥30 mL/minute/1.73 m^2 • Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤2.5 x ULN • Bilirubin ≤1.5 x ULN • Alkaline phosphatase ≤2.5 x ULN
Exclusion criteria	Participation in a clinical study ≤30 days before randomization
	Chemotherapy within the past 3 months (a pre-phase to reduce tumor burden prior to start of R-CHOP was allowed)
	Any major surgical procedure, open biopsy, or significant traumatic injury within 28 days of start of chemotherapy
	Active cardiac disease or uncontrolled hypertension
	Arterial or venous thrombotic or embolic events such as cerebrovascular accident (including transient ischemic attacks), deep vein thrombosis or pulmonary embolism within 6 months before start of chemotherapy
	Ongoing infection or known history of human immunodeficiency virus (HIV) infection, tuberculosis, or chronic hepatitis B or C
	Evidence or history of bleeding diathesis
	Non-healing wound, ulcer, or bone fracture
	Renal failure requiring hemodialysis or peritoneal dialysis
	Treatment with lithium at screening or planned during the study
	Any other conditions that could interfere with study participation or evaluation of the study results

Supplementary Table S2. Summary of observed absolute neutrophil count ($x10^9$/L) during cycle 1 (per-protocol population)

Absolute neutrophil count ($x10^9$/L)	**Lipegfilgrastim (N=41)**	**Pegfilgrastim (N=44)**
Baseline, n	41	44
Mean (SD)	8.0 (2.55)	8.1 (2.67)
Median (range)	8.2 (2.2–14.7)	7.8 (3.2–13.8)
Day 1, n	34	35
Mean (SD)	5.4 (2.43)	6.1 (2.49)
Median (range)	5.2 (1.2–13.5)	5.6 (2.1–13.1)
Day 3, n	40	40
Mean (SD)	8.6 (2.43)	9.2 (5.75)
Median (range)	8.5 (2.2–14.7)	8.8 (3.2–40.7)
Day 5, n	40	44
Mean (SD)	29.8 (11.20)	29.6 (10.39)
Median (range)	28.6 (5.7–64.6)	30.1 (8.7–52.1)
Day 8, n	41	42
Mean (SD)	2.6 (5.30)	2.6 (3.40)
Median (range)	1.0 (0.1–32.7)	0.9 (0.1–14.9)
Day 10, n	38	42
Mean (SD)	2.3 (2.51)	1.5 (2.27)
Median (range)	1.3 (0.1–9.5)	0.9 (0.0–11.5)
Day 12, n	39	43
Mean (SD)	8.4 (6.36)	4.8 (3.45)
Median (range)	6.3 (1.4–32.6)	4.0 (0.0–15.9)
Day 15, n	40	43
Mean (SD)	10.1 (4.47)	7.5 (3.95)
Median (range)	9.6 (2.5–22.9)	6.5 (1.7–18.1)

SD, standard deviation

Supplementary Table S3. Overview of adverse events (safety population)

Number of patients, *n* (%)	**Lipegfilgrastim (N=46)**	**Pegfilgrastim (N=50)**	**Total (N=96)**
At least 1 AE	45 (98)	49 (98)	94 (98)
Individual AEs reported by ≥30% of subjects in either group			
Constipation	18 (39)	16 (32)	34 (35)
Anemia	13 (28)	20 (40)	33 (34)
Neutropenia	17 (37)	15 (30)	32 (33)
Alopecia	16 (35)	13 (26)	29 (30)
Nausea	10 (22)	19 (38)	29 (30)
Fatigue	12 (26)	16 (32)	28 (29)
Diarrhea	9 (20)	16 (32)	25 (26)
At least 1 treatment-related AE	11 (24)	10 (20)	21 (22)
At least 1 SAE	21 (46)	23 (46)	44 (46)
At least 1 treatment-related SAE	0	0	0
At least 1 AE leading to withdrawal from the study	1 (2)	9 (18)	10 (10)
At least 1 AE leading to death*	2 (4)	5 (10)	7 (7)

AE, adverse event; SAE, serious adverse event.
*Causes of death were general physical health deterioration (1 patient) and NHL (1 patient) in the lipegfilgrastim group, and NHL (3 patients), diffuse large B-cell lymphoma (1 patient) and coma (1 patient) in the pegfilgrastim group. One patient randomized to lipegfilgrastim died before starting study treatment.