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

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Corresponding Author: Hartmut Link, Prof. Dr.
Westpfalz-Klinikum, Klinik für Innere Medizin
Kaiserslautern, GERMANY

E-Mail: hlink@kabelmail.de
### 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 10⁹/L |
|                    | • Platelets ≥100 x 10⁹/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 m² |
|                    | • 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 (x10⁹/L) during cycle 1 (per-protocol population)

| Absolute neutrophil count (x10⁹/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**

|                      | Lipegfilgrastim (N=46) | Pegfilgrastim (N=50) | Total (N=96) |
|----------------------|-------------------------|----------------------|--------------|
| 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.