HEXA*FIL*: Non-Interventional Study for supportive treatment of chemotherapy induced neutropenia with Filgrastim HEXAL®

RESULTS

Patients Demographics: Mean age of the total patient (pt) population was 59.3 years (±12.7), 1125 were female and 344 male pts, with 67.0% women and 47.4% men ≥65 years. Tumors were classified to solid (n=1216) and hematologic tumors (n=253). The three main entities were breast (n=846), non-Hodgkin's Lymphoma (NHL, n=207) and lung cancer (n=108), with 73.2% breast cancer, 40.6% NHL and 50.0% lung cancer pts ≥65 years. One third of pts ≥65 years had at least one comorbidity as classified by the Charlson comorbidity score (34.2%, n=189).

Chemotherapy: In total, 3759 Filgrastim supported chemotherapy (Cx) cycles were documented. Supportive treatment of Filgrastim was started for more than half of pts (56.0%) in the first documented Cx cycle, for 18.7% in the second and for 9.3% in the third Cx cycle. One third of pts presented at least one previous Cx treatment (n=475, 32.3%), the other two thirds were Cx naïve (n=994, 67.7%). The present Cx was instituted as neo-adjuvant treatment for 138 (9.4%), adjuvant for 777 (52.9%), and palliative for 491 (33.4%) pts. Furthermore, 193 (13.1%) pts received additional radiotherapy. Most frequently used Cx substances were cyclophosphamide, epirubicin, and docetaxel. The majority of chemotherapy regimens were combination therapies (75.3% of documented Cx cycles vs. 21.9% mono-therapies).

Risk evaluation for febrile neutropenia: Physicians' risk evaluation for febrile neutropenia (applicable for PP/SP patients only, n=1107) stratified 46.8% pts at start of their Filgrastim supported therapy into the high risk (≥20%, n=518), 48.1% pts into the intermediate risk (10-20%, n=533) and 5.1% pts into the low risk (<10%, n=56) group. Main reasons for risk stratification named by physicians were "chemotherapy strategy" (>97%) for all three risk categories followed by "chemotherapy substance" (<10% risk: 51.8%, 10-20% risk: 63.8%, >20% risk: 67.4%), "combination therapy" (<10% risk: 60.7%, 10-20% risk: 44.7%, >20% risk: 40.5%), and "age" (<10% risk: 42.9%, 10-20% risk: 24.2%, >20% risk: 29.3%). A "previous episode of FN" was referred to as reason for risk stratification into intermediate / high risk patient group in 71 cases (10-20% risk: 3.9%, >20% risk: 9.7%).

Filgrastim therapy: Filgrastim treatment was intended for 42.7% (n=627) pts as primary prophylaxis (PP), for 32.7% (n=480) as secondary prophylaxis (SP), and for 24.6% (n=362) as interventional therapy (TX). According to risk categories for development of neutropenia, primary prophylaxis was applied to 28.6% of low risk pts (<10% risk, n=16), 55.7% of intermediate risk pts (risk 10-20%, n=297) and 60.6% of high risk pts (risk >20%, n=314).

The median duration of Filgrastim application for all pts (n=1469) and PP pts (n=627) was 5 days, while the median Filgrastim duration for SP and TX pts was 3 days, respectively. According to tumor type (breast cancer, lung cancer, NHL) the median duration of Filgrastim application was 5 days. The duration of Filgrastim therapy did not differ between physicians' prescription and patients' application (mean days 4.4 vs 4.3, n=1457 and 987, respectively).

EFFICACY RESULTS: In total, 3643 Filgrastim supported Cx cycles with complete data were available for efficacy analysis. Percentages refer to the total number of Cx cycles (n=3643).

- 3297 (90.5%) out of 3643 documented Cx cycles were administered without modifications (i.e. dose modification, substance discontinued, or change of substance).
- In 237 Cx cycles (6.5%) neutropenic complications occurred.
- Main categories of neutropenic complications were infections (3.2% of Cx cycles, where this information was documented), followed by fever and chills.
- In total, 109 Cx cycles (3.0%) were modified due to neutropenic complications with comparable rates for all intentions and the main three tumor types.

- Febrile neutropenia was documented for 45 cycles and occurred slightly more often in lung cancer (3.6% vs. 1.2% overall; NHL: 1.5 %; breast: 1.1%).
- 2.4% of pts (n=35, 17 PP, 11 SP, 7 TX) were hospitalized for neutropenic complications with a median duration of 7 days in case of PP and SP, and 3 days in case of TX.

Of patients without baseline leukopenia at the first documented Cx cycle, 47.4% (n=927) developed grade 3/4 leukopenia at nadir. According to supportive intention, PP pts without baseline leukopenia developed grade 3/4 at nadir less frequently (35.7%, n=497) than SP pts (51.0%, n=241) and TX pts (73.5%, n=189).

Physicians' evaluation of Filgrastim treatment effectiveness indicated benefits for 93.7% of pts, comparable over treatment intentions (PP: 95.5%, SP: 91.9%, TX: 92.8%). Effectiveness aspects considered most important were "ability to maintain Cx regimen" (80.8%, n=1112), "FN prevention" (71.9%, n=989), "reduction in duration of neutropenia" (36%, n=496), and "reduction in severity of neutropenia" (13.0%, n=179).

SAFETY RESULTS: In 119 (8.1%) pts, the attending physicians reported at least one adverse drug reaction (ADR); the most frequently reported ADR was pain. Three serious adverse events were reported (gastrointestinal pain, drug-related; musculoskeletal pain, drug-related; valvular heart disease, not drug-related).

Most pts (n=956, 89.0%) assessed Filgrastim application and handling of the needle protection system easy or very easy, whereof 563 pts (52.4%) had no previous experience in the self-administration of syringes. Two thirds of pts (n=668, 62.1%) applied Filgrastim without help. Most patients reported no symptoms at the needle puncture site (n=897, 81.8%); 81 (7.5%) reported reddening, 73 (6.8%) hematomas, 29 (2.7%) swellings. Handling, transport, storage, and self-administration of the prefilled syringe were mainly explained by the attending physician (25.7%) or a practice nurse (61.9%).

Physicians assessed tolerance to Filgrastim treatment as very well (47.5%) or well (43.7%).

CONCLUSIONS:

The majority of patients received primary (42.7%, PP) or secondary prophylaxis (32.7%, SP) with the biosimilar Filgrastim; however, 24.6% were treated interventionally (TX, i.e. after having experienced neutropenic complications or a drop in leukocytes putting the patient at acute risk of neutropenic complications). The median duration of Filgrastim application was 5 days. Approximately 90% of all documented Filgrastim-supported Cx cycles could be applied without any modification of the Cx regimen. The rate of Cx cycle modifications due to neutropenic events was generally low (3.0%) with small differences (2.8-4.0%) for filgrastim intention and tumor types.

With regard to Filgrastim therapy intention, patients with primary Filgrastim prophylaxis developed less grade 3/4 leukopenia than pts with secondary prophylaxis or interventional treatment. A similar trend was observed for neutropenic events.

The incidence of ADRs was in the expected range (<10% musculoskeletal pain, Filgrastim SmPC). Filgrastim treatment has proved to be effective and well tolerated. The majority of patients assessed the syringe self-administration and needle protection system as easy and safe.