Evolving prevalence of haematological malignancies in orphan designation procedures in the EU

Authors: Benedetta Polsinelli[1], Frauke Naumann-Winter[3], Segundo Mariz[1], Bruno Sepodes[2], Tsigkos Stylianos[1]

European Medicines Agency, 30 Churchill Place Canary Wharf London E14 5EU United Kingdom[1]

University of Lisbon Faculty of Pharmacy, Avenida das Forcas Armadas, 1649 -019 Lisboa, PORTUGAL[2]

Bundesinstitut für Arzneimittel und Medizinprodukte Kurt-Georg-Kiesinger-Allee 3, 53175 Bonn, GERMANY[3]

Background & Objectives:

- In accordance with Regulation (EC) 141/2000 The Committee for Orphan Medicinal Products (COMP), which was established in 2000 by the European Orphan Regulation of 2000, evaluates prevalence of rare conditions as one of the criteria for the recommendation of granting an Orphan Designation.
- Recently the COMP has noted changes in the prevalence of certain haematological malignancies which have been reported in submissions for Orphan Designation and the Maintenance of the Orphan Designation at the time of the submission for Marketing Authorisation.
- The objective of this study was to review the most representative haematological malignancies where a change between the initial orphan designation and review of the orphan designation showed a visible change in the prevalence reported.

Study sample & Methods:

- We did a retrospective analysis and examined the prevalence estimates across time (from 2000 to 2015) reflected in the COMP procedures for orphan medicinal designation for three representative haematological malignancies.
- The criterion applied to choose the conditions to be further analysed was based on the combination of two elements: number of orphan designations granted and number of authorized products. Only positive opinions at the time of initial Orphan Designation and at the time of the Maintenance of the Orphan Designation, and which were reported in the public domain on the EMA website, were included in the retrospective analysis.
- Submissions which were withdrawn were considered inconclusive for the analysis. Those with a high number of designations, where new products have come to market under the orphan designation framework and a change in the prevalence has been observed were selected.

Results

- The selected conditions were: plasma cell myeloma (commonly and also in older designations referred to as multiple myeloma), with 22 orphan designations and 6 authorized products (Thalidomide, Revlimid, Pomalidomide, Neofortex, Farydak and Kyprolis), chronic lymphocytic leukaemia/ small lymphocytic lymphoma with 26 orphan designations and 2 authorized products (Arzerra and Gazyvaro), and acute lymphoblastic leukaemia with 22 orphan designations and 6 authorized products (Evoltra, Glivec, Sprycel, Atriance, Mercaptopurine Nova Laboratories, Iclusig).See (figure 1)
- For multiple myeloma the prevalence estimates accepted by the Committee increased from 1.2 to 3.6 in 10.000 with the last designation granted in 2015. For acute lymphoblastic leukaemia this increased from 0.4 to 1.7 in 10.000 and for chronic lymphocytic leukaemia/ small lymphocytic lymphoma from 2.7 to 4.85 in 10.000 (See figure 2)

Conclusion

- According to the documents analysed, the number of people affected by the three rare haematological malignancies may be rising, as reflected in designation opinions, and this may be due to increase in survival of the patients affected by the conditions analysed. This hypothesis appears to be supported by recent literature data indicating an increase in survival rates for these conditions, partly due to an improvement in treatments and patients' standard of care. However, these reflections have to be interpreted with caution since other factors may play a role and have also an impact to these trends, such as changes in mortality and incidence rates across time, as long as the population ages and the diagnostic methods evolve. Interestingly, it remains to be further investigated to what extent the authorisation of orphan medicinal products may impact on these trends. According to our observational prevalence trends, the highest increasing rates occur in correspondence of the timeframe of approval of new products, which may suggest a critical impact of new authorized medicinal products to the epidemiological changes of these evolving conditions.

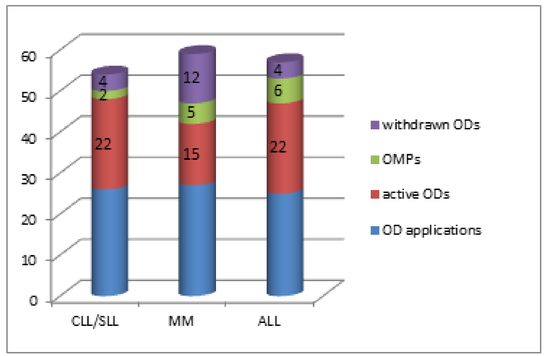

Figure 1 Distribution of Orphan Designation (OD) applications, active ODs, Orphan Medicinal Products (OMPs) and withdrawn ODs for chronic lymphocytic leukaemia/ small lymphocytic lymphoma (CLL/SLL), multiple myeloma (MM), acute lymphocytic leukaemia (ALL).

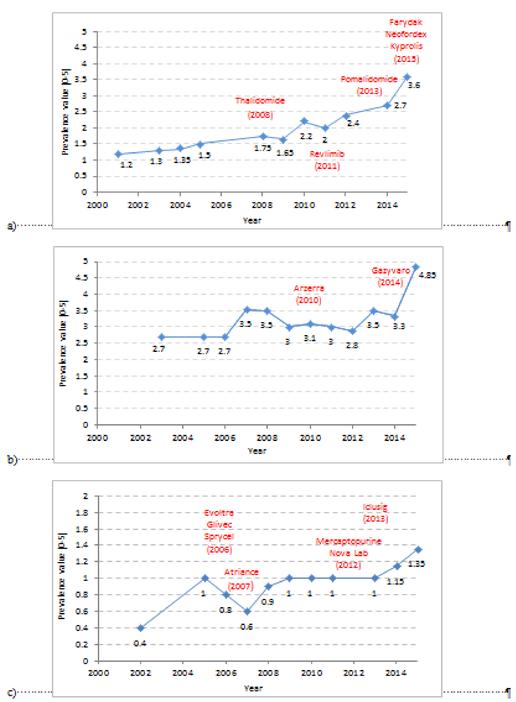

Figure 2 Time-dependent prevalence trends accepted by the COMP for a) multiple myeloma, b) acute lymphocytic leukaemia and c) chronic lymphocytic leukaemia/ small lymphocytic lymphoma during the timeframe 2000-2015. The products with an orphan status that have been authorized for these conditions are shown in red.