Failures to further developing orphan medicinal products after designation granted in Europe

1)Giannuzzi V. 2)Landi A. 3)Bosone E. 4)Giannuzzi F. 5)Nicotri S. 6)Torrent-farnell J. 7)Bonifazi F. 8)Felisi M. 9)Bonifazi D. 10)Ceci A.

Fondazione per la Ricerca Farmacologica Gianni Benzi onlus

The Research&Development process in the field of rare diseases is characterised by many well-known difficulties and a large percentage of orphan drugs does not reach the marketing approval.

This work aims at identifying orphan medicinal products that failed the Research&Development process and at investigating the reasons for failure and possible factors influencing this failure.

Drugs designated under Regulation (EC) 141/2000 in the period 2000-2012 were investigated in terms of failures: 1) Marketing Authorisation failures (refused or withdrawn), and 2) drugs abandoned by the sponsor during the development.

Possible risk factors for failure were analysed using statistical validated methods. This study demonstrated that, out of 788 designations, 437 are under development and 219 failed the developmental process.

Among these failures, 34 failed the Marketing Authorisation process and 185 were abandoned during the developmental process. In the first group of drugs (Marketing Authorisation failures), 50% reached the phase II, 47% the phase III and 3% the phase I while, in the second group (abandoned drugs), apparently, the majority of orphan medicinal products never started the development process, since no data on 48,1% of them was published and the 3,2% did not progress beyond the non-clinical stage.

The reasons for Marketing Authorisation failures were: safety/efficacy issues (26), insufficient data (12), quality issues (7), regulatory issues on trials (4), commercial reasons (1). The main causes for abandoned drugs were safety/efficacy issues reported in 54 cases, inactive companies (25,4%), change of company strategy (8,1%), drug competition (10,8%). No information about the reasons for failure was available for the 23,2%.

This analysis demonstrated that failures accounted for 27,8% of all designations granted in Europe and the main reasons for failure are safety and efficacy issues. Moreover, the stage of development reached by the drug represents a specific risk factor for failures.

References

• Giannuzzi V et al. Orphan medicinal products in Europe and United States to cover needs of patients with rare diseases: an increased common effort is to be foreseen. Orphanet Journal of Rare Diseases 2017.

• Morel T et al. Regulatory watch: The orphan drug pipeline in Europe. Nature Reviews Drug Discovery 2016;15(6):376-376.