Relationship / Association between clinical potential of orphan drugs and registration status assigned by the European Medicines Agency: selected aspects

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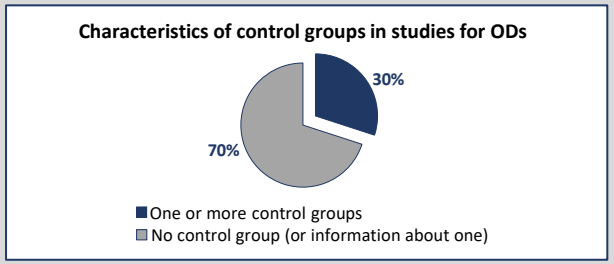
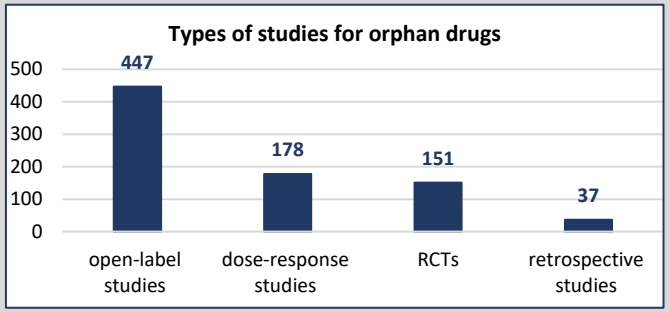
OBJECTIVES

While there have been some attempts to investigate potential factors influencing the registration status of orphan drugs, clinical data for these drugs (such as evidence on effectiveness and cost-effectiveness) are limited. We aimed to assess the association between available clinical data for orphan drugs (ODs) and the registration status assigned by the European Medicines Agency (EMA).



METHODS

The analysis included medicines with an orphan designation available for June 1, 2020, on the EMA website [www.ema.europa.eu]. Clinical data were collected from the EPARs (European public assessment reports) for each orphan drug, containing such information as clinical trial characteristics or drug safety and efficacy. Data were categorized, and statistical analysis was performed.



RESULTS

There were 968 trials identified, reporting the results of 1,342 clinical evaluations of 105 orphan drugs on a total of nearly 130,000 patients. We have extracted 447 open-label studies (46%), 151 RCTs (16%), 37 retrospective studies (4%), and 178 dose-response studies (18%). Single or double-blinding was used in 209 studies (22%), while placebo in 180 trials (19%). At least one control group was included in 294 studies (30%). Each drug could have more than one EMA status or none, summarized by: under additional monitoring (n=72); with accelerated assessment (n=20); conditional approval (n=13); exceptional circumstances (n=12) and without any status (n=24).

KEY FINDINGS: In multiple logistic regression model analysis, each additional dose-response trial was associated with a 33-fold increase in the odds for the drug being under additional monitoring (OR=33.1, 95%CI: 1.90-833.99; p=0.02). Each add-on study with a safety endpoint assessed within 2 months was associated with a 63% reduction in the odds for exceptional circumstances status (OR=0.37, 95%CI: 0.10-0.93; p=0.03). Each additional percent point for a study with a follow-up longer than 2 years was associated with a 98% reduction in the odds for accelerated assessment (OR=0.02, 95%CI: 0.00-0.50; p=0.01).

CONCLUSION

Our innovative quantitative analysis of the EMA authorization decision-making process revealed that the characteristics of a clinical trial and the quality of collected evidence can be significantly associated with the odds of specific registration status. Assessment of clinical robustness of orphan drugs fills an information gap relating to the factors significantly influencing marketing authorization decisions.

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