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Rare Diseases: A Common Problem

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What are rare diseases?

Rare diseases, also commonly referred to as Orphan diseases, are defined on the basis of rarity of occurrence. Although these diseases are individually rare, collectively they are a common problem, affecting between 6-8% of the population [1], or around 30m people in the USA [2], as well as in European Union.

Whilst the regulatory definition varies across regions, the incidence could be considered broadly similar. In the USA, a rare disease is defined as one that affects fewer than 200,000 people [3], whereas in the EU it is defined as effecting less than 5 subjects per 10,000 people [4].

According to EURORDIS, there are between 6,000 and 8,000 known rare diseases [1], out of which the vast majority affect children [5]. A third of children may lose their lives to such diseases before reaching the age of five, with 80% having a genetic origin [2,5,6].

Regulations of orphan diseases generally limit such designation to seriously debilitating or life threatening diseases, without any existing effective treatment or cure.

Why is the issue important?

The importance of rare diseases stem from the fact that in many cases rare diseases are so rare that an individual physician may have never seen a single patient with that disorder. As a consequence, in many of these cases there is insufficient treatment and by the time a diagnosis is made, it may be too late to help the patient. The variability of presentation of these diseases makes it particularly difficult to recognise and diagnose. Furthermore, some of them may present with common symptoms that may be mistakenly attributed to a common disease. This leads to reduced awareness and a delayed diagnosis.

The vast majority of rare diseases are genetically inherited and therefore lifelong. It's also the case that about 30% of subjects are children who die early unless diagnosed early and treated quickly.

How should they be developed?

There are three major aspects that should be considered to achieve successful drug development for a rare disease:

The first, and most common problem, is development leading to regulatory approval for commercialisation. Because of the rarity of the condition, general and very rare occurrences of some of the diseases, it's often not possible to have a significant number of patients included in a clinical trial. This evidently leads to uncertainties in the data analysis, conclusion and evaluation of the results.

While clinical and statistical significance are often considered critical for approvals, because of the rarity of a condition the latter may not always be achievable. Because of this it is sometimes difficult to make definitive conclusions from a regulatory point of view. Additionally, the classical clinical trial designs, such as double blind, controlled and randomised trials, can be challenging to design.

The second main reason why many rare diseases do not have satisfactory treatment is that the cost of developing products is disproportionately high. As there are fewer patients entered into clinical trials a satisfactory method of demonstrating efficacy in safety does not always exist. The general development design that applies to products for common diseases cannot be easily applied in very rare diseases. Because of the cost of development being high and few patients use it after approval, the cost of the product tends to be disproportionately high making reimbursement a significant issue.

The third aspect is the need to include patients and/or carers in the decision making. Since many of these diseases have a huge impact, not only on the patients but also on parents and carers, in their everyday life, it is critical to ensure any benefit achieved with a treatment is relevant to all those involved.

Therefore the way to develop this product is to adapt established methods and to come up with a 'smart' design of the clinical

development. This means maximising the use of fewer patients by ensuring that the design captures all the relevant data in as many patients treated as possible, without at the same time losing the power of the data to sufficiently demonstrate a clinical benefit.

This can be achieved by combining stages of drug development where possible and also planning for continued assessment of patients in the post licensing period. It is common for such products to have registries where information is captured on an on-going basis. Such efforts can help demonstrate the value of the product in real-world clinical use.

There are also other important aspects that are often not satisfactorily captured. This may include quality of life measures that tend to use standard parameters such as SF36, which may not apply to a given indication. In such cases, the sponsors should be encouraged to devise appropriate tools and parameters that are relevant to the patients and the treatment given to them.

Who should be the players?

The traditional development and regulatory approval process involves mainly the industry and medicines regulators. That model is unlikely to be sufficient going forward. It is increasingly becoming obvious that inclusion of both the patients and patient groups is critical for successful development and use of these products.

Whilst patients may be willing to accept the higher risk for the benefit, it is important to ensure that the emotional component does not influence the decision making more than is justifiable.

Another important set of players in this area are those responsible for Health Technology Assessment. The cost; benefit evaluation can be difficult. As mentioned before, the cost can be very high and evaluation of benefit at the moment may not be sufficiently sophisticated in taking into account the benefits all around, both in the short and the long term. New methodologies may need to be applied to assess this aspect appropriately in order to encourage product development in the sector.

Although there are more than 6000 orphan diseases or rare diseases currently in Europe there are only 117 [7] products that are approved in this field. The vast majority of patients, therefore, have not benefited so far by successful drug development, despite the regulatory incentives available.

Where is help available?

But there is help available in most developed countries – USA, Europe, Japan, Singapore and Australia have orphan drug development incentives which encourage sponsors. For example, in Europe, there is 10 year market exclusivity for a product where there is no current licensed product, or alternatively the new product offers significant benefit over an existing product. There is also a cost reduction for scientific advice given by regulatory agencies that are available, for example protocol assistance in the EU, specifically designed for orphan products at reduced cost.

Current status

In the EU, out of 2,127 applications in the years 2000 - 2014, 1,430 received positive opinion for Orphan Product designation, the rest having either had a negative opinion or having withdrawn the application [8]. During this period, 114 products received marketing approval, including those that were later withdrawn or reached expired status.

Oncology indications cover more than a third of the conditions, followed by alimentary tract and metabolism [8]. This is also reflected in the approved products in the EU. Amongst orphan designated products, nearly half are for conditions that affect less than 1 in 10,000. It is broadly similar for products licensed so far.

What does the future hold?

To be successful, drug development needs to take into account the cost of development versus the rarity of the disease and the benefits to the patient and the carers/ parents, and come up with a sensible and practical method of developing and evaluating this class of products. In this regard, it is important to take a global view in more than one sense, in particular the patient's needs given importance, if we are to see more approvals for rare diseases.

References:

1 http://www.eurordis.org/content/what-rare-disease

2 https://globalgenes.org/rare-diseases-facts-statistics/

3 http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/ucm2005525.htm

4 Regulation (EC) No 141/2000 of the European parliament and of the council.

5 http://www.eurordis.org/sites/default/files/publications/Fact_Sheet_RD.pdf

6 http://www.geneticseducation.nhs.uk/for-practitioners-62/rare-diseases-in-clinical-practice

7 http://ec.europa.eu/health/human-use/orphan-medicines/index_en.htm

8 http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/04/WC500185766.pdf