Disease Clustering

What do we mean by disease clustering in Asterix?

Clustering is about a new way to group orphan/rare conditions that has been developed within the Asterix project to make it easier to decide the best way to study the efficacy and safety of a new treatment.
Specifically, this is a systematic grouping of medical conditions that links the clinical and treatment characteristics with the applicability of different methodologies and designs of clinical studies.

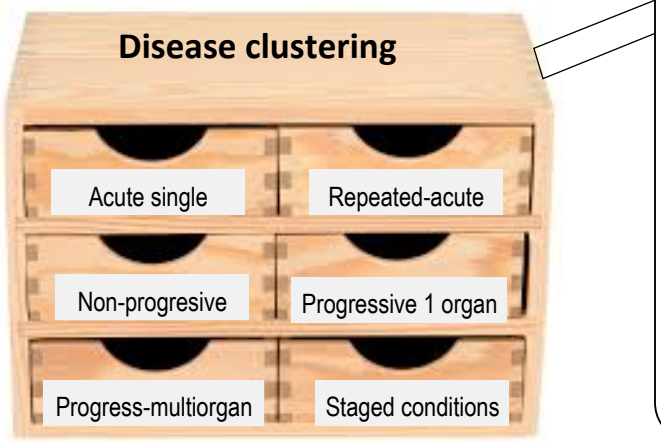
What is the purpose of grouping?

It is often difficult to decide which is the best way to study a new treatment in a way that is quick but also robust to provide credible results.
Guidance on best approaches for a given disease are useful, and can be shared by regulators and investigators to ensure efficient research. However, there are so many different rare diseases, that guidance is unfeasible for all.
Grouping conditions by methodological and statistical requirements allows generalizing recommendations on the applicability of novel methodologies to types or groups of diseases, rather than to single disease models.
These recommendations will facilitate drug development and subsequently the regulatory decisions on the marketing authorization of drugs for orphan diseases.

What is the novelty of this proposal?

Contrary to other classifications available, the focus here is not on the course of the disease but on the specific condition of an orphan disease that is targeted by a drug. For example, drugs that could be under development for Cystic Fibrosis can target either the maintenance treatment aimed to prevent exacerbations or the treatment of acute exacerbations, which both constitute different conditions of the same disease.

Thus, the condition that is being targeted and not the disease in all its spectrum, is the one that defines the methodological and statistical requirements when conducting studies that will support the clinical drug development.



The clusters may describe the type of medical indication to be studied for a given treatment

Some examples follow:

A Single acute episode: Guillen-Barré Syndrome
B Repeated acute episodes: Multiple sclerosis
C Chronic non-progressive conditions: Haemophilia
D Chronic progressive conditions led by one system-organ: Amyotrophic Lateral Sclerosis (ALS)
E Chronic progressive multidimensional conditions: Cystic fibrosis
F Staged conditions: Solid malignancies

Why the clustering of conditions is particularly relevant for orphan diseases

Conducting traditional Randomized Clinical Trials (RCT) in orphan diseases is particularly challenging due to the rarity of the conditions that are often seriously debilitating and affecting children, as well as due to the small number of the eligible patients that can take part in trials. Single-arm trials (where comparative control arm is absent) that are more selected when conducting studies in orphan diseases, are considered as trials with less persuasive evidence to support the authorization of a medicinal product. Thus, the use of some novel methodologies to the design and analysis of studies in these small populations offer an alternative to the single arm trial and in this sense, allows achieving a more robust evidence in a more efficient way.

Orphan diseases usually deal with small populations and the number of different diseases identified so far ranges from 6.000 to 8.000. In this context, it is unrealistic making recommendations on the applicability of those novel methods to each single disease separately. By clustering conditions, we can provide general recommendations on the applicability of the novel methods to the different clusters, and consequently that can be useful for every individual orphan disease and/or condition.

Possible benefits for patients

This clustering method could make it easier to provide guidance on how to conduct safe and efficient clinical trials, including the minimum number of participants necessary to obtain the best possible evidence in each particular orphan clinical situation.

In other words, it may avoid unnecessary patient exposure to experimental and/or placebo treatments, and may also reduce uncertainty at the time of product approval.

Possible downsides

The proposed clustering aims to ease the provision of top level guidance on the conduct of best clinical drug development and trials design for orphan diseases.

By clustering conditions, guidance is given at a group level, but unfortunately no specific advice can be given for each single condition, and there may be complex situations that cannot be addressed with this grouped approach.

More information

. Pontes C et al. (2015) Clustering of rare medical conditions based on clinical features which determine applicability of investigative designs and methods to their study. Clinical Therapeutics

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