Innovative approaches to facilitate paediatric drug development

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The design and implementation of paediatric trials are challenging and often difficult to accomplish. Ethical, practical and even financial considerations have caused the evaluation of efficacy and safety of drugs in children to be based on empirical extrapolations from clinical trials in adults.
The design, analysis and interpretation of clinical studies in this vulnerable population require specific techniques to ensure accurate decision-making regarding the pharmacokinetics, safety and efficacy of drugs. This is also endorsed by the guideline on clinical trials in small populations set by the European Medicine Agency (EMA), which states that 'crude (simple) methods may often be adequate when we have huge amounts of data, but when there are very few data, it is imperative that the most efficient and informative analytical methods should be used' (EMA, 2006).
Extrapolation is a strategic approach that may allow one to circumvent some of the aforementioned difficulties: it consists in extending information and conclusions available from studies in one or more subgroups of the patient population (source population), or in related conditions or with related medicinal products, to make inferences for another subgroup of the population (target population), or condition or product, thus reducing the need to generate additional information (EMA, 2012).
A very useful methodological tool that naturally fits into the context of extending information from a source population to make inferences for another population is Modelling and Simulation (M&S). The added value of M&S in paediatric clinical research has been extensively documented (Tod et al., 2008), and its weight at a regulatory level in supporting extrapolation has constantly been increasing in the last years. However, extrapolation is primarily a clinically related process and should not be intended as a strategy for replacement of clinical studies, especially when dealing with diseases specific to children.
Whenever extrapolation cannot be applied to its full extent and clinical trials in children are required, it should be still used as an optimization procedure in the design of such trials. In fact, extrapolation plays a pivotal role in the identification of the right dose and in the design of clinical studies by means of clinical trial simulation of innovative study designs (Smania et al., 2015), which ultimately allow to reduce the number of patients required, making these techniques appealing, or rather compulsory, for the development of new medicines for children.
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