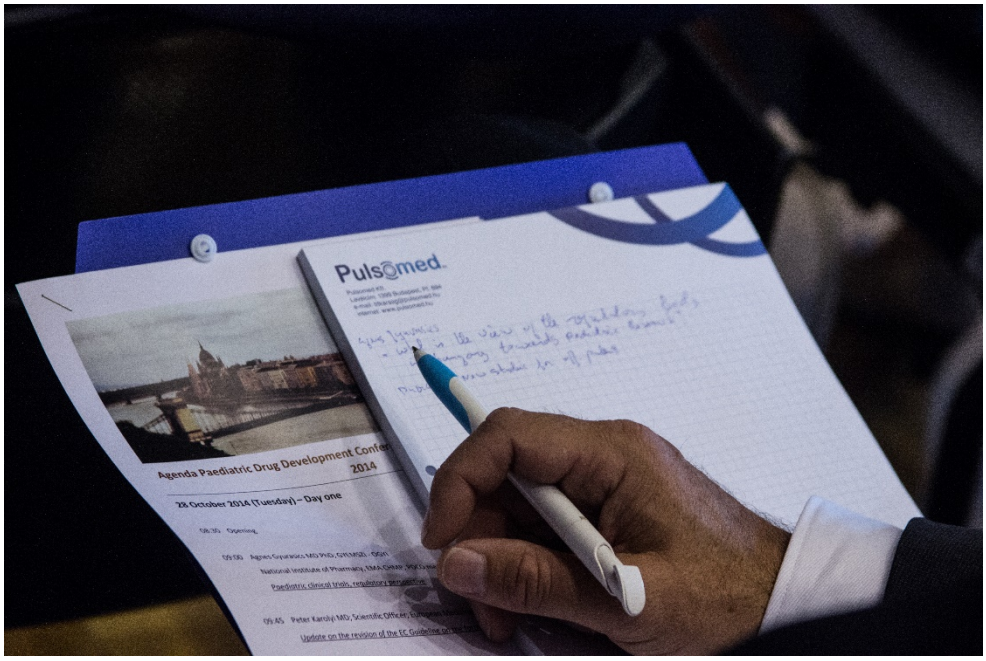
Korábbi konferenciák

2014



Paediatric Clinical Trials of pharmaceuticals pose a number of problems not least to the pharmaceutical industry. Small numbers of small patients provide little opportunity to make a return on the investment required to obtain a licence to market a pharmaceutical product. All the regulatory processes have been set up to provide a framework for first approval in man, then women and then perhaps in children.

The conference set itself the task of identifying the opportunities and impediments, to address the further and try and find ways to solve or avoid the latter and reveal the opportunities which underlie the challenges of using drugs developed for adults in children.

The stakeholders represented at the conference came from two of the regulatory bodies – the EMA PDCO and the FDA. Industry was represented by paediatric specialists from large companies and from the drug delivery and technologies side. Others representing patient groups, academia, and clinical research organisation took part by presenting their concerns and engaging in the plenary debates.

What was discovered?

The initial presentations covered the latest issue of regulations regarding paediatric trials from EMA and the advice of the PDCO in understanding and applying these regulations. This identified that there are both constraints and incentives being offered by the European and US regulators in this area.

Seen from the industry angle the constraints are often seen as disincentives rather to developing paediatric drugs and formulations, as these have been made a mandatory part of all relevant drug developments representing a cost and an erosion of margins. To counteract this perception the incentives of supplementary protection certificates extending patent life, close consultations and expedited review processes and in the US a voucher system to encourage paediatric drug development form part of the platform are the returns regulators can offer.

However there are several major differences between the adult clinical trial process and the practicalities of performing such studies to a similar standard.

1. The patients
   Children are not standard. They range from preterm neonates to adult sized teenagers. Differences in height, weight, metabolism, growth, physical and mental maturity mean that there is no "standard" paediatric population even when segmented by age, or height and weight. This poses a number of challenges.

2. Informed consent
   Below a certain age parents are asked to give consent but there is some difficulty in believing that the consent is fully informed. Later, children will have increasing abilities to choose but this cannot be standardised solely on physical characteristics, either. This is just one of the ethical concerns in this area.

3. Population size
   Many paediatric disease groups are too small to form a population from which a sample can be drawn which will provide statistically meaningful analyses. Moreover the inclusion and exclusion criteria will limit the choice further.
   Access to sufficient number of children to perform a "standard" study may mean having to reach out to a very wide geography and this has implications for conducting trials to ICH standards when centres may have different resources for patient care due to the local economy.

4. Drugs
   There are very few drugs specifically approved for paediatric uses for the reasons mentioned before. Hence there is less standardisation of care. This means that patients may have had different prior treatments making selection harder and mean that centres are not familiar with another "standard of care".
   Existing formulations of drugs are often unsuited to smaller children, so dosing both physically depending on their size and in relation to their metabolism can make the application of a dosing regimen inappropriate for the paediatric patient.
   Drug delivery therefore is a major constraint and this increases as the size of the child decreases.

5. Companies
   Companies also come in different sizes and the requirement to produce a Paediatric Investigation Plan has a disproportionate effect on the finances and financing of smaller companies which are often only funded to produce early trial results in order to attract a buyer among the larger companies. This can distort investor choices in two ways.
   Indications which have no need for paediatric developments may be preferred such as women's health or diseases of the elderly. But, conversely, if the indication has been designated as an Orphan and/or Rare disease the pricing and reimbursement incentives allowed for drugs of this kind attract investors and larger companies. The selection of Rare and Orphan disease candidates is thus likely to deselect those without these designations for private funding.

6. PUMA
   Regulations have been cast to incentivise development of older drugs for paediatric uses. Various means to offer exclusivity and protection are included in these but that cannot prevent hospitals and physicians from using a generically available drug in place of such an 'approved' medication as there is almost no way of enforcing an exclusivity of that kind.
   It was therefore posited that such PUMA developments would best be developed in proprietary formulations protected by patents and other IP to encourage investment.

Overall the conference identified many significant features of paediatric clinical development which do not and cannot be fitted into the current standards, thus requiring adaptations of the expectations and requirements for regulatory approval of drugs for paediatric use. One suggestion to overcome some of the intrinsic constraints of patient numbers and design limitation might be the introduction of a Registry approach comparing individual patients' response to a matched cohort of children who had received the existing standard of care. This was considered worthy of investigation by all, including the regulators. Moreover, the regulatory representatives expressed a strong willingness to discuss individual design proposals in dialogue with industry rather than to expect rigid adherence to the currently published guidelines in order that these may be adapted and continuously updated and approved.

Next year's conference: 6th and 7th October 2015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