Chapter 8

Paediatric clinical trials

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Aim

This chapter aims to provide a comprehensive overview of the challenges related to the paediatric clinical trials. It will, therefore, focus on the novel complexities of the paediatric clinical trials, safety concerns of testing medicines in children, stringent ethical considerations, informed consent, lower prevalence of disease, the need to test different age groups, the possibility of late adverse effects, the requirement for tailored study design and the need for child-appropriate medicine formulations and will highlight relevant questions such as the lack of commercial interest.

Summary

Most drugs for children are prescribed empirically, based on physicians' experiences within an "off-label" regime (the authorization for children is often missing). Conducting paediatric clinical trials are vital to get modern, effective and, in the next step, on-label therapies to paediatric patients. At the same time, children represent one of the vulnerable populations. This is one of the reasons why paediatric population is often overlooked when discussing the topic of clinical trials in general.

EU Paediatric Regulation was published in 2007 to better protect children's health. The Regulation introduces, among others, changes in the development of paediatric drugs such as evaluation of the safety and efficacy in all appropriate paediatric age groups, a requirement on guaranteeing that the product labels contain the known paediatric data, the needs to develop paediatric-appropriate drug formulations and last, but not least, task on providing the Paediatric Investigation Plan for testing the particular drug in children at the time of application submission.

Paediatric trials also face unique challenges regarding concerns around trial interventions and the logistics of subject recruitment and obtaining consent. Attention will therefore be drawn to ethical and recruitment issues, parental permission, and child assent. While conducting research on children, rigorous efforts are required to minimize all the predictable risks. International paediatric trial networks have been established in many countries to address some challenges by improving the infrastructure and research capacity.

This chapter addresses the fundamentals of paediatric clinical trials, principally the rationale for conducting them, the specifics that need to be respected, including the topic of risk management and monitoring safety data.

Methods

E-learning materials (study materials, videos, links to publications), quiz questions, discussion boards, and practical exercises.

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Learning Outcomes

Students will be able to:

1. Discuss the legislation relevant to paediatric clinical trials
2. Outline the ICH GCP principles applicable to paediatric clinical trials
3. Discuss the ethical issues in paediatric clinical trials
4. Explain the difference between child assent versus adult consent
5. Define the specifics of paediatric trials
6. Explain why children are considered vulnerable populations
7. Apply an appropriate drug formulation for the paediatric population
8. Discuss the recruitment and retention issues in paediatric clinical trials

Complementarity to CONSCIOUS I Materials

The issue has been partially covered by the CONSCIOUS I project - the paediatric topic was only marginally mentioned in the 5th lesson– Informed consent in vulnerable populations.

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1 Introduction to the chapter

2 Paediatric regulatory framework
- 2.1 Paediatric Regulation in Europe
  - 2.1.1 The Paediatric Committee (PDCO)
  - 2.1.2 Paediatric Investigational Plan (PIP)
  - 2.1.3 The Paediatric-Use Marketing Authorisation (PUMA)
- 2.2 ICH E11(R1) Guideline

3 Ethics of paediatric clinical trials
- 3.1 Informed consent and assent
  - 3.1.1 Informed consent from the legally designated representative
  - 3.1.2 Participation of minors in the informed consent process and agreement/assent
- 3.2 Payment for participation

4 Study design and conduct of paediatric clinical trials
- 4.1 Characteristics of paediatric clinical trials
  - 4.1.1 Patients´ recruitment and retention
  - 4.1.2 Drug formulations
  - 4.1.3 Trial design and conduction
- 4.2 Trial registration and publication

5 Safety monitoring

6 Paediatric trials initiatives
- 6.1 Infrastructure support
- 6.2 Patient and parent involvement

7 Conclusion

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