The development of fixed-dose combinations (FDCs) through improved methodology

FDCs have been subject to stricter regulations in general as compared to mono-therapies. However, when it comes to specific guidelines for the development of the different categories of FDC’s, the existing clinical development guidelines does not diverge in spite of differences in the amount of existing clinical data. Although EMA and FDA are not in accordance in this regard, both are in the process of finding common ground within the clinical guidelines.

**Optimization of the clinical development of FDC**

This project will monitor and explore the conditions for the development of FDC’s taking into account the differences in the available data for categories. By modelling and simulation of existing trial data for FDC’s obtained through EMA, we will optimize the clinical development conditions. Clinical development is only one of the aspects of FDC development. To keep the developmental costs down and get access to the market, it is important to avoid any superfluous investigations by performing the correct and necessary clinical experiments from the beginning. However, the tools and models for this purpose are only in their infancy. Thus, we would contribute in the current project to the development and validation of such tools.

Drug combination products are still developed through comprehensive clinical development efforts (e.g., factorial design) - all according to existing guidelines. For this type of medicines based on quite extensive and resource demanding activities, it will be valuable to explore if in silico methods as modelling and simulation could have facilitated the entire developmental process by saving time and resources or if the modelling and simulation could have increased the power of some of the studies.

**Focus on recent and relevant examples of approved combination products**

Since drug approval package data for such projects nowadays are official accessible from EMA we will be able to benchmark how modelling methods could have facilitated the process, i.e., could any clinical studies have been omitted or at least been reduced in size and complexity. To facilitate the clinical development plan and further process to reach an NDA, the project will focus on recent and relevant examples of approved combination products. This focus will include the official description of its clinical development process to NDA and give us access to pivotal compound data (clinical efficacy and safety data). Within the project plan there will be a specific selection of a product that is most optimal to explore based on data access, public information of clinical study plans as well as the indication area.

Finally, the findings will be put into a holistic overview of the requirements for development of FDC’s in general. This will include the PK/PD properties, formulation aspects, and the dosing scheme. Hopefully, the generated modelling results could contribute to a revision of the guidelines for the development of FDC’s.

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