The impacts of undetected noncompliance in phase II, III, and IV clinical trials: An overview

Elise Le Flohic[1], Bernard Vrijens[2], and Mickael Hiligsmann[1]

[1]Maastricht University
[2]AARDEX Group

March 7, 2023

Abstract

Aim: This research aims to provide an overview of the consequences of undiagnosed non-adherence in clinical trials. Methods: This research was conducted with a mixed-methods approach. It combines a literature review and qualitative semi-structured interviews with key opinion leaders. Based on this groundwork, the consequences of undiagnosed non-adherence in clinical trials were summarized and reported in a figure. This study focused on phases II, III, and IV in ambulatory settings across a variety of therapeutic areas and indications. Results: Various consequences of non-adherence in trials were investigated. In phase II, drug efficacy may be underestimated, variability in the outcomes may be high, and a distorted picture of side effects could be reported, resulting in an uncertain impression of the investigational product's profile, and complicating decision-making. The sponsor may need to increase the sample size of the upcoming phase III study to improve its power, representing additional costs, or even terminate the study. In phase III, similar phenomena may be observed, making demonstration of efficacy to the regulatory bodies more difficult. Lastly, in phase IV, a distortion in pharmacometrics may occur; the drug may underperform, prescriptions may be refilled less often than expected, or extra expenses may be incurred by the payers. This can result in post-marketing dose reduction, new competitors coming into the market, and eventually, product withdrawal. Conclusion: This research highlighted the many potential adverse consequences of undiagnosed non-adherence in clinical trials, including additional costs. Collecting accurate data appeared to be crucial for decision-making throughout the drug development process.

Hosted file

`Article V3.docx` available at https://authorea.com/users/593324/articles/628404-the-impacts-of-undetected-noncompliance-in-phase-ii-iii-and-iv-clinical-trials-an-overview