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CLINICAL TRIAL

The practical application of adaptive study design in early phase clinical trials: a retrospective analysis of time savings

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Abstract
Background The interest in adaptive study design is evident from the growing amount of clinical research employing this model in the mid to later stages of medicines development. Little has been published on the practical application and merits of adaptive study design in early phase clinical research.
Methods This paper describes a retrospective analysis performed on a sample of 29 industry lead adaptive early phase studies commencing between 1 January 2006 and 31 December 2010 in a clinical trials unit in London, England. All studies containing at least one adaptive feature in the original protocol were included in the analysis. The scope of the analysis was to assess whether the use of adaptive study designs provided tangible benefits over the use of conventional study designs using time savings as the main measure.
Conclusion We conclude that the use of adaptive study design saves time in early phase research programs. This is achieved by abolishing the need for substantial amendments or by mitigating their impact on timelines and by using adaptive scheduling efficiencies.

Keywords Adaptive study design · Early phase · Clinical trials · Protocol · Protocol amendments · Time savings

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Introduction

The aim of using adaptive study design in early phase clinical trials is to develop new medicines in a safe, efficient and cost effective manner, progressing rapidly from first administration in man to proof of concept. Adaptive study designs allow for modification or termination of a study in situations typically occurring in early drug development such as the initial design parameters being inaccurate due to insufficient understanding of the investigational medicinal product; interim data suggesting that the risk/benefit profile of a study has changed or futility of the study realised after the start. Expected benefits of using adaptive study design are to maximise the collection of desired data whilst minimising the collection of unnecessary data, exposure and risk to the participants and time and cost of the development. This paper discusses whether and under what conditions the use of adaptive study designs in early phase clinical trials of non-oncology investigational medicinal products can deliver on the expectation to save time compared to conventional designs.

Background

"Adaptive" in this context means that one or more decision points are built into the trial design and that the subsequent trial conduct following that decision point depends on the data observed to that point "without undermining the validity and integrity of the trial" [1]. The concept is not a new one as it has been used in oncology phase I trials and in many other patient trials where a lack of efficacy leads to the discontinuation of a treatment or study that is showing no benefit [2, 3].