Phase II Trials

Introduction

Phase II trials begin after the successful completion of Phase I. During Phase II, the investigational medicinal product is tested for efficacy (and safety). The studies conducted during Phase II are typically therapeutic exploratory studies which try to discover whether the medicine treats the intended disease or condition. When an investigational medicinal product fails, it is usually because Phase II trials show that it does not work as expected or has unforeseen toxic effects in patients.

Key questions for Phase II trials

- Is the medicine safe in patients? (Safety)
- What does the medicine do to the body? (Pharmacodynamics (PD))
- Does the medicine seem to work in patients? At what dose(s)? (Effect)
- How should confirmatory trials be designed? (Endpoints, target population, other medications being taken (concomitant), etc.)

Characteristics of Phase II trials

Participants

Phase II trials are performed on large groups of participants (usually around 100-500 participants). There are often more than 30 participants per treatment group. Participants are usually selected using strict inclusion criteria, meaning that the study population is relatively homogenous. A homogenous study population helps the interpretation of study results.

Duration

Phase II trials are typically quite short, lasting just several weeks or months.

Exploring therapeutic efficacy: Proof of Concept (POC) studies

Phase II trials must show that the investigational medicinal product treats the intended indication in a particular patient population. This is called ‘Proof of Concept (PoC)’. Proof of Concept studies must clearly show clinical improvement so that the existence of activity or ‘response’ can be determined. The outcomes and results of these trials are considered when making the ‘go/no-go’ decision to progress to Phase III development of the medicine.

Estimating dosage levels and schedules: Dose-response studies

Phase II trials must also gather information about the best dosage levels and schedules. Proof of Concept is usually tested at the maximum tolerated dose (MTD) in order to minimise false-negative results, provide the best test of hypothesis, and maximise the pharmacodynamic (PD) effect.

Dose-response studies seek to:

- Discover a minimum effective dose
    - The smallest dose at which an effect is observed
- Discover an optimal dose
    - The dose at which the optimum (desired) effect is observed
    - Mitigate the risk of the MTD not being tolerated

Typically, dose-response studies use randomised parallel group

studies looking at three or more dosage levels, one of which may be zero (placebo).

Dose-response data are important, and must be gathered not only from formal dose-response studies, but from all other possible sources during previous studies of the investigational medicinal product.

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