Women of childbearing potential in clinical trials

Introduction

There is a lot of concern surrounding the inclusion of women of childbearing potential (WOCBP) in clinical studies. The concern is largely in regard to the unintentional exposure of an embryo or foetus to a candidate compound before enough data has been gathered for a satisfactory analysis of the potential risks and benefits the compound poses to an embryo or foetus. In certain circumstances, WOCBP may be included in early clinical trials without non-clinical embryo-foetal development toxicity studies.

Including women of childbearing potential in clinical trials

Recently, women have been choosing to get more involved in clinical studies earlier in the development programme. In order for them to do so safely, the risk of their falling pregnant must be minimised. There are several methods of minimising these risks, including:

- The completion of reproduction toxicity studies in order to characterise the risk profile of the candidate compound,
- Mitigating or limiting risks by recommending pregnancy prevention measures during clinical trials. Such precautions include:
    - Accurate pregnancy testing (for example, based on human chorionic gonadotropin (hCG))
    - Use of highly effective methods of birth control (with failure rates of less than 1%)

        - Allowing study entry only after a confirmed menstrual period.

In some cases, such as with some biotechnology-derived medicines, it may be difficult to conduct embryo-foetal development toxicity studies in an appropriate animal model. In such cases, there are several options to consider in order to minimize the risk of causing foetal malformations (the risk of teratogenicity):

- Communicate to the participant the potential for possible risks to an embryo or foetus
- Informed consent that is as specific and helpful as possible
- Participant education to ensure compliance
- Testing for pregnancy during the trial
- Knowledge of the mechanism of action of the compound and the extent of foetal exposure.
    - For example, for monoclonal antibodies, embryo-foetal exposure during the development of organs (organogenesis) is low in humans. Based on this knowledge, developmental toxicity studies can conducted.

Generally, before women of childbearing potential are included in clinical trials, preliminary reproduction toxicity data have been made available from two animal species. If precautions to prevent pregnancy in clinical trials are used, (up to 150) women of childbearing potential can be included in trials where they receive investigational treatment for a relatively short duration (up to 3 months) *before* definitive reproduction testing is carried out. The justification for this policy is the very low rate of pregnancy in controlled clinical trials of this size and duration, and the fact that adequately designed preliminary studies could detect most developmental toxicity.

The special situation regarding the inclusion of pregnant

women and children in clinical trials requires that all the relevant non-clinical data should be available and analysed, and preferably information about human exposure from non-pregnant women should be assessed to support efficacy and safety for the clinical situation.

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