

Round table number 2 : Adaptative design : when and how to use it in clinical trials ?

Modifying a trial in process on the basis of accumulated data

The changes made to procedures during on going trials on the basis of accumulated data within a survey is the concern of adaptative design. It allows for changes to the on-going trial on the basis of data collected within that same trial, without putting its validity or integrity at risk.

'This is not an unplanned attempt at rescueing a survey that shows signs of predictable failure but a specific and closely monitored process allowing for changes to the protocol of a survey based on results already collected within that same survey. There are many adaptations possible and they vary depending on the types of tests carried out and which stage they are at.

This round table has reviewed the difficulties and necessary precautions inherent in these methods : the need for rigourous planning to envisage a priori the various cases that might occur, use of an independent statistician for data analysis, designation of an independent committee with access to the results as well as the adaptation regulations which are pre-established in a 'charter' so that the direction that the test should be taking can be decided, logistic constraints...

Before making the decision to use adaptative design all these difficulties should be carefully identified and weighed.

Indeed, this is a choice inferring significant human, intellectual and financial costs . In reverse, adaptative design allows for more precision at the cost of efforts spent in anticipation and planning.

Nowadays academic researchers and manufacturers develop an interest in these methods. A brief survey amongst our round table shows that they are still not used much. There are few initiatives of that sort in academic research. Manufacturers may see it as a mean to shorten the time of drug development in specific circumstances. During Phase I, the use of adaptative tests is well recognized, in particular for trials regarding dosing research. For later stages of

development (II and III) this process is less well accepted and our group has tried to identify when manufacturers may have an interest in developing these methods, in which case they would need close contact with regulating agencies from the start of their project.

The benefits from these methods are well identified : shorter exposition of subjects to toxic or ineffective doses and benefits proved more rapidly and more effectively ; these methods could be encouraged as long as inherent constraints are being observed.