

Round table number 3 : How can the paradigm of clinical development and its segmentation in Phases I, II and III evolve ?

Gaining time overall in order to have more time to spend on dosage

These stages must absolutely not overlap before a drug becomes authorized on the market. Adaptive design is undoubtedly one of the means available to decompartmentalize these stages and speed up surveys without increasing risks. We do not want to expose subjects to more risk ; we are only trying to waste less time.

' Getting Market Authorization (MA) takes several years and manufacturers always think the process too long. Equally patients' associations put pressure on us to speed up the process but they also sue us when things go badly. In these conditions we think that it is important to maintain the structure in phases I, II and III but we are willing to make it evolve. We could try and combine the first two stages, which are exploratory, whilst keeping the third stage of development, which allows for results to be confirmed, clearly separated. Gaining time during phases I and II or doing it differently could allow quicker access to the confirmation stage which, on the contrary, could be extended a little. As an authorization is delivered on the basis of the ratio between a demonstrated benefit and an evaluated risk, the quantity of exposed patients remains globally small compared with the number of patients to whom the product will be offered eventually. The risk is more difficult to assess, especially its extension to the populations who will be treated in real life.

Amongst the ideas debated within our group we have raised the question whether to remove or lighten the stage involving trials on healthy volunteers. In cancerology phase I testing is done on patients and this is an option that is now clearly discussed in other areas. The purpose is to get to work on the patient more quickly in order to do tolerance trials. I do not know whether the important question is to gain time in the end. The review of the procedure would rather allow us to be more precise in evaluating doses to be used in phase III. That is the most difficult part of the development in the end. Finding

the right dosage is being done during phase II and if we reduce phase I trials that would give us more time for this assessment.

We already have ways of shortening the time needed to launch a drug on the market: authorizations under exceptional circumstances, which deal with severe and very rare diseases for which we know that there will not be any further information than what is available in the presented file. One is aware that the elements presented do not allow a full validation of the risk/benefit ratio but in cases where there is no treatment available and strong demands from patients as well as the medical staff, one may give such a type of authorization. There also are conditional authorizations in which an authorization is given providing that the firm undertakes a complementary survey to try and confirm the risk/benefit ratio.

These two procedures are already ways of gaining time and we have simply been looking for more options to be invented. How to reinforce the risk/benefit ratio regarding some populations, in specific conditions of use in real life, after Market Authorization has been delivered? Complementary surveys are possible. The conditions to facilitate them and thus complete the file are still to be defined.'