Improving clinical outcome using TDM

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Extended abstract:

Therapeutic drug monitoring (TDM) offers the option of individualizing patient care by adjusting the dose of the drug, to increase the chances of efficacy, and to reduce the risk of toxicity. Typically TDM is done for drugs with a narrow therapeutic index. For some drugs during drug development TDM is already included in the early phase of registration studies. In Phase I and Phase II studies repetitive measurements of drug exposure assist in selecting the preferred dose and/or target concentrations for subsequent Phase III trials. Based on these studies the drug label will indicate the necessity for TDM, although typically no studies are available that show that clinical outcome is better when TDM is performed, compared to dose adjustments based on clinical grounds. It is generally accepted that this is the way to handle this particular drug, and (all) prescribers will implement TDM.

For other drugs during drug development the concentration-effect relationship has not been explored, and at registration there is no indication that TDM would provide a benefit. After the introduction in patient care such data may become available. Typically drug exposure is correlated to efficacy or toxicity. Based on observational data target ranges are defined. Randomized trials demonstrating the added value of TDM are often not performed. As a result it may be very hard to convince physicians to change the way they dose this drug. For such compounds we often see substantial diversity in patient management.

During my presentation I will highlight the best available evidence that TDM improves clinical outcome. The selection of studies is based on a survey among all scientific committees of IATDMCT. Furthermore, recommendations will be given for future clinical trials that evaluate either an a priori test (e.g. pharmacogenetics) and/or a posteriori measurement (concentration of drugs; pk/pd).