VALIDATION OF SURROGATE ENDPOINTS USING META-ANALYSES OF INDIVIDUAL PATIENT DATA

Marc Buyse[1]

International Drug Development Institute, Brussels, Belgium

Email: *marc.buyse@iddi.com*

Ten years ago, Fleming and Demets drew attention to the fact that a correlate does not make a surrogate. The area of surrogate endpoint validation has made much progress since. The key concept involved in surrogate endpoint validation today is that a good surrogate endpoint should predict a treatment effect on the true endpoint, rather than just be correlated with this true endpoint. Several approaches have been suggested to implement the prediction paradigm, but all of them share the need for repeated measurements (perhaps in several independent trials) of the effects of treatment on both the surrogate and the true endpoint. This paper illustrates an approach to prediction based on individual patient data from several independent trials addressing the same therapeutic questions. The strength of association between the treatment effects on the surrogate and the true endpoints is quantified through a standard correlation-type measure. In addition, the "surrogate threshold effect" is defined as the smallest effect on the surrogate endpoint that predicts a significant effect on the true endpoint.