as well as from intent-to-treat (ITT) analysis, and reporting the confidence interval. For non-inferiority trials, per protocol analysis is preferred, while ITT analysis is secondary (97,98). In the context of a non-inferiority trial, per protocol analysis may provide conclusions that are more conservative or careful, than conclusions provided by ITT analysis (99,100).

The confidence interval defines the difference between the efficacy of the study drug and the active control drug. Moreover, these authors recommend reporting the number of subjects dropping out of the trial.

In view of the fact that non-inferiority trials are conducted with the expectation that efficacy of the study drug and active control drug are the same, Dignam (101) has warned against the early termination of clinical trials where the available data implicate the study drug as superior to the active control. Thus, during the early phases of any clinical trial, the available data may show that the study drug clearly works better than the control treatment. But often, data available during the first weeks or months of a clinical trial are of a sporadic nature, that is, early indications of remarkable efficacy or unusual toxicity typically disappear as more and more data are collected. Thus, in the context of a non-inferiority trial, where there is an expectation of no difference in efficacy, investigators should refrain from deciding that the study drug is more effective than the active control, where the clinical trial is only partly completed.

[97] Sanjay Mitter, personal communication of May 13, 2011.

[98] The author thanks Dr. Jenna Elder for this advice.

[99] Matsuyama Y. A comparison of the results of intent-to-treat, per-protocol, and g-estimation in the presence of non-random treatment changes in a time-to-event non-inferiority trial. *Stat Med*. 2010;29:2107–2116.

[100] Matilde Sanchez M, Chen X. Choosing the analysis population in non-inferiority studies: per protocol or intent-to-treat. *Stat Med*. 2006;25:1169–1181.

[101] Dignam JJ. Early viewing of noninferiority trials in progress. *J Clin Oncol*. 2005;23:5461–5463.