XII. STATISTICAL ANALYSIS BY SUPERIORITY ANALYSIS VERSUS BY NONINFERIORITY ANALYSIS

The two arms found in a typical Kaplan–Meier plot can be compared or analyzed by various statistical methods, including superiority analysis and noninferiority analysis. Where the study drug is compared to a placebo, superiority analysis is used. But where the study drug is compared with an active control drug, or with the standard or traditional treatment, both superiority analysis and noninferiority analysis are used (84).

While sponsors and investigators prefer that their drug be superior to the control treatment, the difference in efficacy may be insignificant. Where the difference is insignificant, the clinical trial can be rescued, at least in some situations, by noninferiority analysis.

Following the clinical trial, the statistician analyzes the results to determine whether the study drug is superior to the active control drug. The statistician also analyzes the results to determine whether the study drug is not significantly inferior to the active control.

With noninferiority analysis, the goal of the investigator is to prove that the efficacy of the study drug is better than, equivalent to, or only trivially worse than the active control, in terms of efficacy (85). D'Agostino et al. (86), emphasize that, in designing a noninferiority clinical trial, the comparator drug should be the *best available* comparator drug.

In addition to the superiority trial design, and the noninferiority trial design, another type of trial design is the equivalence trial. The goal of this type of trial is to demonstrate that the study drug is both insignificantly better than and insignificantly worse than an active control drug. Paggio et al. (87), document the fact that published reports of clinical trials frequently confuse the concepts of noninferiority and equivalence.

In conducting a clinical trial, the sponsor prefers to show that its study drug is superior to an active control drug, in terms of efficacy. However, if superiority in terms of efficacy cannot be shown, and where the investigator is not willing to scrap the results from the clinical trial, the results can be salvaged by using noninferiority analysis. In practice, statisticians conduct the noninferiority analysis first, and once this is complete, they conduct the superiority analysis (88). The following situation concerns a finding of noninferiority where the efficacy of the study drug is found to be not statistically better than that of the active control drug (comparator drug). In this case, regulatory approval can be granted based on the fact that the study drug is safer, cheaper to produce, easier to administer (injected vs oral),

[84]US Department of Health and Human Services. Food and Drug Administration. Guidance for Industry. Non-inferiority clinical trials. 2010 (66 pages).

[85]Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJ; CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. J. Am. Med. Assoc. 2006;295:1152–60.

[86]D'Agostino RB Sr, Massaro JM, Sullivan LM. Non-inferiority trials: design concepts and issues—the encounters of academic consultants in statistics. Stat. Med. 2003;22:169–86.

[87]Piaggio G, Elbourne DR, Altman DG, Pocock SJ, Evans SJ; CONSORT Group. Reporting of noninferiority and equivalence randomized trials: an extension of the CONSORT statement. J. Am. Med. Assoc. 2006;295:1152–60.

[88]The author thanks Dr Jenna Elder for this fact.