Statistical Frameworks of Clinical Trial Design for Evaluating Treatment Effect in Subpopulations

H.M. James Hung
Office of Biostatistics, OTS/CDER, Food and Drug Administration, U.S.A.

Classical designs for clinical trial were founded with an implicit assumption that the treatment effect under study is relatively homogeneous in the patients recruited for study. Such an assumption is probably reasonable in a relatively localized geographical region. Under such a paradigm, subgroup effects that stand out become surprising and often are thought of as spurious observations, particularly if the overall treatment effect is inconclusive. Interpretation of such apparent subgroup effects is often controversial. In the current era, drug development is frequently and more and more so based on global clinical trials. An individual global clinical trial may cover many geographical regions. In another context, more or more drug evaluation processes are stimulated by incorporation of some biomarkers in defining patient subpopulations. Evaluation of treatment effect in a particular patient subgroup becomes more or more of interest, regardless of whether the treatment effect is established globally or not. This presentation will stipulate a few statistical frameworks for such evaluation from the perspective of statistical design.

[H.M. James Hung, Division of Biometrics I, OB/OTS/CDER, FDA, 10903 New Hampshire Ave Bldg 22 Rm 4238, HFD-710, Mail stop 4105, Silver Spring, MD 20993-0002, USA; hsienming.hung@fda.hhs.gov]