Detecting Rare Adverse Events in Post-Marketing Safety Studies: Statistical Considerations

Yu-Te Wu
Food and Drug Administration, USA

A rising concern in drug development is the long-term monitoring of safety, especially for those rare, and severe/irreversible adverse drug reactions (ADRs) that are unable to be detected in pre-marketing studies. The observational cohort study often is the design used to detect causal relationships between drugs and ADRs when it is unfeasible to conduct prospective, randomized clinical trials. The single-group study has the disadvantage of lacking a comparator group while the two-group prospective study requires a prohibitively large sample size. In this presentation, I will discuss other alternative designs which can reduce the sample size requirement and reach the safety decision more quickly while satisfying the advantages of two-group design. New sample size formulae will be proposed for the alternative hybrid designs and the feasibility these designs is evaluated under different study scenarios. Simulation results of the performance of the proposed formulae will be presented.

[Yu-te Wu, US Food and Drug Administration, 1401 Blair Mill Rd, apt 418, Silver Spring, MD, USA; yu-te.wu@fda.hhs.gov]