SEQUENTIAL TESTING OF HYPOTHESES WITHIN THE SAME STAGE OF A MULTI-STAGE PHASE II DESIGN

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In Fleming's multi-stage Phase II design (1982 Biometrics 38, 143-151) the basic hypothesis H_o: $p \leq p_o$ versus H_A: $p \geq p_A$ is tested in a phase II clinical trial. This hypothesis consists of two non-complementary events and as mentioned by Store (1992 Biometrics 48, 55-60) this can introduce ambiguity in the evaluation of type I and II errors and the choice of the appropriate practical decision at the end of the study. In the majority of the suggested multi-stage phase II designs and particularly in the optimal designs (Gehan, Simon and Chen) this problem is addressed by considering designs that allow acceptance of the therapy only at the last stage of the study. Thus, only one of the non-complementary events is tested at each stage. In order to address the testing of non-complementary events at the same stage, instead of testing the hypothesis H_o: $p \leq p_o$ versus H_A: $p \geq p_A$, we propose a class of designs in which testing of two hypotheses is performed sequentially at each stage, with first testing: H_{o1}: $p \leq p_o$ versus H_{A1}: $p > p_o$; and second: H_{o2}: $p < p_A$ versus H_{A2}: $p \geq p_A$. For this class of designs the overall type I and II errors and the study average sample size (ASN) are evaluated and compared to the corresponding designs that test the two non-complementary events.