Multiplicity in adaptive designs aiming to combine learning data and confirming data

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To make use of the available information more efficiently, the temptation of combining phase II data and phase III data to increase the study power for the assessment of a new experimental treatment is growing. Newer adaptive designs are heading this direction making it inescapably attractive to drug sponsors. We will call such consideration novel two-stage adaptive designs. In statistical literature, it is well-known that when the learning data is used to both generate the hypothesis and test the hypothesis, the conventional type I error rate is not controlled. I will present a variety of novel adaptive designs, their relevant statistical hypotheses originally set out for versus the statistical hypotheses of eventual interest. When different randomization schemes are involved in different stages, it is not clear what the appropriate statistical analysis methods should be used. In addition, for data analysis, frequentist p-value may not always be computable. Statistical principles will be highlighted under the frequentist settings. Some regulatory perspectives will be presented and the above concerned issues will bring up for panel discussions.