A case study of refining testing strategy using graphical approach

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Abstract: For clinical trials with multiple treatment arms or endpoints a variety of sequentially rejective, weighted Bonferroni-type tests have been proposed, such as gatekeeping procedures, fixed sequence tests, and fallback procedures. The graphic approach (Bretz et al., 2009) is a simple iterative method to construct and perform such Bonferroni-type tests, where the resulting multiple test procedures are represented by directed, weighted graphs, where each node corresponds to an elementary hypothesis, together with a simple algorithm to generate such graphs while sequentially testing the individual hypotheses. We apply the graphic approach to a complex case study with multiple endpoints, multiple doses and multiple comparators to tailor the multiple test procedure to given study objectives. It is a good communication tool for the team with clinicians and medical doctors on this complicated multiple testing strategy. The hierarchy of the decision points with the alpha splitting of the hypotheses is described for each of the potential options. The overall power calculation based on the multiple testing strategy takes the correlations between different endpoints.