

Key Multiplicity Issues in Clinical Trials (Part I)

Online training course by Alex Dmitrienko available at www.sprmm.com

Papers

Alosh, M., Bretz, F., Huque, M. (2014). Advanced multiplicity adjustment methods in clinical trials. *Statistics in Medicine*. 33, 693-713.

Beer, T.M., Armstrong, A.J., Rathkopf, D.E., Loriot, Y., Sternberg, C.N., Higano, C.S., Iversen, P., Bhattacharya, S., Carles, J., Chowdhury, S., Davis, I.D., de Bono, J.S., Evans, C.P., Fizazi, K., Joshua, A.M., Kim, C.S., Kimura, G., Mainwaring, P., Mansbach, H., Miller, K., Noonberg, S.B., Perabo, F., Phung, D., Saad, F., Scher, H.I., Taplin, M.E., Venner, P.M., Tombal, B. (2014). Enzalutamide in metastatic prostate cancer before chemotherapy. *The New England Journal of Medicine*. 371, 424-433.

Benda, N., Branson, M., Maurer, W., Friede, T. (2010). Aspects of modernizing drug development using clinical scenario planning and evaluation. *Drug Information Journal*. 44, 299-315.

Brechenmacher, T., Xu, J., Dmitrienko, A., Tamhane, A.C. (2011). A mixture gatekeeping procedure based on the Hommel test for clinical trial applications. *Journal of Biopharmaceutical Statistics*. 21, 748-767.

Bretz, F., Maurer, W., Brannath, W., Posch, M. (2009). A graphical approach to sequentially rejective multiple test procedures. *Statistics in Medicine*. 28, 586-604.

Bofinger, E. (1987). Step-down procedures for comparison with a control. *Australian Journal of Statistics*. 29, 348-364.

Burman, C.F., Sonesson, C., Guilbaud, O. (2009). A recycling framework for the construction of Bonferroni-based multiple tests. *Statistics in Medicine*. 28, 739-761.

Cappuzzo, F., Ciuleanu, T., Stelmakh, L., Cicenas, S., Szczesna, A., Juhisz, E., Esteban, E., Molinier, O., Brugger, W., Melezinek, I., Klingelschmitt, G., Klughammer, B., Giaccone, G. (2010). Erlotinib as maintenance treatment in advanced non-small-cell lung cancer: A multicentre, randomized, placebo-controlled phase 3 study. *Lancet Oncology*. 11, 521-529.

Dmitrienko, A., Tamhane, A.C. (2011). Mixtures of multiple testing procedures for gatekeeping applications in clinical trials. *Statistics in Medicine*. 30, 1473-1488.

Dmitrienko, A., Millen, B.A., Brechenmacher, T., Paux, G. (2011). Development of gatekeeping strategies in confirmatory clinical trials. *Biometrical Journal*. 53, 875-893.

Dmitrienko, A., D'Agostino, R.B., Huque, M.F. (2013). Key multiplicity issues in clinical drug development. *Statistics in Medicine*. 32, 1079-1111.

- Dmitrienko, A., Tamhane, A.C. (2013). General theory of mixture procedures for gatekeeping. *Biometrical Journal*. 55, 402-419.
- Dmitrienko, A., D'Agostino, R.B. (2013). Tutorial in Biostatistics: Traditional Multiplicity Adjustment Methods in Clinical Trials. *Statistics in Medicine*. 32, 5172-5218.
- Dmitrienko, A., Paux, G., Brechenmacher, T. (2015). Power calculations in clinical trials with complex clinical objectives. *Journal of the Japanese Society of Computational Statistics*. 28, 15-50.
- Dmitrienko, A., Kordzakhia, G., Brechenmacher, T. (2016). Mixture-based gatekeeping procedures for multiplicity problems with multiple sequences of hypotheses. *Journal of Biopharmaceutical Statistics*. 26, 758-780.
- Dmitrienko, A., Paux, G., Pulkstenis, E., Zhang, J. (2016). Tradeoff-based optimization criteria in clinical trials with multiple objectives and adaptive designs. *Journal of Biopharmaceutical Statistics*. 26, 120-140.
- Dunnnett, C.W. (1955). A multiple comparison procedure for comparing several treatments with a control. *Journal of the American Statistical Association*. 50, 1096-1121.
- Dunnnett, C.W., Tamhane, A.C. (1991). Step-down multiple tests for comparing treatments with a control in unbalanced one-way layouts. *Statistics in Medicine*. 10, 939-947.
- Dunnnett, C.W., Tamhane, A.C. (1992). A step-up multiple test procedure. *Journal of the American Statistical Association*. 87, 162-170.
- Friede, T., Nicholas, R., Stallard, N., Todd, S., Parsons, N. R., Valdes-Marquez, E., Chataway, J. (2010). Refinement of the clinical scenario evaluation framework for assessment of competing development strategies with an application to multiple sclerosis. *Drug Information Journal*. 44, 713-718.
- Guilbaud, O. (2008). Simultaneous confidence regions corresponding to Holm's stepdown procedure and other closed-testing procedures. *Biometrical Journal*. 50, 678-692.
- Guilbaud, O. (2009). Alternative confidence regions for Bonferroni-based closed-testing procedures that are not alpha-exhaustive. *Biometrical Journal*. 51, 721-735.
- Guilbaud, O. (2012). Simultaneous confidence regions for closed tests, including Holm, Hochberg and Hommel related procedures. *Biometrical Journal*. 54, 317-342.
- Guilbaud, O., Karlsson, P. (2011). Confidence regions for Bonferroni-based closed tests extended to more general closed tests. *Journal of Biopharmaceutical Statistics*. 21, 682-707.
- Hochberg, Y. (1988). A sharper Bonferroni procedure for multiple significance testing. *Biometrika*. 75, 800-802.
- Hochberg, Y., Tamhane, A.C. (1987). *Multiple Comparison Procedures*. Wiley, New York.

- Holm, S. (1979). A simple sequentially rejective multiple test procedure. *Scandinavian Journal of Statistics*. 6, 65-70.
- Hommel, G. (1988). A stagewise rejective multiple test procedure based on a modified Bonferroni test. *Biometrika*. 75, 383-386.
- Hothorn, T., Bretz, F., Westfall, P. (2008). Simultaneous inference in general parametric models. *Biometrical Journal*. 50, 346-363.
- Huque, M.F., Alosch, M. (2008). A flexible fixed-sequence testing method for hierarchically ordered correlated multiple endpoints in clinical trials. *Journal of Statistical Planning and Inference*. 138, 321-335.
- Huque, M.F., Dmitrienko, A., D'Agostino, R.B. (2013). Multiplicity issues in clinical trials with multiple objectives. *Statistics in Biopharmaceutical Research*. 5, 321-337.
- Huque, M.F. (2016). Validity of the Hochberg procedure revisited for clinical trial applications. *Statistics in Medicine*. 35, 5-20.
- Marcus, R., Peritz, E., Gabriel, K.R. (1976). On closed testing procedures with special reference to ordered analysis of variance. *Biometrika*. 63, 655-660.
- Maurer, W., Hothorn, L. A., Lehmacher, W. (1995). Multiple comparisons in drug clinical trials and preclinical assays: a priori ordered hypotheses. *Biometrie in der Chemisch-in-Pharmazeutischen Industrie*. 6. Vollman, J. (editor). Fischer-Verlag, Stuttgart, 3-18.
- Millen, B.A., Dmitrienko, A. (2011). Chain procedures: A class of flexible closed testing procedures with clinical trial applications. *Statistics in Biopharmaceutical Research*. 3, 14-30.
- Naik, U.D. (1975). Some selection rules for comparing p processes with a standard. *Communications in Statistics. Series A*. 4, 519-535.
- Rosenstock, J., Aguilar-Salinas, C., Klein, E., Nepal, S., List, J., Chen, R. (2009). Effect of saxagliptin monotherapy in treatment-naïve patients with type 2 diabetes. *Current Medical Research And Opinion*. 25, 2401-2411.
- Sarkar, S., Chang, C.K. (1997). Simes' method for multiple hypothesis testing with positively dependent test statistics. *Journal of the American Statistical Association*. 92, 1601-1608.
- Sarkar, S.K. (1998). Some probability inequalities for censored MTP2 random variables: A proof of the Simes conjecture. *The Annals of Statistics*. 26, 494-504.
- Sarkar, S.K. (2008). On the Simes inequality and its generalization. *Beyond Parametrics in Interdisciplinary Research: Festschrift in Honor of Professor Pranab K. Sen*. Balakrishnan, N., Pena, E.A., Silvapulle, M.J. (editors). Institute of Mathematical Statistics, Beachwood, Ohio, 231-242.

Simes, R.J. (1986). An improved Bonferroni procedure for multiple tests of significance. *Biometrika*. 63, 655-660.

Stefansson, G., Kim, W.-C., Hsu, J.C. (1988). On confidence sets in multiple comparisons. *Statistical Decision Theory and Related Topics IV*. Gupta, S.S., Berger, J.O. (editors). Academic Press, New York, 89-104.

Strassburger, K., Bretz, F. (2008). Compatible simultaneous lower confidence bounds for the Holm procedure and other Bonferroni based closed tests. *Statistics in Medicine*. 27, 4914-4927.

Wang, S., O'Neill, R., Hung, H. (2007). Approaches to evaluation of treatment effect in randomized clinical trials with genomic subset. *Pharmaceutical Statistics*. 6, 227-244.

Wiens, B. (2003). A fixed-sequence Bonferroni procedure for testing multiple endpoints. *Pharmaceutical Statistics*. 2, 211-215.

Wiens, B., Dmitrienko, A. (2005). The fallback procedure for evaluating a single family of hypotheses. *Journal of Biopharmaceutical Statistics*. 15, 929-942.

Winblad, B., Grossberg, G., Frölich, D., Farlow, M., Zechner, S., Nagel, J., Lane, R. (2007). A 6-month, double-blind, placebo-controlled study of the first skin patch for Alzheimer disease. *Neurology*. 69, S14-S22.

Zhao, Y.D., Dmitrienko, A., Tamura, R. (2010). Design and analysis considerations in clinical trials with a sensitive subpopulation. *Statistics in Biopharmaceutical Research*. 2, 72-83.

Books

Dmitrienko, A., Tamhane, A.C., Bretz, F. (editors). (2009). *Multiple Testing Problems in Pharmaceutical Statistics*. Chapman and Hall/CRC Press, New York.

Dmitrienko, A., Pulkstenis, E. (editors). (2017). *Clinical Trial Optimization Using R*. Chapman and Hall/CRC Press, New York.