MEDICAL UNIVERSITY OF VIENNA

Wiener Biometrische Sektion
der Internationalen Biometrischen Gesellschaft
Region Österreich – Schweiz

Please join the Biometric Colloquium

January 21st, 2025 at 16:00 – 17:30

The colloquium features two talks on combined analyses of multiple trials by
Dong Xi (Gilead Sciences) and Marc Vandemeulebroecke (UCB Farchim SA)
Host: Martin Posch (Medical University of Vienna)

You can join using this Webex Link

Abstracts:

WHEN CONVENTION MEETS PRACTICALITY: COMBINED ANALYSIS TESTING UNDER THE TWO-TRIALS CONVENTION

DONG XI[1], FRANK BRETZ[2] , WILLI MAURER[2]
[1] Gilead Sciences; [2] Novartis AG

Regulatory guidance suggests controlling the family-wise error rate (FWER) in confirmatory clinical trials. The two-trial paradigm represents a further requirement to demonstrate efficacy in a clinical submission: A statistically significant outcome in at least two adequate and well-controlled clinical trials. Within each trial, different endpoints may require different sample size to achieve the adequacy of power. Sometimes the sample size driven by one endpoint could be twice as large as that required by other endpoints. These unbalanced requirements of resources in a single trial are amplified under the two-trial convention and may lead to financial and logistical challenges for the trial sponsor. It is, therefore, often of interest to combine the data from the two trials for an endpoint to make a confirmatory claim without doubling the sample size. However, it remains unclear what approaches could be used to manage multiplicity adjustments for the combined analysis using data from two identically designed trials. In this talk, we provide principles of controlling the submission-wise error rate (SWER) with combined analyses when success claims for endpoints tested in individual trials should be based on significance in both trials. We also discuss examples of SWER under other requirements where success claims could be based on significance from a single trial.

References

1. Bretz, F., Maurer, W., & Xi, D. (2019). Replicability, reproducibility, and multiplicity in drug development. *Chance*, 32(4), 4-11.
2. Bretz, F., & Xi, D. (2019). Commentary on “Statistics at FDA: Reflections on the Past Six Years”. *Statistics in Biopharmaceutical Research*, 11(1), 20-25.
3. Vandemeulebroecke, M., Häring, D., Hua, E., Wei, X., & Xi, D. (2024): New strategies for confirmatory testing of secondary hypotheses on combined data from multiple trials. *Clinical Trials*, 21(2) 171–179

CONFIRMATORY TESTING OF SECONDARY HYPOTHESES ON COMBINED DATA FROM MULTIPLE TRIALS – CASE STUDIES AND REFLECTIONS

MARC VANDEMEULEBROECKE[1] , DIETER HÄRING[2] , EVA HUA[2] , XIAOLING WEI[2] , DONG XI[3]

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In this talk, we present case studies that generated pivotal evidence on important secondary endpoints using combined data from multiple pivotal trials in an overarching formal testing hierarchy. For the primary endpoint, the case studies still adhere to the traditional two-trials convention which requires independent pivotal evidence from (at least) two trials, separately. For each case study, we discuss the situation and rationale, the approach taken with its advantages and caveats, any experiences with health authorities, and the final outcomes such as resulting label claims.

References

1. Vandemeulebroecke, M., Häring, D., Hua, E., Wei, X., & Xi, D. (2024): New strategies for confirmatory testing of secondary hypotheses on combined data from multiple trials. *Clinical Trials*, 21(2) 171–179