# Traditional design with multiple outcomes

## Description

The simulation report presents key operating characteristics of a multiple testing procedure (gatekeeping procedure) for multiple endpoints and multiple treatment-control comparisons in a trial with a normally distributed endpoint.

## Table 1. Number of enrolled patients

| **Trial arm** | **Sample size** |
| --- | --- |
| Control | 115 |
| Treatment 1 | 115 |
| Treatment 2 | 115 |
| Treatment 3 | 115 |

## Table 2. Treatment effect assumptions

| **Endpoint** | **Trial arm** | **Parameter** | **Value** |
| --- | --- | --- | --- |
| Endpoint 1 | Control | Mean | -15 |
|  |  | SD | 20 |
| Endpoint 1 | Treatment 1 | Mean | -20 |
|  |  | SD | 20 |
| Endpoint 1 | Treatment 2 | Mean | -21 |
|  |  | SD | 20 |
| Endpoint 1 | Treatment 3 | Mean | -23 |
|  |  | SD | 20 |
| Endpoint 2 | Control | Mean | -1 |
|  |  | SD | 1 |
| Endpoint 2 | Treatment 1 | Mean | -1.35 |
|  |  | SD | 1 |
| Endpoint 2 | Treatment 2 | Mean | -1.4 |
|  |  | SD | 1 |
| Endpoint 2 | Treatment 3 | Mean | -1.45 |
|  |  | SD | 1 |

A lower value of the endpoint indicates a beneficial effect.

## Table 3. Hypothesis definitions

| **Hypothesis** | **Definition** |
| --- | --- |
| Hypothesis 1 | Null hypothesis of no difference between Treatment 1 and control with respect to Endpoint 1 |
| Hypothesis 2 | Null hypothesis of no difference between Treatment 2 and control with respect to Endpoint 1 |
| Hypothesis 3 | Null hypothesis of no difference between Treatment 3 and control with respect to Endpoint 1 |
| Hypothesis 4 | Null hypothesis of no difference between Treatment 1 and control with respect to Endpoint 2 |
| Hypothesis 5 | Null hypothesis of no difference between Treatment 2 and control with respect to Endpoint 2 |
| Hypothesis 6 | Null hypothesis of no difference between Treatment 3 and control with respect to Endpoint 2 |

## Table 4. Endpoint correlation matrix

| **Endpoint** | **Endpoint 1** | **Endpoint 2** |
| --- | --- | --- |
| Endpoint 1 | 1 | 0.5 |
| Endpoint 2 | 0.5 | 1 |

## Table 5. Multiple testing procedure (Gatekeeping procedure)

| **Parameter** | **Value** |
| --- | --- |
| Component procedure | Hochberg |
| Mixture method | Modified |
| Truncation parameters | 0.8, 1 |

## Table 6. Other design parameters

| **Parameter** | **Value** |
| --- | --- |
| Dropout rate (%) | 10 |

## Table 7. Simulation parameters

| **Parameter** | **Value** |
| --- | --- |
| One-sided Type I error rate | 0.025 |
| Number of simulations | 10000 |

## Table 8. Simulation results: Hypothesis-specific power

| **Hypothesis** | **Power (%)** | **Adjusted power (%)** |
| --- | --- | --- |
| Hypothesis 1 | 47.1 | 40.4 |
| Hypothesis 2 | 61 | 51.5 |
| Hypothesis 3 | 85.5 | 75.9 |
| Hypothesis 4 | 75.6 | 34.3 |
| Hypothesis 5 | 85.7 | 44.1 |
| Hypothesis 6 | 92.1 | 63.6 |

Power: Probability of rejecting each hypothesis of no effect without a multiplicity adjustment. Adjusted power: Probability of rejecting each hypothesis of no effect using a multiplicity adjustment based on the specified multiple testing procedure.

## Table 9. Simulation results: Overall power

| **Endpoint family** | **Overall power** | **Power (%)** |
| --- | --- | --- |
| Endpoint 1 | Disjunctive power | 80.4 |
|  | Conjunctive power | 32.9 |
| Endpoint 2 | Disjunctive power | 69 |
|  | Conjunctive power | 28.2 |

Disjunctive power: Probability of rejecting at least one hypothesis of no effect within each endpoint family using a multiplicity adjustment based on the specified multiple testing procedure. Conjunctive power: Probability of rejecting all hypotheses of no effect within each endpoint family using a multiplicity adjustment based on the specified multiple testing procedure.