# Adaptive design with sample size re-estimation

## Description

The simulation report presents key operating characteristics of an adaptive design for a two-arm Phase III clinical trial with two interim analyses. The first interim analysis supports early stopping for futility and the second interim analysis supports an option to increase the sample size in the trial.

## Table 1. Number of enrolled patients

| **Trial arm** | **Sample size** |
| --- | --- |
| Control | 200 |
| Treatment | 200 |

## Table 2. Primary efficacy endpoint

| **Population** | **Value** |
| --- | --- |
| Endpoint type | Normal |
| Direction of favorable outcome | A lower value of the endpoint indicates a more favorable outcome |

## Table 3. Treatment effect assumptions

| **Trial arm** | **Parameter** | **Value** |
| --- | --- | --- |
| Control | Mean | -15 |
|  | SD | 25 |
| Treatment | Mean | -22.5 |
|  | SD | 25 |

## Table 4. Number of patients at the interim and final analyses

| **Decision point** | **Total number of patients** | **Information fraction (%)** |
| --- | --- | --- |
| Interim analysis 1 | 96 | 30 |
| Interim analysis 2 | 224 | 70 |
| Final analysis (before sample size re-estimation) | 320 | 100 |
| Final analysis (after sample size re-estimation) | Up to 416 | 130 |

The number of patients at the interim and final analyses may be reduced due to patient dropout.

## Table 5. Decision rule at Interim analysis 1

| **Parameter** | **PPS (%)** |
| --- | --- |
| Futility threshold | 10 |

PPS: Predicted probability of success at Interim analysis 1. The trial will be stopped for futility at Interim analysis 1 if the predicted probability of success is less than the futility threshold.

## Table 6. Decision rules at Interim analysis 2

| **Parameter** | **PPS (%)** |
| --- | --- |
| Promising interval (lower limit) | 50 |
| Promising interval (upper limit) | 90 |
| Target probability of success at Final analysis | 90 |

PPS: Predicted probability of success at Interim analysis 2. The sample size will be increased after Interim analysis 2 to achieve the target probability of success at Final analysis if the predicted probability of success lies within the promising interval.

## Table 7. Other design parameters

| **Parameter** | **Value** |
| --- | --- |
| Dropout rate at the end of the treatment period (%) | 20 |

## Table 8. Simulation parameters

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

## Table 9. Simulation results: Outcome probabilities

| **Parameter** | **Value** |
| --- | --- |
| Probability of stopping for futility at Interim analysis 1 (%) | 15.9 |
| Probability of increasing the sample size at Interim analysis 2 (%) | 18.3 |
| Traditional design: Power (%) | 69.9 |
| Adaptive design: Power (%) | 71.7 |

## Table 10. Simulation results: Comparison of traditional and adaptive designs

| **Interval** | **Design** | **Power (%)** |
| --- | --- | --- |
| Unfavorable interval | Traditional design | 20.1 |
|  | Adaptive design | 20.1 |
| Promising interval | Traditional design | 81 |
|  | Adaptive design | 91.1 |
| Favorable interval | Traditional design | 97.8 |
|  | Adaptive design | 97.8 |

Unfavorable interval: Predicted probability of success at Interim analysis 2 (PPS) is less than 50% (original sample size is retained). Promising interval: PPS is between 50% and 90% (sample size is increased). Favorable interval: PPS is greater than 90% (original sample size is retained).