# Optimal futility stopping rule

## Description

The simulation report presents operating characteristics of a multi-arm trial design with a single interim analysis. A futility stopping rule will be applied at this interim look and the trial will be stopped early for futility if the predicted probability of success (conditional power) is less than a pre-defined futility threshold in all treatment arms. An optimal value of the futility threshold is computed by maximizing the sensitivity and specificity rates.

## Table 1. Primary efficacy endpoint

| **Parameter** | **Value** |
| --- | --- |
| Endpoint type | Time-to-event |
| Direction of favorable outcome | A higher value of the endpoint indicates a more favorable outcome |

## Table 2. Number of enrolled patients

| **Trial arm** | **Sample size** |
| --- | --- |
| Control | 230 |
| Treatment | 230 |

## Table 3. Treatment effect assumptions

| **Trial arm** | **Parameter** | **Value** |
| --- | --- | --- |
| Control | Median time | 16 |
| Treatment | Median time | 22.9 |

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

| **Decision point** | **Total number of events** | **Information fraction (%)** |
| --- | --- | --- |
| Interim analysis | 165 | 50 |
| Final analysis | 330 | 100 |

## Table 5. Other design parameters

| **Parameter** | **Value** |
| --- | --- |
| Patient enrollment period | 36 |
| Median enrollment time | 24 |
| Annual dropout rate (%) | 5 |

## Table 6. Simulation parameters

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

## Figure 1. Sensitivity and specificity rates as functions of the futility threshold



Red curve: Sensitivity rate (probability of correctly retaining at least one treatment arm at the interim analysis, evaluated under the alternative hypothesis of beneficial effect, i.e., all treatments are effective). Blue curve: Specificity rate (probability of correctly stopping all treatment arms at the interim analysis due to futility, evaluated under the null hypothesis of no effect, i.e., all treatments are ineffective).

## Figure 2. Accuracy rate as a function of the futility threshold



The accuracy rate is defined as the average of the sensitivity and specificity rates and an optimal futility threshold is defined as the threshold that maximizes the accuracy rate. Optimal futility threshold: 27%. 95% optimal interval: (5%, 77%).