child2

# *Executive summary*

For the planned study, a total of **250** patients with a possible infection must be observed given the below assumptions.

For the proposed randomized clinical study, the sample size considerations are given with the following suppositions:

* 2 arms (arm A, B)
* binary outcome variable (ie. rates between groups)
* aim: to show statistical significant difference between the two arms
* arm A is hypothecized to be 30%
* arm B is hypothecized to be 15%
* Power of 80%
* Type I error rate of 5% (2-sided, equal to 2.5% one-sided)
* 1 interim analysis (at 50% of cases, but this is flexible), 1 final analysis
* Hwang, Shi & DeCani alpha spending function, gamma = 1
* 1:1 randomization

# Working Environment

# Load the package `ggplot2`  
library(ggplot2)  
# Load the package `rpact`  
library(rpact)

Warning: package 'rpact' was built under R version 4.4.2

# Design

## R command

design <- getDesignGroupSequential(typeOfDesign = "asHSD", informationRates = c(0.5, 1),  
 gammaA = -2)  
print(design)  
getDesignCharacteristics(design)  
designPlan <- getSampleSizeRates(design, pi1 = 0.3, pi2 = 0.15)  
summary(designPlan)  
print(designPlan)

*Design parameters and output of group sequential design*

*User defined parameters*

* *Type of design*: Hwang, Shi & DeCani alpha spending
* *Information rates*: 0.500, 1.000
* *Parameter for alpha spending function*: -2

*Derived from user defined parameters*

* *Maximum number of stages*: 2
* *Stages*: 1, 2
* *Futility bounds (non-binding)*: -Inf

*Default parameters*

* *Significance level*: 0.0250
* *Type II error rate*: 0.2000
* *Binding futility*: FALSE
* *Test*: one-sided
* *Tolerance*: 1e-08
* *Type of beta spending*: none

*Output*

* *Cumulative alpha spending*: 0.006724, 0.025000
* *Critical values*: 2.472, 2.025
* *Stage levels (one-sided)*: 0.006724, 0.021451 *Group sequential design characteristics*
* *Number of subjects fixed*: 7.8489
* *Shift*: 8.0900
* *Inflation factor*: 1.0307
* *Informations*: 4.045, 8.090
* *Power*: 0.3226, 0.8000
* *Rejection probabilities under H1*: 0.3226, 0.4774
* *Futility probabilities under H1*: 0
* *Ratio expected vs fixed sample size under H1*: 0.8645
* *Ratio expected vs fixed sample size under a value between H0 and H1*: 0.9940
* *Ratio expected vs fixed sample size under H0*: 1.0273 *Design plan parameters and output for rates*

*Design parameters*

* *Information rates*: 0.500, 1.000
* *Critical values*: 2.472, 2.025
* *Futility bounds (non-binding)*: -Inf
* *Cumulative alpha spending*: 0.006724, 0.025000
* *Local one-sided significance levels*: 0.006724, 0.021451
* *Significance level*: 0.0250
* *Type II error rate*: 0.2000
* *Test*: one-sided

*User defined parameters*

* *Assumed treatment rate*: 0.300
* *Assumed control rate*: 0.150

*Default parameters*

* *Risk ratio*: FALSE
* *Theta H0*: 0
* *Normal approximation*: TRUE
* *Treatment groups*: 2
* *Planned allocation ratio*: 1

*Sample size and output*

* *Direction upper*: TRUE
* *Maximum number of subjects*: 248.3
* *Maximum number of subjects (1)*: 124.2
* *Maximum number of subjects (2)*: 124.2
* *Number of subjects [1]*: 124.2
* *Number of subjects [2]*: 248.3
* *Reject per stage [1]*: 0.3226
* *Reject per stage [2]*: 0.4774
* *Early stop*: 0.3226
* *Expected number of subjects under H0*: 247.5
* *Expected number of subjects under H0/H1*: 239.5
* *Expected number of subjects under H1*: 208.3
* *Critical values (treatment effect scale) [1]*: 0.191
* *Critical values (treatment effect scale) [2]*: 0.103

*Legend*

* *(i)*: values of treatment arm i
* *[k]*: values at stage k

*Sample size calculation for a binary endpoint*

Sequential analysis with a maximum of 2 looks (group sequential design), one-sided overall significance level 2.5%, power 80%. The results were calculated for a two-sample test for rates (normal approximation), H0: pi(1) - pi(2) = 0, H1: pi(1) = 0.3, control rate pi(2) = 0.15.

| Stage | 1 | 2 |
| --- | --- | --- |
| Planned information rate | 50% | 100% |
| Cumulative alpha spent | 0.0067 | 0.0250 |
| Stage levels (one-sided) | 0.0067 | 0.0215 |
| Efficacy boundary (z-value scale) | 2.472 | 2.025 |
| Efficacy boundary (t) | 0.191 | 0.103 |
| Cumulative power | 0.3226 | 0.8000 |
| Number of subjects | 124.2 | 248.3 |
| Expected number of subjects under H1 |  | 208.3 |
| Exit probability for efficacy (under H0) | 0.0067 |  |
| Exit probability for efficacy (under H1) | 0.3226 |  |

Legend:

* *(t)*: treatment effect scale *Design plan parameters and output for rates*

*Design parameters*

* *Information rates*: 0.500, 1.000
* *Critical values*: 2.472, 2.025
* *Futility bounds (non-binding)*: -Inf
* *Cumulative alpha spending*: 0.006724, 0.025000
* *Local one-sided significance levels*: 0.006724, 0.021451
* *Significance level*: 0.0250
* *Type II error rate*: 0.2000
* *Test*: one-sided

*User defined parameters*

* *Assumed treatment rate*: 0.300
* *Assumed control rate*: 0.150

*Default parameters*

* *Risk ratio*: FALSE
* *Theta H0*: 0
* *Normal approximation*: TRUE
* *Treatment groups*: 2
* *Planned allocation ratio*: 1

*Sample size and output*

* *Direction upper*: TRUE
* *Maximum number of subjects*: 248.3
* *Maximum number of subjects (1)*: 124.2
* *Maximum number of subjects (2)*: 124.2
* *Number of subjects [1]*: 124.2
* *Number of subjects [2]*: 248.3
* *Reject per stage [1]*: 0.3226
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* *Early stop*: 0.3226
* *Expected number of subjects under H0*: 247.5
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* *Expected number of subjects under H1*: 208.3
* *Critical values (treatment effect scale) [1]*: 0.191
* *Critical values (treatment effect scale) [2]*: 0.103

*Legend*

* *(i)*: values of treatment arm i
* *[k]*: values at stage k