Sample size calculation for future trials

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2021/2/8

Sample size calculation

Meta-analysis

Nanni 2018, Pimentel 2019, Zhao 2017

```
df <- read.csv("data.csv", sep="," , header=T)
metaprop(event=Event,
         n=Sample,
         data=df,
         studlab=Study,
         sm="Plogit",
         comb.fixed=FALSE,
         comb.random=TRUE,
         hakn=F,
         method.tau="DL")
```

```
##      proportion           95%-CI %W(random)
## id12     0.7692 [0.6481; 0.8647]       42.1
## id16     0.8636 [0.6509; 0.9709]       21.7
## id28     0.6000 [0.4060; 0.7734]       36.2
##
## Number of studies combined: k = 3
##
##                       proportion           95%-CI
## Random effects model     0.7417 [0.5832; 0.8549]
##
## Quantifying heterogeneity:
##  tau^2 = 0.2330 [0.0000; 18.0661]; tau = 0.4827 [0.0000; 4.2504]
##  I^2 = 59.0% [0.0%; 88.3%]; H = 1.56 [1.00; 2.93]
##
## Test of heterogeneity:
##     Q d.f. p-value
##  4.88    2  0.0874
##
## Details on meta-analytical method:
## - Inverse variance method
## - DerSimonian-Laird estimator for tau^2
## - Jackson method for confidence interval of tau^2 and tau
## - Logit transformation
## - Clopper-Pearson confidence interval for individual studies
```

The pooled 3-year mortality was calculated.

Sample size calculation

```
tref <- 3 #time at which mortalities estimated
Nsim <- seq(5000,6000, 100)
mc <- 0.74 #tref-year mortality, control
hr <- 1.13 #hazard ratio.
r <- (1-((1-(1-mc)^hr)/mc))*100 #% reduction in mc by intervention
accrual <- 2 #duration of accrual period
tmin <- 2/12 #minimum follow-up time
pwr.res<-c()
for (i in 1:length(Nsim) ){
  pwr.tmp<-cpower(tref=tref,
                  n=Nsim[i],
                  mc=mc,
                  r=r,
                  accrual=accrual,
                  tmin=tmin,
                  noncomp.c=0,
                  noncomp.i=0,
                  alpha=0.05,
                  pr=FALSE)
  pwr.res[i]<-pwr.tmp["Power"]
}
pwr.res.all<-cbind(Nsim, pwr.res)
pwr.res.all
```

```
##       Nsim   pwr.res
##  [1,] 5000 0.7846554
##  [2,] 5100 0.7925657
##  [3,] 5200 0.8002270
##  [4,] 5300 0.8076448
##  [5,] 5400 0.8148243
##  [6,] 5500 0.8217713
##  [7,] 5600 0.8284910
##  [8,] 5700 0.8349890
##  [9,] 5800 0.8412709
## [10,] 5900 0.8473419
## [11,] 6000 0.8532077
```

A total of 5200 patients will be needed.

Methods

Sample size calculation for future trials
We performed sample size calculation for future trials targeting at patients with metastatic/recurrent breast cancer receiving chemotherapy or endocrine therapy. First, we picked up the median follow-up period among the included studies and calculated the pooled event rates using the random-effects model. Then, we simulated trials of comparing the entire survival curves between metformin group and placebo group.

We used the following data; $\alpha = 0.05$, $power = 0.8$, study accrual period, percent of drop-ins and non-adherers, the pooled event rates of placebo during the median follow-up period, and the pooled hazard ratio. Parameters were based on the results of systematic review. R version 3.6.0 (R core Team, Vienna, Austria) and packages "meta" (version. 4.16-2) and "Hmisc" (version 4.4-0) were used for sample size calculation.

Results

Sample size calculation for future trials

Based on the information gathered from our systematic review, we set the parameters as following; study accrual period of 1 year, no drop-ins or non-adherers, the pooled event rates of 0.74 among the placebo group during the 3-year follow-up period, and the pooled hazard ratio of 1.13. When randomised controlled trials with a allocation ratio of 1:1 are conducted, a total of 5200 patients will be needed to detect the difference assuming $\alpha = 0.05$ and $power = 0.8$.