

## Supplementary material

### Sample size calculation for time to event analysis

Two interventions Standard (S) and Test (T).

#### Parameters

**Significance level, Alpha ( $\alpha$ ):** Type I error rate

**Power ( $1 - \beta$ ):** Type II error rate

**Standard group proportion,  $\pi_S$ :** proportion alive at fixed time point  $\pi_s$ . The proportion surviving without MACE at 5 years of follow-up is estimated to be 0.95.

**HR<sub>Plan</sub>:** Planned hazard ratio for the study

**Allocation ratio,  $\phi$ :** Refers to the ratio of intended numbers of participants in each of the comparison treatment groups. For two-groups trials, the allocation ratio is usually 1:1, however unequal allocation (such as 1:2) is also sometimes used. Kindly enter 1 for 1:1 ratio, 1.5 for 2:3 ratio, 2 for 1:2 ratio, 3 for 1:3 ratio and so on.

**Events, E:** The total number of events required to give a test with significance  $\alpha$  and power  $1-\beta$ .

Sample size refers to the minimum number of patients required to be accrued to perform the trial.

nS denotes the number of patients required in standard group

nT denotes the number of patients required in test group

nS = nT if the allocation ratio,  $\phi = 1$

Total sample size is the sum of the number of patients in all the treatment groups.

Parameters	Option 1	Option 2	Option 3	Option 4	Option 5
Significance level, $\alpha$	.05	.05	.05	.05	.05
Power, $1-\beta$	.80	.90	.80	.80	.80
Standard group proportion, $\pi_S$	.95	.95	.9	.95	.95
Hazard ratio, HR <sub>Plan</sub>	.85	.90	.85	.95	.80
Allocation ratio, $\phi$	1	1	1	1	1
One-sided or Two-sided	Two-sided	Two-sided	Two-sided	Two-sided	Two-sided
Total Number of Events, E	1194	3794	1194	11940	636
Standard group, nS	12886	39889	6431	122386	7051
Test group, nT	12886	39889	6431	122386	7051
Total Sample Size, N	25772	79778	12862	244772	14102

More than two groups should be calculated as a series of two group studies.

We have four groups, with one group as the reference group.

Thus, using option 1 as an example, assuming equal allocation, both groups have same sample size of 12886. Therefore, the total sample size required is  $4 \times 12886 = 51544$ , and total number of events is approximately  $2 \times 1194 = 2388$ .

## References

1. Machin D, Campbell MJ, Tan SB, et al. Survival Time Outcomes. Sample Sizes for Clinical, Laboratory and Epidemiology Studies. 2018:99-116.
2. Department of Obstetrics and Gynaecology of The Chinese University of Hong Kong. StatTools: Survival - Kaplan Meier Log Rank Test Explained [Internet]. [cited 2020 Jul 15]. Available from: [http://www.obg.cuhk.edu.hk/ResearchSupport/StatTools/Survival\\_Exp.php](http://www.obg.cuhk.edu.hk/ResearchSupport/StatTools/Survival_Exp.php)