

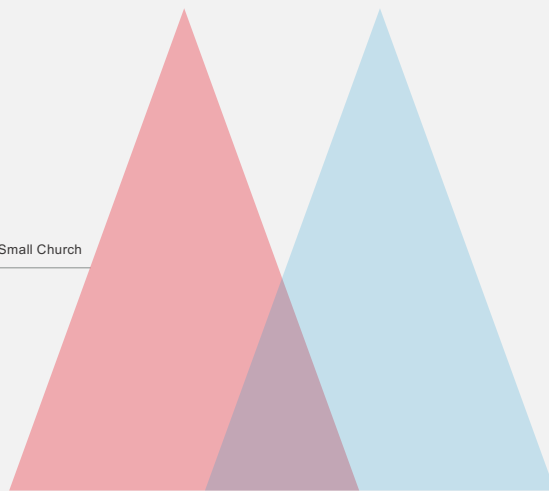
KIOSC

Korean Incubating Organization for Small Church

Study Design and Power & Sample Size

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#KIOSC #TRAINING



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Last week summary

Outcome	Method	Comparison
Continuous	t-test	Means of two groups
Continuous	ANOVA	Means of 2 or more groups
Continuous	ANCOVA	Adjusted Means of 2 or more groups
Continuous	MMRM	Adjusted Means and more
Categorical	Chi-square	Proportion of 2 or more groups
Categorical	Logistic Regression	Odds ratio and more
Time to Event	Survival Analysis	Hazard ratio and more

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Study types

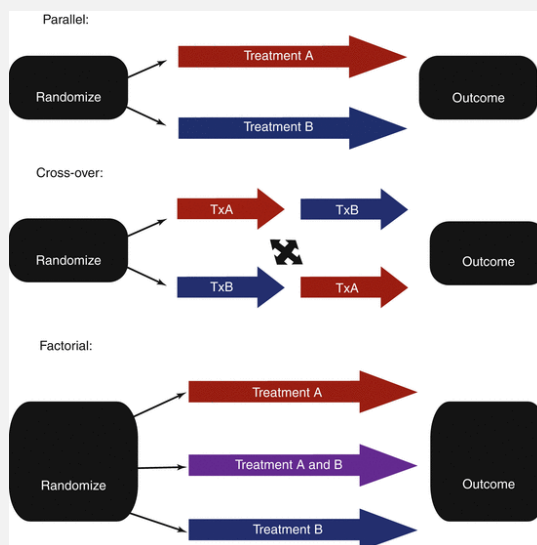
- **Observational Study**
 - **Case-control**
 - **Cohort study**
- **Experimental Study/Trial**
 - **Intervention**

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Trial Design

- **Parallel group**
- **Cross-over design**
- **Factorial design**
- **Sequential design**



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Power and Sample Size

Significance level (α)

	Reject H_0	Fail to reject H_0
H_0 is True	Type I error (α)	correct
H_a is True	correct	Type II error (β)

Power ($1-\beta$)

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Power and Sample Size

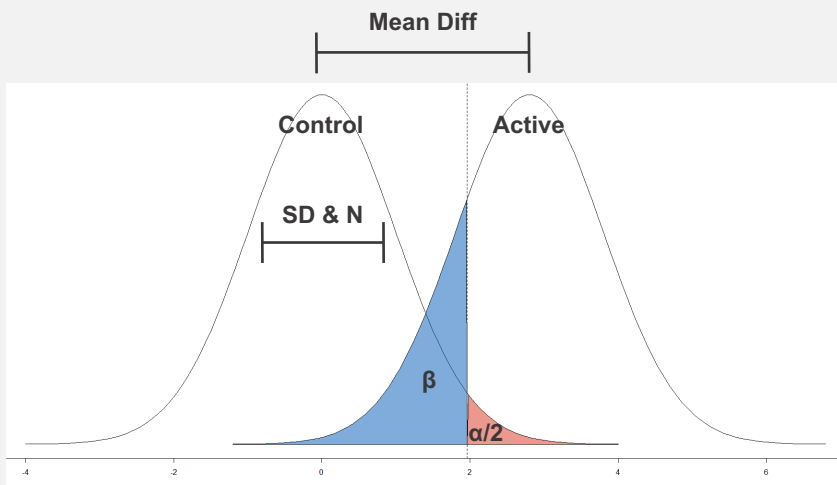
- Sample Size
- Power ($1-\beta$)
- Effect Size (difference and standard deviation)
- Significance level (α)

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Power and Sample Size

- Comparing two means



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Power and Sample Size

- Example from last week

15.4.1 Rationale for Sample Size

The sample size was calculated in reference to the point estimate and its 95% confidence interval of the percent change from baseline in pruritus VAS at Week 12 in the phase II clinical study (CIM003JG) (ITT, including data after rescue therapy, without imputation) because there is no efficacy data in this design of the study though this study is to verify superiority of nemolizumab compared to placebo at Week 16 under concomitant use of topical corticosteroid or Topical calcineurin inhibitor (Table 15-2).

Table 15-2 Point estimate of the percent change from baseline in pruritus VAS (%) at Week 12 using MMRM and the two-sided 95% confidence interval (ITT, including data after rescue therapy, without supplement)

Placebo group (N=53)	0.5 mg/kg group (N=54)	2.0 mg/kg group (N=52)
-27.63 (-36.56 to -18.70)	-61.76 (-70.47 to -53.04)	-66.07 (-74.96 to -57.17)

In reference to the upper bound of the 95% confidence limit at Week 12 in Table 15-2, the percent change from baseline in pruritus VAS of the nemolizumab group was assumed as **53%**. In reference to the lower bound of the 95% confidence limit at Week 12, the percent change from baseline in pruritus VAS of the placebo group was assumed as **36%**. If the standard deviation of the percent change from baseline in pruritus VAS at Week 16 of both groups is assumed as **35%**, the number of subjects required to confirm superiority of the nemolizumab group compared to the placebo group was calculated to be 204 (total of both treatment groups) using the SAS Power procedure based on a significance level of **2.5% (one sided)**, **90% power**, and randomization ratio 2:1. Since the subjects who discontinue the study can be included in the analysis of the primary analysis (MMRM), the target sample size was determined to be 204 subjects (136 subjects in the nemolizumab group and 68 subjects in the placebo group).

End Point	Nemolizumab (N=143)	Placebo (N=72)	Difference (95% CI)
Primary end point: percent change in pruritus VAS score from baseline to wk 16	-42.8±2.6	-21.4±3.6	percentage points -21.5 (-30.2 to -12.7)†

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Power and Sample Size

- Comparing two proportion
 - chisq is approximately normal when N is large
 - Difference in prop \approx Difference in mean
 - Standard deviation related to overall proportion

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Power and Sample Size

- Example from last week

Sample Size Determination

Approximately 545 subjects in total will be enrolled into the study. Sample size is estimated based on the primary endpoint of the proportion of subjects in remission at Week 8 and the key secondary endpoint of the proportion of subjects achieving mucosal healing at Week8. Subjects will be randomized in a 4:1 ratio to either tofacitinib 10mg BID or placebo. With a sample size of approximately 545, there will be at least 90% power to detect a treatment difference assuming a difference of 17.5% between treatment groups in remission rate at Week8 using Chi-square test at the significant level of 5% (2-sided) under the assumption of placebo rate of 15%. With this sample size, there will be at least 90% power to detect a treatment difference assuming a difference of 17.5% between treatment groups in the proportion of subjects achieving mucosal healing at Week8 using Chi-square test at the significant level of 5% under the assumption of placebo rate of 35%.



End Point	OCTAVE Induction 1			
	Placebo (N = 122)	Tofacitinib, 10 mg (N = 476)	Difference (95% CI)	P Value
	percentage points			
Based on Mayo score†				
Primary end point: remission at wk 8 — no. (%)	10 (8.2)	88 (18.5)	10.3 (4.3 to 16.3)	0.007

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Power and Sample Size

- Comparing hazard ratio
 - α and β
 - Accrual time and follow-up time
 - Median survival time/hazard rate
 - Careful considerations

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Thank You

Biostatistics for Non-statistician

- ☐ Basic I - Various Statistical Analysis Methods I
- ☐ Basic II - Various Statistical Analysis Methods II
- ☐ Advanced I - Study Design and Power & Sample Size
- ☐ Advanced II - Adaptive Trial Design

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