

**A randomized, controlled, double blind study to evaluate the efficacy
of intralesional triamcinolone in the treatment of hidradenitis
suppurativa**

STATISTICAL ANALYSIS PLAN

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Statistical approach for IRB 16-0773, A randomized, controlled, double-blind study to evaluate the efficacy of intralesional triamcinolone in the treatment of hidradenitis suppurativa.

The calculations for power justification are outlined below demonstrating 80% power to demonstrate our primary aim. The power to tell a difference between our 2 treatment groups is only 28%, but this is acceptable as a secondary aim. In our final analysis we will use a mixed effects regression model to account for the variation in number of lesions evaluated in each patient. This will account for some correlation among lesions treated within the same patient due to how patient reported lesion clearance may be somewhat effected by individual patient perception. 95% confidence intervals will be created for each group and p-values for comparisons between each group will be calculated in the final analysis for each study end point.

Our secondary aim of finding differences in pain scores are appropriately powered with power nearing 100%.

For our third aim demonstrating improved perception of treatment, the analysis is more straightforward as data is gathered at only one time point. We will perform descriptive analysis and report the average ratings and the corresponding confidence intervals.

Simulation settings for power analysis

There are 30 patients in which 12 have 1 lesion, 6 have 2 lesions and 12 have 3 lesions. Each lesion is then randomized to one of 3 treatment groups (say, A, B, C) with equal chance. For patient k , lesion j , let T be the treatment assigned. We generate data as following:

$$Y_{kj} = \beta_1 I(T_{kj} = A) + \beta_2 I(T_{kj} = B) + \beta_3 I(T_{kj} = C) + b_k + e_{kj}$$

b_k is a patient-specific random effect, e_{kj} is a random error.

We consider two scenarios, where the first one corresponds to the outcome of days to resolution, and the second one is for the pain scores.

Scenario 1:

$$\beta_1 = 6, \beta_2 = 8, \beta_3 = 10;$$

b_k is patient-specific random effect from normal with mean 0 and standard deviation $5\sqrt{0.2}$;

e_{kj} is random error from normal with mean 0 and standard deviation $5\sqrt{0.8}$.

Scenario 2:

$$\beta_1 = 2, \beta_2 = 4, \beta_3 = 6;$$

b_k is patient-specific random effect from normal with mean 0 and standard deviation $\sqrt{0.2}$;

e_{kj} is random error from normal with mean 0 and standard deviation $\sqrt{0.8}$.

After simulating the data 100 times, we fit the same model, and perform two tests as follows:

- a. Test $\frac{\beta_1 + \beta_2}{2} < \beta_3$, report the probability of rejecting the null (one side p-value < 0.05), report the standard error of the estimates for $\frac{\beta_1 + \beta_2}{2} - \beta_3$.
- b. Test $\beta_1 < \beta_2$, report the probability of rejecting the null (one side p-value < 0.05), report the standard error of the estimates for $\beta_1 - \beta_2$.

The results are given in the following table. It shows that for the primary outcome (days to resolution), there is 80% power to test that the combined treatment groups have less number of the days than the control group. The power to detect the difference between two treatment groups is 28%. For the secondary outcome of the pain scores, these numbers become 100%.

The average 95% confidence interval for the difference between the combined treatment groups and the control group is (2.6, 5.6) for days to resolution and (2.46, 3.52) for pain scores.

Results of the two scenarios						
Scenario	Compare combined treatments vs control			Compare two treatment groups		
	$\frac{\beta_1 + \beta_2}{2} - \beta_3$	SE	power	$\beta_1 - \beta_2$	Std err (estimates)	power
	True value			True value		

1: days to resolution	-3	1.331	0.8	-2	1.540	0.28
2: pain scores	-3	0.266	1	-2	0.300	1

Final analysis of data:

For each aim we will calculate means with 95% confidence intervals and p-values for comparisons between each treatment group and the placebo group. The treatment groups will also be combined for comparison to the placebo group.