

A Phase III dose-finding clinical trial in patients with pancreatic cancer was conducted to determine if at least one of two doses of a new experimental treatment has a beneficial effect on 1-year mortality. Occasionally, for serious illnesses such as pancreatic cancer, the FDA allows the sponsor to skip Phase II and go directly to a Phase III dose-finding study in order to expedite product testing and get the product on the market as soon as possible, especially when there is no current treatment for the disease being studied. However, the usual appropriate statistical rigor required for Phase III (i.e., control the probability of a false positive study at 0.05) needs to be applied.

Treatment Group	Died Within 1 Year of Randomization	
	Yes	No
Control	30	16
Low Dose	23	22
High Dose	13	31

- $H_0: p_{low} = p_P$       The proportion of death is the same in the low experimental dose and placebo groups.  
 $H_A: p_{low} \neq p_P$       The proportion of death is not the same in the low experimental dose and placebo groups.
- $H_0: p_{high} = p_P$       The proportion of death is the same in the low experimental dose and placebo groups.  
 $H_A: p_{high} \neq p_P$       The proportion of death is not the same in the low experimental dose and placebo groups.

2 tests will be performed, so the Bonferroni correction is  $\frac{0.05}{2} = 0.025$ .

## Pairwise Comparison between Low Dose and Placebo

### The FREQ Procedure

Frequency Row Pct	Table of trt by outcome			
	trt	outcome(Death)		
		Alive	Died	Total
	Low Dose	22 48.89	23 51.11	45
	Placebo	16 34.78	30 65.22	46
	Total	38	53	91

## Pairwise Comparison between High Dose and Placebo

### The FREQ Procedure

Frequency Row Pct	Table of trt by outcome			
	trt	outcome(Death)		
		Alive	Died	Total
	High Dose	31 70.45	13 29.55	44
	Placebo	16 34.78	30 65.22	46
	Total	47	43	90

There are 14.11% (95% CI: -37.06%, 8.84%,) fewer cases of death in the low dose group than in the placebo group. The risk of death in the low dose group is 78.36% (95% CI: 52.21%, 117.65%) of the risk in the placebo group.

There are 35.67% (95% CI: -57.70%, -13.64%) fewer cases of death in the high dose group than in the placebo group. The risk of death in the high dose group is 45.30% (95% CI: 25.49%, 80.50%) of the risk in the placebo group.

$$\begin{aligned} \text{low dose vs placebo } p - \text{value} &= 0.1725 \\ \text{adjusted } p - \text{value} &= 2 \times 0.1725 = 0.3454 \end{aligned}$$

$$\begin{aligned} \text{high dose vs placebo } p - \text{value} &= 0.0007 \\ \text{adjusted } p - \text{value} &= 2 \times 0.0007 = 0.0014 \end{aligned}$$

The low doses' adjusted p-value was 0.3454, which is greater than the  $\alpha=0.05$  significance level, while the high dose's adjusted p-value was 0.0014, which is less than the  $\alpha=0.05$  significance level. Only the null hypothesis of the proportion of death being the same as the placebo group can be rejected for the high dose comparison.

The low dose's 95% confidence interval for the risk difference contains 0 and the risk ratio contains 1, so those effects were not significant. On the other hand, the high dose's 95% confidence interval for the risk difference doesn't contain 0 and the risk ratio doesn't contain 1, so those effects are statistically significant. Since at least one dose, the high dose, was found to be significantly more effective than the control at reducing mortality, the study was found to be a success.