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.

The goal of the trial is to detect if at least one of the doses of the experimental treatment is significantly more effective than the control at reducing mortality of pancreatic cancer patients. State the pairwise (null and alternative) hypotheses of interest in both words and notation, and the Bonferroni comparison-wise error rates that will control the family-wise error rate (probability of a false positive study) at the 0.05 level of significance.

	Died Within 1 Year of Randomization	
Treatment Group	**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 $\frac{0.05}{2} = 0.025$.

Use PROC FREQ to set up a formal contingency table relating treatment to mortality. Please highlight the risk of death within 1 year for each treatment group. Report the Bonferroni-adjusted chi-square p-values for the comparison of each dose versus control.

Pairwise Comparison between Low Dose and Placebo

The FREQ Procedure

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

Calculate the risk difference and risk ratios for death between (a) the low dose group and the control group; and (b) the high dose and the control group. Calculate the Bonferroni-adjusted 2-sided 95%confidence interval for the risk difference and risk difference in each case, appropriately controlling the family-wise error rate at the 0.05 level of significance.

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.

Explain whether or not the study is a success based on the definition of success in and the results you generated; please state the dose(s), if any, that you feel should be marketed and why.

$$low\ dose\ vs\ placebo\ p-value\ =\ 0.1725$$
$$adjusted\ p-value\ =\ 2\times 0.1725\ =\ 0.3454$$

$$high\ dose\ vs\ placebo\ p-value\ =\ 0.0007$$
$$adjusted\ p-value\ =\ 2\times 0.0007\ =\ 0.0014$$

The low doses' adjusted p-value was 0.3454, which is greater than the α=0.05 significance level, while the high dose's adjusted p-value was 0.0014, which is less than the α=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.