A randomized trial for Hepatitis C is planned with 1:1 randomization to a new treatment versus a standard of care treatment (control) is planned. The initial goal is to enroll 1500 patients in both treatments combined. The primary outcome is sustained virological response ("SVR") at 6 months after randomization (meaning hepatitis C virus is not detected in the blood). The investigators plan to carry out 4 interim analyses (plus the final analysis) and will consider stopping the study at an interim analysis if there is a significant difference in SVR at 6 months between the two treatments using O'Brien-Fleming two-sided significance levels. Suppose we are at the design stage of the study, and we are planning on enrolling 1500 patients. Suppose that the first interim analysis is scheduled after the first 600 patients (300 per group) are treated and followed for 6 months, the second interim analysis is scheduled after the first 750 patients (375 per group) are treated and followed for 6 months, the third interim analysis is scheduled after the first 1000 patients (500 per group) are treated and followed for 6 months, the fourth interim analysis is scheduled after the first 1200 (600 per group) are treated and followed for 6 months, and the final analysis is planned after all 1500 patients have been treated and followed.

O'Brien-Fleming Two-sided Significance Levels for the Five Analysis

n	s	$\alpha(s)$	Z	Significance Level
600	0.4	0.00079	3.3569	0.000788
750	0.5	0.00306	2.9885	0.00280
1,000	0.6667	0.01210	2.5396	0.01110
1,200	0.8	0.02442	2.3154	0.02058
1,500	1	0.05	2.0337	0.04198

n	s	$\alpha(s)$	Z	Significance Level
560	0.3733	0.00048	3.4873	0.000488
750	0.5	0.00306	2.9790	0.00290
1,000	0.6667	0.01210	2.5391	0.01112
1,200	0.8	0.02442	2.3153	0.02060
1,500	1	0.05	2.0337	0.04198

n	s	$\alpha(s)$	Z	Significance Level
560	0.3111	0.00048	3.4917	0.00048
750	0.4167	0.00306	2.9775	0.00290
1,000	0.5556	0.01210	2.5392	0.01112
1,200	0.6667	0.02442	2.3154	0.02060
1,800	1	0.05	2.0766	0.03784

n	s	$\alpha(s)$	Z	Significance Level
560	0.3111	0.00048	3.4917	0.00048
822	0.4567	0.00306	2.9832	0.00286
1,000	0.5556	0.01210	2.5290	0.01144
1,200	0.6667	0.02442	2.3133	0.02070
1,800	1	0.05	2.0762	0.03788

	No SVR	**SVR**	Total
Active Control	289 (70.32%)	122 (29.68%)	411
New Treatment	251 (61.07%)	160 (38.93%)	411
Total	540	282	822

A chi-squared test was used to test whether there was a difference in the proportion of sustained virological response between treatment groups. The chi-squared statistic was 7.7946 with 1 degree of freedom and the resulting p-value was 0.0052. With a p-value greater than the α=0.00286 O'Brien-Fleming significance level, the null hypothesis of there being no difference in in the proportion of sustained virological response between treatment groups was not rejected. There is insufficient statistical evidence to suggest early efficacy of the new treatment. The Data Safety and Monitoring Board should not recommend stopping the study early.