

Development of Early Stopping Guidelines for Slow Accruing Trials

The guidelines were developed on a database of 239 CTEP-sponsored phase III trial that were initiated on or prior to 2000 and stayed open for more than 15 months. This data base was randomly split into two subsets: training subset (115 trials) and validation subset (124 trials). Early accrual feasibility was measured in terms of the fraction of the projected accrual in quarters 5-6 (e.g., quarter 5-6 accrual over 20% of projected accrual for quarter 5-6). The overall trial success was judged by whether the final trial accrual was over 80% of projected. Training Data Set results are presented in Table 1. Based on these results the cut-off of 20% of projected accrual was selected for termination of the study. The results were validated on the validation data set Table 2. The results on the entire 239 patient data base are given in Table 3.

Table 1 Training subset

		quarter5-6 accrual over 20% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	6*	25	31
	YES	0	84	84
Total		6	109	115
		quarter5-6 accrual over 30% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	11**	20	31
	YES	2	82	84
Total		13	102	115
		quarter5-6 accrual over 40% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	16	15	31
	YES	4	80	84
Total		20	95	115
		quarter5-6 accrual over 50% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	21	10	31
	YES	7	77	84
Total		28	87	115
		quarter5-6 accrual over 60% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	24	7	31
	YES	13	71	84
Total		37	78	115

*Final percentages of total accrual were: 43%, 6%, 5%, 4%, 2% and 2%.

**Final percentages of total accrual were: 63%, 43%, 28%, 28%, 25%, 19%, 6%, 5%, 4%, 2%, 2%

Table 2 Validation subset

		quarter5-6 accrual over 20% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	9	30	39
	YES	0	85	85
Total		9	115	124
		quarter5-6 accrual over 30% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	21	18	39
	YES	3	82	85
Total		24	100	124
		quarter5-6 accrual over 50% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	27	12	39
	YES	12	73	85
Total		39	85	124

Table 3 Entire 239-trial database

		quarter5-6 accrual over 20% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	15*	55	70
	YES	0	169	169
Total		15	224	239
		quarter5-6 accrual over 50% of projected		
		NO	YES	Total
Total accrual over 80% of projected	NO	48	22	70
	YES	19	150	169
Total		67	172	239

*Final percentages of total accrual were: **45%, 43%, 38%, 35%, 14%, 8%, 7%, 6%, 6%, 6%, 5%, 4%, 3%, 2%, 2%.**