

Supporting Information for “Generalized Phase I-II Designs to Increase Long Term Therapeutic Success Rate” by P.F. Thall, Y. Zang and Y. Yuan.

Definition of the Adaptive Randomization Probabilities

For the fixed design parameter $0 \leq \zeta \leq 1$, $n = n_1 + 1, \dots, n_{1,2} = n_1 + n_2$, and acceptable dose set \mathcal{A}_n , given the data \mathcal{D}_n , the adaptive randomization used in stage 2 of the Gen I-II design gives dose $d_j \in \mathcal{A}_n$ to the n^{th} patient with the following probability:

$$r_{j,n} = \frac{(\hat{\phi}_{j,n})^\zeta}{\sum_{l:d_l \in \mathcal{A}_n} (\hat{\phi}_{l,n})^\zeta}.$$

Values $\zeta < 1$ shrink $r_{j,n}$ toward the fair randomization probability $1/|\mathcal{A}_n|$, which corresponds to $\zeta = 0$. The value $\zeta = 1/2$ was used for the design in the simulation study.

Likelihood and Generation of Outcome Variables for the Simulations

The joint likelihood of data \mathcal{D}_n from n patients is given by the product

$$\mathcal{L}(\mathcal{D}_n, \boldsymbol{\theta}) = \prod_{i=1}^n \pi_Y(Y_i | d_{[i]}, \boldsymbol{\theta}) \left[\{f_Z(Z_i^o | Y_i, d_{[i]}, \boldsymbol{\theta})\}^{\delta_i} \{S_Z(Z_i^o | Y_i, d_{[i]}, \boldsymbol{\theta})\}^{(1-\delta_i)} \right]^{I[Y'_{i,R} > 0]}$$

and the posterior is $p(\boldsymbol{\theta} | \mathcal{D}_n) \propto \mathcal{L}(\mathcal{D}_n, \boldsymbol{\theta})p(\boldsymbol{\theta} | \tilde{\boldsymbol{\theta}})$.

To generate (Y'_R, Y_T) , we assumed latent variables $\mathbf{W} = (W_{R'}, W_T)$ following a bivariate

normal distribution with mean (0,0), variances 1, and correlation .20, and defined

$$Y_T = \begin{cases} 0 & \text{if } W_T < \kappa_T(d_j) \\ 1 & \text{if } W_T \geq \kappa_T(d_j) \end{cases}, \quad Y_{R'} = \begin{cases} 0 & \text{if } W_{R'} < \kappa_{R'1}(d_j) \\ 1 & \text{if } \kappa_{R'1}(d_j) \leq W_{R'} < \kappa_{R'2}(d_j) \\ 2 & \text{if } W_{R'} \geq \kappa_{R'2}(d_j) \end{cases}.$$

To generate PFS time, we assumed $[Z \mid Y_{R'} > 0, Y_T, d_j]$ followed a piecewise exponential distribution with probability density function

$$f_Z(Z \mid Y_{R'}, Y_T, d_j) = \exp\{-Z/\tilde{\lambda}(Z)\}, \quad 0 < Z \leq 5,$$

with piecewise log hazard

$$\log\{\tilde{\lambda}(Z)\} = \begin{cases} \tilde{\beta}_{01} + \tilde{\beta}_{R1}I[Y_{R'} = 2] + \tilde{\beta}_{T1}Y_T + \tilde{\gamma}_{j1}I[j > 1] & \text{if } 0 < Z \leq 2.5 \\ \tilde{\beta}_{02} + \tilde{\beta}_{R2}I[Y_{R'} = 2] + \tilde{\beta}_{T2}Y_T + \tilde{\gamma}_{j2}I[j > 1] & \text{if } 2.5 < Z \leq 5 \end{cases}$$

The parameters $\kappa_T(d_j)$, $\kappa_{R'1}(d_j)$, $\kappa_{R'2}(d_j)$, $\tilde{\beta}_{0l}$, $\tilde{\beta}_{Rl}$, $\tilde{\beta}_{Tl}$ and $\tilde{\gamma}_{j1}$, $\tilde{\gamma}_{j2}$ were derived under each scenario to match the pre-determined $\phi(d_j)^{true}$ and $\xi(d_j)^{true}$ values for $j = 1, \dots, 4$.

Table S1. Sensitivity analysis for the effect of AR in stage 2 of the Gen I-II design.

Designs		Dose levels					Sample size	R (%)
		0	1	2	3	4		
<i>Scenario 1</i>								
With AR	$\pi_T^{true}(d_j)$		0.1	0.2	0.4	0.5		
	$\pi_R^{true}(d_j)$		0.3	0.4	0.5	0.55		
	$\bar{U}^{true}(d_j)$		59.1	62.5	60.9	59.9		
	$\xi^{true}(d_j)$		0.05	0.1	0.15	0.3		
	Selection (%)	93.5	0	0.5	2.6	3.3	35.6	NA
Without AR	Patients (#)		9.5	13.5	8.8	3.7		
	Selection (%)	94.8	0	0.5	1.8	2.9	41.4	NA
	Patients (#)		10.8	16.2	10.1	4.2		
<i>Scenario 2</i>								
With AR	$\pi_T^{true}(d_j)$		0.05	0.2	0.4	0.5		
	$\pi_R^{true}(d_j)$		0.6	0.65	0.55	0.4		
	$\bar{U}^{true}(d_j)$		76.7	68.0	54.0	40.4		
	$\xi^{true}(d_j)$		0.1	0.15	0.15	0.15		
	Selection (%)	83.8	2.3	9.6	4.1	0.2	48.2	NA
Without AR	Patients (#)		21.5	16.4	7.4	2.8		
	Selection (%)	86.7	0.8	8.1	3.8	0.5	60.4	NA
	Patients (#)		32.7	18.2	6.9	2.7		
<i>Scenario 3</i>								
With AR	$\pi_T^{true}(d_j)$		0.04	0.06	0.08	0.1		
	$\pi_R^{true}(d_j)$		0.4	0.5	0.6	0.6		
	$\bar{U}^{true}(d_j)$		61.2	67.0	74.2	75.0		
	$\xi^{true}(d_j)$		0.2	0.4	0.5	0.7		
	Selection (%)	2.9	0.3	7.0	19.3	70.5	52.7	91.0
Without AR	Patients (#)		10.6	13.0	14.9	14.3		
	Selection (%)	3.0	0.1	5.4	16.4	75.0	69.7	92.7
	Patients (#)		11.6	15.2	21.4	21.5		
<i>Scenario 4</i>								
With AR	$\pi_T^{true}(d_j)$		0.01	0.03	0.06	0.08		
	$\pi_R^{true}(d_j)$		0.6	0.7	0.7	0.7		
	$\bar{U}^{true}(d_j)$		72.1	80.9	81.3	80.6		
	$\xi^{true}(d_j)$		0.4	0.45	0.65	0.5		
	Selection (%)	0.1	4.3	9.2	69.1	17.2	58.1	91.5
Without AR	Patients (#)		13.9	15.1	14.8	14.4		
	Selection (%)	0	4.0	8.7	70.1	17.1	75.9	91.8
	Patients (#)		14.6	21.0	20.8	19.6		
<i>Scenario 5</i>								
With AR	$\pi_T^{true}(d_j)$		0.03	0.05	0.1	0.15		
	$\pi_R^{true}(d_j)$		0.4	0.6	0.75	0.65		
	$\bar{U}^{true}(d_j)$		63.1	75.2	82.3	72.7		
	$\xi^{true}(d_j)$		0.3	0.45	0.5	0.65		
	Selection (%)	1.2	1.4	14.2	24.1	59.1	54.3	89.1
Without AR	Patients (#)		10.5	14.7	15.8	13.3		
	Selection (%)	1.1	1.3	15.0	23.6	59.0	71.3	89.0
	Patients (#)		10.4	18.9	27.0	15.1		

Table S1. (continued)

		<i>Scenario 6</i>							
			$\pi_T^{true}(d_j)$	0.02	0.04	0.07	0.1		
			$\pi_R^{true}(d_j)$	0.4	0.6	0.65	0.75		
			$\bar{U}^{true}(d_j)$	54.4	72.6	72.5	77.8		
			$\xi^{true}(d_j)$	0.45	0.7	0.5	0.45		
With AR	Selection (%)	0.6	5.4	68.4	15.7	9.8	54.3	90.0	
	Patients (#)		10.0	14.4	14.7	15.2			
Without AR	Selection (%)	0.7	5.5	70.7	14.5	8.6	70.2	90.8	
	Patients (#)		9.4	19.4	18.5	22.9			
		<i>Scenario 7</i>							
			$\pi_T^{true}(d_j)$	0.03	0.05	0.1	0.15		
			$\pi_R^{true}(d_j)$	0.4	0.5	0.6	0.5		
			$\bar{U}^{true}(d_j)$	66.1	70.3	73.5	68.6		
			$\xi^{true}(d_j)$	0.3	0.45	0.65	0.4		
With AR	Selection (%)	3.3	2.0	15.0	70.9	8.8	52.2	90.6	
	Patients (#)		11.2	13.7	15.1	12.1			
Without AR	Selection (%)	2.8	1.8	13.9	74.6	7.0	69.9	91.9	
	Patients (#)		13.7	18.8	21.9	15.5			
		<i>Scenario 8</i>							
			$\pi_T^{true}(d_j)$	0.15	0.2	0.25	0.4		
			$\pi_R^{true}(d_j)$	0.6	0.7	0.6	0.5		
			$\bar{U}^{true}(d_j)$	71.8	77.8	68.5	56.4		
			$\xi^{true}(d_j)$	0.45	0.6	0.45	0.4		
With AR	Selection (%)	9.1	23.4	56.9	9.0	1.6	47.7	90.5	
	Patients (#)		17.7	14.8	9.9	5.3			
Without AR	Selection (%)	8.0	20.2	62.5	7.8	1.6	62.7	91.8	
	Patients (#)		21.2	24.3	11.8	5.4			
		<i>Scenario 9</i>							
			$\pi_T^{true}(d_j)$	0.02	0.1	0.2	0.5		
			$\pi_R^{true}(d_j)$	0.6	0.6	0.6	0.6		
			$\bar{U}^{true}(d_j)$	76.3	73.5	70.2	60.4		
			$\xi^{true}(d_j)$	0.4	0.45	0.6	0.65		
With AR	Selection (%)	1.3	18.2	22.5	51.2	6.8	51.6	88.7	
	Patients (#)		17.2	15.6	12.8	5.9			
Without AR	Selection (%)	1.1	13.7	23.2	53.8	8.2	68.2	90.2	
	Patients (#)		25.0	21.1	15.9	6.2			

Table S2. Sensitivity analysis of ρ for determining the candidate dose set.

ρ		Dose levels				Sample size	R (%)	
		0	1	2	3			4
<i>Scenario 1</i>								
	$\pi_T^{true}(d_j)$		0.1	0.2	0.4	0.5		
	$\pi_R^{true}(d_j)$		0.3	0.4	0.5	0.55		
	$\bar{U}^{true}(d_j)$		59.1	62.5	60.9	59.9		
	$\xi^{true}(d_j)$		0.05	0.1	0.15	0.3		
0.6	Selection (%)	93.6	0	0.5	2.6	3.3	35.4	NA
	Patients (#)		9.5	13.5	8.7	3.6		
0.7	Selection (%)	93.5	0	0.5	2.6	3.3	35.6	NA
	Patients (#)		9.5	13.5	8.8	3.7		
0.8	Selection (%)	93.9	0	0.5	2.0	3.5	35.0	NA
	Patients (#)		9.4	13.4	8.6	3.6		
0.9	Selection (%)	95.0	0	0.5	2.2	2.3	35.2	NA
	Patients (#)		9.4	13.5	8.7	3.6		
<i>Scenario 2</i>								
	$\pi_T^{true}(d_j)$		0.05	0.2	0.4	0.5		
	$\pi_R^{true}(d_j)$		0.6	0.65	0.55	0.4		
	$\bar{U}^{true}(d_j)$		76.7	68.0	54.0	40.4		
	$\xi^{true}(d_j)$		0.1	0.15	0.15	0.15		
0.6	Selection (%)	82.3	2.2	9.8	5.1	0.6	48.5	NA
	Patients (#)		21.2	16.6	7.8	3.0		
0.7	Selection (%)	83.8	2.3	9.6	4.1	0.2	48.2	NA
	Patients (#)		21.5	16.4	7.4	2.8		
0.8	Selection (%)	86.4	2.4	8.5	2.5	0.2	47.9	NA
	Patients (#)		21.7	16.2	7.1	2.8		
0.9	Selection (%)	90.0	2.4	6.5	1.0	0	47.6	NA
	Patients (#)		21.3	16.4	7.1	2.8		
<i>Scenario 3</i>								
	$\pi_T^{true}(d_j)$		0.04	0.06	0.08	0.1		
	$\pi_R^{true}(d_j)$		0.4	0.5	0.6	0.6		
	$\bar{U}^{true}(d_j)$		61.2	67.0	74.2	75.0		
	$\xi^{true}(d_j)$		0.2	0.4	0.5	0.7		
0.6	Selection (%)	3.1	0.4	6.9	19.3	70.4	53.2	91.0
	Patients (#)		11.0	13.2	14.9	14.1		
0.7	Selection (%)	2.9	0.3	7.0	19.3	70.5	52.7	91.0
	Patients (#)		10.6	13.0	14.9	14.3		
0.8	Selection (%)	3.3	0.3	6.9	20.5	69.0	51.6	90.7
	Patients (#)		10.2	12.8	14.6	14.0		
0.9	Selection (%)	3.2	0.7	8.5	28.9	58.6	50.0	87.1
	Patients (#)		9.8	12.2	14.3	13.6		
<i>Scenario 4</i>								
	$\pi_T^{true}(d_j)$		0.01	0.03	0.06	0.08		
	$\pi_R^{true}(d_j)$		0.6	0.7	0.7	0.7		
	$\bar{U}^{true}(d_j)$		72.1	80.9	81.3	80.6		
	$\xi^{true}(d_j)$		0.4	0.45	0.65	0.5		
0.6	Selection (%)	0.1	4.8	9.6	69.0	16.4	58.6	91.3
	Patients (#)		14.1	15.2	14.8	14.5		
0.7	Selection (%)	0.1	4.3	9.5	69.1	17.2	58.1	91.5
	Patients (#)		13.9	15.1	14.8	14.4		
0.8	Selection (%)	0	4.2	12.3	65.1	18.3	56.5	90.3
	Patients (#)		13.0	14.8	14.5	14.1		
0.9	Selection (%)	0.2	5.7	17.6	54.5	22.0	53.2	87.2
	Patients (#)		12.1	14.1	13.8	13.2		

Table S2. (continued)

ρ		Dose levels				Sample size	R (%)	
		0	1	2	3			4
<i>Scenario 5</i>								
	$\pi_T^{true}(d_j)$		0.03	0.05	0.1	0.15		
	$\pi_R^{true}(d_j)$		0.4	0.6	0.75	0.65		
	$\bar{U}^{true}(d_j)$		63.1	75.2	82.3	72.7		
	$\xi^{true}(d_j)$		0.3	0.45	0.5	0.65		
0.6	Selection (%)	1.4	1.4	13.3	22.9	61.0	54.8	89.6
	Patients (#)		10.7	14.7	15.8	13.6		
0.7	Selection (%)	1.2	1.4	14.2	24.1	59.1	54.3	89.1
	Patients (#)		10.5	14.7	15.8	13.3		
0.8	Selection (%)	1.1	12.8	16.3	30.9	50.5	52.8	86.8
	Patients (#)		9.8	14.4	15.7	12.8		
0.9	Selection (%)	1.6	11.2	18.4	48.8	30.0	50.6	81.9
	Patients (#)		9.3	13.8	15.6	12.0		
<i>Scenario 6</i>								
	$\pi_T^{true}(d_j)$		0.02	0.04	0.07	0.1		
	$\pi_R^{true}(d_j)$		0.4	0.6	0.65	0.75		
	$\bar{U}^{true}(d_j)$		54.4	72.6	72.5	77.8		
	$\xi^{true}(d_j)$		0.45	0.7	0.5	0.45		
0.6	Selection (%)	0.8	5.0	71.4	14.3	8.6	55.2	91.0
	Patients (#)		10.4	14.7	14.8	15.3		
0.7	Selection (%)	0.6	5.4	68.4	15.7	9.8	54.3	90.0
	Patients (#)		10.0	14.4	14.7	15.2		
0.8	Selection (%)	0.6	4.2	64.5	17.0	13.6	52.6	88.7
	Patients (#)		9.2	14.3	14.2	14.9		
0.9	Selection (%)	0.9	1.9	45.8	23.0	28.4	50.8	82.4
	Patients (#)		8.9	13.6	13.7	14.5		
<i>Scenario 7</i>								
	$\pi_T^{true}(d_j)$		0.03	0.05	0.1	0.15		
	$\pi_R^{true}(d_j)$		0.4	0.5	0.6	0.5		
	$\bar{U}^{true}(d_j)$		66.1	70.3	73.5	68.6		
	$\xi^{true}(d_j)$		0.3	0.45	0.65	0.4		
0.6	Selection (%)	3.0	2.1	14.9	72.4	7.6	52.2	91.1
	Patients (#)		11.1	13.9	15.3	12.0		
0.7	Selection (%)	3.3	2.0	15.0	70.9	8.8	52.2	90.6
	Patients (#)		11.2	13.7	15.1	12.1		
0.8	Selection (%)	3.1	2.3	15.8	70.4	8.4	51.5	90.4
	Patients (#)		10.8	13.5	15.3	11.8		
0.9	Selection (%)	3.6	4.3	20.6	60.6	11.0	50.0	86.7
	Patients (#)		10.5	13.4	14.8	11.3		
<i>Scenario 8</i>								
	$\pi_T^{true}(d_j)$		0.15	0.2	0.25	0.4		
	$\pi_R^{true}(d_j)$		0.6	0.7	0.6	0.5		
	$\bar{U}^{true}(d_j)$		71.8	77.8	68.5	56.4		
	$\xi^{true}(d_j)$		0.45	0.6	0.45	0.4		
0.6	Selection (%)	8.6	22.5	58.1	9.2	1.6	48.2	90.7
	Patients (#)		17.8	14.9	10.2	5.4		
0.7	Selection (%)	9.1	23.4	56.8	9.0	1.6	47.7	90.5
	Patients (#)		17.7	14.8	9.9	5.3		
0.8	Selection (%)	8.9	22.5	59.2	8.3	1.1	47.2	91.1
	Patients (#)		17.5	15.0	9.7	4.9		
0.9	Selection (%)	9.1	23.3	59.4	7.7	0.5	46.1	91.2
	Patients (#)		17.1	14.8	9.5	4.7		

Table S2. (continued)

ρ	Dose levels					Sample size	R (%)	
	0	1	2	3	4			
<i>Scenario 9</i>								
	$\pi_T^{true}(d_j)$		0.02	0.1	0.2	0.5		
	$\pi_R^{true}(d_j)$		0.6	0.6	0.6	0.6		
	$\bar{U}^{true}(d_j)$		76.3	73.5	70.2	60.4		
	$\xi^{true}(d_j)$		0.4	0.45	0.6	0.65		
0.6	Selection (%)	1.0	13.7	21.4	55.3	8.6	51.8	90.7
	Patients (#)		17.1	15.6	13.2	5.9		
0.7	Selection (%)	1.3	18.2	22.5	51.2	6.8	51.6	88.7
	Patients (#)		17.2	15.6	12.8	5.9		
0.8	Selection (%)	1.1	21.0	27.0	45.8	5.1	50.6	86.5
	Patients (#)		17.1	15.6	12.5	5.5		
0.9	Selection (%)	2.3	34.0	30.8	30.5	2.4	49.4	80.7
	Patients (#)		17.0	14.7	12.3	5.4		

Table S3. Sensitivity analysis for sample size allocation between stage 2 and stage 3, with stage 1 sample size fixed at $n_1 = 15$.

$n_2; N(d)$		Dose levels				Sample size	R (%)	
		0	1	2	3			4
<i>Scenario 1</i>								
$n_2 = 39; N(d) = 9$	$\pi_T^{true}(d_j)$		0.1	0.2	0.4	0.5		
	$\pi_R^{true}(d_j)$		0.3	0.4	0.5	0.55		
$n_2 = 33; N(d) = 15$	$\bar{U}^{true}(d_j)$		59.1	62.5	60.9	59.9		
	$\xi^{true}(d_j)$		0.05	0.1	0.15	0.3		
$n_2 = 27; N(d) = 21$	Selection (%)	94.9	0	0.5	1.8	2.8	37.4	NA
	Patients (#)		9.6	14.6	9.6	3.6		
$n_2 = 33; N(d) = 15$	Selection (%)	93.5	0	0.5	2.6	3.3	35.6	NA
	Patients (#)		9.5	13.5	8.8	3.7		
$n_2 = 27; N(d) = 21$	Selection (%)	94.1	0	0.6	2.1	3.2	35.8	NA
	Patients (#)		9.8	13.2	8.9	4.0		
<i>Scenario 2</i>								
$n_2 = 39; N(d) = 9$	$\pi_T^{true}(d_j)$		0.05	0.2	0.4	0.5		
	$\pi_R^{true}(d_j)$		0.6	0.65	0.55	0.4		
$n_2 = 33; N(d) = 15$	$\bar{U}^{true}(d_j)$		76.7	68.0	54.0	40.4		
	$\xi^{true}(d_j)$		0.1	0.15	0.15	0.15		
$n_2 = 39; N(d) = 9$	Selection (%)	85.5	1.7	8.4	4.1	0.3	52.8	NA
	Patients (#)		23.9	18.5	7.6	2.8		
$n_2 = 33; N(d) = 15$	Selection (%)	83.8	2.3	9.6	4.1	0.2	48.2	NA
	Patients (#)		21.5	16.4	7.4	2.8		
$n_2 = 27; N(d) = 21$	Selection (%)	88.6	1.4	7.6	2.1	0.3	50.8	NA
	Patients (#)		21.7	17.8	8.4	3.0		
<i>Scenario 3</i>								
$n_2 = 39; N(d) = 9$	$\pi_T^{true}(d_j)$		0.04	0.06	0.08	0.1		
	$\pi_R^{true}(d_j)$		0.4	0.5	0.6	0.6		
$n_2 = 33; N(d) = 15$	$\bar{U}^{true}(d_j)$		61.2	67.0	74.2	75.0		
	$\xi^{true}(d_j)$		0.2	0.4	0.5	0.7		
$n_2 = 39; N(d) = 9$	Selection (%)	3.1	0.3	6.8	19.8	70.0	53.2	90.9
	Patients (#)		10.3	13.0	15.4	14.5		
$n_2 = 33; N(d) = 15$	Selection (%)	2.9	0.3	7.0	19.3	70.5	52.7	91.0
	Patients (#)		10.6	13.0	14.9	14.3		
$n_2 = 27; N(d) = 21$	Selection (%)	2.7	0.4	5.1	16.9	74.9	65.2	92.5
	Patients (#)		12.9	16.0	18.4	17.9		
<i>Scenario 4</i>								
$n_2 = 39; N(d) = 9$	$\pi_T^{true}(d_j)$		0.01	0.03	0.06	0.08		
	$\pi_R^{true}(d_j)$		0.6	0.7	0.7	0.7		
$n_2 = 33; N(d) = 15$	$\bar{U}^{true}(d_j)$		72.1	80.9	81.3	80.6		
	$\xi^{true}(d_j)$		0.4	0.45	0.65	0.5		
$n_2 = 39; N(d) = 9$	Selection (%)	0.1	5.0	10.6	66.8	17.6	54.2	90.7
	Patients (#)		12.9	14.3	13.8	13.2		
$n_2 = 33; N(d) = 15$	Selection (%)	0.1	4.3	9.2	69.1	17.2	58.1	91.5
	Patients (#)		13.9	15.1	14.8	14.4		
$n_2 = 27; N(d) = 21$	Selection (%)	0.1	3.2	8.1	73.9	14.6	77.0	92.8
	Patients (#)		17.6	20.0	19.9	19.5		

Table S3. (continued)

$n_2; N(d)$		Dose levels					Sample size	R (%)
		0	1	2	3	4		
<i>Scenario 5</i>								
	$\pi_T^{true}(d_j)$		0.03	0.05	0.1	0.15		
	$\pi_R^{true}(d_j)$		0.4	0.6	0.75	0.65		
	$\bar{U}^{true}(d_j)$		63.1	75.2	82.3	72.7		
	$\xi^{true}(d_j)$		0.3	0.45	0.5	0.65		
$n_2 = 39; N(d) = 9$	Selection (%)	1.2	1.4	14.7	22.7	60.0	53.7	89.2
	Patients (#)		9.7	14.9	16.2	12.9		
$n_2 = 33; N(d) = 15$	Selection (%)	1.2	1.4	14.2	24.1	59.1	54.3	89.1
	Patients (#)		10.5	14.7	15.8	13.3		
$n_2 = 27; N(d) = 21$	Selection (%)	1.1	1.1	13.6	22.9	61.3	68.9	89.7
	Patients (#)		13.0	18.9	19.9	17.1		
<i>Scenario 6</i>								
	$\pi_T^{true}(d_j)$		0.02	0.04	0.07	0.1		
	$\pi_R^{true}(d_j)$		0.4	0.6	0.65	0.75		
	$\bar{U}^{true}(d_j)$		54.4	72.6	72.5	77.8		
	$\xi^{true}(d_j)$		0.45	0.7	0.5	0.45		
$n_2 = 39; N(d) = 9$	Selection (%)	0.7	5.6	70.3	14.6	8.8	53.9	90.6
	Patients (#)		9.8	14.6	14.4	15.0		
$n_2 = 33; N(d) = 15$	Selection (%)	0.6	5.4	68.4	15.7	9.8	54.3	90.0
	Patients (#)		10.0	14.4	14.7	15.2		
$n_2 = 27; N(d) = 21$	Selection (%)	0.7	4.3	72.8	14.1	8.1	67.7	91.5
	Patients (#)		11.3	18.4	18.7	19.3		
<i>Scenario 7</i>								
	$\pi_T^{true}(d_j)$		0.03	0.05	0.1	0.15		
	$\pi_R^{true}(d_j)$		0.4	0.5	0.6	0.5		
	$\bar{U}^{true}(d_j)$		66.1	70.3	73.5	68.6		
	$\xi^{true}(d_j)$		0.3	0.45	0.65	0.4		
$n_2 = 39; N(d) = 9$	Selection (%)	3.7	2.0	14.1	71.2	9.1	53.2	90.8
	Patients (#)		11.1	14.1	16.0	12.0		
$n_2 = 33; N(d) = 15$	Selection (%)	3.3	2.0	15.0	70.9	8.8	52.2	90.6
	Patients (#)		11.2	13.7	15.1	12.1		
$n_2 = 27; N(d) = 21$	Selection (%)	2.4	1.5	13.3	75.9	7.0	63.9	92.3
	Patients (#)		13.3	16.7	18.6	15.2		
<i>Scenario 8</i>								
	$\pi_T^{true}(d_j)$		0.15	0.2	0.25	0.4		
	$\pi_R^{true}(d_j)$		0.6	0.7	0.6	0.5		
	$\bar{U}^{true}(d_j)$		71.8	77.8	68.5	56.4		
	$\xi^{true}(d_j)$		0.45	0.6	0.45	0.4		
$n_2 = 39; N(d) = 9$	Selection (%)	8.7	22.6	58.0	9.0	1.6	50.0	90.7
	Patients (#)		18.9	16.1	10.0	5.0		
$n_2 = 33; N(d) = 15$	Selection (%)	9.1	23.4 ₉	56.9	9.0	1.6	47.7	90.5
	Patients (#)		17.7	14.8	9.9	5.3		
$n_2 = 27; N(d) = 21$	Selection (%)	8.1	20.9	61.2	8.7	1.1	56.6	91.5
	Patients (#)		19.8	17.4	12.9	6.4		

Table S3. (continued)

$n_2; N(d)$		Dose levels					Sample size	R (%)
		0	1	2	3	4		
		<i>Scenario 9</i>						
	$\pi_T^{true}(d_j)$		0.02	0.1	0.2	0.5		
	$\pi_R^{true}(d_j)$		0.6	0.6	0.6	0.6		
	$\bar{U}^{true}(d_j)$		76.3	73.5	70.2	60.4		
	$\xi^{true}(d_j)$		0.4	0.45	0.6	0.65		
$n_2 = 39; N(d) = 9$	Selection (%)	1.4	14.3	24.2	51.8	8.3	53.7	89.7
	Patients (#)		17.8	17.0	13.5	5.4		
$n_2 = 33; N(d) = 15$	Selection (%)	1.3	18.2	22.5	51.2	6.8	51.6	88.7
	Patients (#)		17.2	15.6	12.8	5.9		
$n_2 = 27; N(d) = 21$	Selection (%)	1.0	14.3	21.9	55.7	7.1	62.0	90.2
	Patients (#)		19.4	18.9	16.6	7.0		