

Table 1A: Simulated rejection probabilities for noninferiority testing under three event-rate settings with 3 years of accrual followed by 3 years of follow-up using proportional hazards (Cox) and RMST methods with  $\tau=5$

Noninferiority designs										
NI Margin		Sample size per arm	Simulated powers				Simulated levels			
HR	RMST (years)		5-yr surv (Exp arm)	5-yr surv (contr arm)	RMST* ( $\tau=5$ )	Proportional Hazards **	5-yr surv (Exp arm)	5-yr surv (contr arm)	RMST* ( $\tau=5$ )	Proportional Hazards**
<u>Low</u> event-rate setting: 90% 3-year survival on the best arm(s)										
2	.37	250	84%	84%	<b>.956</b>	<b>.834</b>	70%	84%	<b>.0260</b>	<b>.0258</b>
1.75	.28	450	84%	84%	<b>.964</b>	<b>.889</b>	74%	84%	<b>.0261</b>	<b>.0258</b>
1.5	.19	1000	84%	84%	<b>.967</b>	<b>.932</b>	77%	84%	<b>.0262</b>	<b>.0262</b>
1.25	.10	3750	84%	84%	<b>.961</b>	<b>.957</b>	80%	84%	<b>.0249</b>	<b>.0246</b>
<u>Moderate</u> event-rate setting: 60% 3-year survival on the best arm(s)										
2	.96	75	43%	43%	<b>.913</b>	<b>.863</b>	18%	43%	<b>.0237</b>	<b>.0253</b>
1.75	.77	125	43%	43%	<b>.925</b>	<b>.892</b>	23%	43%	<b>.0242</b>	<b>.0255</b>
1.5	.54	250	43%	43%	<b>.925</b>	<b>.907</b>	28%	43%	<b>.0245</b>	<b>.0256</b>
1.25	.29	1000	43%	43%	<b>.951</b>	<b>.953</b>	35%	43%	<b>.0251</b>	<b>.0253</b>
<u>High</u> event-rate setting: 20% 3-year survival on the best arm(s)***										
2	.81	50	7%	7%	<b>.787</b>	<b>.900</b>	0.5%	7%	<b>.0292</b>	<b>.0249</b>
1.75	.68	75	7%	7%	<b>.806</b>	<b>.897</b>	1%	7%	<b>.0280</b>	<b>.0246</b>
1.5	.52	150	7%	7%	<b>.854</b>	<b>.913</b>	2%	7%	<b>.0265</b>	<b>.0250</b>
1.25	.30	450	7%	7%	<b>.853</b>	<b>.888</b>	4%	7%	<b>.0256</b>	<b>.0251</b>

\* RMST analysis with  $\tau=5$  performed after 3 years of accrual followed by 3 years of follow-up (6 years after study activation)

\*\* Proportional hazards analysis performed after 3 years of accrual followed by 3 years of follow-up (6 years after study activation)

\*\*\* In trial replications where the minimum of the longest observed times on each arm was less than 5 years  $\tau$  was set to the minimum of the longest observed times on the two arms (Tian et al.<sup>31</sup>)

Table 2A: Simulated rejection probabilities for superiority testing under three event-rate settings with 3 years of accrual followed by 3 years of follow-up using proportional hazards (Cox) and RMST methods with  $\tau=5$

Superiority designs										
Target effect		Sample size per arm	Simulated powers				Simulated levels			
HR	RMST (years)		5-yr surv (Exp arm)	5-yr surv (Contr arm)	RMST* ( $\tau=5$ )	Proportional Hazards**	5-yr surv (Exp arm)	5-yr surv (contr arm)	RMST* ( $\tau=5$ )	Proportional Hazards**
<u>Low</u> event-rate setting: 90% 3-year survival on the best arm(s)										
½	.37	250	84%	70%	<b>.892</b>	<b>.933</b>	70%	70%	<b>.0249</b>	<b>.0241</b>
1/1.75	.28	450	84%	74%	<b>.919</b>	<b>.954</b>	74%	74%	<b>.0252</b>	<b>.0247</b>
1/1.5	.19	1000	84%	77%	<b>.938</b>	<b>.967</b>	77%	77%	<b>.0256</b>	<b>.0251</b>
1/1.25	.10	3750	84%	80%	<b>.945</b>	<b>.973</b>	80%	80%	<b>.0247</b>	<b>.0243</b>
<u>Moderate</u> event-rate setting: 60% 3-year survival on the best arm(s)										
½	.96	75	43%	18%	<b>.912</b>	<b>.925</b>	18%	18%	<b>.0265</b>	<b>.0247</b>
1/1.75	.77	125	43%	23%	<b>.922</b>	<b>.937</b>	23%	23%	<b>.0263</b>	<b>.0245</b>
1/1.5	.54	250	43%	28%	<b>.920</b>	<b>.939</b>	28%	28%	<b>.0253</b>	<b>.0251</b>
1/1.25	.29	1000	43%	35%	<b>.948</b>	<b>.965</b>	35%	35%	<b>.0256</b>	<b>.0254</b>
<u>High</u> event-rate setting: 20% 3-year survival on the best arm(s)***										
½	.81	50	7%	0.5%	<b>.899</b>	<b>.913</b>	0.5%	0.5%	<b>.0236</b>	<b>.0263</b>
1/1.75	.68	75	7%	1%	<b>.900</b>	<b>.909</b>	1%	1%	<b>.0236</b>	<b>.0256</b>
1/1.5	.52	150	7%	2%	<b>.919</b>	<b>.922</b>	2%	2%	<b>.0242</b>	<b>.0250</b>
1/1.25	.30	450	7%	4%	<b>.892</b>	<b>.895</b>	4%	4%	<b>.0254</b>	<b>.0252</b>

\* RMST analysis with  $\tau=5$  performed after 3 years of accrual followed by 3 years of follow-up (6 years after study activation)

\*\* Proportional hazards analysis performed after 3 years of accrual followed by 3 years of follow-up (6 years after study activation)

\*\*\* In trial replications where the minimum of the longest observed times on each arm was less than 5 years  $\tau$  was set to the minimum of the longest observed times on the two arms (Tian et al.<sup>31</sup>)

Table 3A: Simulated rejection probabilities for noninferiority testing **rare event setting**: 96% 3-year survival on the best arm(s)

<b>Noninferiority designs</b>										
NI Margin		Sample size per arm	Simulated powers				Simulated levels			
HR	RMST (years)		5-yr surv (Exp arm)	5-yr surv (contr arm)	RMST* ( $\tau=5$ )	Proportional Hazards**	5-yr surv (Exp arm)	5-yr surv (contr arm)	RMST* ( $\tau=5$ )	Proportional Hazards**
Rare event-rate setting: 96% 3-year survival on the best arm(s)										
2	.16	500	93%	93%	<b>.926</b>	<b>.752</b>	87%	93%	<b>.0288</b>	<b>.0260</b>
1.75	.12	900	93%	93%	<b>.931</b>	<b>.817</b>	89%	93%	<b>.0275</b>	<b>.0258</b>
1.5	.08	2000	93%	93%	<b>.932</b>	<b>.872</b>	90%	93%	<b>.0254</b>	<b>.0251</b>
1.25	.04	7500	93%	93%	<b>.921</b>	<b>.913</b>	92%	93%	<b>.0257</b>	<b>.0255</b>

\* RMST analysis with  $\tau=5$  performed after 3 years of accrual followed by 3 years of follow-up (6 years after study activation)

\*\* Proportional hazards analysis performed after 3 years of accrual followed by 3 years of follow-up (6 years after study activation)

Table 4A: Simulated rejection probabilities for superiority testing under **rare event setting**: 96% 3-year survival on the best arm(s)

<b>Superiority designs</b>										
Target effect		Sample size per arm	Simulated powers				Simulated levels			
HR	RMST (years)		5-yr surv (Exp arm)	5-yr surv (Contr arm)	RMST* ( $\tau=5$ )	Proportional Hazards**	5-yr surv (Exp arm)	5-yr surv (contr arm)	RMST* ( $\tau=5$ )	Proportional Hazards**
Rare event-rate setting: 96% 3-year survival on the best arm(s)										
1/2	.16	500	93%	87%	<b>.824</b>	<b>.882</b>	87%	87%	<b>.0258</b>	<b>.0246</b>
1/1.75	.12	900	93%	89%	<b>.854</b>	<b>.910</b>	89%	89%	<b>.0256</b>	<b>.0246</b>
1/1.5	.08	2000	93%	90%	<b>.879</b>	<b>.929</b>	90%	90%	<b>.0243</b>	<b>.0241</b>
1/1.25	.04	7500	93%	92%	<b>.893</b>	<b>.940</b>	92%	92%	<b>.0254</b>	<b>.0249</b>

\* RMST analysis with  $\tau=5$  performed after 3 years of accrual followed by 3 years of follow-up (6 years after study activation)

\*\* Proportional hazards analysis performed after 3 years of accrual followed by 3 years of follow-up (6 years after study activation)