Impact of informative censoring on the Kaplan-Meier estimate of progression-free survival in phase II clinical trials

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Supplemental materials

The piecewise exponential model for the survival function S(t) used in the simulations is

$$S(t) = (1-p) \exp(-\lambda_1 (t-a_1) I(t \geq a_1)) + (p) \exp(-\lambda_2 (t-a_2) I(t \geq a_2));$$

where I(a) is the indicator function which is equal to 1 if $t \geq a$ and 0 otherwise, $a1=a2=2$ in the WM simulations, $a1=2$ and $a2=6$ in the MM simulations, t is the time from the first day of the first cycle of investigational treatment, p is the proportion of patients who are informatively censored, λ_1 is the hazard rate per month for the patients who continue on therapy until progression and λ_2 is the hazard rate per month for those who initiate non-protocol therapy or undergo transplantation prior to progression.

The piecewise model allows for the two different hazard rate parameters for those who stay on study (λ_1) versus those who are informatively censored (λ_2) and for flexibility in defining when failure times start. For example, WM and MM disease evaluations are often not done until after 2 cycles of therapy (approximately 2 months). Therefore, no failures are generated before 2 months in the simulations. In addition for MM, no failures are generated before 6 months for the patients who continue to transplant since patients usually receive a 4 to 6 induction cycles prior to transplant. For the WM simulated data, the time of NPT prior to progression are generated dependent on the failure time and is restricted to occur 1 to 2 months prior to progression time based on uniform distribution. The data is generated in this manner because in practice if patients are taken off study due to inadequate response or clinical signs of progression, another therapy is often initiated, indicating potential higher risk for progression. For the MM simulations, the time of ASCT are generated based on random uniform distribution between 4 and 6 months.

For 5 newly diagnosed WM scenarios, there were at most 6/2000 (0.3%) simulations where the median PFS was not reached. In those cases, the mean and the standard error of the bias were calculated using the simulated data sets where the median PFS was reached. The mean of the 2000 estimates is compared to the true values based on the piecewise model and percent relative mean bias (defined as [mean of 2000 estimates-true value]/true value) are reported. The mean of the 2000 estimated Greenwood' standard errors of the KM estimate and the standard error of the 2000 biases of the KM estimates are also provided.

Supplementary tables

Table 1. Distribution of the relative (%) bias of the 12-month progression-free survival estimation (in months) of newly diagnosed WM patients by scenario. We assumed that the hazard rate of progression for those who remained on therapy is 0.03 (to simulate upfront WM patients), and that the administrative censoring started from 48 months after initiation of therapy. Number of simulated data: B=2000.

N	λ₂	% discontinued prior to PD	True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS median	Mean Std. error	min	max	Relative (%) bias: Median PFS mean	Std. error	min	max	True 12-month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS median	Mean Std. error	min	max	Relative (%) bias: 12 Month PFS mean	Std. error	min	max
25	0.03	0.01	25.10	25.30	0.10	9.51	56.55	3.62	0.62	-62.13	125.27	0.74	0.76	0.09	0.44	0.96	0.15	0.26	-40.58	29.64
		0.1	25.10	27.50	0.10	9.51	60.64	12.41	0.68	-62.13	141.55	0.74	0.76	0.08	0.44	1.00	2.91	0.26	-40.53	35.58
		0.2	25.10	30.64	0.11	11.21	78.40	26.12	0.77	-55.36	212.29	0.73	0.79	0.08	0.43	1.00	6.96	0.25	-40.79	36.18
		0.3	25.10	35.15	0.11	11.31	84.40	45.01	0.89	-54.95	236.18	0.73	0.83	0.08	0.49	1.00	11.28	0.24	-33.62	36.79
		0.4	25.10	39.25	0.12	12.59	84.40	61.42	0.99	-49.86	251.84	0.73	0.83	0.07	0.53	1.00	14.46	0.23	-26.53	37.40
	0.06	0.01	24.94	25.30	0.10	9.51	56.55	4.31	0.63	-61.88	126.77	0.74	0.76	0.08	0.44	0.96	0.43	0.26	-40.41	30.01
		0.1	22.19	26.68	0.10	9.51	60.64	23.61	0.75	-57.16	173.28	0.72	0.76	0.08	0.43	1.00	5.46	0.27	-39.91	39.49
		0.2	21.96	28.69	0.11	9.51	78.40	34.78	0.84	-56.70	257.05	0.69	0.78	0.09	0.43	1.00	12.38	0.28	-37.26	44.30
		0.3	20.54	31.46	0.12	11.31	84.40	58.57	1.00	-44.94	310.89	0.67	0.81	0.09	0.46	1.00	20.09	0.28	-30.77	49.46
		0.4	19.23	33.70	0.12	11.22	84.40	81.54	1.13	-41.68	338.78	0.65	0.82	0.09	0.46	1.00	27.31	0.28	-28.05	55.00
	0.12	0.01	24.81	25.30	0.10	9.51	56.55	4.84	0.63	-61.69	127.92	0.74	0.76	0.08	0.44	0.96	0.77	0.26	-40.21	30.45
		0.1	22.19	25.62	0.10	8.35	57.67	19.27	0.73	-62.38	159.89	0.69	0.75	0.08	0.41	1.00	8.65	0.29	-41.18	44.53
		0.2	19.37	27.16	0.11	9.51	63.04	45.10	0.95	-50.91	225.46	0.64	0.77	0.09	0.41	1.00	19.51	0.32	-36.45	55.52
		0.3	16.79	28.23	0.12	9.96	65.83	74.29	1.14	-40.66	292.04	0.59	0.80	0.09	0.40	1.00	32.54	0.35	-32.53	68.32
		0.4	14.57	29.44	0.13	9.87	84.40	110.82	1.43	-32.29	479.23	0.55	0.81	0.09	0.41	1.00	47.08	0.37	-24.98	83.42
40	0.03	0.01	25.10	25.03	0.08	12.41	46.60	1.54	0.46	-50.57	85.61	0.74	0.75	0.07	0.50	0.95	-0.07	0.21	-32.48	28.29
		0.1	25.10	27.51	0.08	13.04	51.82	11.64	0.51	-48.04	106.40	0.74	0.77	0.07	0.51	0.95	3.27	0.20	-30.69	28.63
		0.2	25.10	30.50	0.08	13.19	66.96	23.70	0.58	-47.45	166.74	0.73	0.79	0.07	0.52	0.97	6.66	0.19	-28.59	32.69
		0.3	25.10	34.55	0.09	14.57	75.94	40.13	0.66	-41.95	202.47	0.73	0.81	0.06	0.57	0.98	10.44	0.19	-21.88	33.37
		0.4	25.10	39.93	0.09	17.23	88.47	61.72	0.79	-31.38	252.40	0.73	0.84	0.06	0.63	1.00	14.44	0.18	-13.97	37.40
	0.06	0.01	24.94	25.03	0.08	12.41	46.60	2.22	0.46	-50.24	86.85	0.74	0.75	0.08	0.50	0.95	0.21	0.21	-32.29	28.65
		0.1	22.19	26.80	0.08	12.74	51.12	22.32	0.56	-42.56	130.37	0.72	0.76	0.08	0.50	0.95	5.74	0.21	-29.85	32.34
		0.2	21.96	28.67	0.09	12.24	66.96	32.88	0.62	-44.26	204.97	0.69	0.78	0.09	0.51	0.97	12.06	0.21	-26.06	40.60
		0.3	20.54	31.31	0.09	13.45	66.96	54.52	0.74	-34.50	226.02	0.67	0.80	0.09	0.55	0.98	19.27	0.22	-18.21	45.73
		0.4	19.23	34.06	0.10	14.57	72.61	80.52	0.89	-24.23	277.53	0.65	0.83	0.09	0.60	1.00	27.35	0.22	-6.88	55.00
	0.12	0.01	24.81	25.03	0.08	12.41	46.60	2.73	0.46	-49.98	87.80	0.74	0.75	0.08	0.50	0.95	0.55	0.21	-32.06	29.09
		0.1	22.19	26.07	0.08	12.00	51.12	19.37	0.56	-45.94	130.37	0.69	0.76	0.08	0.50	0.95	8.78	0.22	-28.15	36.92
		0.2	19.37	26.99	0.09	11.97	66.96	41.27	0.68	-38.19	245.75	0.64	0.77	0.09	0.50	0.97	19.13	0.24	-22.55	51.32
		0.3	16.79	28.00	0.09	12.24	60.26	71.08	0.84	-27.11	258.90	0.59	0.79	0.09	0.52	0.97	31.78	0.26	-12.20	63.89

N	λ_2	% discontinued prior to PD	True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS				Relative (%) bias: Median PFS				True 12-month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS				Relative (%) bias: 12 Month PFS			
				median	Mean Std. error	min	max	mean	Std. error	min	max		median	Mean Std. error	min	max	mean	Std. error	min	max
		0.4	14.57	29.66	0.10	13.12	72.61	108.65	1.09	-9.99	398.37	0.55	0.81	0.09	0.55	1.00	47.18	0.29	0.72	83.42
60	0.03	0.01	25.10	25.37	0.06	14.43	43.95	2.15	0.38	-42.53	75.07	0.74	0.75	0.06	0.53	0.92	0.50	0.17	-27.98	23.71
		0.1	25.10	27.42	0.07	14.83	47.49	10.58	0.43	-40.93	89.18	0.74	0.76	0.05	0.56	0.92	3.32	0.17	-23.88	24.28
		0.2	25.10	30.46	0.07	16.19	51.96	22.75	0.49	-35.51	106.96	0.73	0.79	0.05	0.59	0.95	6.86	0.16	-20.09	29.30
		0.3	25.10	34.36	0.07	19.56	58.97	38.57	0.56	-22.08	134.88	0.73	0.81	0.05	0.63	0.95	10.47	0.16	-14.33	29.83
		0.4	25.10	39.26	0.07	21.77	74.52	59.24	0.65	-13.30	196.83	0.73	0.83	0.05	0.67	0.98	14.27	0.15	-8.51	34.81
	0.06	0.01	24.94	25.20	0.06	13.99	43.95	2.25	0.38	-43.91	76.24	0.74	0.75	0.08	0.53	0.92	0.70	0.17	-27.77	23.98
		0.1	22.19	26.66	0.07	14.83	45.21	21.78	0.47	-33.17	103.76	0.72	0.76	0.08	0.56	0.92	5.80	0.17	-21.94	27.87
		0.2	21.96	28.58	0.07	15.91	47.56	31.80	0.52	-27.55	116.59	0.69	0.78	0.09	0.57	0.95	12.26	0.18	-17.45	36.88
		0.3	20.54	30.86	0.07	17.99	52.95	52.14	0.61	-12.41	157.78	0.67	0.80	0.09	0.61	0.95	19.31	0.18	-8.94	41.68
		0.4	19.23	33.64	0.08	19.34	61.02	77.94	0.72	0.54	217.26	0.65	0.82	0.09	0.63	0.98	27.15	0.18	-1.90	51.84
	0.12	0.01	24.81	25.05	0.07	13.99	43.95	2.38	0.38	-43.62	77.13	0.74	0.75	0.08	0.53	0.92	0.92	0.17	-27.53	24.37
		0.1	22.19	25.88	0.07	13.99	44.78	18.27	0.47	-36.96	101.81	0.69	0.75	0.08	0.55	0.92	8.87	0.18	-19.86	32.44
		0.2	19.37	26.90	0.07	13.62	46.21	40.75	0.56	-29.66	138.57	0.64	0.77	0.09	0.55	0.95	19.37	0.20	-14.75	47.27
		0.3	16.79	28.02	0.08	15.83	50.77	69.16	0.70	-5.72	202.39	0.59	0.78	0.09	0.58	0.95	31.81	0.22	-2.53	59.18
		0.4	14.57	29.40	0.08	16.21	58.63	104.83	0.87	11.27	302.36	0.55	0.80	0.09	0.59	0.98	46.91	0.24	9.13	79.06
1000	0.03	0.01	25.10	25.32	0.02	21.87	28.61	1.01	0.09	-12.89	13.95	0.74	0.74	0.01	0.69	0.79	0.33	0.04	-6.59	6.25
		0.1	25.10	27.56	0.02	23.65	31.64	9.88	0.10	-5.79	26.04	0.74	0.76	0.01	0.72	0.80	3.38	0.04	-2.64	9.07
		0.2	25.10	30.66	0.02	26.62	34.87	22.13	0.11	6.02	38.89	0.73	0.79	0.01	0.74	0.83	6.91	0.04	1.06	12.66
		0.3	25.10	34.57	0.02	30.20	39.43	37.77	0.13	20.30	57.04	0.73	0.81	0.01	0.76	0.85	10.57	0.04	4.43	15.79
		0.4	25.10	39.84	0.02	34.26	45.56	58.59	0.15	36.46	81.50	0.73	0.83	0.01	0.79	0.87	14.39	0.04	8.65	18.92
	0.06	0.01	24.94	25.25	0.02	21.86	28.57	1.40	0.09	-12.36	14.55	0.74	0.74	0.08	0.69	0.79	0.57	0.04	-6.39	6.55
		0.1	22.19	26.77	0.02	23.33	30.51	20.76	0.11	5.13	37.50	0.72	0.76	0.08	0.71	0.80	5.87	0.04	-0.55	11.80
		0.2	21.96	28.71	0.02	24.80	32.62	30.89	0.12	12.94	48.56	0.69	0.78	0.09	0.73	0.82	12.33	0.04	5.63	18.58
		0.3	20.54	31.09	0.02	27.21	35.55	51.27	0.14	32.46	73.06	0.67	0.80	0.09	0.75	0.84	19.43	0.04	12.29	25.43
		0.4	19.23	33.92	0.02	29.08	38.96	76.58	0.17	51.18	102.57	0.65	0.82	0.09	0.78	0.86	27.31	0.04	20.37	32.89
	0.12	0.01	24.81	25.19	0.02	21.86	28.47	1.63	0.09	-11.92	14.72	0.74	0.74	0.08	0.69	0.79	0.83	0.04	-6.18	6.84
		0.1	22.19	25.97	0.02	22.69	29.80	17.19	0.11	2.25	34.30	0.69	0.75	0.08	0.71	0.80	8.94	0.04	2.03	15.31
		0.2	19.37	26.99	0.02	23.11	30.92	39.45	0.13	19.30	59.64	0.64	0.77	0.09	0.72	0.81	19.46	0.05	11.63	26.48
		0.3	16.79	28.13	0.02	23.86	32.57	67.67	0.17	42.12	93.97	0.59	0.78	0.09	0.73	0.83	31.97	0.05	22.80	39.19
		0.4	14.57	29.50	0.02	24.81	34.08	102.56	0.21	70.26	133.88	0.55	0.80	0.09	0.75	0.84	47.11	0.06	37.29	54.55

Table 2. Distribution of the relative (%) bias of the 12-month progression-free survival estimation (in months) of newly diagnosed WM patients by scenario. We assumed that the hazard rate of progression for those who remained on therapy is 0.06 (to simulate R/R WM patients), and that the administrative censoring started from 48 months after initiation of therapy. Number of simulated data: B=2000.

parameters			True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS				Relative (%) bias: Median PFS				True 12-month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS				Relative (%) bias: 12 Month PFS			
N	λ_2	% discontinued prior to PD		median	Mean Std. err	min	max	mean	Std. err	min	max		median	Mean Std. error	min	max	mean	Std. err	min	max
25	0.06	0.01	13.55	13.65	0.10	5.75	29.28	3.35	0.58	-57.55	116.03	0.55	0.56	0.10	0.24	0.84	0.49	0.40	-56.23	53.19
		0.1	13.55	14.70	0.10	5.75	31.32	11.03	0.63	-57.55	131.10	0.54	0.58	0.10	0.22	0.88	5.78	0.41	-59.80	60.82
		0.2	13.55	16.25	0.11	6.38	38.84	23.36	0.71	-52.90	186.61	0.54	0.62	0.10	0.26	0.91	13.94	0.41	-51.72	68.54
		0.3	13.55	18.35	0.11	6.65	48.47	40.49	0.83	-50.90	257.63	0.53	0.66	0.10	0.31	0.96	22.76	0.40	-41.32	79.24
		0.4	13.55	20.40	0.12	7.29	52.92	56.23	0.94	-46.18	290.50	0.53	0.69	0.10	0.33	0.96	29.65	0.39	-37.13	81.15
	0.12	0.01	13.47	13.65	0.10	5.75	29.28	3.98	0.58	-57.28	117.36	0.55	0.56	0.10	0.24	0.84	0.95	0.40	-56.03	53.89
		0.1	12.09	14.23	0.10	5.17	31.32	20.92	0.69	-57.23	158.96	0.52	0.57	0.10	0.22	0.88	9.42	0.44	-58.12	68.56
		0.2	11.98	15.21	0.11	5.75	32.42	30.68	0.76	-51.97	170.62	0.49	0.60	0.10	0.18	0.90	21.84	0.48	-62.51	84.78
		0.3	11.27	16.43	0.12	5.98	43.20	51.02	0.91	-46.92	283.30	0.46	0.63	0.11	0.25	0.96	36.56	0.51	-44.75	108.48
		0.4	10.62	17.64	0.12	6.61	48.47	70.93	1.03	-37.75	356.51	0.43	0.65	0.11	0.27	0.96	51.62	0.54	-36.94	122.88
	0.24	0.01	13.41	13.65	0.10	5.75	29.28	4.47	0.58	-57.08	118.38	0.54	0.56	0.10	0.24	0.84	1.30	0.41	-55.88	54.42
		0.1	12.09	13.76	0.10	5.17	29.83	17.29	0.67	-57.23	146.67	0.50	0.57	0.10	0.22	0.88	11.91	0.46	-56.55	74.90
		0.2	10.68	14.52	0.11	4.65	32.42	40.13	0.86	-56.45	203.41	0.45	0.58	0.11	0.16	0.90	27.30	0.54	-65.56	99.23
		0.3	9.40	14.83	0.12	5.93	36.10	63.61	1.01	-36.86	284.21	0.40	0.60	0.11	0.14	0.96	46.89	0.64	-64.67	137.23
		0.4	8.29	15.44	0.13	5.93	43.20	93.47	1.25	-28.40	421.38	0.35	0.61	0.12	0.16	0.96	71.01	0.75	-55.43	169.70
40	0.06	0.01	13.55	13.52	0.08	7.21	24.30	1.42	0.42	-46.83	79.30	0.55	0.55	0.08	0.33	0.80	0.12	0.31	-40.73	45.89
		0.1	13.55	14.70	0.08	7.52	26.49	10.40	0.47	-44.50	95.45	0.54	0.58	0.08	0.32	0.82	6.52	0.31	-40.99	50.26
		0.2	13.55	16.16	0.08	7.12	34.14	21.07	0.54	-47.47	151.90	0.54	0.61	0.08	0.38	0.84	13.54	0.31	-29.78	55.53
		0.3	13.55	18.10	0.09	7.73	34.14	35.55	0.61	-42.99	151.90	0.53	0.65	0.08	0.40	0.87	21.39	0.31	-24.52	62.14
		0.4	13.55	20.65	0.09	9.61	43.55	54.85	0.72	-29.07	221.34	0.53	0.69	0.08	0.44	0.91	29.97	0.30	-17.51	72.26
	0.12	0.01	13.47	13.52	0.08	7.21	24.30	2.05	0.43	-46.51	80.40	0.55	0.55	0.08	0.33	0.80	0.57	0.32	-40.46	46.56
		0.1	12.09	14.29	0.08	7.37	26.06	19.97	0.52	-39.05	115.51	0.52	0.57	0.08	0.31	0.81	9.83	0.33	-40.41	56.69
		0.2	11.98	15.20	0.09	7.12	32.96	28.93	0.57	-40.56	175.11	0.49	0.60	0.08	0.35	0.83	21.35	0.36	-28.55	70.38
		0.3	11.27	16.35	0.09	7.12	32.96	47.53	0.67	-36.83	192.42	0.46	0.62	0.08	0.36	0.86	35.37	0.39	-21.22	86.69
		0.4	10.62	17.73	0.10	8.29	34.14	69.84	0.80	-21.95	221.55	0.43	0.66	0.09	0.36	0.91	52.24	0.42	-15.54	110.83
	0.24	0.01	13.41	13.52	0.08	7.21	24.30	2.53	0.43	-46.26	81.25	0.54	0.55	0.08	0.33	0.80	0.92	0.32	-40.25	47.07
		0.1	12.09	13.99	0.08	7.00	26.06	17.54	0.51	-42.14	115.51	0.50	0.56	0.08	0.29	0.81	11.90	0.35	-41.73	62.19
		0.2	10.68	14.36	0.09	6.94	32.96	36.22	0.62	-35.06	208.45	0.45	0.57	0.08	0.29	0.83	26.72	0.41	-36.23	83.42
		0.3	9.40	14.81	0.09	7.07	30.13	60.93	0.75	-24.73	220.66	0.40	0.59	0.09	0.28	0.85	46.13	0.48	-29.51	111.65
		0.4	8.29	15.60	0.10	7.07	32.96	91.92	0.94	-14.64	297.76	0.35	0.61	0.09	0.29	0.90	71.68	0.59	-19.49	153.18
60	0.06	0.01	13.55	13.68	0.06	8.21	22.98	1.95	0.35	-39.39	69.53	0.55	0.55	0.06	0.35	0.75	1.11	0.26	-36.17	36.78
		0.1	13.55	14.65	0.07	8.41	24.75	9.45	0.39	-37.91	82.60	0.54	0.58	0.06	0.36	0.77	6.58	0.26	-34.37	42.31

N	λ_2	% discontinued prior to PD	True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS				Relative (%) bias: Median PFS				True 12-month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS				Relative (%) bias: 12 Month PFS			
				median	Mean Std. err	min	max	mean	Std. err	min	max		median	Mean Std. error	min	max	mean	Std. err	min	max
		0.2	13.55	16.13	0.07	9.10	26.98	20.30	0.45	-32.89	99.06	0.54	0.61	0.06	0.37	0.80	13.75	0.26	-31.60	48.95
		0.3	13.55	17.98	0.07	10.78	30.48	34.17	0.51	-20.45	124.93	0.53	0.65	0.06	0.45	0.82	21.36	0.26	-15.90	54.04
		0.4	13.55	20.25	0.07	11.88	34.47	52.06	0.59	-12.32	154.37	0.53	0.69	0.06	0.49	0.86	29.70	0.25	-6.73	61.63
	0.12	0.01	13.47	13.60	0.06	7.99	22.98	2.04	0.35	-40.65	70.58	0.55	0.55	0.06	0.35	0.75	1.29	0.26	-35.88	37.40
		0.1	12.09	14.27	0.07	8.41	23.61	19.36	0.43	-30.43	95.18	0.52	0.57	0.07	0.35	0.77	9.94	0.28	-33.04	48.15
		0.2	11.98	15.16	0.07	8.95	24.78	27.91	0.48	-25.25	106.85	0.49	0.60	0.07	0.34	0.80	21.59	0.30	-31.25	63.00
		0.3	11.27	16.15	0.07	9.82	27.47	45.36	0.55	-12.86	143.78	0.46	0.62	0.07	0.41	0.82	35.27	0.33	-11.22	77.71
		0.4	10.62	17.41	0.08	10.67	31.22	67.39	0.65	0.49	194.06	0.43	0.65	0.07	0.44	0.85	51.83	0.34	1.48	97.52
	0.24	0.01	13.41	13.52	0.07	7.99	22.98	2.18	0.35	-40.37	71.38	0.54	0.55	0.06	0.35	0.75	1.33	0.26	-35.66	37.62
		0.1	12.09	13.89	0.07	7.99	23.39	16.35	0.43	-33.90	93.39	0.50	0.56	0.07	0.34	0.76	12.01	0.30	-32.40	52.32
		0.2	10.68	14.29	0.07	7.81	23.61	35.53	0.51	-26.88	120.95	0.45	0.57	0.07	0.32	0.79	26.97	0.34	-29.85	73.82
		0.3	9.40	14.78	0.08	8.72	25.02	59.49	0.62	-7.14	166.35	0.40	0.59	0.07	0.35	0.80	45.97	0.40	-12.42	98.90
		0.4	8.29	15.36	0.08	8.91	29.58	88.65	0.76	7.52	257.03	0.35	0.61	0.08	0.37	0.83	71.13	0.47	3.04	132.94
1000	0.06	0.01	13.55	13.66	0.02	11.93	15.30	0.90	0.09	-11.94	12.92	0.55	0.55	0.02	0.50	0.61	0.72	0.06	-8.92	10.57
		0.1	13.55	14.73	0.02	12.82	16.68	8.76	0.09	-5.40	23.10	0.54	0.58	0.02	0.53	0.64	6.70	0.06	-2.95	16.88
		0.2	13.55	16.21	0.02	14.17	18.38	19.61	0.10	4.58	35.65	0.54	0.61	0.02	0.56	0.67	13.87	0.06	3.87	24.39
		0.3	13.55	18.08	0.02	15.94	20.63	33.44	0.12	17.65	52.22	0.53	0.65	0.02	0.60	0.71	21.58	0.06	11.99	33.05
		0.4	13.55	20.58	0.02	17.82	23.52	51.87	0.14	31.51	73.53	0.53	0.69	0.02	0.64	0.75	29.97	0.06	20.55	41.51
	0.12	0.01	13.47	13.62	0.02	11.93	15.28	1.25	0.09	-11.45	13.47	0.55	0.55	0.02	0.50	0.61	1.01	0.06	-8.78	10.88
		0.1	12.09	14.32	0.02	12.63	16.21	18.47	0.10	4.43	34.06	0.52	0.57	0.02	0.52	0.63	10.04	0.07	-0.04	21.12
		0.2	11.98	15.20	0.02	13.29	17.07	27.09	0.11	10.94	42.49	0.49	0.60	0.02	0.54	0.66	21.74	0.07	10.30	34.10
		0.3	11.27	16.31	0.02	14.26	18.48	44.66	0.13	26.53	63.96	0.46	0.62	0.02	0.57	0.69	35.57	0.08	23.71	50.36
		0.4	10.62	17.62	0.02	15.24	20.12	66.20	0.15	43.57	89.53	0.43	0.65	0.02	0.60	0.72	52.21	0.09	39.94	68.38
	0.24	0.01	13.41	13.58	0.02	11.93	15.23	1.45	0.09	-11.03	13.62	0.54	0.55	0.02	0.50	0.60	1.17	0.06	-8.59	11.10
		0.1	12.09	13.91	0.02	12.30	15.85	15.20	0.10	1.66	31.08	0.50	0.56	0.02	0.51	0.62	12.11	0.07	1.29	23.93
		0.2	10.68	14.35	0.02	12.35	16.39	34.44	0.12	15.58	53.42	0.45	0.57	0.02	0.51	0.64	27.11	0.08	12.91	41.12
		0.3	9.40	14.83	0.02	12.79	17.20	58.12	0.15	36.15	83.06	0.40	0.59	0.02	0.53	0.66	46.24	0.10	30.73	64.42
		0.4	8.29	15.44	0.02	13.27	17.63	86.53	0.19	60.11	112.77	0.35	0.61	0.02	0.55	0.69	71.50	0.12	54.13	93.79

Table 3. Distribution of the relative (%) bias of the KM estimation of the median and 12-month progression-free survival (in months) of newly diagnosed MM patients by scenario. We assumed that no patient progresses within the first six months of induction treatment for patients who undergone ASCT, that the hazard rate of progression for those not eligible for transplantation is 0.036, and that the administrative censoring started from 200 months after induction treatment. Number of simulated data: B=2000.

Parameters			True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS				Relative (%) bias: Median PFS				True 12-month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS				Relative (%) bias: 12 Month PFS			
N	λ₂	% ASCT		median	Mean Std. err	min	max	mean	Std. err	min	max		median	Mean Std. err	min	max	mean	Std.err	min	max
	0.036	0.01	21.30	20.96	0.10	9.37	51.88	2.42	0.61	-56.01	143.58	0.70	0.68	0.09	0.40	0.96	-0.31	0.29	-42.76	37.39
		0.1	21.68	21.38	0.10	6.88	47.89	0.92	0.61	-68.29	120.90	0.71	0.70	0.09	0.35	0.96	-1.24	0.30	-50.05	35.01
		0.2	22.10	22.61	0.11	8.88	58.94	5.62	0.67	-59.81	166.67	0.72	0.72	0.10	0.36	1.00	-0.62	0.30	-50.25	39.03
		0.3	22.52	22.08	0.12	8.37	64.19	2.05	0.69	-62.82	185.09	0.73	0.73	0.10	0.37	1.00	-0.80	0.32	-49.60	36.97
		0.4	22.92	22.24	0.13	7.48	50.44	0.89	0.68	-67.37	120.04	0.74	0.75	0.11	0.33	1.00	-0.82	0.33	-55.05	34.97
	0.018	0.01	21.40	21.22	0.10	7.75	48.60	2.43	0.61	-63.77	127.11	0.70	0.68	0.09	0.36	1.00	-0.30	0.30	-48.55	42.92
		0.1	22.77	21.58	0.10	7.26	48.89	-2.95	0.59	-68.11	114.67	0.72	0.70	0.09	0.36	1.00	-1.23	0.30	-49.24	39.33
		0.2	24.45	22.40	0.11	8.21	56.82	-4.71	0.60	-66.43	132.37	0.74	0.72	0.10	0.37	1.00	-3.27	0.30	-49.38	35.56
		0.3	26.30	21.68	0.12	7.78	57.40	-13.70	0.59	-70.43	118.23	0.76	0.73	0.10	0.25	1.00	-4.57	0.32	-67.18	31.98
		0.4	28.34	22.24	0.13	7.48	50.44	-18.39	0.55	-73.60	77.98	0.78	0.75	0.11	0.33	1.00	-5.50	0.32	-57.17	28.58
25	0.012	0.01	21.44	21.15	0.10	7.78	49.08	1.00	0.59	-63.73	128.90	0.70	0.72	0.09	0.32	0.92	-0.29	0.29	-54.29	31.43
		0.1	23.26	21.30	0.10	6.96	44.73	-5.52	0.57	-70.07	92.35	0.72	0.70	0.09	0.39	0.96	-2.30	0.29	-45.31	33.15
		0.2	25.61	22.47	0.11	6.07	48.12	-9.87	0.56	-76.28	87.90	0.74	0.72	0.10	0.37	0.96	-4.21	0.30	-49.92	29.00
		0.3	28.39	22.05	0.12	7.30	68.75	-19.50	0.54	-74.29	142.16	0.77	0.73	0.10	0.25	1.00	-5.56	0.31	-67.24	30.29
		0.4	31.68	22.30	0.13	8.08	65.08	-26.44	0.52	-74.49	105.41	0.79	0.74	0.11	0.31	1.00	-7.31	0.32	-60.38	26.45
	0.009	0.01	21.46	21.32	0.10	7.46	45.69	1.38	0.57	-65.24	112.90	0.70	0.68	0.09	0.32	0.96	-0.46	0.29	-54.30	37.10
		0.1	23.53	21.17	0.10	7.81	50.61	-6.95	0.57	-66.80	115.10	0.72	0.70	0.09	0.27	1.00	-2.46	0.30	-62.60	38.37
		0.2	26.31	22.31	0.11	8.81	48.66	-12.19	0.55	-66.52	84.94	0.75	0.72	0.10	0.32	1.00	-4.47	0.30	-57.56	33.76
		0.3	29.75	22.06	0.12	8.00	64.07	-23.66	0.50	-73.12	115.35	0.77	0.73	0.10	0.31	1.00	-6.11	0.31	-59.32	29.43
		0.4	34.05	22.04	0.13	8.22	55.62	-32.28	0.47	-75.86	63.33	0.80	0.74	0.11	0.30	1.00	-8.44	0.31	-61.79	25.38
	0.036	0.01	21.30	21.34	0.08	10.24	42.31	2.31	0.47	-51.93	98.69	0.70	0.70	0.07	0.45	0.95	-0.05	0.23	-35.60	35.96
		0.1	21.68	22.03	0.08	8.77	43.49	3.28	0.49	-59.57	100.58	0.71	0.71	0.07	0.43	0.95	-0.07	0.24	-39.80	33.69
		0.2	22.10	22.05	0.09	10.21	46.73	2.70	0.52	-53.80	111.43	0.72	0.71	0.08	0.44	0.97	-0.84	0.24	-38.16	34.68
		0.3	22.52	22.37	0.09	8.38	45.87	1.58	0.53	-62.80	103.74	0.73	0.73	0.08	0.41	0.96	-1.05	0.25	-43.27	32.08
		0.4	22.92	22.91	0.10	9.58	50.35	1.64	0.58	-58.21	119.66	0.74	0.74	0.09	0.41	0.97	-0.91	0.27	-45.29	30.32
40	0.018	0.01	21.40	21.15	0.08	9.43	40.60	0.09	0.44	-55.93	89.73	0.70	0.70	0.07	0.43	0.93	-0.61	0.24	-39.26	32.20
		0.1	22.77	22.04	0.08	9.50	47.28	-1.72	0.49	-58.29	107.60	0.72	0.70	0.07	0.42	0.97	-1.60	0.24	-40.94	35.47
		0.2	24.45	22.15	0.09	9.36	49.06	-7.87	0.47	-61.71	100.67	0.74	0.72	0.08	0.42	1.00	-3.21	0.24	-43.05	35.56
		0.3	26.30	22.50	0.09	10.03	43.78	-12.95	0.45	-61.86	66.45	0.76	0.73	0.08	0.37	0.95	-4.88	0.24	-50.64	25.38
		0.4	28.34	22.91	0.10	9.58	50.35	-17.79	0.47	-66.20	77.67	0.78	0.74	0.09	0.41	0.97	-5.59	0.26	-47.87	24.16
	0.012	0.01	21.44	21.50	0.08	10.00	38.12	1.57	0.46	-53.35	77.80	0.70	0.70	0.07	0.43	0.93	0.04	0.24	-39.29	32.14
		0.1	23.26	22.03	0.08	10.16	41.95	-3.69	0.47	-56.29	80.39	0.72	0.70	0.07	0.45	0.98	-2.29	0.24	-37.10	35.23

N	λ_2	% ASCT	True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS				Relative (%) bias: Median PFS				True 12-month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS				Relative (%) bias: 12 Month PFS			
				median	Mean Std. err	min	max	mean	Std. err	min	max		median	Mean Std. err	min	max	mean	Std.err	min	max
		0.2	25.61	22.28	0.09	9.64	41.48	-11.63	0.44	-62.35	61.97	0.74	0.72	0.08	0.46	0.98	-3.90	0.24	-38.85	31.01
		0.3	28.39	22.33	0.09	9.38	46.90	-19.52	0.43	-66.95	65.20	0.77	0.72	0.08	0.44	0.98	-5.99	0.24	-43.23	27.04
		0.4	31.68	22.62	0.10	10.06	50.17	-26.89	0.40	-68.25	58.36	0.79	0.73	0.09	0.39	0.98	-7.84	0.24	-50.08	23.29
	0.009	0.01	21.46	21.31	0.08	11.20	46.66	0.48	0.45	-47.83	117.41	0.70	0.70	0.07	0.48	0.95	-0.53	0.23	-32.16	35.68
		0.1	23.53	21.84	0.08	10.83	46.97	-5.54	0.44	-53.97	99.62	0.72	0.70	0.07	0.45	0.92	-2.39	0.23	-37.32	27.20
		0.2	26.31	22.08	0.09	9.97	44.68	-14.68	0.43	-62.10	69.82	0.75	0.72	0.08	0.46	0.94	-4.35	0.23	-39.07	25.40
		0.3	29.75	22.45	0.09	10.02	46.81	-22.88	0.41	-66.34	57.34	0.77	0.73	0.08	0.45	0.96	-6.17	0.24	-41.72	24.81
		0.4	34.05	22.80	0.10	10.21	59.64	-31.25	0.38	-70.02	75.15	0.80	0.73	0.09	0.45	1.00	-7.90	0.24	-43.18	25.38
60	0.036	0.01	21.30	21.32	0.07	11.95	40.50	1.45	0.39	-43.91	90.18	0.70	0.70	0.06	0.49	0.90	0.35	0.19	-29.52	28.56
		0.1	21.68	21.89	0.07	11.69	37.27	2.47	0.41	-46.06	71.90	0.71	0.71	0.06	0.45	0.88	-0.08	0.20	-36.48	23.93
		0.2	22.10	21.86	0.07	11.64	46.31	0.38	0.41	-47.31	109.52	0.72	0.71	0.06	0.48	0.96	-0.90	0.20	-33.21	33.80
		0.3	22.52	22.34	0.08	9.35	38.92	0.23	0.42	-58.46	72.85	0.73	0.73	0.07	0.47	0.92	-0.95	0.21	-35.07	25.34
		0.4	22.92	22.52	0.08	9.87	43.08	0.54	0.47	-56.94	87.94	0.74	0.73	0.07	0.45	0.94	-1.33	0.22	-39.03	26.63
	0.018	0.01	21.40	21.14	0.07	11.02	36.03	-0.12	0.38	-48.50	68.37	0.70	0.70	0.06	0.46	0.90	0.01	0.19	-34.49	28.50
		0.1	22.77	21.69	0.07	10.68	38.46	-3.48	0.37	-53.11	68.87	0.72	0.71	0.06	0.42	0.93	-1.76	0.19	-41.69	29.07
		0.2	24.45	21.76	0.07	11.22	38.58	-9.50	0.37	-54.12	57.79	0.74	0.71	0.06	0.49	0.90	-3.21	0.19	-34.20	22.42
		0.3	26.30	22.24	0.08	10.81	40.96	-14.23	0.38	-58.89	55.72	0.76	0.72	0.07	0.46	0.92	-4.71	0.20	-38.91	21.21
		0.4	28.34	22.52	0.08	9.87	43.08	-18.68	0.38	-65.17	52.02	0.78	0.73	0.07	0.45	0.94	-5.99	0.21	-41.92	20.65
	0.012	0.01	21.44	21.20	0.07	11.37	37.07	0.17	0.38	-46.98	72.92	0.70	0.70	0.06	0.48	0.88	-0.39	0.19	-32.03	26.01
		0.1	23.26	21.74	0.07	11.15	37.47	-5.15	0.37	-52.04	61.13	0.72	0.71	0.06	0.49	0.90	-2.00	0.19	-31.80	24.13
		0.2	25.61	21.88	0.07	10.58	39.51	-13.47	0.35	-58.69	54.28	0.74	0.72	0.06	0.48	0.92	-3.82	0.19	-36.01	24.24
		0.3	28.39	22.29	0.08	12.03	42.95	-20.36	0.34	-57.63	51.26	0.77	0.73	0.07	0.50	0.93	-5.76	0.19	-34.53	20.56
		0.4	31.68	22.51	0.08	10.74	47.29	-27.72	0.34	-66.09	49.27	0.79	0.73	0.07	0.45	0.96	-7.70	0.21	-43.44	20.79
	0.009	0.01	21.46	21.20	0.07	11.83	36.44	-0.36	0.37	-44.87	69.76	0.70	0.70	0.06	0.49	0.86	-0.19	0.19	-29.72	23.49
		0.1	23.53	21.80	0.07	11.43	38.63	-6.08	0.37	-51.44	64.16	0.72	0.71	0.06	0.47	0.89	-2.23	0.19	-34.74	23.65
		0.2	26.31	21.88	0.07	11.89	41.33	-15.79	0.34	-54.80	57.09	0.75	0.72	0.06	0.50	0.89	-4.80	0.19	-33.79	18.43
		0.3	29.75	22.10	0.08	9.76	42.79	-24.43	0.33	-67.18	43.81	0.77	0.72	0.07	0.44	0.90	-6.73	0.20	-43.02	17.11
		0.4	34.05	22.61	0.08	11.47	43.31	-32.11	0.32	-66.31	27.18	0.80	0.74	0.07	0.46	0.96	-8.20	0.20	-42.80	19.77
100	0.036	0.01	21.30	21.40	0.05	13.96	31.38	0.74	0.29	-34.46	47.34	0.70	0.70	0.57	0.84	0.19	0.15	-18.94	20.09	0.70
		0.1	21.68	21.53	0.05	14.59	34.95	0.04	0.29	-32.70	61.20	0.71	0.71	0.55	0.84	-0.47	0.15	-22.15	18.30	0.71
		0.2	22.10	21.79	0.06	13.52	34.47	-0.84	0.32	-38.81	55.95	0.71	0.71	0.55	0.88	-0.86	0.15	-24.20	21.96	0.71
		0.3	22.52	22.22	0.06	12.95	35.31	-0.34	0.33	-42.49	56.81	0.72	0.72	0.51	0.87	-1.02	0.16	-30.05	19.41	0.72
		0.4	22.92	22.56	0.07	12.60	38.84	-1.12	0.34	-45.03	69.43	0.73	0.73	0.53	0.89	-1.31	0.17	-28.49	19.90	0.73
	0.018	0.01	21.40	21.22	0.05	14.00	31.30	-0.18	0.28	-34.60	46.26	0.70	0.70	0.05	0.56	0.87	-0.14	0.15	-20.54	24.21
		0.1	22.77	21.55	0.05	12.54	36.08	-4.47	0.28	-44.95	58.43	0.72	0.71	0.05	0.52	0.87	-1.50	0.15	-27.52	21.40
		0.2	24.45	21.89	0.06	14.46	35.67	-9.81	0.28	-40.84	45.90	0.74	0.71	0.05	0.54	0.90	-3.13	0.15	-26.80	22.06
		0.3	26.30	22.14	0.06	13.59	36.94	-14.85	0.29	-48.33	40.43	0.76	0.72	0.05	0.55	0.88	-4.76	0.16	-27.41	15.93
		0.4	28.34	22.56	0.07	12.60	38.84	-20.02	0.28	-55.54	37.04	0.78	0.73	0.06	0.53	0.89	-5.97	0.16	-31.86	14.23

N	λ_2	% ASCT	True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS				Relative (%) bias: Median PFS				True 12-month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS				Relative (%) bias: 12 Month PFS			
				median	Mean Std. err	min	max	mean	Std. err	min	max		median	Mean Std. err	min	max	mean	Std.err	min	max
	0.012	0.01	21.44	21.18	0.05	12.48	31.29	-0.19	0.29	-41.81	45.95	0.70	0.70	0.05	0.51	0.85	-0.31	0.15	-27.70	21.27
		0.1	23.26	21.43	0.05	12.42	32.91	-7.39	0.28	-46.60	41.51	0.72	0.71	0.05	0.51	0.84	-2.37	0.15	-29.31	16.26
		0.2	25.61	21.93	0.06	13.36	34.34	-13.74	0.27	-47.82	34.08	0.74	0.71	0.05	0.55	0.88	-4.08	0.15	-26.04	17.71
		0.3	28.39	22.37	0.06	13.85	35.27	-20.72	0.26	-51.23	24.21	0.77	0.73	0.05	0.53	0.90	-5.59	0.15	-30.42	17.21
		0.4	31.68	22.47	0.07	13.34	39.30	-28.21	0.25	-57.89	24.05	0.79	0.73	0.06	0.53	0.90	-7.83	0.16	-32.63	13.82
	0.009	0.01	21.46	21.24	0.05	11.76	30.90	-0.41	0.30	-45.20	43.97	0.70	0.70	0.05	0.49	0.85	-0.23	0.15	-30.59	21.28
		0.1	23.53	21.54	0.05	13.31	32.90	-7.72	0.28	-43.42	39.80	0.72	0.71	0.05	0.55	0.85	-2.44	0.15	-23.59	17.31
		0.2	26.31	22.01	0.06	13.13	35.71	-15.94	0.27	-50.10	35.72	0.75	0.72	0.05	0.53	0.90	-4.57	0.15	-28.46	20.01
		0.3	29.75	22.25	0.06	13.78	33.64	-24.91	0.25	-53.69	13.07	0.77	0.72	0.05	0.54	0.88	-6.60	0.15	-30.74	13.76
		0.4	34.05	22.44	0.07	13.71	37.31	-33.36	0.24	-59.74	9.57	0.80	0.73	0.06	0.53	0.91	-8.24	0.16	-34.10	13.60
	0.036	0.01	21.30	21.35	0.02	18.61	25.15	0.27	0.09	-12.63	18.07	0.70	0.70	0.01	0.65	0.75	0.09	0.05	-6.65	6.78
		0.1	21.68	21.58	0.02	18.41	24.78	-0.44	0.10	-15.10	14.29	0.71	0.71	0.02	0.65	0.76	-0.40	0.05	-8.71	6.65
		0.2	22.10	21.91	0.02	18.46	25.11	-0.82	0.10	-16.46	13.62	0.72	0.71	0.02	0.66	0.77	-0.71	0.05	-8.13	7.24
		0.3	22.52	22.21	0.02	19.26	25.61	-1.23	0.11	-14.47	13.73	0.73	0.72	0.02	0.67	0.78	-1.07	0.05	-8.59	6.40
		0.4	22.92	22.60	0.02	18.28	26.66	-1.26	0.11	-20.26	16.30	0.74	0.73	0.02	0.66	0.80	-1.26	0.05	-10.38	7.31
	0.018	0.01	21.40	21.28	0.02	18.46	24.23	-0.49	0.09	-13.75	13.24	0.70	0.70	0.01	0.65	0.75	-0.16	0.05	-7.35	7.50
		0.1	22.77	21.56	0.02	18.25	24.87	-5.19	0.09	-19.88	9.20	0.72	0.71	0.02	0.66	0.75	-1.66	0.05	-8.65	4.47
		0.2	24.45	21.90	0.02	18.75	25.10	-10.31	0.09	-23.33	2.66	0.74	0.71	0.02	0.65	0.77	-3.20	0.05	-11.55	4.20
		0.3	26.30	22.22	0.02	18.52	25.93	-15.44	0.09	-29.58	-1.42	0.76	0.72	0.02	0.67	0.78	-4.66	0.05	-11.93	2.89
		0.4	28.34	22.60	0.02	18.28	26.66	-20.14	0.09	-35.50	-5.93	0.78	0.73	0.02	0.66	0.80	-5.93	0.05	-14.61	2.24
1000	0.012	0.01	21.44	21.32	0.02	18.25	24.42	-0.53	0.09	-14.89	13.89	0.70	0.70	0.01	0.65	0.75	-0.16	0.05	-6.94	6.73
		0.1	23.26	21.56	0.02	18.58	25.46	-7.16	0.09	-20.09	9.49	0.72	0.71	0.02	0.65	0.76	-2.21	0.05	-10.29	4.97
		0.2	25.61	21.86	0.02	19.17	26.24	-14.46	0.09	-25.13	2.46	0.74	0.71	0.02	0.66	0.77	-4.04	0.05	-11.02	2.92
		0.3	28.39	22.26	0.02	18.90	26.07	-21.63	0.08	-33.45	-8.16	0.77	0.72	0.02	0.66	0.77	-5.89	0.05	-13.60	0.78
		0.4	31.68	22.55	0.02	19.22	26.58	-28.74	0.08	-39.32	-16.12	0.79	0.73	0.02	0.67	0.79	-7.49	0.05	-14.66	-0.67
	0.009	0.01	21.46	21.22	0.02	17.80	24.90	-0.97	0.09	-17.08	16.03	0.70	0.70	0.01	0.65	0.75	-0.33	0.05	-7.70	6.58
		0.1	23.53	21.54	0.02	18.73	25.02	-8.37	0.09	-20.38	6.34	0.72	0.71	0.02	0.66	0.76	-2.38	0.05	-9.17	5.16
		0.2	26.31	21.90	0.02	18.93	25.19	-16.67	0.08	-28.05	-4.28	0.75	0.72	0.02	0.66	0.77	-4.45	0.05	-11.86	2.47
		0.3	29.75	22.23	0.02	18.71	25.72	-25.24	0.08	-37.11	-13.57	0.77	0.72	0.02	0.67	0.78	-6.50	0.05	-13.78	0.52
		0.4	34.05	22.52	0.02	19.03	26.17	-33.71	0.08	-44.11	-23.14	0.80	0.73	0.02	0.67	0.80	-8.30	0.05	-15.90	0.55

Table 4. Distribution of the relative (%) bias of the KM estimation of the median and 12-month progression-free survival (in months) of newly diagnosed MM patients by scenario. We assumed that no patient progresses within the first six months of induction treatment for patients who undergone ASCT, that the hazard rate of progression for those not eligible for transplantation is 0.108, and that the administrative censoring started from 200 months after induction treatment. Number of simulated data: B=2000.

| N	λ_2	% ASCT	True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS				Relative (%) bias: Median PFS				True 12 month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS				Relative (%) bias: 12 Month PFS			
				median	Mean Std.err	min	max	mean	Std.err	min	max		median	Mean Std.err	min	max	mean	Std.err	min	max
25	0.108	0.01	8.47	8.32	0.10	4.46	18.63	1.61	0.51	-47.38	119.95	0.34	0.32	0.09	0.08	0.64	-0.91	0.62	-76.57	87.45
		0.1	8.91	8.60	0.10	3.80	17.30	-1.08	0.47	-57.37	94.24	0.36	0.36	0.10	0.05	0.74	-2.05	0.63	-87.21	108.07
		0.2	9.37	9.07	0.11	4.83	20.98	-0.13	0.51	-48.39	123.94	0.38	0.37	0.11	0.05	0.74	-3.39	0.67	-85.86	95.33
		0.3	9.81	9.64	0.12	5.11	25.52	1.53	0.54	-47.89	160.20	0.39	0.39	0.12	0.00	0.77	-2.91	0.69	-100.00	94.00
		0.4	10.23	9.88	0.13	5.35	21.16	0.45	0.54	-47.74	106.87	0.41	0.39	0.13	0.00	0.85	-4.28	0.71	-100.00	105.63
	0.054	0.01	8.49	8.41	0.10	3.92	17.53	1.78	0.51	-53.85	106.56	0.34	0.32	0.09	0.08	0.64	-0.64	0.62	-76.70	86.37
		0.1	9.15	8.62	0.10	4.46	17.63	-3.29	0.47	-51.32	92.59	0.38	0.36	0.10	0.09	0.75	-6.30	0.59	-76.64	97.49
		0.2	9.96	9.05	0.11	5.12	20.27	-5.94	0.47	-48.63	103.47	0.42	0.37	0.11	0.05	0.72	-12.25	0.60	-87.00	72.88
		0.3	10.85	9.57	0.12	4.68	24.99	-8.87	0.49	-56.90	130.27	0.45	0.38	0.12	0.00	0.78	-15.94	0.59	-100.00	72.03
		0.4	11.82	9.88	0.13	5.35	21.16	-13.04	0.47	-54.76	79.09	0.49	0.39	0.13	0.00	0.85	-19.81	0.60	-100.00	72.24
	0.036	0.01	8.50	8.38	0.10	3.93	17.69	0.66	0.49	-53.80	108.25	0.34	0.32	0.09	0.08	0.76	-1.98	0.62	-76.76	120.74
		0.1	9.26	8.60	0.10	4.59	16.24	-4.74	0.46	-50.39	75.50	0.39	0.36	0.10	0.04	0.70	-8.60	0.58	-88.37	80.79
		0.2	10.25	9.03	0.11	4.70	17.37	-9.43	0.44	-54.12	69.58	0.43	0.37	0.11	0.05	0.72	-16.15	0.57	-87.41	67.44
		0.3	11.42	9.65	0.12	4.76	24.25	-13.04	0.46	-58.35	112.41	0.48	0.38	0.12	0.00	0.82	-19.84	0.56	-100.00	71.78
		0.4	12.80	9.88	0.13	5.25	23.93	-19.39	0.44	-58.99	86.90	0.53	0.40	0.13	0.00	0.81	-24.23	0.55	-100.00	53.34
	0.027	0.01	8.50	8.44	0.10	3.82	16.56	1.02	0.48	-55.05	94.89	0.34	0.32	0.09	0.08	0.68	-1.42	0.59	-76.79	97.27
		0.1	9.31	8.53	0.10	4.15	18.20	-5.62	0.46	-55.42	95.48	0.39	0.35	0.10	0.09	0.66	-11.03	0.57	-77.17	69.47
		0.2	10.41	9.01	0.11	4.68	18.17	-10.58	0.44	-55.06	74.50	0.44	0.37	0.11	0.05	0.69	-17.90	0.56	-88.28	56.54
		0.3	11.78	9.63	0.12	5.14	22.69	-16.20	0.43	-56.34	92.58	0.49	0.38	0.12	0.00	0.72	-23.78	0.55	-100.00	46.71
		0.4	13.50	9.87	0.13	5.56	24.70	-24.11	0.41	-58.79	83.01	0.54	0.39	0.13	0.00	0.89	-27.36	0.53	-100.00	63.89
40	0.108	0.01	8.47	8.45	0.08	4.75	15.44	1.51	0.39	-43.96	82.31	0.34	0.35	0.07	0.13	0.63	-0.29	0.51	-63.39	83.05
		0.1	8.91	8.72	0.08	4.99	15.83	-0.51	0.39	-43.95	77.75	0.36	0.35	0.08	0.12	0.62	-1.66	0.50	-67.59	74.52
		0.2	9.37	9.13	0.09	5.44	16.91	-0.19	0.39	-41.98	80.50	0.38	0.37	0.08	0.10	0.65	-2.13	0.52	-73.10	72.48
		0.3	9.81	9.50	0.10	5.54	16.90	-1.32	0.40	-43.52	72.34	0.39	0.38	0.09	0.12	0.69	-3.68	0.53	-69.12	75.37
		0.4	10.23	9.87	0.10	5.90	19.74	-1.55	0.42	-42.37	92.96	0.41	0.40	0.10	0.06	0.77	-4.11	0.55	-86.51	85.23
	0.054	0.01	8.49	8.38	0.08	4.48	14.87	-0.18	0.37	-47.25	75.15	0.34	0.33	0.07	0.10	0.65	-2.33	0.48	-70.88	89.28
		0.1	9.15	8.74	0.08	4.98	17.09	-3.12	0.39	-45.63	86.73	0.38	0.35	0.08	0.09	0.65	-6.59	0.48	-75.93	72.25
		0.2	9.96	9.16	0.09	5.43	17.75	-6.80	0.37	-45.46	78.11	0.42	0.37	0.08	0.10	0.65	-12.44	0.48	-75.47	55.30
		0.3	10.85	9.56	0.09	5.30	16.62	-10.59	0.36	-51.15	53.15	0.45	0.38	0.09	0.08	0.72	-16.12	0.46	-82.05	57.29
		0.4	11.82	9.87	0.10	5.90	19.74	-14.77	0.36	-50.11	67.04	0.49	0.40	0.10	0.06	0.77	-19.67	0.46	-88.68	55.14
	0.036	0.01	8.50	8.50	0.08	4.67	14.04	1.14	0.39	-45.06	65.26	0.34	0.35	0.07	0.03	0.58	-0.55	0.49	-92.74	67.01
		0.1	9.26	8.72	0.08	4.75	15.32	-4.17	0.38	-48.65	65.49	0.39	0.35	0.08	0.12	0.60	-8.42	0.46	-69.55	55.59
		0.2	10.25	9.19	0.09	5.66	15.44	-9.18	0.35	-44.71	50.66	0.43	0.37	0.08	0.10	0.65	-15.20	0.44	-75.99	50.00
		0.3	11.42	9.49	0.09	5.70	18.68	-15.21	0.35	-50.05	63.59	0.48	0.38	0.09	0.08	0.67	-20.80	0.43	-82.46	39.05
		0.4	12.80	9.86	0.10	5.90	20.84	-21.28	0.34	-53.94	62.78	0.53	0.39	0.10	0.00	0.71	-25.09	0.44	-100.00	34.54
	0.027	0.01	8.50	8.44	0.08	5.07	16.89	0.26	0.38	-40.40	98.68	0.34	0.35	0.07	0.08	0.58	-1.25	0.48	-78.24	66.81
		0.1	9.31	8.65	0.08	5.16	17.09	-5.40	0.36	-44.56	83.55	0.39	0.35	0.08	0.09	0.60	-10.52	0.45	-77.60	53.98
		0.2	10.41	9.15	0.09	5.48	16.83	-11.11	0.35	-47.36	61.62	0.44	0.37	0.08	0.11	0.68	-17.29	0.42	-74.90	55.00

N	λ_2	% ASCT	True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS				Relative (%) bias: Median PFS				True 12 month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS				Relative (%) bias: 12 Month PFS			
				median	Mean Std.err	min	max	mean	Std.err	min	max		median	Mean Std.err	min	max	mean	Std.err	min	max
		0.3	11.78	9.51	0.09	5.51	19.64	-17.58	0.34	-53.23	66.70	0.49	0.38	0.09	0.08	0.67	-22.77	0.42	-83.20	35.23
		0.4	13.50	9.90	0.10	6.14	21.76	-24.97	0.33	-54.48	61.17	0.54	0.40	0.10	0.05	0.69	-27.12	0.43	-90.55	26.13
60	0.108	0.01	8.47	8.44	0.07	5.32	14.83	0.79	0.32	-37.23	75.18	0.34	0.34	0.06	0.15	0.60	0.42	0.41	-55.05	74.65
		0.1	8.91	8.83	0.07	5.24	13.76	0.17	0.32	-41.11	54.47	0.36	0.35	0.06	0.16	0.62	-0.38	0.42	-55.73	73.65
		0.2	9.37	9.18	0.07	5.92	16.78	-1.01	0.32	-36.83	79.11	0.38	0.37	0.07	0.16	0.61	-2.30	0.42	-56.99	63.26
		0.3	9.81	9.53	0.08	6.07	15.33	-1.62	0.32	-38.14	56.32	0.39	0.38	0.08	0.14	0.62	-3.61	0.43	-64.24	56.06
		0.4	10.23	9.88	0.08	6.23	15.86	-1.62	0.34	-39.14	55.02	0.41	0.40	0.08	0.13	0.64	-3.89	0.45	-69.68	53.88
	0.054	0.01	8.49	8.38	0.07	5.01	13.34	-0.36	0.32	-41.01	57.20	0.34	0.34	0.06	0.12	0.55	-1.22	0.40	-65.06	58.91
		0.1	9.15	8.76	0.07	4.92	14.15	-3.38	0.30	-46.24	54.62	0.38	0.35	0.06	0.12	0.60	-7.14	0.38	-68.97	59.37
		0.2	9.96	9.11	0.07	5.77	14.55	-7.44	0.29	-42.09	46.04	0.42	0.37	0.07	0.14	0.61	-11.77	0.37	-66.80	46.07
		0.3	10.85	9.48	0.08	5.59	17.59	-11.25	0.30	-48.51	62.13	0.45	0.38	0.08	0.09	0.63	-15.94	0.37	-80.10	39.39
		0.4	11.82	9.88	0.08	6.23	15.86	-14.83	0.30	-47.32	34.20	0.49	0.40	0.08	0.13	0.64	-19.49	0.38	-74.59	28.90
	0.036	0.01	8.50	8.40	0.07	5.12	13.69	-0.04	0.32	-39.71	61.15	0.34	0.34	0.06	0.15	0.56	-0.70	0.40	-55.30	62.88
		0.1	9.26	8.78	0.07	5.55	13.82	-4.07	0.29	-40.03	49.36	0.39	0.35	0.06	0.17	0.56	-8.39	0.37	-55.23	44.12
		0.2	10.25	9.14	0.07	5.87	15.97	-10.01	0.29	-42.70	55.89	0.43	0.36	0.07	0.14	0.63	-15.50	0.36	-67.24	45.06
		0.3	11.42	9.49	0.08	6.09	15.75	-15.63	0.28	-46.65	37.99	0.48	0.38	0.08	0.16	0.65	-20.34	0.35	-65.62	35.79
		0.4	12.80	9.78	0.08	6.47	18.55	-22.06	0.27	-49.44	44.92	0.53	0.39	0.08	0.07	0.68	-25.05	0.36	-86.31	30.07
	0.027	0.01	8.50	8.40	0.07	5.28	13.48	-0.45	0.31	-37.91	58.58	0.34	0.34	0.06	0.12	0.56	-1.19	0.40	-65.36	62.69
		0.1	9.31	8.80	0.07	5.37	14.21	-4.59	0.30	-42.39	52.58	0.39	0.35	0.06	0.16	0.57	-9.47	0.37	-59.89	46.12
		0.2	10.41	9.10	0.07	5.58	15.11	-11.29	0.29	-46.43	45.12	0.44	0.36	0.07	0.15	0.61	-17.50	0.36	-65.91	37.03
		0.3	11.78	9.49	0.08	6.26	16.24	-18.49	0.27	-46.90	37.79	0.49	0.38	0.08	0.11	0.64	-22.95	0.34	-76.79	29.24
		0.4	13.50	9.89	0.08	6.21	16.71	-25.50	0.27	-54.03	23.82	0.54	0.40	0.08	0.13	0.67	-26.66	0.35	-76.15	22.65
100	0.108	0.01	8.47	8.47	0.05	5.99	11.79	0.20	0.24	-29.31	39.27	0.34	0.34	0.05	0.19	0.50	0.24	0.31	-43.60	45.24
		0.1	8.91	8.75	0.05	6.34	13.43	-1.03	0.24	-28.86	50.79	0.36	0.35	0.05	0.21	0.53	-1.31	0.31	-42.11	47.00
		0.2	9.37	9.10	0.06	6.42	12.95	-2.29	0.25	-31.46	38.23	0.38	0.36	0.05	0.17	0.59	-3.19	0.33	-55.49	55.61
		0.3	9.81	9.45	0.06	6.31	14.36	-2.52	0.25	-35.64	46.41	0.39	0.38	0.06	0.16	0.59	-3.25	0.33	-60.14	50.65
		0.4	10.23	9.84	0.07	6.85	14.77	-3.16	0.26	-32.99	44.40	0.41	0.39	0.06	0.09	0.61	-4.63	0.35	-78.03	48.72
	0.054	0.01	8.49	8.41	0.05	6.00	11.77	-0.41	0.24	-29.33	38.61	0.34	0.34	0.05	0.18	0.50	-1.08	0.31	-46.83	44.47
		0.1	9.15	8.77	0.05	5.69	13.64	-3.51	0.23	-37.80	49.00	0.38	0.36	0.05	0.17	0.55	-6.14	0.29	-54.07	44.63
		0.2	9.96	9.15	0.06	6.56	13.58	-7.61	0.22	-34.17	36.32	0.42	0.37	0.05	0.20	0.58	-11.99	0.29	-52.15	38.19
		0.3	10.85	9.49	0.06	6.89	14.06	-11.96	0.23	-36.52	29.55	0.45	0.38	0.06	0.15	0.61	-16.43	0.29	-66.86	34.66
		0.4	11.82	9.84	0.07	6.85	14.77	-16.17	0.23	-41.99	25.01	0.49	0.39	0.06	0.09	0.61	-20.12	0.29	-81.59	24.56
	0.036	0.01	8.50	8.39	0.05	5.51	11.76	-0.34	0.25	-35.19	38.47	0.34	0.34	0.05	0.18	0.49	-1.10	0.30	-46.85	41.39
		0.1	9.26	8.73	0.05	5.85	13.10	-5.21	0.23	-36.84	41.53	0.39	0.35	0.05	0.20	0.53	-9.30	0.29	-49.09	37.31
		0.2	10.25	9.14	0.06	6.32	12.97	-10.09	0.22	-38.35	26.61	0.43	0.37	0.05	0.20	0.53	-15.30	0.27	-53.60	22.16
		0.3	11.42	9.53	0.06	6.69	13.78	-15.95	0.22	-41.38	20.70	0.48	0.38	0.06	0.19	0.59	-20.13	0.27	-61.31	22.22
		0.4	12.80	9.86	0.07	6.91	15.42	-22.24	0.21	-46.06	20.48	0.53	0.40	0.07	0.13	0.62	-24.37	0.27	-75.37	18.48
	0.027	0.01	8.50	8.41	0.05	5.28	11.63	-0.49	0.25	-37.83	36.87	0.34	0.34	0.05	0.19	0.49	-1.13	0.31	-43.95	41.02
		0.1	9.31	8.75	0.05	6.20	12.86	-5.33	0.23	-33.45	38.07	0.39	0.35	0.05	0.16	0.53	-9.96	0.30	-58.36	34.81
		0.2	10.41	9.20	0.06	6.10	13.83	-11.40	0.22	-41.37	32.78	0.44	0.37	0.05	0.22	0.57	-16.77	0.27	-50.81	28.90
		0.3	11.78	9.49	0.06	6.80	13.61	-19.03	0.21	-42.30	15.48	0.49	0.38	0.06	0.18	0.56	-23.13	0.27	-64.31	12.80
		0.4	13.50	9.83	0.07	6.73	15.04	-26.59	0.20	-50.11	11.40	0.54	0.39	0.06	0.17	0.60	-27.67	0.27	-69.59	10.00
1000	0.108	0.01	8.47	8.48	0.02	7.60	9.73	0.10	0.08	-10.28	14.87	0.34	0.34	0.02	0.29	0.40	0.08	0.10	-14.41	16.98
		0.1	8.91	8.78	0.02	7.83	9.71	-1.44	0.08	-12.04	9.05	0.36	0.35	0.02	0.30	0.40	-1.37	0.10	-16.94	12.21
		0.2	9.37	9.13	0.02	8.15	10.23	-2.47	0.08	-12.96	9.16	0.38	0.37	0.02	0.31	0.43	-2.54	0.10	-17.24	14.11

| parameters			True Median PFS	Summary Statistics from simulations of the estimated KM Median PFS				Relative (%) bias: Median PFS				True 12 month PFS	Summary Statistics from simulations of the estimated KM 12 month PFS				Relative (%) bias: 12 Month PFS			
N	λ_2	% ASCT		median	Mean Std.err	min	max	mean	Std.err	min	max		median	Mean Std.err	min	max	mean	Std.err	min	max
		0.3	9.81	9.50	0.02	8.41	10.61	-3.24	0.08	-14.25	8.11	0.39	0.38	0.02	0.32	0.44	-3.34	0.11	-19.13	11.84
		0.4	10.23	9.87	0.02	8.60	11.17	-3.52	0.08	-15.90	9.16	0.41	0.40	0.02	0.33	0.47	-3.92	0.11	-20.16	13.20
	0.054	0.01	8.49	8.45	0.02	7.52	9.46	-0.37	0.08	-11.39	11.46	0.34	0.34	0.02	0.29	0.41	-0.73	0.10	-14.91	18.38
		0.1	9.15	8.77	0.02	7.84	9.83	-4.05	0.08	-14.36	7.37	0.38	0.35	0.02	0.30	0.41	-6.61	0.09	-19.44	8.84
		0.2	9.96	9.13	0.02	8.11	10.23	-8.30	0.07	-18.63	2.71	0.42	0.37	0.02	0.32	0.42	-11.96	0.09	-24.29	0.77
		0.3	10.85	9.49	0.02	8.22	10.68	-12.55	0.07	-24.25	-1.54	0.45	0.38	0.02	0.31	0.45	-16.21	0.09	-31.12	-1.89
		0.4	11.82	9.87	0.02	8.60	11.17	-16.48	0.07	-27.19	-5.50	0.49	0.40	0.02	0.33	0.47	-19.51	0.09	-33.12	-5.17
	0.036	0.01	8.50	8.46	0.02	7.43	9.50	-0.35	0.08	-12.52	11.81	0.34	0.34	0.02	0.29	0.39	-0.87	0.10	-15.97	12.69
		0.1	9.26	8.77	0.02	7.73	10.13	-5.13	0.08	-16.50	9.42	0.39	0.35	0.02	0.30	0.41	-8.57	0.09	-21.96	6.06
		0.2	10.25	9.12	0.02	8.18	10.27	-10.84	0.07	-20.14	0.22	0.43	0.37	0.02	0.31	0.43	-15.34	0.09	-28.63	-1.48
		0.3	11.42	9.49	0.02	8.27	10.78	-16.85	0.07	-27.53	-5.62	0.48	0.38	0.02	0.31	0.45	-20.57	0.09	-35.44	-6.49
		0.4	12.80	9.83	0.02	8.58	11.29	-23.07	0.07	-32.96	-11.80	0.53	0.40	0.02	0.31	0.46	-24.77	0.09	-40.68	-12.26
	0.027	0.01	8.50	8.43	0.02	7.37	9.64	-0.67	0.08	-13.35	13.43	0.34	0.34	0.02	0.28	0.40	-1.19	0.10	-18.48	15.29
		0.1	9.31	8.77	0.02	7.95	9.87	-5.81	0.07	-14.67	5.94	0.39	0.35	0.02	0.31	0.42	-9.73	0.09	-21.19	6.76
		0.2	10.41	9.13	0.02	8.13	10.33	-12.22	0.07	-21.93	-0.76	0.44	0.37	0.02	0.31	0.42	-16.95	0.09	-30.22	-4.39
		0.3	11.78	9.47	0.02	8.26	10.55	-19.49	0.07	-29.85	-10.46	0.49	0.38	0.02	0.31	0.44	-22.77	0.09	-36.81	-10.94
		0.4	13.50	9.82	0.02	8.44	11.19	-27.09	0.06	-37.50	-17.13	0.54	0.40	0.02	0.33	0.46	-27.25	0.08	-39.44	-16.18

Supplementary figure 1. Distribution of relative (%) bias by proportion of relapsed and/or refractory WM patients who receive NPT prior to progression (Panels A and B) and by ratio between hazard rate of the group of patients who remain on study and the hazard rate of the group of patients who come off study prior to progression and by the specific value of the hazard rates themselves (Panels C and D assuming 20% of the patients are informatively censored.) Results are shown with n=40 patients and assume non-informative censoring exists. Panels A and C show the impact on the 12-month PFS estimates and Panels B and D show the impact on the median PFS. The x-axis in Panels A and B is the proportion of patients who receive NPT prior to progression. The x-axis in Panels C and D is the hazard ratio ($\lambda_2(t)/\lambda_1(t)$). The white boxes in Panels C and D correspond to $\lambda_1(t)=0.03$ and the grey boxes correspond to $\lambda_1(t)=0.06$.

Supplementary figure 2. Distribution of relative (%) bias by proportion of MM patients who undergo transplant prior to progression (Panels A and B) and by ratio between hazard rate of the group of patients who remain on study and the hazard rate of the group of patients who undergo transplant prior to progression and by the specific value of the hazard rates themselves (Panels C and D assuming 40% of the patients are informatively censored.) Results are shown with n=60 patients and assuming non-informative censoring exists. Panels A and C show the impact on the 12-month PFS estimates and Panels B and D show the impact on the median PFS. The x-axis in Panels A and B is the proportion of patients who undergo transplant prior to progression. The x-axis in Panels C and D is the hazard ratio ($\lambda_2(t)/\lambda_1(t)$). The white boxes in Panels C and D correspond to $\lambda_1(t)=0.036$ and the grey boxes correspond to $\lambda_1(t)=0.108$.

**Panel A: WM, N=40, 12 month estimate. Case with NI censoring**

$\lambda_1=0.06$; $\lambda_2=0.24$

% relative bias

proportion of patients with NPT
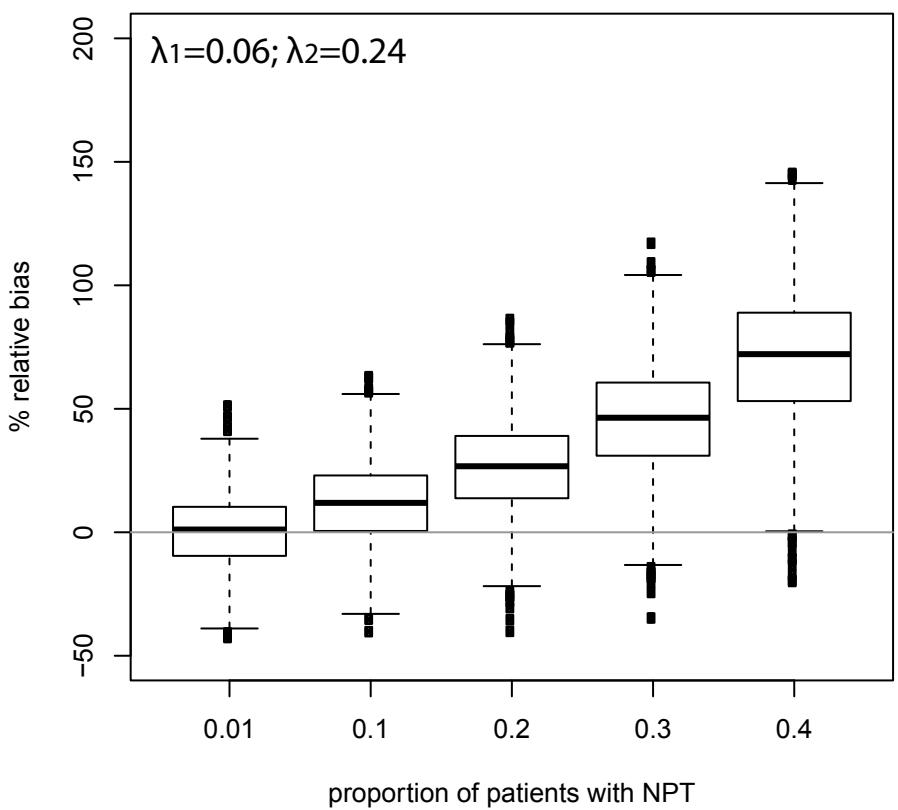
Panel B: WM, N=40, median estimate. Case with NI censoring

$\lambda_1=0.06$; $\lambda_2=0.24$

% relative bias

proportion of patients with NPT
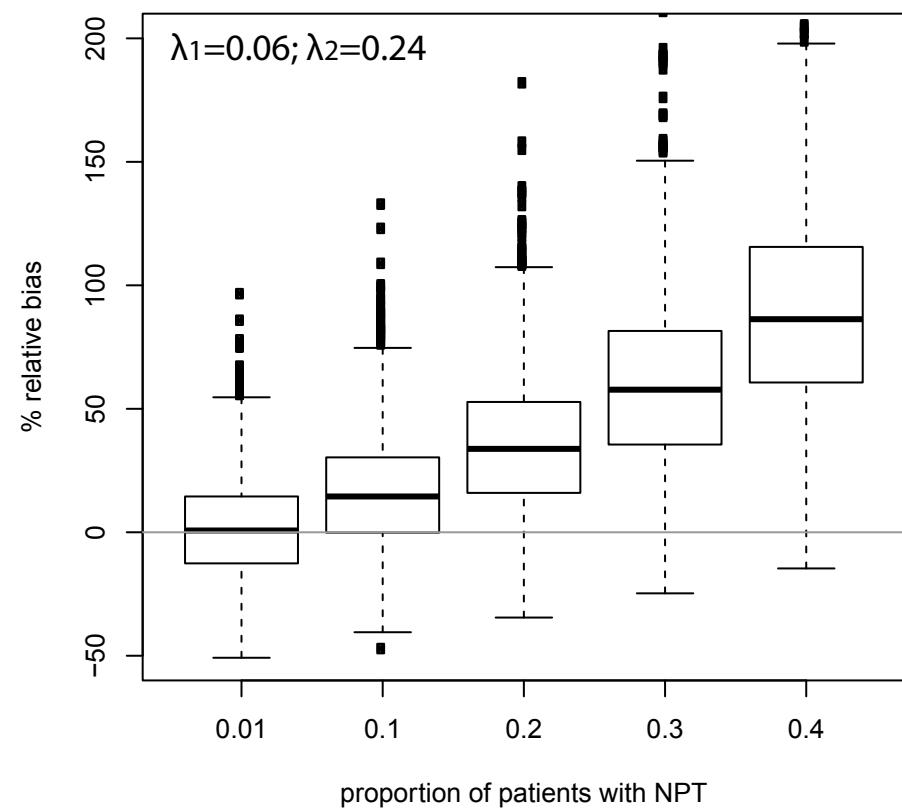
Panel C: WM, N=40, 12 month estimate, proportion=0.20. Case with NI censoring

% relative bias

$\lambda_1 = 0.03$
$\lambda_1 = 0.06$

hazard ratio ($\lambda 2/\lambda 1$)
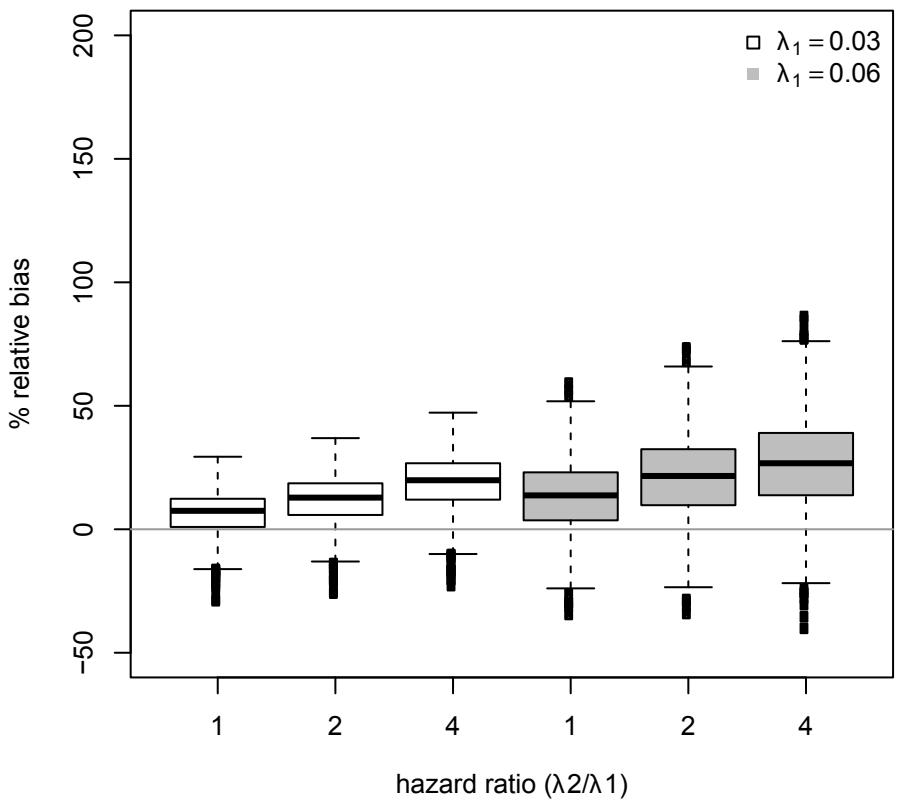
Panel D: WM, N=40, median estimate, proportion=0.20. Case with NI censoring

% relative bias

$\lambda_1 = 0.03$
$\lambda_1 = 0.06$

hazard ratio ($\lambda 2/\lambda 1$)
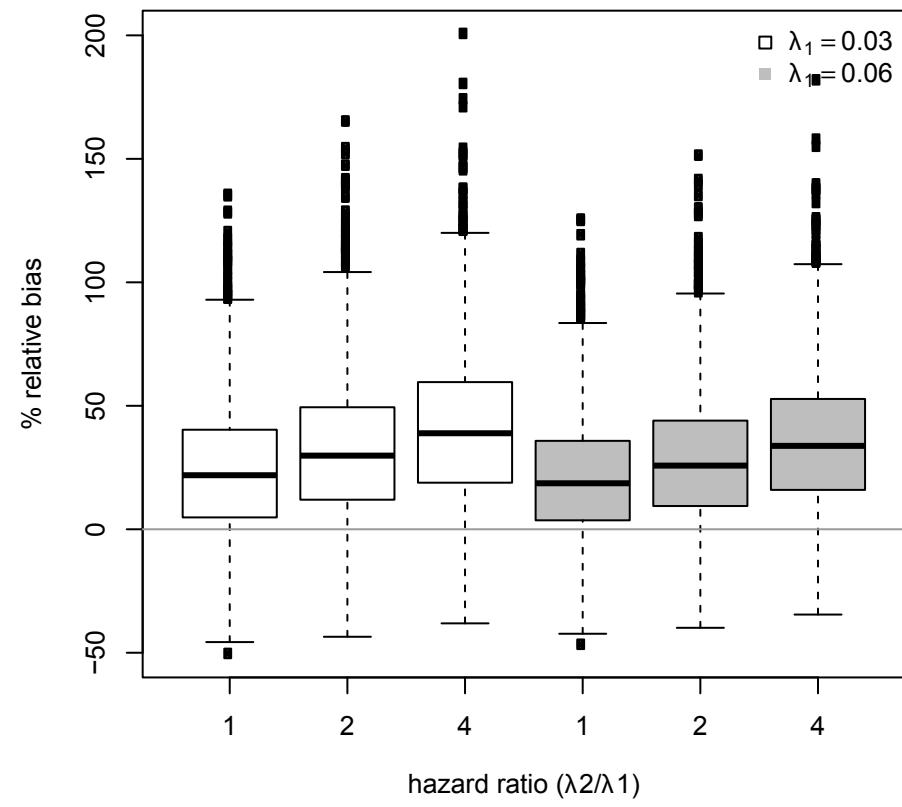
Panel A: MM, N=60, 12 month estimate. Case with NI censoring

$\lambda_1=0.108; \lambda_2=0.054$

% relative bias

proportion of patients with ASCT
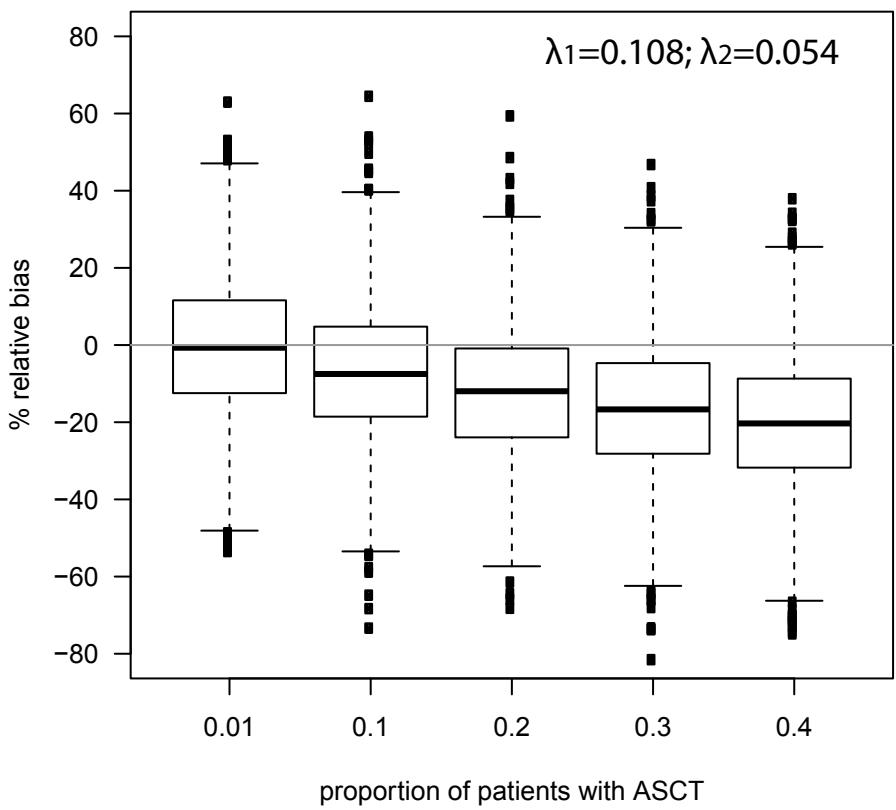
Panel B: MM, N=60, median estimate. Case with NI censoring

$\lambda_1=0.108; \lambda_2=0.054$

% relative bias

proportion of patients with ASCT
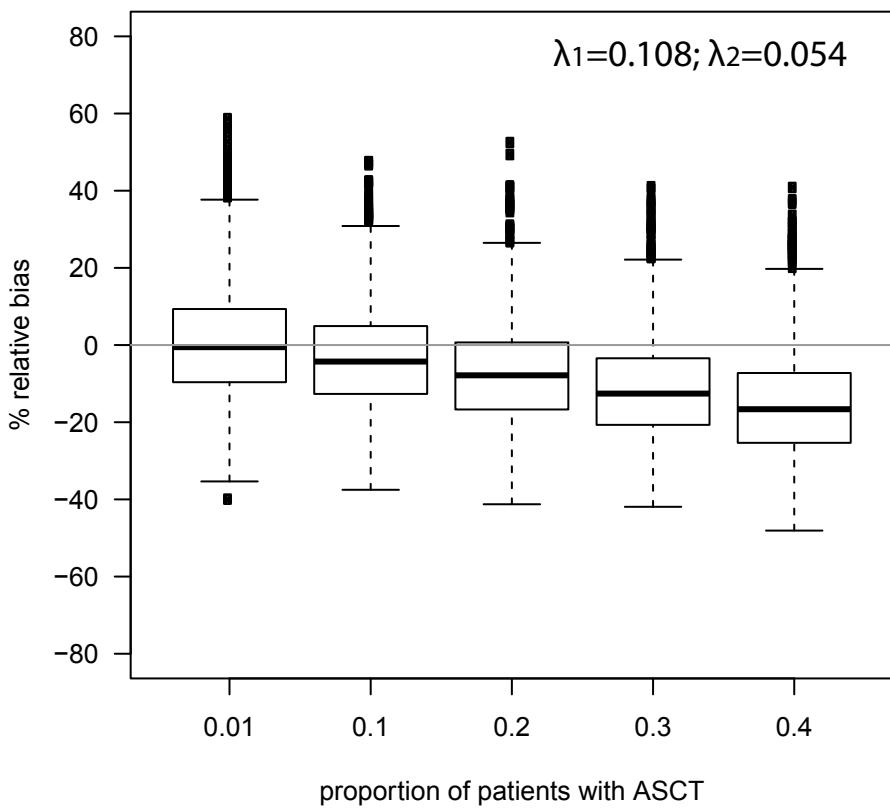
Panel C: MM, N=60, 12 month estimate, proportion=0.40. Case with NI censoring

$\lambda_1 = 0.036$
$\lambda_1 = 0.108$

% relative bias

hazard ratio (λ_2/λ_1)
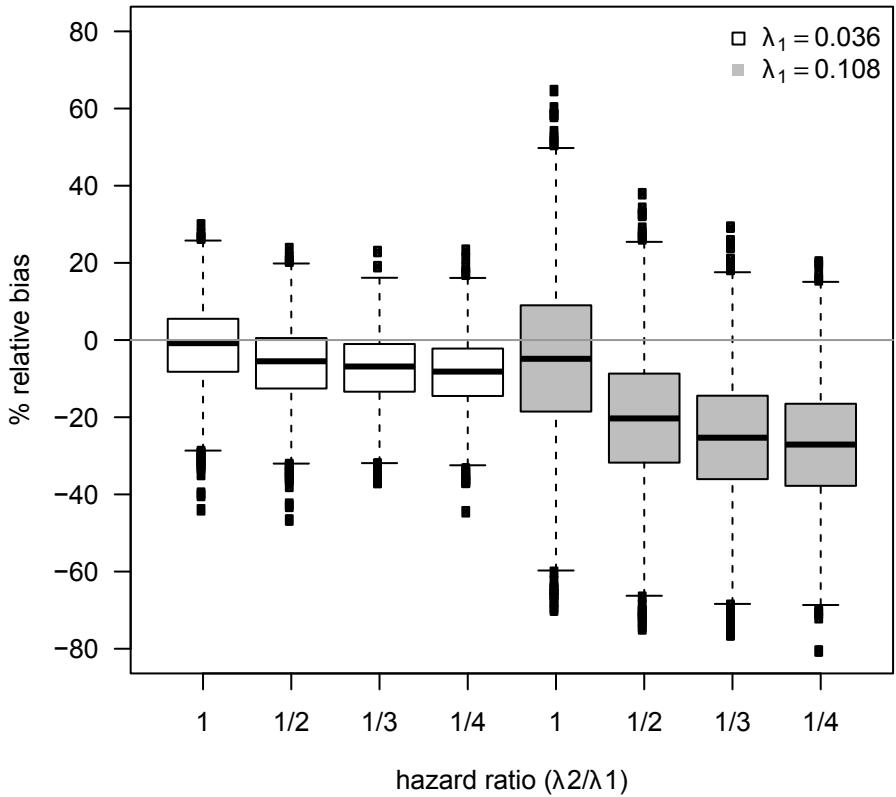
Panel D: MM, N=60, median estimate, proportion=0.40. Case with NI censoring

$\lambda_1 = 0.036$
$\lambda_1 = 0.108$

% relative bias

hazard ratio (λ_2/λ_1)