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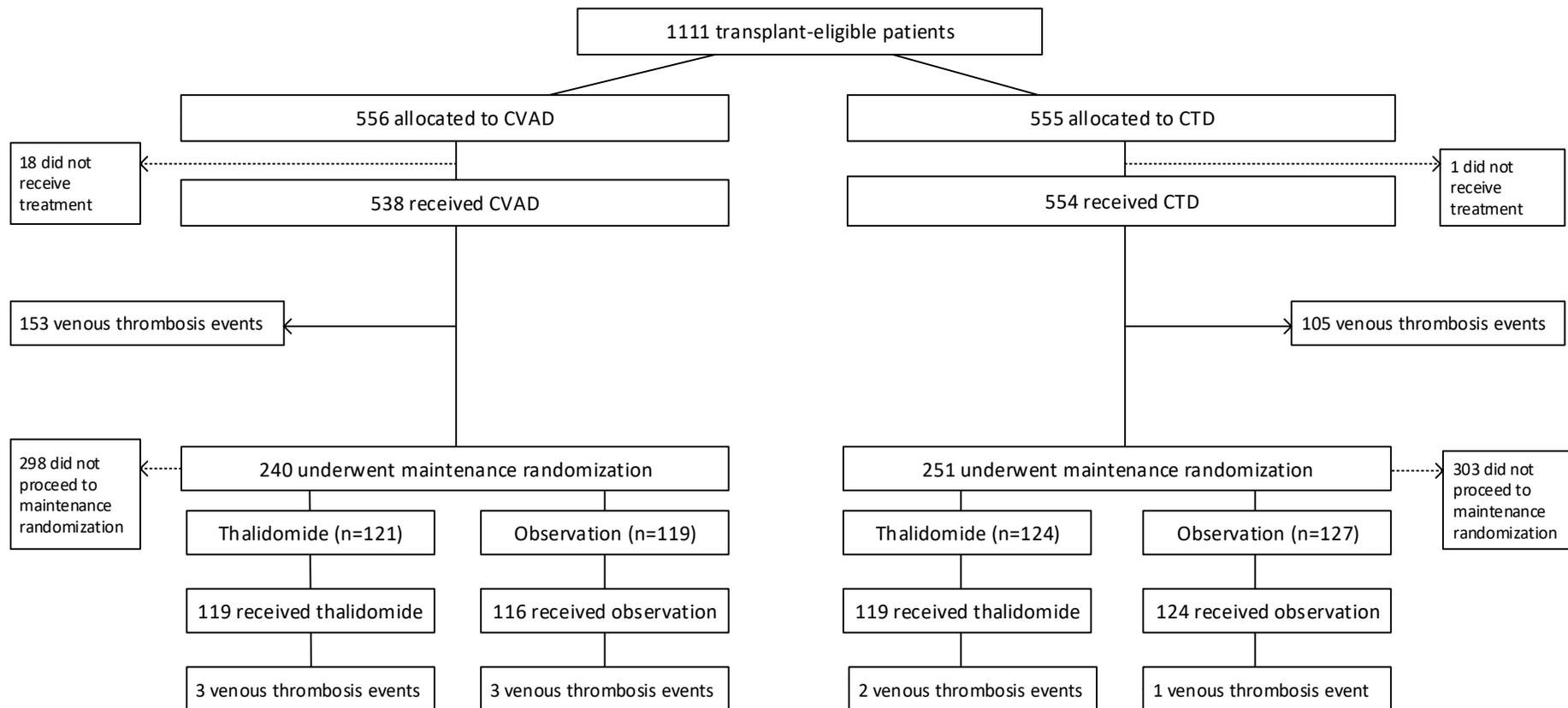


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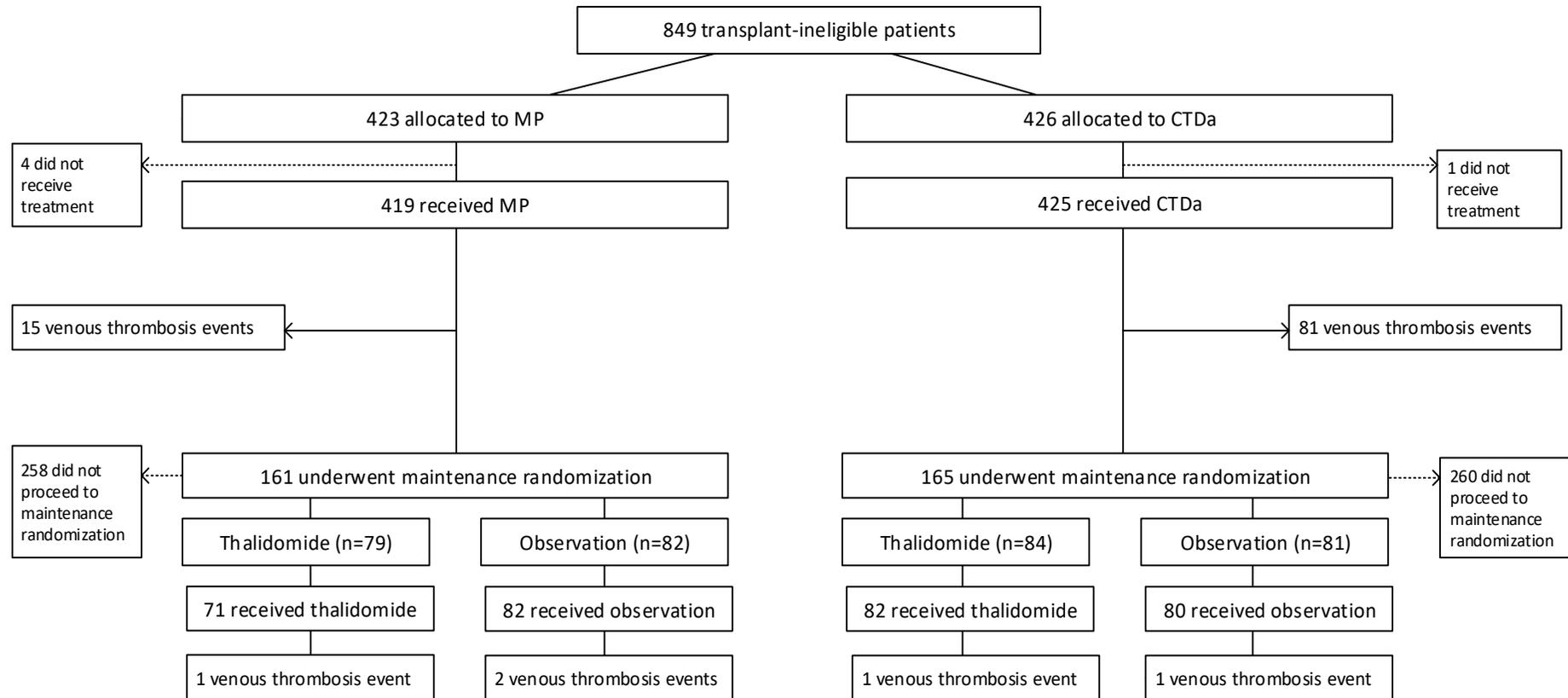
Supplementary material

Figure 1. CONSORT flow diagram for Myeloma IX transplant-eligible (A) and transplant-ineligible (B) pathways and Myeloma XI transplant-eligible (C) and transplant-ineligible (D) pathways

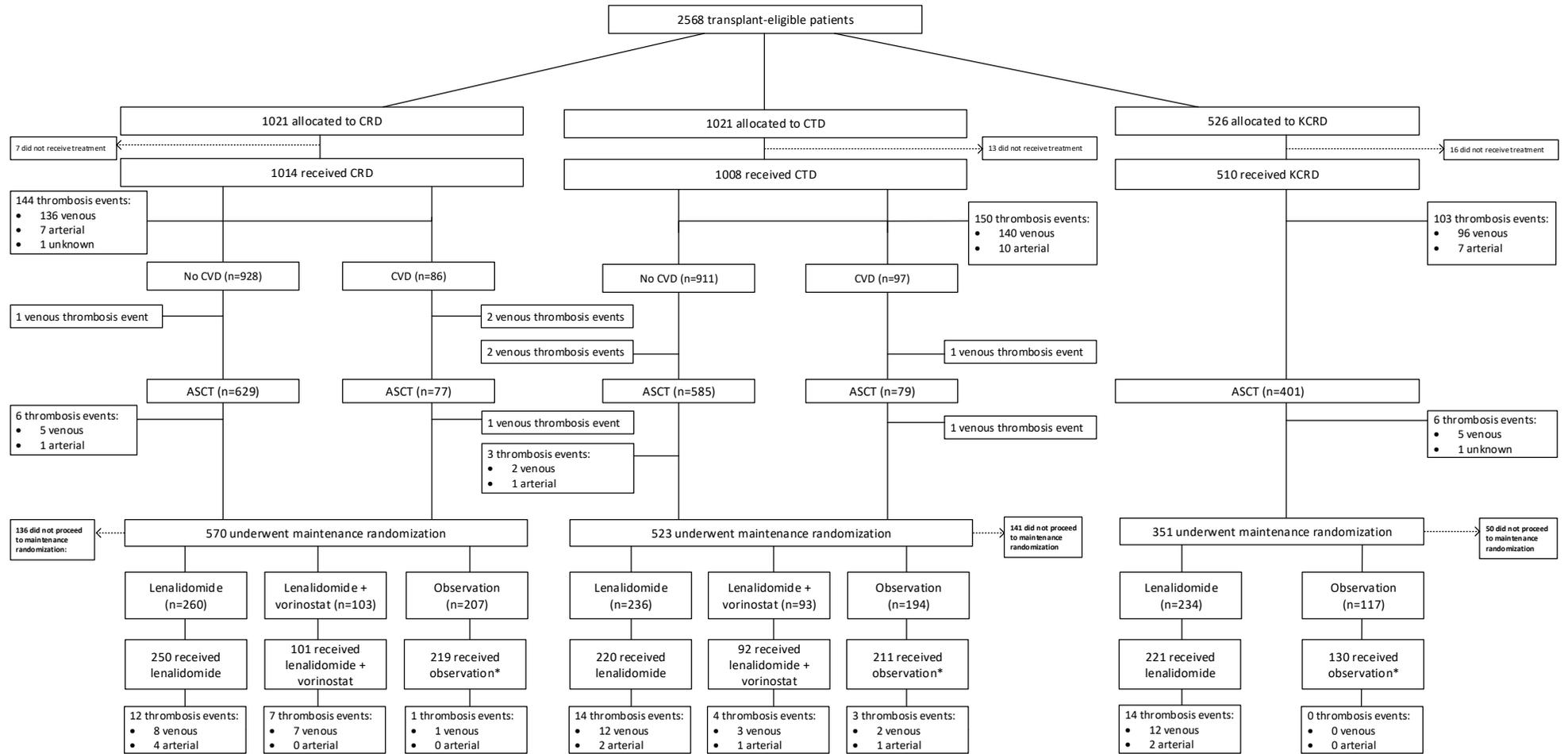
A



B



C



* Includes 12 who were randomised to lenalidomide ± vorinostat but did not received this treatment

* Includes 17 who were randomised to lenalidomide ± vorinostat but did not received this treatment

* Includes 13 who were randomised to lenalidomide but did not received this treatment

D

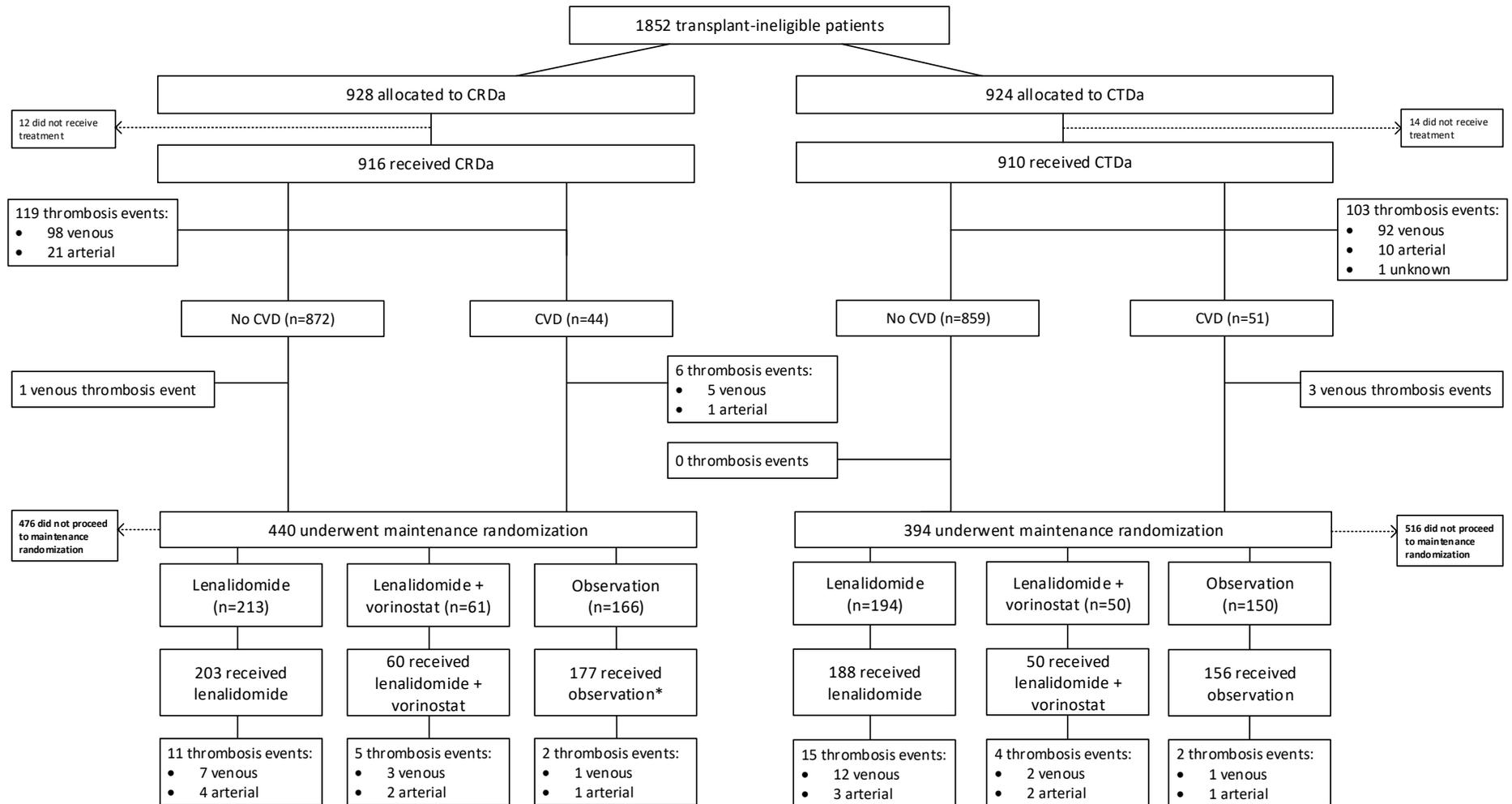


Table 1. Myeloma IX and Myeloma XI baseline characteristics

Characteristic	Myeloma IX					Myeloma IX					
	Transplant-eligible pathway		Transplant-ineligible pathway		Total (n=1936)	Transplant-eligible pathway			Transplant-ineligible pathway		Total (n=4358)
	CVAD (n=538)	CTD (n=554)	MP (n=419)	CTDa (n=425)		CTD (n=1008)	CRD (n=1014)	KCRD (n=510)	CTDa (n=910)	CRDa (n=916)	
Age											
Median (range)	58 (31, 74)	59 (33, 79)	73 (57, 89)	73 (58, 87)	65 (31, 89)	61 (29, 80)	61 (28, 75)	60 (33, 80)	74 (54, 89)	74 (60, 92)	67 (28, 92)
Sex											
Male	339 (63.0%)	339 (61.2%)	231 (55.1%)	241 (56.7%)	1150 (59.4%)	605 (60.0%)	605 (59.7%)	309 (60.6%)	529 (58.1%)	503 (54.9%)	2551 (58.5%)
Female	199 (37.0%)	215 (38.8%)	188 (44.9%)	184 (43.3%)	786 (40.6%)	403 (40.0%)	409 (40.3%)	201 (39.4%)	381 (41.9%)	413 (45.1%)	1807 (41.5%)
Ethnicity											
White	528 (98.1%)	526 (94.9%)	411 (98.1%)	413 (97.2%)	1878 (97.0%)	932 (92.5%)	938 (92.5%)	479 (93.9%)	868 (95.4%)	857 (93.6%)	4074 (93.5%)
Black (black Caribbean, black African, other)	4 (0.7%)	12 (2.2%)	6 (1.4%)	5 (1.2%)	27 (1.4%)	13 (1.3%)	21 (2.1%)	9 (1.8%)	20 (2.2%)	12 (1.3%)	75 (1.7%)
Asian (Indian, Pakistani, Bangladeshi, other)	4 (0.7%)	8 (1.4%)	1 (0.2%)	2 (0.5%)	15 (0.8%)	26 (2.6%)	28 (2.8%)	9 (1.8%)	10 (1.1%)	19 (2.1%)	92 (2.1%)
Other	2 (0.4%)	8 (1.4%)	1 (0.2%)	5 (1.2%)	16 (0.8%)	14 (1.4%)	10 (1.0%)	8 (1.6%)	3 (0.3%)	4 (0.4%)	39 (0.9%)
Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	23 (2.3%)	17 (1.7%)	5 (1.0%)	9 (1.0%)	24 (2.6%)	78 (1.8%)
WHO performance status											
0	158 (29.4%)	151 (27.3%)	70 (16.7%)	86 (20.2%)	465 (24.0%)	435 (43.2%)	420 (41.4%)	216 (42.4%)	227 (24.9%)	248 (27.1%)	1546 (35.5%)

Characteristic	Myeloma IX					Myeloma IX					
	Transplant-eligible pathway		Transplant-ineligible pathway		Total (n=1936)	Transplant-eligible pathway			Transplant-ineligible pathway		Total (n=4358)
	CVAD (n=538)	CTD (n=554)	MP (n=419)	CTDa (n=425)		CTD (n=1008)	CRD (n=1014)	KCRD (n=510)	CTDa (n=910)	CRDa (n=916)	
1	222 (41.3%)	240 (43.3%)	208 (49.6%)	201 (47.3%)	871 (45.0%)	364 (36.1%)	361 (35.6%)	192 (37.6%)	398 (43.7%)	404 (44.1%)	1719 (39.4%)
2	102 (19.0%)	91 (16.4%)	83 (19.8%)	88 (20.7%)	364 (18.8%)	135 (13.4%)	120 (11.8%)	56 (11.0%)	187 (20.5%)	147 (16.0%)	645 (14.8%)
3	47 (8.7%)	58 (10.5%)	51 (12.2%)	42 (9.9%)	198 (10.2%)	32 (3.2%)	46 (4.5%)	19 (3.7%)	48 (5.3%)	61 (6.7%)	206 (4.7%)
4	4 (0.7%)	7 (1.3%)	5 (1.2%)	6 (1.4%)	22 (1.1%)	2 (0.2%)	8 (0.8%)	1 (0.2%)	5 (0.5%)	6 (0.7%)	22 (0.5%)
Missing	5 (0.9%)	7 (1.3%)	2 (0.5%)	2 (0.5%)	16 (0.8%)	40 (4.0%)	59 (5.8%)	26 (5.1%)	45 (4.9%)	50 (5.5%)	220 (5.0%)
Haemoglobin g/dl											
Mean (s.d.)	10.7 (2.0)	10.8 (2.0)	10.7 (4.2)	10.8 (4.5)	10.8 (3.2)	10.9 (1.98)	10.9 (2.0)	11.1 (2.0)	10.5 (1.7)	10.5 (1.7)	10.8 (1.9)
Missing	1	0	0	0	1	1	0	0	1	0	2
Platelets (*10/l)											
Mean (s.d.)	251.3 (93.3)	256.0 (97.7)	249.9 (102.5)	233.8 (94.8)	248.5 (97.2)	255.0 (105.0)	249.3 (97.7)	249.1 (90.7)	235.5 (89.9)	239.0 (94.5)	245.6 (96.6)
Missing	1	0	0	0	1	0	0	0	0	0	0
Creatinine (µmol/l)											
Mean (s.d.)	118.3 (65.4)	116.1 (67.1)	116.6 (52.6)	121.3 (62.7)	118.0 (62.7)	98.0 (56.2)	97.8 (52.1)	92.9 (43.6)	105.7 (52.1)	106.5 (59.3)	100.7 (54.0)
Missing	17	23	10	17	67	1	0	0	0	0	1
β2 microglobulin (mg/l)											
Mean (s.d.)	5.8 (5.6)	5.8 (7.5)	6.2 (4.4)	6.4 (5.0)	6.0 (5.9)	4.7 (3.9)	4.8 (4.1)	4.6 (3.5)	5.8 (4.2)	5.9 (5.1)	5.2 (4.3)
Missing	43	40	33	46	162	354	360	176	342	339	1571

Characteristic	Myeloma IX					Myeloma IX					
	Transplant-eligible pathway		Transplant-ineligible pathway		Total (n=1936)	Transplant-eligible pathway			Transplant-ineligible pathway		Total (n=4358)
	CVAD (n=538)	CTD (n=554)	MP (n=419)	CTDa (n=425)		CTD (n=1008)	CRD (n=1014)	KCRD (n=510)	CTDa (n=910)	CRDa (n=916)	
Calcium (µmol/l)											
Mean (s.d.)	2.4 (0.5)	2.4 (1.1)	2.4 (0.2)	2.4 (0.2)	2.4 (0.7)	2.4 (0.2)	2.4 (0.3)	2.4 (0.2)	2.4 (0.2)	2.4 (0.2)	2.4 (0.2)
Missing	17	25	16	18	76	1	1	0	0	1	3
Paraprotein type											
IgG	319 (59.3%)	331 (59.7%)	256 (61.1%)	249 (58.6%)	1155 (59.7%)	596 (59.1%)	632 (62.3%)	292 (57.3%)	576 (63.3%)	572 (62.4%)	2668 (61.2%)
IgA	120 (22.3%)	119 (21.5%)	100 (23.9%)	98 (23.1%)	437 (22.6%)	266 (26.4%)	221 (21.8%)	126 (24.7%)	229 (25.2%)	234 (25.5%)	1076 (24.7%)
IgM	3 (0.6%)	2 (0.4%)	1 (0.2%)	2 (0.5%)	8 (0.4%)	3 (0.3%)	4 (0.4%)	4 (0.8%)	2 (0.2%)	3 (0.3%)	16 (0.4%)
IgD	9 (1.7%)	14 (2.5%)	3 (0.7%)	10 (2.4%)	36 (1.9%)	9 (0.9%)	11 (1.1%)	4 (0.8%)	3 (0.3%)	8 (0.9%)	35 (0.8%)
Non-secretor	11 (2.0%)	9 (1.6%)	5 (1.2%)	7 (1.6%)	32 (1.7%)	7 (0.7%)	5 (0.5%)	4 (0.8%)	5 (0.5%)	5 (0.5%)	26 (0.6%)
Light chain only	71 (13.2%)	72 (13.0%)	49 (11.7%)	54 (12.7%)	246 (12.7%)	127 (12.6%)	140 (13.8%)	79 (15.5%)	95 (10.4%)	91 (9.9%)	532 (12.2%)
Missing	5 (0.9%)	7 (1.3%)	5 (1.2%)	5 (1.2%)	22 (1.1%)	0 (0.0%)	1 (0.1%)	1 (0.2%)	0 (0.0%)	3 (0.3%)	5 (0.1%)
Light Chain Type											
Lambda	171 (31.8%)	168 (30.3%)	148 (35.3%)	133 (31.3%)	620 (32.0%)	337 (33.4%)	344 (33.9%)	180 (35.3%)	296 (32.5%)	291 (31.8%)	1448 (33.2%)
Kappa	312 (58.0%)	342 (61.7%)	241 (57.5%)	258 (60.7%)	1153 (59.6%)	661 (65.6%)	660 (65.1%)	325 (63.7%)	609 (66.9%)	611 (66.7%)	2866 (65.8%)
Missing	55 (10.2%)	44 (7.9%)	30 (7.2%)	34 (8.0%)	163 (8.4%)	10 (1.0%)	10 (1.0%)	5 (1.0%)	5 (0.5%)	14 (1.5%)	44 (1.0%)

Table 2. Myeloma IX baseline characteristics by thrombosis occurrence, split by pathway

Characteristic	Transplant-eligible pathway				Transplant-ineligible pathway			
	Thrombosis (n=210)	No thrombosis (n=882)	Total (n=1092)	P	Thrombosis (n=85)	No thrombosis (n=759)	Total (n=844)	P
Sex								
Male	120 (57.1%)	558 (63.3%)	678 (62.1%)	0.1003	34 (40.0%)	438 (57.7%)	472 (55.9%)	0.0018
Female	90 (42.9%)	324 (36.7%)	414 (37.9%)		51 (60.0%)	321 (42.3%)	372 (44.1%)	
Age								
Mean (SD)	57.1 (7.44)	57.8 (7.44)	57.7 (7.44)	0.1941	73.2 (5.47)	73.4 (5.48)	73.3 (5.48)	0.8444
Median (Range)	58.0 (31.0, 74.0)	59.0 (31.0, 79.0)	59.0 (31.0, 79.0)		73.0 (63.0, 87.0)	73.0 (57.0, 89.0)	73.0 (57.0, 89.0)	
Ethnicity								
White	207 (98.6%)	847 (96.0%)	1054 (96.5%)	0.7172	85 (100.0%)	739 (97.4%)	824 (97.6%)	1.0000
Black (black Caribbean, black African, other)	1 (0.5%)	15 (1.7%)	16 (1.5%)		0 (0.0%)	11 (1.5%)	11 (1.3%)	
Asian (Indian, Pakistani, Bangladeshi, other)	1 (0.5%)	11 (1.2%)	12 (1.1%)		0 (0.0%)	3 (0.4%)	3 (0.4%)	
Other	1 (0.5%)	9 (1.0%)	10 (0.9%)		0 (0.0%)	6 (0.8%)	6 (0.7%)	
WHO performance status								
0	61 (29.0%)	248 (28.1%)	309 (28.3%)	0.8722	18 (21.2%)	138 (18.2%)	156 (18.5%)	0.7529
1	90 (42.9%)	372 (42.2%)	462 (42.3%)		44 (51.8%)	365 (48.1%)	409 (48.5%)	
2	38 (18.1%)	155 (17.6%)	193 (17.7%)		13 (15.3%)	158 (20.8%)	171 (20.3%)	
3	19 (9.0%)	86 (9.8%)	105 (9.6%)		10 (11.8%)	83 (10.9%)	93 (11.0%)	
4	1 (0.5%)	10 (1.1%)	11 (1.0%)		0 (0.0%)	11 (1.4%)	11 (1.3%)	
Missing	1 (0.5%)	11 (1.2%)	12 (1.1%)		0 (0.0%)	4 (0.5%)	4 (0.5%)	
β2 microglobulin (mg/l)								
Mean (SD)	5.7 (5.62)	5.9 (6.87)	5.8 (6.65)	0.5614	5.5 (3.48)	6.4 (4.82)	6.3 (4.71)	0.2383

Characteristic	Transplant-eligible pathway				Transplant-ineligible pathway			
	Thrombosis (n=210)	No thrombosis (n=882)	Total (n=1092)	P	Thrombosis (n=85)	No thrombosis (n=759)	Total (n=844)	P
Median (Range)	4.1 (0.2, 58.0)	4.0 (0.1, 114.1)	4.0 (0.1, 114.1)		4.5 (0.4, 21.2)	5.0 (0.3, 64.0)	4.9 (0.3, 64.0)	
Missing	17	66	83		10	69	79	
Creatinine (µmol/l)								
Mean (SD)	115.8 (61.17)	117.6 (67.38)	117.2 (66.22)	0.6675	122.2 (83.06)	118.6 (54.42)	118.9 (57.88)	0.0547
Median (Range)	98.0 (49.0, 439.0)	98.0 (2.4, 462.0)	98.0 (2.4, 462.0)		95.0 (50.0, 495.0)	102.0 (42.0, 468.0)	102.0 (42.0, 495.0)	
Missing	9	31	40		3	24	27	
Calcium (µmol/l)								
Mean (SD)	2.4 (0.24)	2.4 (0.93)	2.4 (0.84)	0.3175	2.4 (0.29)	2.4 (0.22)	2.4 (0.23)	0.7035
Median (Range)	2.4 (1.6, 3.4)	2.4 (1.3, 26.4)	2.4 (1.3, 26.4)		2.4 (1.6, 3.5)	2.4 (1.4, 3.5)	2.4 (1.4, 3.5)	
Missing	8	34	42		3	31	34	
Platelets (*10/l)								
Mean (SD)	260.3 (93.57)	252.1 (95.97)	253.7 (95.53)	0.2652	238.4 (96.54)	242.2 (99.26)	241.8 (98.94)	0.7386
Median (Range)	251.0 (43.0, 540.0)	241.0 (17.0, 647.0)	242.0 (17.0, 647.0)		230.0 (82.0, 642.0)	228.0 (15.0, 825.0)	228.0 (15.0, 825.0)	
Missing	0	1	1		0	0	0	
Haemoglobin g/dl								
Mean (SD)	10.8 (1.89)	10.8 (2.04)	10.8 (2.01)	0.7923	10.4 (1.77)	10.8 (4.54)	10.7 (4.34)	0.1614
Median (Range)	10.8 (6.5, 17.8)	10.6 (4.0, 17.8)	10.7 (4.0, 17.8)		10.4 (6.5, 14.9)	10.5 (5.3, 95.0)	10.4 (5.3, 95.0)	
Missing	0	1	1		0	0	0	
Paraprotein type								
IgG	139 (66.2%)	511 (57.9%)	650 (59.5%)	0.0096	54 (63.5%)	451 (59.4%)	505 (59.8%)	0.9399
IgA	38 (18.1%)	201 (22.8%)	239 (21.9%)		21 (24.7%)	177 (23.3%)	198 (23.5%)	

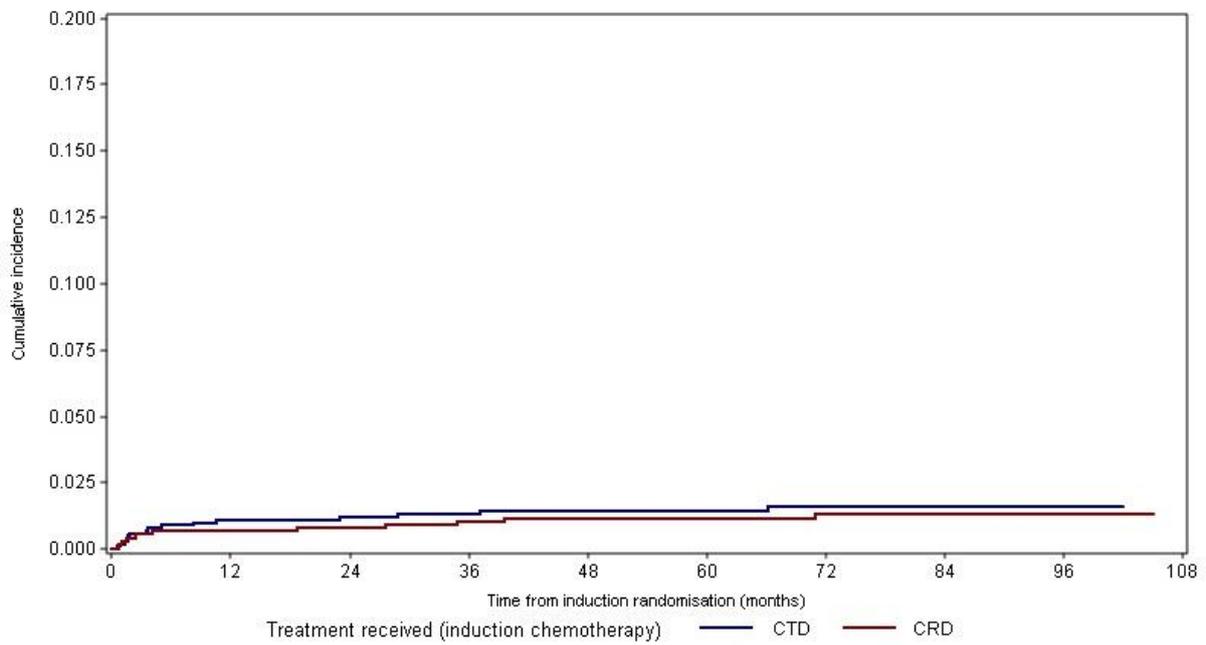
Characteristic	Transplant-eligible pathway				Transplant-ineligible pathway			
	Thrombosis (n=210)	No thrombosis (n=882)	Total (n=1092)	P	Thrombosis (n=85)	No thrombosis (n=759)	Total (n=844)	P
IgM	0 (0.0%)	5 (0.6%)	5 (0.5%)		0 (0.0%)	3 (0.4%)	3 (0.4%)	
IgD	8 (3.8%)	15 (1.7%)	23 (2.1%)		1 (1.2%)	12 (1.6%)	13 (1.5%)	
Non-secretor	6 (2.9%)	14 (1.6%)	20 (1.8%)		0 (0.0%)	12 (1.6%)	12 (1.4%)	
Light chain only	17 (8.1%)	126 (14.3%)	143 (13.1%)		9 (10.6%)	94 (12.4%)	103 (12.2%)	
Missing	2 (1.0%)	10 (1.1%)	12 (1.1%)		0 (0.0%)	10 (1.3%)	10 (1.2%)	
Light Chain Type								
Lambda	69 (32.9%)	270 (30.6%)	339 (31.0%)	0.5987	32 (37.6%)	249 (32.8%)	281 (33.3%)	0.4344
Kappa	124 (59.0%)	530 (60.1%)	654 (59.9%)		48 (56.5%)	451 (59.4%)	499 (59.1%)	
Missing	17 (8.1%)	82 (9.3%)	99 (9.1%)		5 (5.9%)	59 (7.8%)	64 (7.6%)	

	Transplant-eligible pathway				Transplant-ineligible pathway			
Characteristic	Thrombosis (n=371)	No thrombosis (n=2161)	Total (n=2532)	P	Thrombosis (n=228)	No thrombosis (n=1598)	Total (n=1826)	P
Mean (SD)	4.2 (2.86)	4.8 (4.02)	4.7 (3.88)	0.0472	5.6 (4.17)	5.9 (4.75)	5.9 (4.68)	0.3798
Median (Range)	3.3 (1.4, 19.3)	3.6 (0.9, 57.9)	3.5 (0.9, 57.9)		4.3 (0.9, 33.9)	4.6 (0.0, 88.0)	4.6 (0.0, 88.0)	
Missing	136	754	890		85	596	681	
Creatinine (μmol/l)								
Mean (SD)	92.7 (40.17)	97.6 (54.00)	96.9 (52.22)	0.9541	108.3 (54.13)	105.8 (56.09)	106.1 (55.84)	0.3361
Median (Range)	84.0 (32.0, 340.0)	83.0 (32.0, 609.0)	83.0 (32.0, 609.0)		90.5 (34.0, 390.0)	91.0 (34.0, 551.0)	91.0 (34.0, 551.0)	
Missing	0	1	1		0	0	0	
Calcium (mmol/l)								
Mean (SD)	2.4 (0.21)	2.4 (0.26)	2.4 (0.25)	0.0175	2.4 (0.22)	2.4 (0.24)	2.4 (0.24)	0.6913
Median (Range)	2.4 (1.6, 3.6)	2.4 (1.6, 4.9)	2.4 (1.6, 4.9)		2.4 (2.0, 3.5)	2.4 (1.3, 4.4)	2.4 (1.3, 4.4)	
Missing	0	2	2		0	1	1	
Platelets (*10/l)								
Mean (SD)	252.8 (103.48)	251.3 (98.60)	251.5 (99.31)	0.8123	229.7 (78.12)	238.3 (94.00)	237.2 (92.19)	0.1288
Median (Range)	239.0 (57.0, 1112.0)	242.0 (2.0, 1093.0)	241.0 (2.0, 1112.0)		223.5 (3.0, 534.0)	227.0 (19.0, 726.0)	226.0 (3.0, 726.0)	
Haemoglobin g/dl								
Mean (SD)	11.4 (2.0)	10.9 (2.0)	11.0 (2.0)	0.0001	10.7 (1.7)	10.6 (1.7)	10.6 (1.7)	0.3344
Median (Range)	11.3 (5.2, 16.8)	10.9 (3.3, 17.4)	110.0 (3.3, 17.4)		10.5 (7.2, 14.8)	10.4 (3.4, 16.6)	10.4 (3.4, 16.6)	
Missing	0	1	1		1	0	1	
Paraprotein type								
IgG	230 (62.0%)	1290 (59.7%)	1520 (60.0%)	0.3891	142 (62.3%)	1006 (63.0%)	1148 (62.9%)	0.3323

	Transplant-eligible pathway				Transplant-ineligible pathway			
Characteristic	Thrombosis (n=371)	No thrombosis (n=2161)	Total (n=2532)	P	Thrombosis (n=228)	No thrombosis (n=1598)	Total (n=1826)	P
IgA	85 (22.9%)	528 (24.4%)	613 (24.2%)		53 (23.2%)	410 (25.7%)	463 (25.4%)	
IgM	1 (0.3%)	10 (0.5%)	11 (0.4%)		0 (0.0%)	5 (0.3%)	5 (0.3%)	
IgD	0 (0.0%)	24 (1.1%)	24 (0.9%)		1 (0.4%)	10 (0.6%)	11 (0.6%)	
Non-secretor	3 (0.8%)	13 (0.6%)	16 (0.6%)		3 (1.3%)	7 (0.4%)	10 (0.5%)	
Light chain only	52 (14.0%)	294 (13.6%)	346 (13.7%)		29 (12.7%)	157 (9.8%)	186 (10.2%)	
Missing	0 (0.0%)	2 (0.1%)	2 (0.1%)		0 (0.0%)	3 (0.2%)	3 (0.2%)	
Light chain type								
Lambda	108 (29.1%)	753 (34.8%)	861 (34.0%)	0.0385	71 (31.1%)	516 (32.3%)	587 (32.1%)	0.7504
Kappa	257 (69.3%)	1389 (64.3%)	1646 (65.0%)		154 (67.5%)	1066 (66.7%)	1220 (66.8%)	
Missing	6 (1.6%)	19 (0.9%)	25 (1.0%)		3 (1.3%)	16 (1.0%)	19 (1.0%)	

Figure 2. Arterial CIF curves for Myeloma XI transplant-eligible (A) and transplant-ineligible (B) pathways

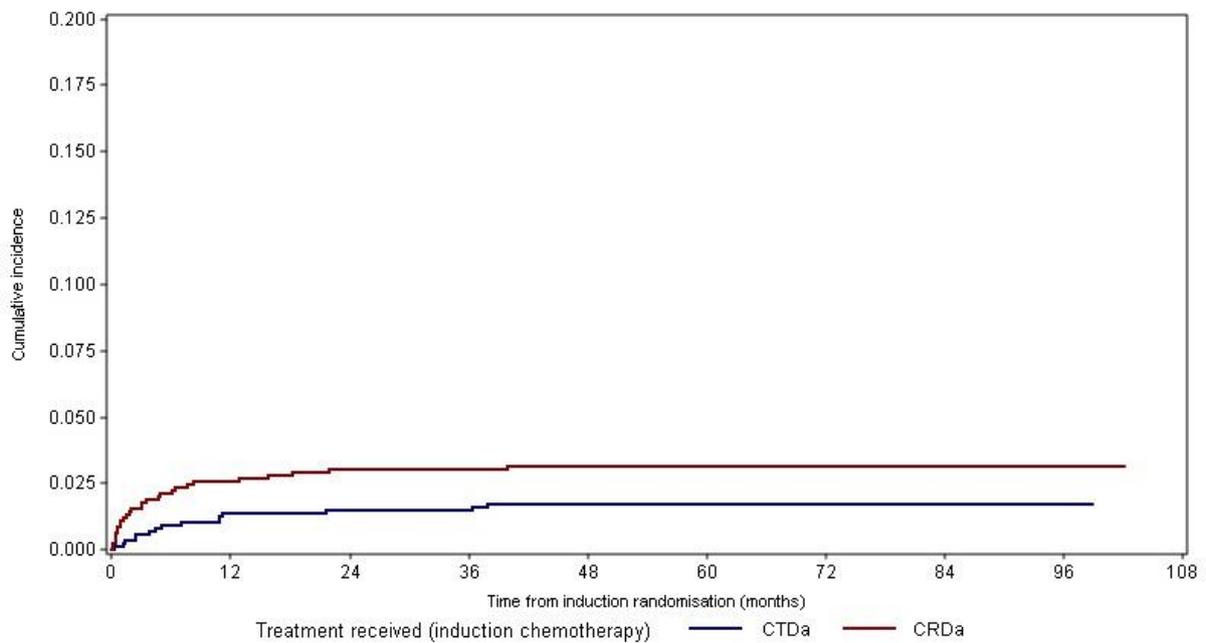
A



Number at risk

CTD	1008	910	821	699	559	411	224	95	8	0
CRD	1014	920	852	761	596	448	253	97	16	0

B



Number at risk

CTDa	910	699	588	483	340	199	100	26	4	0
CRDa	916	731	635	515	355	202	93	32	6	0

Figure 3. Myeloma XI PFS, by arterial thrombosis occurrence

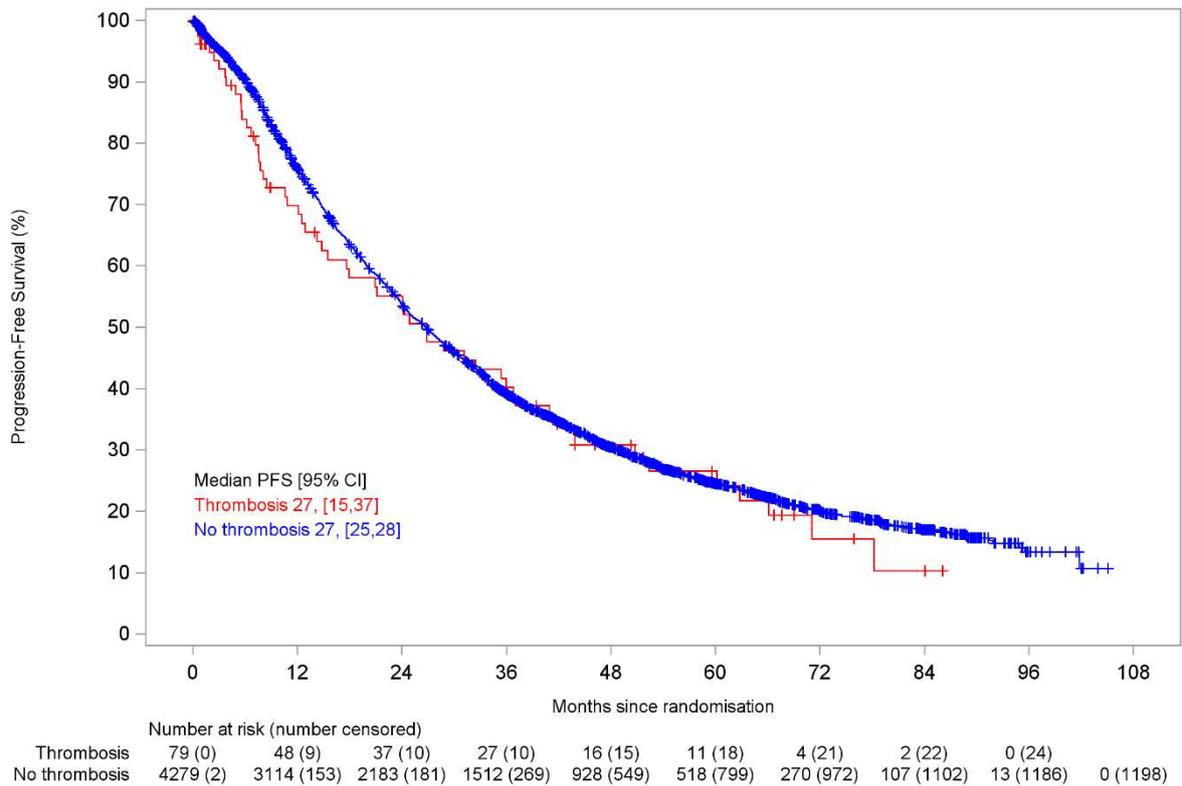


Figure 4. Myeloma XI OS, by arterial thrombosis occurrence

