

Supplementary materials

Study, year	Group	median follow-up (month)	Intervention
			Drugs (day administered)×no. of cycles (duration, days)
Mateos 2014	VMP	72	V:1.3mg/m ² (1,4,8,11,22,25,29,32)×1(42) then 1.3mg/m ² (1,8,15,22)×5(35), M:9mg/m ² (1-4)×1(42)then 9mg/m ² (1-4)×5(35), P:60mg/m ² (1-4)×1(42) then 60mg/m ² (1-4)×5(35)
	VTD		V:1.3mg/m ² (1,4,8,11,22,25,29,32)×1(42)then 1.3mg/m ² (1,8,15,22)×5(35), P:60mg/m ² (1-4)×1(42)then 60mg/m ² (1-4)×5(35), T:50mg(1-15)×1(42)then 100mg(1-35)×5(35)
Palumbo 2014	VMPT-VT	23.2	V: 1.3mg/m ² (1,4,8,11,22,25,29,32)×4(42) then 1.3mg/m ² (1,8,22,29)×5(42),M:9mg/m ² (1-4)×9(42), P:60mg/m ² (1-4)×9(42), T:50mg per day continuously, maintenance: V: 1.3mg/m ² every 14 days, T:50mg per day continuously
	VMP		V: 1.3mg/m ² (1,4,8,11,22,25,29,32)×4(42) then 1.3mg/m ² (1,8,22,29)×5(42), M:9 mg/m ² (1-4)×9(42), P:60 mg/m ² (1-4)×9(42)
Miguel 2013	VMP	30	V: 1.3mg/m ² (1,4,8,11,22,25,29,32)×4(42) then 1.3mg/m ² (1,8,22,29)×5(42), M:9mg/m ² (1-4)×9(42), P:60 mg/m ² (1-4)×9(42)
	MP		M:9mg/m ² (1-4)×9(42), P:60 mg/m ² (1-4)×9(42)
Miguel 2014	VMPS	23.3	V: 1.3mg/m ² (1,4,8,11,22,25,29,32)×4(42) then 1.3mg/m ² (1,8,22,29)×5(42), M:9mg/m ² (1-4)×9(42), P:60 mg/m ² (1-4)×9(42), S: 11 mg/kg every 3 weeks
	VMP		V: 1.3mg/m ² (1,4,8,11,22,25,29,32)×4(42) then 1.3mg/m ² (1,8,22,29)×5(42), M:9mg/m ² (1-4)×9(42), P:60 mg/m ² (1-4)×9(42)
Beksac 2010	MPT-T	23	M:9mg/m ² (1-4)×8(42), P:60mg/m ² (1-4)×8(42), T:100mg per day continuously
	MP		M:9mg/m ² (1-4)×8(42), P:60mg/m ² (1-4)×8(42)
Waage 2010	MPT-T	42	M:0.25mg/kg(1-4)×X(42)to plateau phase, P:100mg(1-4)×X(42) to plateau phase, T:400 mg daily until plateau phase and thereafter 200 mg daily until progression
	MP		M:0.25mg/kg(1-4)×X(42)to plateau phase, P:100mg(1-4)×X(42) to plateau phase, placebo:400 mg daily until plateau phase and thereafter 200 mg daily until progression
Hulin 2009	MPT	47.5	M:0.2mg/kg(1-4)×12(42), P:2mg/kg(1-4)×12(42), T:100mg per day for 72 weeks
	MP		M:0.2mg/kg(1-4)×12(42), P:2mg/kg(1-4)×12(42), placebo:100mg per day for 72 weeks
Wijermans 2009	MPT-T	39	M:0.25mg/kg(1-5)×8(28), P:1mg/kg(1-5)×8(28), T:200 mg/d until 4 weeks after the last MP-T cycle, then T:50mg per day until disease progression
	MP		M:0.25mg/kg(1-5)×8(28), P:1mg/kg(1-5)×8(28)
Morgan 2011	MP	44	M:7mg/m ² (1-4)×6-9(28), P:40mg(1-4)
	CTD		C:500mg(1,8,15,22)×6-9(28), D:20mg(1-4,15-18)×6-9(28), T:50 mg for 4 weeks and increased every 4 weeks in 50-mg increments to a maximum of 200 mg/day and maintenance
Ludwig 2009	TD	28.1	T:50-400mg per day, D:40mg(1-4,15-18)×5(28) or 40mg(1-4)×4(28)
	MP		M:0.25mg/kg(1-4)×9(28/42), P:2mg/kg(1-4)×9(28/42)
Benboubker 2014	Ld	37	L:25mg(1-21)×continuous(28), D:40mg(1,8,15,22)×continuous(28)
	continuous Ld 18cycle MPT		L:25mg(1-21)×18(28), D:40mg(1,8,15,22)×18(28) M:0.25mg/kg(1-4)×12(42), P:2mg/kg(1-4)×12(42), T:200mg(1-42)×12(42)
Palumbo 2012	MPR-R	30	M:0.18mg(1-4)×9(28), P:2mg/kg(1-4)×9(28), L:10mg(1-21)×9(28), maintenance:L:10mg(1-21)×X(28)
	MPR		M:0.18mg(1-4)×9(28), P:2mg/kg(1-4)×9(28), placebo
Facon 2007	MP	51.5	M:0.25mg/kg(1-4)×12(42), P:2mg/kg(1-4)×12(42)
	MPT		M:0.25mg/kg(1-4)×12(42), P:2mg/kg(1-4)×12(42), T: < 400mg(1-42)×12(42)
palumbo 2006	MEL100	17.6	Vi:9 mg/m ² (1-4)×2(28), A:9 mg/m ² (1-4)×2(28), D:40mg(1-4)×2(28),M: 100mg/m ² MEL100 was repeated once after 2 months
	MPT-T		M:4 mg/m ² (1-7)×6(28), P:40mg/m ² (1-7)×6(28), T:100mg(1-28)×6(28), maintenance T:100mg per day until relapsed
Palumbo 2004	MP	41	M:4 mg/m ² (1-7)×6(28),P:40mg/m ² (1-7)×6(28)
	MEL100		Vi:1mg(1)×2(28), A:50mg/m ² (1)×2(28), D:40mg(1-4)×2(28), M: 100mg/m ² MEL100 was repeated once after 2 months
Stewart 2015	MP	40.7	M:6mg/m ² (1-7)×6(28),P:60 mg/m ² (1-7)×6(28)
	MPT-T		M:9mg/m ² (1-4)×12(28), P:100mg(1-4)×12(28), T:100mg per day until disease progression
Niesvizky 2015	MPR-R	42.7	M:5mg/m ² (1-4)×12(28), P:100mg(1-4)×12(28), L:10mg(1-21)×12(28),maintenance:L 10mg per day until disease progression
	VD		V:1.3mg/m ² (1,4,8,11)×8(21), D:20mg(1,2,4,5,8,9,11,12)×4(21)or(1,2,4,5)×4(21)
Zweegman 2016	VTD	36	V:1.3mg/m ² (1,4,8,11)×8(21), D:20mg(1,2,4,5,8,9,11,12)×4(21) or (1,2,4,5)×4(21), T:100mg(1-21)×8(21)
	VMP		V:1.3mg/m ² (1,4,8,11)×8(21), M:9mg/m ² (1-4)×8(21), P:60mg/m ² (1-4)×8(21),every other cycle, then V:1.6mg/m ² (1,8,15,22)×5(35)
Magarotto 2016	MPT-T	39	M:0.18mg(1-4)×9(28),P:2mg/kg(1-4)×9(28), T: 200mg/day until 4 weeks after the last cycle of MP, then maintenance: with T 100 mg daily
	MPR-R		M:0.18mg(1-4)×9(28), P:2mg/kg(1-4)×9(28), L:10mg(1-21) every cycles until disease progression
Magarotto 2016	MPR	39	M: 0.18 or 0.13mg(1-4)×9(28), P: 1.5mg/kg(1-4)×9(28), L:10mg(1-21)×9(28)
	CPR		C:50mg every other day×9(21/28), P: 25mg every other day×9(28), L:10mg(1-21)×9(28)
	Ld 9 cycles		L:25mg(1-21)×9(28), D:40 or 20mg(1,8,15,22)×9(28)

Supplementary table 1 Details of initial treatments of elderly multiple myeloma patients

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

Study, year	randomization	blinding	follow-up	total
Mateos 2010	2	0	1	3
Palumbo 2010	2	0	1	3
Miguel 2008	2	0	1	3
Miguel 2014	2	0	0	2
Beksac 2010	2	0	1	3
Waage 2010	2	2	1	5
Hulin 2009	2	0	1	3
Wijermans 2009	2	0	1	3
Morgan 2011	2	0	1	3
Ludwig 2009	2	1	1	3
Benboubker 2014	2	0	1	3
Palumbo 2012	2	2	1	5
Facon 2007	2	0	1	3
palumbo 2006	2	0	1	3
Palumbo 2004	2	1	1	4
Stewart 2015	2	0	1	3
Niesvizky 2015	2	0	1	3
Zweegman 2016	2	0	1	3
Magarotto 2016	2	0	1	3

Supplementary table 2 Methodological quality of each article, assessed according to the Jadad scale

Study, year	Group	number	Median age	male(%)	M Protein(%)				ISS stage(%)			Median β -microglobulin,mg/L(range)	Median albumin(range)
					IgG	IgA	Light chain	Other	I	II	III		
Mateos 2010	VMP	130	73	69(53)	81(62)	37(28)	12(9)	0	39(30)	52(40)	39(30)	NA	NA
	VTD	130	73	61(47)	72(55)	42(32)	16(12)	0	26(20)	56(43)	48(37)	NA	NA
Palumbo 2010	VMPT-VT	254	71	130(51)	NA	NA	NA	NA	59(23)	100(39)	47(19)	3.8(NA)	37.9(NA)
	VMP	257	71	122(47)	NA	NA	NA	NA	56(22)	88(34)	57(22)	4(NA)	37.5(NA)
Miguel 2008	VMP	344	71	175(51)	220(64)	83(24)	28(8)	14(4)	65(19)	169(47)	120(35)	4.2(1.7-21.6)	3.3(1.3-4.7)
	VP	338	71	166(49)	210(62)	88(26)	27(8)	14(4)	64(19)	159(47)	115(34)	4.3(0.6-60.9)	3.3(1.4-5.0)
Miguel 2014	SVMP	52	71	NA	22(42)	219(41)	8(15)	1(2)	4(8)	20(38)	54(28)	NA	NA
	VMP	54	70	NA	37(69)	10(19)	6(11)	1(2)	3(5)	22(41)	54(29)	NA	NA
Beksac 2010	MPT	58	69	35(60)	44(83)	7(13)	1(2)	1(2)	1(2)	34 (59)	23(40)	5.1(0.3-80)	36(20-49)
	MP	57	72	27(47)	35(71)	10(20)	1(2)	3(6)	5(9)	26(47)	23(44)	4.9(0.43-39.9)	36(22-46)
Waage 2010	MPT	182	74	93(51)	NA	NA	NA	NA	22 (12)	75(41)	78(43)	4.5(NA)	NA
	MP	175	74	107(61)	NA	NA	NA	NA	32 (18)	51(31)	81(46)	4.2(NA)	NA
Hulin 2009	MPT	113	78	43(38)	NA	NA	NA	NA	25(25)	39(40)	34(35)	NA	NA
	MP	116	78	61(43)	NA	NA	NA	NA	26(25)	47(45)	31(30)	NA	NA
Wijermans 2009	MPT	165	72	94(57)	97(59)	50(31)	17(10)	1(1)	44(27)	42(25)	32(19)	4(NA)	34(NA)
	MP	168	73	92(55)	103(61)	49(29)	16(10)	0	39(23)	39(23)	29(17)	4(NA)	34(NA)
Morgan 2011	MP	423	73	231(55)	257(61)	101(24)	49(12)	16(4)	64(15)	156(37)	165(39)	4.9(0.3-40.4)	NA
	CTD	426	73	242(47)	248(58)	100(24)	54(13)	24(6)	46(11)	156(37)	168(39)	5(0.4-64)	NA
Ludwig 2009	TD	145	72	74(51)	91(63)	33(23)	17(12)	4(3)	6(4)	40(28)	99(68)	4.2(1-43.5)	36.9(1.8-50.2)
	MP	143	72	70(50)	94(66)	32(22)	15(11)	2(1)	5(4)	44(31)	94(65)	3.9(1.4-41.8)	38(0.95-53.7)
Benboubker 2014	Ld continuous	535	73	294(55)	334(62)	138(26)	46(9)	17(3)	319(60)		216(40)	NA	NA
	Ld 18cycle	541	73	273(50)	331(61)	142(26)	54(10)	14(3)	322(60)		219(40)	NA	NA
	MPT	547	73	287(52)	350(64)	123(26)	57(10)	17(3)	323(59)		224(41)	NA	NA
Palumbo 2012	MPR-R	152	71	71(47)	NA	NA	NA	NA	28(18)	50(33)	74(49)	NA	NA
	MPR	153	71	82(54)	NA	NA	NA	NA	32(21)	47(31)	74(49)	NA	NA
	MP	154	72	75(49)	NA	NA	NA	NA	28(18)	48(31)	78(51)	NA	NA
Facon 2007	MP	196		109(56)	NA	NA	NA	NA	61(34)	67(37)	54(30)	NA	NA
	MPT	125		63(50)	NA	NA	NA	NA	38(34)	42(38)	32(29)	NA	NA
	MEL100	126		66(52)	NA	NA	NA	NA	33(28)	42(36)	41(35)	NA	NA
palumbo 2006	MPT	129	72	NA	83(64)	31(24)	15(12)	0	0	54(42)	75(58)	3.7(0.36-40)	NA
	MP	126	72	NA	73(58)	37(29)	16(13)	0	0	52(41)	74(59)	3.7(0.2-37.5)	NA

Palumbo 2004	MEL100	44	65	51 (54)	64 (67)	22 (23)	8 (9)	1 (1)	0	37(39)	58(61)	2.9	NA
	MP	36	63	54 (55)	59 (60)	27 (27)	11 (11)	2 (2)	0	37(37)	59(63)	2.9	NA
Stewart 2015	MPT-T	154	75.8	86 (55.8)	92 (71.3)	32 (24.8)	NA	5 (3.9)	45 (29.6)	58 (38.2)	49 (32.2)	NA	NA
	mPR-R	152	76.6	81 (53.3)	90 (72.6)	32 (25.8)	NA	2 (1.6)	36 (23.7)	70 (46.0)	46 (30.3)	NA	NA
Niesvizky 2015	VD	168	74.5	101(60)	101 (62)	41 (25)	21 (13)	1 (< 1)	33 (22)	70 (46)	50 (33)	4.5	3.5
	VTD	167	73	70(42)	89 (58)	43 (28)	20 (13)	2(1)	50 (33)	53 (35)	49 (32)	3.9	3.7
	VMP	167	72	90(54)	100 (62)	40 (25)	18 (11)	3(2)	41 (25)	63 (39)	58 (36)	4.1	3.5
Zweegman 2016	MPT-T	318	72	161(51)	202(64)	87(27)	22(7)	2(1)	75(24)	153(48)	83(26)	NA	NA
	MPR-R	319	73	185(58)	202(63)	75(24)	38(12)	1 (< 1)	82(26)	151(47)	82(26)	NA	NA
Magarotto 2016	MPR	218	74	108(50)	NA	NA	NA	NA	61(28)	97(45)	59(27)	NA	NA
	CPR	222	73	106(48)	NA	NA	NA	NA	59(27)	103(46)	60(27)	NA	NA
	Ld 9 cycles	222	74	108(49)	NA	NA	NA	NA	62(28)	99(45)	60(27)	NA	NA

Supplementary table 3 Patient demographics and baseline disease characteristics.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

CPR	0.37 (0.16-0.86)	0.29 (0.14-0.59)	0.61 (0.44-0.84)	0.29 (0.14-0.58)	0.47 (0.23-0.94)	2.08 (1.25-3.45)	0.78 (0.56-1.11)	0.78 (0.49-1.24)	0.44 (0.22-0.87)	0.78 (0.48-1.26)	1.05 (0.52-2.15)	0.45 (0.22-0.91)	0.4 (0.21-0.75)	0.28 (0.14-0.58)	0.33 (0.17-0.64)	0.33 (0.17-0.65)
2.68 (1.17-6.15)	CTD	0.78 (0.34-1.77)	1.63 (0.73-3.68)	0.76 (0.34-1.73)	1.25 (0.55-2.82)	5.56 (2.88-10.75)	2.1 (0.99-4.48)	2.09 (1.02-4.27)	1.18 (0.53-2.63)	2.08 (1.02-4.22)	2.82 (1.23-6.45)	1.21 (0.54-2.73)	1.06 (0.49-2.28)	0.76 (0.33-1.74)	0.89 (0.41-1.95)	0.89 (0.4-1.96)
3.44 (1.7-6.93)	1.28 (0.57-2.91)	Ld 18 cycles	2.1 (1.06-4.14)	0.98 (0.85-1.12)	1.61 (1.11-2.32)	7.14 (4.39-11.6)	2.7 (1.46-4.97)	2.68 (1.53-4.68)	1.52 (1.29-1.79)	2.67 (1.54-4.63)	3.62 (1.8-7.26)	1.55 (0.78-3.06)	1.36 (0.73-2.53)	0.97 (0.48-1.96)	1.14 (0.6-2.18)	1.14 (0.59-2.19)
1.64 (1.19-2.26)	0.61 (0.27-1.38)	0.48 (0.24-0.94)	Ld 9 cycles	0.47 (0.24-0.92)	0.77 (0.39-1.5)	3.4 (2.12-5.47)	1.28 (0.96-1.73)	1.28 (0.83-1.96)	0.72 (0.37-1.4)	1.27 (0.82-1.99)	1.72 (0.87-3.44)	0.74 (0.38-1.45)	0.65 (0.35-1.2)	0.46 (0.23-0.93)	0.54 (0.29-1.03)	0.54 (0.28-1.04)
3.5 (1.74-7.07)	1.31 (0.58-2.97)	1.02 (0.89-1.17)	2.14 (1.09-4.22)	Ld continuous	1.64 (1.13-2.36)	7.28 (4.48-11.83)	2.75 (1.49-5.07)	2.73 (1.56-4.78)	1.55 (1.31-1.82)	2.72 (1.57-4.72)	3.69 (1.84-7.41)	1.58 (0.8-3.12)	1.39 (0.74-2.58)	0.99 (0.49-2)	1.17 (0.61-2.22)	1.16 (0.6-2.23)
2.14 (1.07-4.3)	0.8 (0.35-1.81)	0.62 (0.43-0.9)	1.31 (0.67-2.56)	0.61 (0.42-0.88)	MEL100	4.45 (2.76-7.17)	1.68 (0.92-3.08)	1.67 (0.96-2.9)	0.94 (0.68-1.31)	1.66 (0.97-2.86)	2.25 (1.13-4.5)	0.97 (0.49-1.9)	0.85 (0.46-1.57)	0.6 (0.3-1.22)	0.71 (0.38-1.35)	0.71 (0.37-1.36)
0.48 (0.29-0.8)	0.18 (0.09-0.35)	0.14 (0.09-0.23)	0.29 (0.18-0.47)	0.14 (0.08-0.22)	0.22 (0.14-0.36)	MP	0.38 (0.26-0.55)	0.38 (0.28-0.49)	0.21 (0.13-0.34)	0.37 (0.29-0.48)	0.51 (0.31-0.84)	0.22 (0.13-0.35)	0.19 (0.13-0.28)	0.14 (0.08-0.23)	0.16 (0.11-0.24)	0.16 (0.1-0.25)
1.27 (0.9-1.8)	0.48 (0.22-1.01)	0.37 (0.2-0.68)	0.78 (0.58-1.05)	0.36 (0.2-0.67)	0.6 (0.33-1.09)	2.65 (1.83-3.84)	MPR	0.99 (0.73-1.35)	0.56 (0.31-1.01)	0.99 (0.71-1.38)	1.34 (0.72-2.5)	0.57 (0.31-1.05)	0.5 (0.29-0.86)	0.36 (0.19-0.68)	0.42 (0.24-0.74)	0.42 (0.24-0.75)
1.28 (0.81-2.04)	0.48 (0.23-0.98)	0.37 (0.21-0.65)	0.78 (0.51-1.2)	0.37 (0.21-0.64)	0.6 (0.35-1.04)	2.66 (2.02-3.51)	1.01 (0.74-1.37)	MPR-R	0.57 (0.33-0.97)	1 (0.86-1.16)	1.35 (0.76-2.39)	0.58 (0.33-1)	0.51 (0.31-0.82)	0.36 (0.2-0.65)	0.43 (0.26-0.71)	0.42 (0.25-0.71)
2.27 (1.15-4.48)	0.85 (0.38-1.89)	0.66 (0.56-0.78)	1.38 (0.72-2.67)	0.65 (0.55-0.76)	1.06 (0.76-1.47)	4.71 (2.98-7.43)	1.78 (0.99-3.2)	MPT	1.77 (1.04-3.01)	1.76 (1.04-2.98)	2.39 (1.21-4.7)	1.02 (0.53-1.98)	0.9 (0.49-1.63)	0.64 (0.32-1.27)	0.75 (0.4-1.4)	0.75 (0.4-1.41)
1.29 (0.8-2.08)	0.48 (0.24-0.98)	0.37 (0.22-0.65)	0.79 (0.5-1.23)	0.37 (0.21-0.64)	0.6 (0.35-1.04)	2.67 (2.06-3.46)	1.01 (0.72-1.41)	1 (0.87-1.16)	0.57 (0.34-0.96)	MPT-T	1.36 (0.77-2.38)	0.58 (0.34-1)	0.51 (0.32-0.81)	0.36 (0.21-0.64)	0.43 (0.26-0.7)	0.43 (0.26-0.71)
0.95 (0.47-1.94)	0.35 (0.16-0.81)	0.28 (0.14-0.55)	0.58 (0.29-1.16)	0.27 (0.14-0.54)	0.44 (0.22-0.89)	1.97 (1.2-3.25)	0.75 (0.4-1.39)	0.74 (0.42-1.31)	0.42 (0.21-0.82)	0.74 (0.42-1.3)	TD	0.43 (0.21-0.86)	0.38 (0.2-0.71)	0.27 (0.13-0.55)	0.32 (0.16-0.61)	0.31 (0.16-0.61)
2.22 (1.1-4.45)	0.83 (0.37-1.87)	0.65 (0.33-1.27)	1.35 (0.69-2.65)	0.63 (0.32-1.25)	1.04(0.53- 2.04)	4.6 (2.86-7.42)	1.74 (0.95-3.18)	1.73 (1-3)	0.98 (0.51-1.89)	1.72 (1-2.96)	2.33 (1.17-4.66)	VD	0.88 (0.67-1.15)	0.63 (0.41-0.96)	0.74 (0.54-1.01)	0.73 (0.56-0.95)
2.53 (1.33-4.79)	0.94 (0.44-2.03)	0.74 (0.39-1.37)	1.54 (0.84-2.85)	0.72 (0.39-1.34)	1.18 (0.64-2.19)	5.25 (3.55-7.76)	1.98 (1.16-3.4)	1.97 (1.22-3.18)	1.12 (0.61-2.03)	1.96 (1.23-3.14)	2.66 (1.41-5.02)	1.14 (0.87-1.5)	VMP	0.71 (0.52-0.99)	0.84 (0.72-0.99)	0.84 (0.68-1.03)
3.54 (1.73-7.26)	1.32 (0.57-3.04)	1.03 (0.51-2.08)	2.16 (1.08-4.33)	1.01 (0.5-2.04)	1.65 (0.82-3.32)	7.35 (4.42-12.23)	2.78 (1.48-5.21)	2.76 (1.55-4.92)	1.56 (0.79-3.09)	2.75 (1.55-4.87)	3.73 (1.83-7.61)	1.6 (1.04-2.45)	1.4 (1.01-1.94)	VMPS	1.18 (0.82-1.69)	1.17 (0.8-1.72)
3 (1.55-5.81)	1.12 (0.51-2.46)	0.87 (0.46-1.66)	1.84 (0.97-3.46)	0.86 (0.45-1.63)	1.4 (0.74-2.66)	6.24 (4.09-9.52)	2.36 (1.34-4.14)	2.34 (1.41-3.88)	1.33 (0.71-2.47)	2.34 (1.42-3.83)	3.16 (1.64-6.09)	1.36 (0.99-1.86)	1.19 (1.01-1.4)	0.85 (0.59-1.22)	VMPT-VT	0.99 (0.77-1.29)
3.02 (1.54-5.92)	1.13 (0.51-2.5)	0.88 (0.46-1.69)	1.85 (0.97-3.53)	0.86 (0.45-1.66)	1.41 (0.74-2.71)	6.28 (4.04-9.76)	2.37 (1.33-4.22)	2.36 (1.4-3.96)	1.33 (0.71-2.52)	2.35 (1.41-3.92)	3.18 (1.63-6.2)	1.36 (1.05-1.77)	1.2 (0.97-1.47)	0.85 (0.58-1.26)	1.01 (0.77-1.31)	VTD

Supplementary table 4 Effect of initial regimens for elderly MM patients on CR/nCR rates. Therapies are reported in alphabetical order. The values in the matrix represent the weighted relative risk (RR) and 95% confidence interval for the row-defining treatment vs. the column-defining treatment.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

Outcomes				
Rank	CR/nCR	ORR	PFS	OS
1st	VMPS (P=0.8711)	Ld continuous (P=0.951)	Ld continuous (P=0.9506)	Ld continuous (P=0.9384)
2nd	Ld continuous (P=0.8549)	Ld 18 cycles (P=0.9096)	MPR-R (P=0.8012)	Ld 18 cycles (P=0.8762)
3rd	Ld 18cycles (P=0.8405)	VMPT-VT (P=0.7922)	MPT (P=0.7977)	MPT (P=0.8061)
4th	VTD (P=0.7796)	VMPS (P=0.7851)	Ld 18 cycles (P=0.7404)	VMPT-VT (P=0.7506)
5th	VMPT-VT (P=0.7766)	VTD (P=0.7382)	MPT-T (P=0.6226)	VMP (P=0.7461)
6th	CTD (P=0.6841)	MPT (P=0.6969)	MEL100 (P=0.5093)	VTD (P=0.538)
7th	VMP (P=0.6263)	CTD (P=0.6368)	MPR (P=0.4093)	VD (P=0.5269)
8th	MPT (P=0.5641)	VD (P=0.6066)	MP (P=0.3197)	MPR-R (P=0.4844)
9th	VD (P=0.5349)	VMP (P=0.5902)	Ld 9 cycles (P=0.246)	MEL100 (P=0.4253)
10th	MEL100 (P=0.5321)	MEL100 (P=0.4491)	CPR (P=0.2409)	MPT-T (P=0.41)
11th	Ld 9 cycles (P=0.4175)	MPR-R (P=0.3346)	CTD (P=0.1959)	MP (P=0.387)
12th	MPR-R (P=0.26)	MPT-T (P=0.3019)	TD (P=0.1665)	CTD (P=0.2759)
13th	MPR (P=0.2528)	Ld 9 cycles (P=0.2364)	VMPT-VT [#] (P=0.8759)	MPR (P=0.2692)
14th	MPT-T (P=0.2358)	TD (P=0.1995)	VMPS [#] (P=0.5251)	CPR (P=0.2553)
15th	CPR (p=0.1377)	MPR (P=0.1616)	VMP [#] (P=0.4522)	Ld 9 cycles (P=0.2267)
16th	TD (P=0.1311)	CPR (P=0.1131)	VTD [#] (P=0.3612)	TD (P=0.084)
17th	MP (P=0.0009)	MP (P=0.0007)	VD [#] (P=0.2856)	NA

Supplementary table 5 initial treatments for the elderly patients with the highest probability of ranking from best to worst (1st to 15th) for the outcomes of interest.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

Note: “#” means the ranks of treatments within the second subgroup regarding PFS

CPR	0.66 (0.51-0.84)	0.53 (0.4-0.71)	0.92 (0.82-1.04)	0.52 (0.39-0.69)	0.76 (0.57-1)	1.27 (1.04-1.55)	0.96 (0.85-1.09)	0.85 (0.71-1.03)	0.63 (0.48-0.82)	0.86 (0.71-1.05)	0.94 (0.71-1.24)	0.66 (0.5-0.88)	0.66 (0.52-0.85)	0.6 (0.44-0.81)	0.6 (0.47-0.78)	0.62 (0.48-0.81)
1.53 (1.19-1.96)	CTD	0.81 (0.63-1.05)	1.4 (1.1-1.8)	0.79 (0.62-1.02)	1.15 (0.9-1.48)	1.94 (1.67-2.27)	1.46 (1.18-1.82)	1.3 (1.08-1.57)	0.96 (0.75-1.22)	1.32 (1.1-1.58)	1.43 (1.12-1.84)	1.01 (0.78-1.3)	1.01 (0.81-1.25)	0.92 (0.69-1.21)	0.92 (0.73-1.16)	0.95 (0.75-1.19)
1.88 (1.41-2.49)	1.23 (0.95-1.58)	Ld 18 cycles	1.73 (1.31-2.29)	0.98 (0.91-1.05)	1.42 (1.16-1.74)	2.39 (1.95-2.92)	1.8 (1.4-2.32)	1.6 (1.28-2.01)	1.18 (1.08-1.28)	1.62 (1.3-2.03)	1.76 (1.33-2.34)	1.24 (0.93-1.65)	1.24 (0.97-1.59)	1.13 (0.83-1.53)	1.13 (0.87-1.47)	1.16 (0.89-1.52)
1.09 (0.96-1.23)	0.71 (0.56-0.91)	0.58 (0.44-0.77)	Ld 9 cycles	0.57 (0.43-0.75)	0.82 (0.62-1.09)	1.38 (1.14-1.68)	1.04 (0.93-1.17)	0.93 (0.77-1.11)	0.68 (0.52-0.89)	0.94 (0.78-1.13)	1.02 (0.77-1.35)	0.72 (0.54-0.95)	0.72 (0.56-0.92)	0.65 (0.48-0.88)	0.66 (0.51-0.85)	0.67 (0.52-0.88)
1.92 (1.45-2.55)	1.26 (0.98-1.62)	1.02 (0.95-1.1)	1.77 (1.34-2.34)	Ld continuous	1.45 (1.19-1.78)	2.45 (2-2.99)	1.84 (1.43-2.38)	1.64 (1.31-2.06)	1.21 (1.11-1.31)	1.66 (1.33-2.08)	1.8 (1.36-2.39)	1.27 (0.96-1.68)	1.27 (0.99-1.63)	1.15 (0.85-1.56)	1.16 (0.89-1.5)	1.19 (0.91-1.56)
1.32 (1-1.75)	0.87 (0.67-1.12)	0.7 (0.58-0.86)	1.22 (0.92-1.61)	0.69 (0.56-0.84)	MEL100	1.68 (1.38-2.06)	1.27 (0.98-1.63)	1.13 (0.9-1.41)	0.83 (0.69-1)	1.14 (0.92-1.43)	1.24 (0.94-1.64)	0.87 (0.66-1.16)	0.87 (0.68-1.12)	0.79 (0.58-1.08)	0.8 (0.62-1.03)	0.82 (0.63-1.07)
0.79 (0.64-0.96)	0.51 (0.44-0.6)	0.42 (0.34-0.51)	0.72 (0.6-0.88)	0.41 (0.33-0.5)	0.59 (0.49-0.73)	MP	0.75 (0.64-0.88)	0.67 (0.6-0.74)	0.49 (0.41-0.59)	0.68 (0.62-0.75)	0.74 (0.61-0.9)	0.52 (0.43-0.63)	0.52 (0.45-0.6)	0.47 (0.37-0.59)	0.47 (0.4-0.56)	0.49 (0.41-0.58)
1.04 (0.92-1.18)	0.68 (0.55-0.85)	0.56 (0.43-0.72)	0.96 (0.85-1.08)	0.54 (0.42-0.7)	0.79 (0.61-1.02)	1.33 (1.14-1.55)	MPR	0.89 (0.78-1.02)	0.65 (0.51-0.83)	0.9 (0.78-1.04)	0.98 (0.76-1.26)	0.69 (0.54-0.89)	0.69 (0.56-0.86)	0.63 (0.47-0.83)	0.63 (0.5-0.79)	0.65 (0.51-0.82)
1.17 (0.98-1.41)	0.77 (0.64-0.93)	0.62 (0.5-0.78)	1.08 (0.9-1.29)	0.61 (0.49-0.77)	0.89 (0.71-1.11)	1.49 (1.34-1.66)	1.12 (0.98-1.29)	MPR-R	0.74 (0.6-0.91)	1.01 (0.95-1.08)	1.1 (0.88-1.38)	0.77 (0.62-0.97)	0.78 (0.65-0.93)	0.7 (0.55-0.91)	0.71 (0.58-0.86)	0.73 (0.59-0.89)
1.59 (1.22-2.09)	1.04 (0.82-1.33)	0.85 (0.78-0.92)	1.47 (1.12-1.92)	0.83 (0.76-0.9)	1.21 (1-1.45)	2.03 (1.69-2.44)	1.53 (1.2-1.94)	1.36 (1.1-1.68)	MPT	1.38 (1.12-1.7)	1.5 (1.14-1.96)	1.05 (0.8-1.38)	1.05 (0.83-1.34)	0.96 (0.71-1.28)	0.96 (0.75-1.23)	0.99 (0.77-1.27)
1.16 (0.96-1.4)	0.76 (0.63-0.91)	0.62 (0.49-0.77)	1.06 (0.88-1.28)	0.6 (0.48-0.75)	0.87 (0.7-1.09)	1.47 (1.34-1.62)	1.11 (0.96-1.28)	0.99 (0.93-1.05)	0.73 (0.59-0.89)	MPT-T	1.09 (0.87-1.35)	0.76 (0.61-0.95)	0.76 (0.64-0.91)	0.69 (0.54-0.89)	0.7 (0.58-0.85)	0.72 (0.59-0.88)
1.06 (0.8-1.41)	0.7 (0.54-0.9)	0.57 (0.43-0.75)	0.98 (0.74-1.29)	0.55 (0.42-0.73)	0.81 (0.61-1.07)	1.36 (1.11-1.65)	1.02 (0.79-1.31)	0.91 (0.73-1.14)	0.67 (0.51-0.87)	0.92 (0.74-1.15)	TD	0.7 (0.53-0.93)	0.7 (0.55-0.9)	0.64 (0.47-0.87)	0.64 (0.5-0.83)	0.66 (0.51-0.86)
1.51 (1.14-2.01)	0.99 (0.77-1.28)	0.81 (0.61-1.07)	1.39 (1.05-1.84)	0.79 (0.59-1.04)	1.14 (0.86-1.52)	1.93 (1.58-2.35)	1.45 (1.13-1.87)	1.29 (1.03-1.62)	0.95 (0.72-1.24)	1.31 (1.05-1.63)	1.42 (1.07-1.88)	VD	1 (0.88-1.14)	0.91 (0.73-1.13)	0.91 (0.79-1.06)	0.94 (0.83-1.06)
1.51 (1.18-1.94)	0.99 (0.8-1.23)	0.81 (0.63-1.04)	1.39 (1.09-1.78)	0.79 (0.61-1.01)	1.14 (0.89-1.47)	1.93 (1.66-2.24)	1.45 (1.17-1.8)	1.29 (1.07-1.55)	0.95 (0.75-1.2)	1.31 (1.09-1.56)	1.42 (1.11-1.82)	1 (0.88-1.14)	VMP	0.91 (0.76-1.08)	0.91 (0.85-0.98)	0.94 (0.86-1.03)
1.67 (1.23-2.26)	1.09 (0.83-1.44)	0.89 (0.65-1.21)	1.54 (1.14-2.08)	0.87 (0.64-1.18)	1.26 (0.93-1.71)	2.12 (1.69-2.68)	1.6 (1.21-2.11)	1.42 (1.1-1.83)	1.05 (0.78-1.4)	1.44 (1.12-1.85)	1.57 (1.16-2.12)	1.1 (0.88-1.37)	1.1 (0.92-1.32)	VMPS	1.01 (0.83-1.22)	1.03 (0.85-1.26)
1.66 (1.28-2.15)	1.09 (0.87-1.36)	0.88 (0.68-1.15)	1.53 (1.18-1.97)	0.86 (0.66-1.12)	1.25 (0.97-1.63)	2.11 (1.79-2.49)	1.59 (1.27-2)	1.41 (1.16-1.72)	1.04 (0.81-1.33)	1.43 (1.18-1.74)	1.56 (1.2-2.01)	1.1 (0.94-1.27)	1.1 (1.02-1.18)	0.99 (0.82-1.2)	VMPT-VT	1.03 (0.91-1.16)
1.61 (1.24-2.1)	1.06 (0.84-1.33)	0.86 (0.66-1.12)	1.48 (1.14-1.93)	0.84 (0.64-1.09)	1.22 (0.94-1.59)	2.05 (1.72-2.44)	1.55 (1.22-1.95)	1.38 (1.12-1.69)	1.01 (0.79-1.3)	1.39 (1.14-1.7)	1.51 (1.16-1.97)	1.07 (0.94-1.21)	1.07 (0.97-1.17)	0.97 (0.79-1.18)	0.97 (0.87-1.09)	VTD

Supplementary table 6 Effect of initial regimens for elderly MM patients on ORR rates. Therapies are reported in alphabetical order. The values in the matrix represent the weighted relative risk (RR) and 95% confidence interval for the row-defining treatment vs. the column-defining treatment.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

CPR	0.95 (0.39-2.31)	1.99 (0.76-5.23)	1.01 (0.6-1.68)	2.84 (1.08-7.5)	1.43 (0.62-3.3)	1.16 (0.57-2.38)	1.25 (0.72-2.18)	2 (0.97-4.11)	2.05 (0.91-4.63)	1.62 (0.77-3.37)	0.89 (0.35-2.26)
1.05 (0.43-2.54)	CTD	2.08 (0.9-4.81)	1.06 (0.44-2.56)	2.98 (1.29-6.89)	1.5 (0.76-2.96)	1.22 (0.72-2.06)	1.31 (0.66-2.62)	2.09 (1.11-3.95)	2.15 (1.11-4.13)	1.69 (0.94-3.06)	0.94 (0.43-2.06)
0.5 (0.19-1.32)	0.48 (0.21-1.11)	Ld 18 cycles	0.51 (0.19-1.33)	1.43 (0.85-2.41)	0.72 (0.35-1.48)	0.59 (0.3-1.12)	0.63 (0.29-1.39)	1 (0.48-2.12)	1.03 (0.61-1.73)	0.81 (0.4-1.65)	0.45 (0.19-1.08)
0.99 (0.6-1.66)	0.95 (0.39-2.3)	1.98 (0.75-5.2)	Ld 9 cycles	2.82 (1.07-7.45)	1.42 (0.62-3.28)	1.16 (0.57-2.36)	1.24 (0.71-2.17)	1.98 (0.96-4.08)	2.03 (0.9-4.6)	1.61 (0.77-3.35)	0.89 (0.35-2.25)
0.35 (0.13-0.93)	0.34 (0.15-0.78)	0.7 (0.42-1.18)	0.35 (0.13-0.94)	Ld continuous	0.5 (0.24-1.04)	0.41 (0.21-0.79)	0.44 (0.2-0.98)	0.7 (0.33-1.49)	0.72 (0.43-1.22)	0.57 (0.28-1.16)	0.32 (0.13-0.76)
0.7 (0.3-1.61)	0.67 (0.34-1.32)	1.39 (0.67-2.86)	0.7 (0.3-1.62)	1.99 (0.96-4.1)	MEL100	0.81 (0.53-1.25)	0.88 (0.47-1.64)	1.4 (0.79-2.45)	1.43 (0.87-2.36)	1.13 (0.67-1.89)	0.63 (0.3-1.3)
0.86 (0.42-1.76)	0.82 (0.49-1.38)	1.71 (0.89-3.28)	0.87 (0.42-1.77)	2.44 (1.27-4.71)	1.23 (0.8-1.9)	MP	1.08 (0.69-1.69)	1.72 (1.2-2.46)	1.76 (1.19-2.61)	1.39 (1.05-1.83)	0.77 (0.43-1.39)
0.8 (0.46-1.39)	0.76 (0.38-1.52)	1.59 (0.72-3.51)	0.8 (0.46-1.4)	2.27 (1.02-5.03)	1.14 (0.61-2.14)	0.93 (0.59-1.46)	MPR	1.59 (1.01-2.53)	1.63 (0.9-2.97)	1.29 (0.8-2.09)	0.71 (0.34-1.5)
0.5 (0.24-1.03)	0.48 (0.25-0.9)	1 (0.47-2.1)	0.5 (0.24-1.04)	1.42 (0.67-3.01)	0.72 (0.41-1.26)	0.58 (0.41-0.84)	0.63 (0.4-0.99)	MPR-R	1.02 (0.6-1.75)	0.81 (0.58-1.12)	0.45 (0.22-0.89)
0.49 (0.22-1.1)	0.47 (0.24-0.9)	0.97 (0.58-1.63)	0.49 (0.22-1.11)	1.39 (0.82-2.35)	0.7 (0.42-1.15)	0.57 (0.38-0.84)	0.61 (0.34-1.11)	0.98 (0.57-1.67)	MPT	0.79 (0.49-1.28)	0.44 (0.22-0.89)
0.62 (0.3-1.29)	0.59 (0.33-1.07)	1.23 (0.61-2.5)	0.62 (0.3-1.3)	1.76 (0.86-3.59)	0.89 (0.53-1.48)	0.72 (0.55-0.95)	0.78 (0.48-1.26)	1.24 (0.89-1.71)	1.27 (0.78-2.05)	MPT-T	0.55(0.29-1.06)
1.12(0.44-2.82)	1.07 (0.48-2.34)	2.22 (0.92-5.35)	1.12 (0.45-2.84)	3.17 (1.31-7.67)	1.6 (0.77-3.32)	1.3 (0.72-2.34)	1.4 (0.67-2.94)	2.23 (1.12-4.45)	2.29 (1.13-4.65)	1.81 (0.94-3.46)	TD

Supplementary table 7a Effect of initial regimens for elderly MM patients on PFS of sub-network a. Therapies are reported in alphabetical order. The values in the matrix represent the weighted hazard ratio and 95% confidence interval for the row-defining treatment vs. the column-defining treatment

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L; lenalidomide, MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles, Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

VD	1.13 (0.69-1.85)	1.21 (0.48-3.05)	1.68 (0.81-3.52)	1.06 (0.65-1.75)
0.89 (0.54-1.45)	VMP	1.08 (0.49-2.34)	1.49 (0.86-2.58)	0.94 (0.64-1.38)
0.82 (0.33-2.07)	0.93 (0.43-2.02)	VMPS	1.39 (0.54-3.59)	0.88 (0.37-2.08)
0.59 (0.28-1.24)	0.67 (0.39-1.16)	0.72 (0.28-1.86)	VMPT-VT	0.63 (0.32-1.23)
0.94 (0.57-1.55)	1.06 (0.73-1.55)	1.14 (0.48-2.71)	1.58 (0.81-3.09)	VTD

Supplementary table 7b Effect of initial regimens for elderly MM patients on PFS of sub-network b. Therapies are reported in alphabetical order. The values in the matrix represent the weighted hazard ratio (HR) and 95% confidence interval for the row-defining treatment vs. the column-defining treatment.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

CPR	1.05 (0.6-1.87)	2.15 (1.16-3.97)	0.95 (0.8-1.13)	2.4 (1.3-4.44)	1.14 (0.63-2.03)	1.18 (0.69-2.03)	1.02 (0.72-1.45)	1.29 (0.76-2.16)	1.88 (1.05-3.36)	1.19 (0.7-2.03)	0.76 (0.4-1.48)	1.35 (0.68-2.71)	1.7 (0.94-3.1)	1.85 (0.82-4.18)	1.37 (0.72-2.61)
0.95 (0.54-1.68)	CTD	2.04 (1.44-2.89)	0.9 (0.51-1.58)	2.28 (1.6-3.24)	1.08 (0.8-1.44)	1.12 (0.93-1.36)	0.97 (0.62-1.52)	1.22 (0.91-1.64)	1.79 (1.34-2.38)	1.13 (0.88-1.45)	0.72 (0.47-1.11)	1.28 (0.8-2.06)	1.62 (1.17-2.23)	1.76 (0.93-3.33)	1.3 (0.87-1.94)
0.47 (0.25-0.86)	0.49 (0.35-0.7)	Ld 18 cycles	0.44 (0.24-0.81)	1.12 (0.91-1.37)	0.53 (0.38-0.73)	0.55 (0.41-0.74)	0.48 (0.29-0.79)	0.6 (0.41-0.87)	0.88 (0.72-1.07)	0.55 (0.39-0.77)	0.36 (0.22-0.58)	0.63 (0.37-1.07)	0.79 (0.54-1.17)	0.86 (0.44-1.7)	0.64 (0.4-1.01)
1.05 (0.88-1.26)	1.11 (0.63-1.96)	2.27 (1.23-4.17)	Ld 9 cycles	2.53 (1.37-4.66)	1.2 (0.67-2.13)	1.25 (0.73-2.13)	1.08 (0.77-1.52)	1.35 (0.81-2.27)	1.99 (1.12-3.53)	1.25 (0.74-2.13)	0.81 (0.42-1.55)	1.43 (0.72-2.84)	1.8 (0.99-3.25)	1.95 (0.87-4.39)	1.44 (0.76-2.74)
0.42 (0.23-0.77)	0.44 (0.31-0.62)	0.9 (0.73-1.1)	0.4 (0.21-0.73)	Ld continuous	0.47 (0.34-0.66)	0.49 (0.37-0.66)	0.43 (0.26-0.71)	0.54 (0.37-0.78)	0.78 (0.64-0.96)	0.49 (0.35-0.7)	0.32 (0.2-0.52)	0.56 (0.33-0.96)	0.71 (0.48-1.05)	0.77 (0.39-1.52)	0.57 (0.36-0.9)
0.88 (0.49-1.58)	0.93 (0.69-1.24)	1.89 (1.37-2.62)	0.84 (0.47-1.49)	2.12 (1.52-2.93)	MEL100	1.04 (0.84-1.3)	0.9 (0.57-1.43)	1.13 (0.82-1.55)	1.66 (1.28-2.14)	1.05 (0.79-1.38)	0.67 (0.43-1.05)	1.19 (0.73-1.94)	1.5 (1.07-2.11)	1.63 (0.85-3.12)	1.21 (0.79-1.83)
0.84 (0.49-1.45)	0.89 (0.74-1.08)	1.81 (1.35-2.44)	0.8 (0.47-1.37)	2.03 (1.51-2.73)	0.96 (0.77-1.2)	MP	0.86 (0.57-1.3)	1.08 (0.87-1.36)	1.59 (1.28-1.98)	1 (0.85-1.18)	0.65 (0.44-0.94)	1.14 (0.74-1.77)	1.44 (1.11-1.86)	1.56 (0.85-2.88)	1.16 (0.81-1.65)
0.98 (0.69-1.39)	1.03 (0.66-1.62)	2.1 (1.27-3.48)	0.93 (0.66-1.31)	2.35 (1.42-3.89)	1.11 (0.7-1.77)	1.16 (0.77-1.74)	MPR	1.26 (0.85-1.85)	1.84 (1.16-2.92)	1.16 (0.77-1.74)	0.75 (0.43-1.31)	1.32 (0.73-2.41)	1.67 (1.03-2.7)	1.81 (0.87-3.78)	1.34 (0.78-2.3)
0.78 (0.46-1.31)	0.82 (0.61-1.1)	1.67 (1.15-2.43)	0.74 (0.44-1.24)	1.87 (1.29-2.72)	0.88 (0.64-1.21)	0.92 (0.74-1.16)	0.8 (0.54-1.17)	MPR-R	1.47 (1.07-2.01)	0.92 (0.77-1.11)	0.59 (0.38-0.93)	1.05 (0.64-1.72)	1.33 (0.94-1.87)	1.44 (0.75-2.76)	1.07 (0.7-1.62)
0.53 (0.3-0.95)	0.56 (0.42-0.75)	1.14 (0.94-1.39)	0.5 (0.28-0.9)	1.28 (1.04-1.56)	0.6 (0.47-0.78)	0.63 (0.51-0.78)	0.54 (0.34-0.86)	0.68 (0.5-0.93)	MPT	0.63 (0.48-0.83)	0.41 (0.26-0.63)	0.72 (0.44-1.17)	0.91 (0.65-1.27)	0.98 (0.51-1.88)	0.73 (0.48-1.1)
0.84 (0.49-1.44)	0.89 (0.69-1.14)	1.81 (1.29-2.54)	0.8 (0.47-1.36)	2.02 (1.44-2.84)	0.96 (0.72-1.26)	1 (0.84-1.18)	0.86 (0.57-1.29)	1.08 (0.9-1.3)	1.58 (1.21-2.08)	MPT-T	0.64 (0.42-0.97)	1.14 (0.71-1.82)	1.43 (1.05-1.95)	1.56 (0.83-2.93)	1.15 (0.78-1.7)
1.31 (0.68-2.53)	1.38 (0.9-2.11)	2.81 (1.74-4.55)	1.24 (0.64-2.39)	3.14 (1.94-5.09)	1.49 (0.96-2.31)	1.55 (1.06-2.27)	1.34 (0.77-2.34)	1.68 (1.08-2.62)	2.46 (1.59-3.82)	1.55 (1.03-2.36)	TD	1.77 (0.99-3.16)	2.23 (1.41-3.53)	2.42 (1.18-4.98)	1.79 (1.06-3.01)
0.74 (0.37-1.48)	0.78 (0.48-1.25)	1.59 (0.94-2.69)	0.7 (0.35-1.4)	1.77 (1.05-3.01)	0.84 (0.51-1.37)	0.88 (0.57-1.35)	0.76 (0.42-1.37)	0.95 (0.58-1.55)	1.39 (0.85-2.26)	0.88 (0.55-1.4)	0.56 (0.32-1.01)	VD	1.26 (0.89-1.79)	1.37 (0.71-2.63)	1.01 (0.72-1.41)
0.59 (0.32-1.07)	0.62 (0.45-0.85)	1.26 (0.85-1.87)	0.56 (0.31-1.01)	1.41 (0.95-2.09)	0.67 (0.47-0.94)	0.7 (0.54-0.9)	0.6 (0.37-0.97)	0.75 (0.53-1.06)	1.1 (0.79-1.55)	0.7 (0.51-0.95)	0.45 (0.28-0.71)	0.79 (0.56-1.13)	VMP	1.09 (0.63-1.89)	0.8 (0.63-1.02)
0.54 (0.24-1.22)	0.57 (0.3-1.08)	1.16 (0.59-2.28)	0.51 (0.23-1.15)	1.3 (0.66-2.56)	0.61 (0.32-1.17)	0.64 (0.35-1.18)	0.55 (0.26-1.15)	0.69 (0.36-1.33)	1.02 (0.53-1.94)	0.64 (0.34-1.21)	0.41 (0.2-0.85)	0.73 (0.38-1.41)	0.92 (0.53-1.6)	VMPT-VT	0.74 (0.4-1.35)
0.73 (0.38-1.39)	0.77 (0.52-1.15)	1.57 (0.99-2.49)	0.69 (0.37-1.31)	1.75 (1.11-2.79)	0.83 (0.55-1.26)	0.87 (0.61-1.23)	0.75 (0.44-1.28)	0.94 (0.62-1.43)	1.38 (0.91-2.08)	0.87 (0.59-1.28)	0.56 (0.33-0.94)	0.99 (0.71-1.38)	1.25 (0.98-1.58)	1.35 (0.74-2.47)	VTD

Supplementary table 8 Effect of initial regimens for elderly MM patients on OS. Therapies are reported in alphabetical order. The values in the matrix represent the weighted hazard ratio (HR) and 95% confidence interval for the row-defining treatment vs. the column-defining treatment.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100,

reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

CPR	0.4 (0.17-0.91)	0.48 (0.19-1.23)	0.61 (0.44-0.84)	0.47 (0.19-1.2)	2.21 (1.33-3.68)	0.78 (0.56-1.11)	0.77 (0.48-1.22)	0.73 (0.29-1.83)	0.76 (0.47-1.22)	1.12 (0.55-2.29)	0.48 (0.24-0.97)	0.42 (0.22-0.8)	0.35 (0.18-0.69)	0.35 (0.18-0.69)
2.52 (1.09-5.8)	CTD	1.22 (0.44-3.38)	1.54 (0.68-3.47)	1.19 (0.43-3.31)	5.56 (2.88-10.75)	1.98 (0.92-4.22)	1.93 (0.94-3.96)	1.85 (0.68-5.05)	1.91 (0.93-3.89)	2.82 (1.23-6.45)	1.21 (0.54-2.73)	1.06 (0.49-2.28)	0.89 (0.41-1.95)	0.89 (0.4-1.96)
2.07 (0.82-5.24)	0.82 (0.3-2.27)	Ld 18 cycles	1.26 (0.51-3.14)	0.98 (0.85-1.12)	4.56 (2.1-9.93)	1.62 (0.68-3.85)	1.58 (0.69-3.63)	1.52 (1.29-1.79)	1.56 (0.69-3.57)	2.31 (0.92-5.83)	0.99 (0.4-2.47)	0.87 (0.36-2.07)	0.73 (0.3-1.77)	0.73 (0.3-1.78)
1.64 (1.19-2.26)	0.65 (0.29-1.47)	0.79 (0.32-1.97)	Ld 9 cycles	0.78 (0.31-1.94)	3.62 (2.24-5.84)	1.28 (0.96-1.73)	1.25 (0.82-1.92)	1.2 (0.49-2.95)	1.24 (0.79-1.94)	1.83 (0.92-3.66)	0.79 (0.4-1.54)	0.69 (0.37-1.28)	0.58 (0.31-1.1)	0.58 (0.3-1.1)
2.11 (0.83-5.34)	0.84 (0.3-2.32)	1.02 (0.89-1.17)	1.29 (0.52-3.21)	Ld continuous	4.66 (2.14-10.13)	1.65 (0.7-3.92)	1.61 (0.7-3.7)	1.55 (1.31-1.82)	1.6 (0.7-3.64)	2.36 (0.94-5.95)	1.01 (0.41-2.52)	0.89 (0.37-2.12)	0.75 (0.31-1.81)	0.74 (0.3-1.81)
0.45 (0.27-0.75)	0.18 (0.09-0.35)	0.22 (0.1-0.48)	0.28 (0.17-0.45)	0.21 (0.1-0.47)	MP	0.36 (0.24-0.52)	0.35 (0.26-0.46)	0.33 (0.16-0.71)	0.34 (0.26-0.45)	0.51 (0.31-0.84)	0.22 (0.13-0.35)	0.19 (0.13-0.28)	0.16 (0.11-0.24)	0.16 (0.1-0.25)
1.27 (0.9-1.8)	0.51 (0.24-1.08)	0.62 (0.26-1.46)	0.78 (0.58-1.05)	0.6 (0.25-1.43)	2.81 (1.93-4.1)	MPR	0.98 (0.72-1.33)	0.94 (0.4-2.18)	0.96 (0.69-1.35)	1.43 (0.76-2.67)	0.61 (0.33-1.12)	0.54 (0.31-0.92)	0.45 (0.26-0.79)	0.45 (0.25-0.8)
1.31 (0.82-2.08)	0.52 (0.25-1.06)	0.63 (0.28-1.45)	0.8 (0.52-1.22)	0.62 (0.27-1.42)	2.88 (2.16-3.85)	1.02 (0.75-1.4)	MPR-R	0.96 (0.43-2.16)	0.99 (0.85-1.15)	1.46 (0.82-2.6)	0.63 (0.36-1.09)	0.55 (0.34-0.89)	0.46 (0.28-0.77)	0.46 (0.27-0.78)
1.36 (0.55-3.4)	0.54 (0.2-1.48)	0.66 (0.56-0.78)	0.83 (0.34-2.04)	0.65 (0.55-0.76)	3.01 (1.41-6.43)	1.07 (0.46-2.5)	1.04 (0.46-2.35)	MPT	1.03 (0.46-2.31)	1.53 (0.61-3.79)	0.65 (0.27-1.6)	0.57 (0.24-1.35)	0.48 (0.2-1.15)	0.48 (0.2-1.15)
1.32 (0.82-2.13)	0.52 (0.26-1.07)	0.64 (0.28-1.46)	0.81 (0.52-1.26)	0.63 (0.27-1.43)	2.92 (2.22-3.84)	1.04 (0.74-1.45)	1.01 (0.87-1.17)	0.97 (0.43-2.17)	MPT-T	1.48 (0.84-2.62)	0.63 (0.37-1.1)	0.56 (0.34-0.9)	0.47 (0.28-0.77)	0.46 (0.28-0.78)
0.89 (0.44-1.83)	0.35 (0.16-0.81)	0.43 (0.17-1.09)	0.55 (0.27-1.09)	0.42 (0.17-1.07)	1.97 (1.2-3.25)	0.7 (0.37-1.31)	0.68 (0.38-1.22)	0.66 (0.26-1.63)	0.68 (0.38-1.2)	TD	0.43 (0.21-0.86)	0.38 (0.2-0.71)	0.32 (0.16-0.61)	0.31 (0.16-0.61)
2.08 (1.04-4.19)	0.83 (0.37-1.87)	1.01 (0.41-2.51)	1.27 (0.65-2.5)	0.99 (0.4-2.46)	4.6 (2.86-7.42)	1.64 (0.89-3)	1.6 (0.91-2.79)	1.53 (0.62-3.75)	1.58 (0.91-2.74)	2.33 (1.17-4.66)	VD	0.88 (0.67-1.15)	0.74 (0.54-1.01)	0.73 (0.56-0.95)
2.38 (1.25-4.52)	0.94 (0.44-2.03)	1.15 (0.48-2.75)	1.45 (0.78-2.69)	1.13 (0.47-2.69)	5.25 (3.55-7.76)	1.87 (1.08-3.21)	1.82 (1.12-2.96)	1.74 (0.74-4.1)	1.8 (1.12-2.9)	2.66 (1.41-5.02)	1.14 (0.87-1.5)	VMP	0.84 (0.72-0.99)	0.84 (0.68-1.03)
2.83 (1.46-5.48)	1.12 (0.51-2.46)	1.37 (0.56-3.31)	1.73 (0.91-3.27)	1.34 (0.55-3.25)	6.24 (4.09-9.52)	2.22 (1.26-3.9)	2.16 (1.3-3.61)	2.07 (0.87-4.95)	2.14 (1.29-3.54)	3.16 (1.64-6.09)	1.36 (0.99-1.86)	1.19 (1.01-1.4)	VMP-T	0.99 (0.77-1.29)
2.84 (1.45-5.58)	1.13 (0.51-2.5)	1.38 (0.56-3.36)	1.74 (0.91-3.33)	1.35 (0.55-3.3)	6.28 (4.04-9.76)	2.23 (1.25-3.98)	2.18 (1.29-3.69)	2.09 (0.87-5.02)	2.15 (1.28-3.62)	3.18 (1.63-6.2)	1.36 (1.05-1.77)	1.2 (0.97-1.47)	1.01 (0.77-1.31)	VTD

Supplementary table 9 Sensitive analysis of effect of initial regimens for elderly MM patients on CR/nCR rates. Therapies are reported in alphabetical order. The values in the matrix represent the weighted relative risk (RR) and 95% confidence interval for the row-defining treatment vs. the column-defining treatment.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

CPR	0.65 (0.51-0.84)	0.55 (0.37-0.8)	0.92 (0.82-1.04)	0.53 (0.37-0.78)	1.27 (1.04-1.55)	0.96 (0.85-1.09)	0.85 (0.71-1.03)	0.64 (0.44-0.93)	0.87 (0.72-1.05)	0.94 (0.71-1.24)	0.66 (0.5-0.87)	0.66 (0.51-0.85)	0.6 (0.46-0.78)	0.62 (0.47-0.81)
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1.53 (1.19-1.97)	CTD	0.84 (0.58-1.2)	1.41 (1.1-1.8)	0.82 (0.57-1.17)	1.94 (1.67-2.27)	1.47 (1.18-1.83)	1.31 (1.08-1.57)	0.98 (0.69-1.39)	1.32 (1.1-1.59)	1.43 (1.12-1.84)	1.01 (0.78-1.3)	1.01 (0.81-1.25)	0.92 (0.73-1.16)	0.95 (0.75-1.19)
1.83 (1.25-2.67)	1.2 (0.84-1.71)	Ld 18 cycles	1.68 (1.15-2.46)	0.98 (0.91-1.05)	2.32 (1.68-3.21)	1.75 (1.22-2.51)	1.56 (1.11-2.19)	1.18 (1.08-1.28)	1.58 (1.13-2.22)	1.71 (1.17-2.5)	1.21 (0.82-1.76)	1.21 (0.84-1.72)	1.1 (0.77- 1.58)	1.13 (0.78-1.63)
1.09 (0.96-1.23)	0.71 (0.55-0.91)	0.59 (0.41-0.87)	Ld 9 cycles	0.58 (0.4-0.85)	1.38 (1.14-1.68)	1.04 (0.93-1.17)	0.93 (0.78-1.11)	0.7 (0.48-1.01)	0.94 (0.78-1.13)	1.02 (0.77-1.34)	0.72 (0.54-0.95)	0.72 (0.56-0.92)	0.65 (0.51-0.85)	0.67 (0.52-0.87)
1.87 (1.28-2.74)	1.22 (0.86-1.75)	1.02 (0.95-1.1)	1.72 (1.18-2.51)	Ld continuous	2.38 (1.72-3.29)	1.8 (1.25-2.57)	1.6 (1.14-2.25)	1.21 (1.11-1.31)	1.62 (1.16-2.27)	1.75 (1.2-2.56)	1.23 (0.84-1.8)	1.24 (0.87-1.76)	1.13 (0.78-1.62)	1.16 (0.8-1.67)
0.79 (0.64-0.96)	0.51 (0.44-0.6)	0.43 (0.31-0.59)	0.72 (0.6-0.88)	0.42 (0.3-0.58)	MP	0.75 (0.65-0.88)	0.67 (0.6-0.75)	0.51 (0.37-0.69)	0.68 (0.62-0.75)	0.74 (0.61-0.9)	0.52 (0.43-0.63)	0.52 (0.45-0.6)	0.47 (0.4-0.56)	0.49 (0.41-0.58)
1.04 (0.92-1.18)	0.68 (0.55-0.85)	0.57 (0.4-0.82)	0.96 (0.85-1.08)	0.56 (0.39-0.8)	1.33 (1.13-1.55)	MPR	0.89 (0.78-1.02)	0.67 (0.47-0.95)	0.9 (0.78-1.04)	0.98 (0.76-1.26)	0.69 (0.53-0.89)	0.69 (0.55-0.85)	0.63 (0.5-0.79)	0.65 (0.51-0.82)
1.17 (0.97-1.41)	0.77 (0.64-0.92)	0.64 (0.46-0.9)	1.08 (0.9-1.29)	0.63 (0.45-0.88)	1.49 (1.34-1.66)	1.12 (0.98-1.29)	MPR-R	0.75 (0.54-1.05)	1.01 (0.95-1.08)	1.1 (0.88-1.37)	0.77 (0.62-0.97)	0.77 (0.64-0.93)	0.71 (0.58-0.86)	0.73(0.59- 0.89)
1.55 (1.07-2.25)	1.02 (0.72-1.44)	0.85 (0.78-0.92)	1.43 (0.99-2.07)	0.83 (0.76-0.9)	1.97 (1.44-2.7)	1.49 (1.05-2.11)	1.33 (0.95-1.85)	MPT	1.34 (0.97-1.87)	1.46 (1.01-2.11)	1.02 (0.71-1.48)	1.02 (0.72-1.45)	0.94 (0.66-1.33)	0.96 (0.67-1.38)
1.16 (0.95-1.4)	0.76 (0.63-0.91)	0.63 (0.45-0.89)	1.06 (0.88-1.28)	0.62 (0.44-0.87)	1.47 (1.33-1.62)	1.11 (0.96-1.28)	0.99 (0.93-1.05)	0.74 (0.54-1.03)	MPT-T	1.08 (0.87-1.35)	0.76 (0.61-0.95)	0.76 (0.64-0.91)	0.7 (0.57-0.84)	0.72 (0.58-0.87)
1.07 (0.81-1.41)	0.7 (0.54-0.9)	0.58 (0.4-0.85)	0.98 (0.74-1.3)	0.57 (0.39-0.83)	1.36 (1.11-1.65)	1.02 (0.8-1.32)	0.91 (0.73-1.14)	0.69 (0.47-0.99)	0.92 (0.74-1.15)	TD	0.7 (0.53-0.93)	0.7 (0.55-0.9)	0.64 (0.5-0.83)	0.66 (0.51-0.86)
1.52 (1.14-2.01)	0.99 (0.77-1.28)	0.83 (0.57-1.21)	1.4 (1.06-1.85)	0.81 (0.55-1.18)	1.93 (1.58-2.35)	1.45 (1.13-1.87)	1.29 (1.03-1.62)	0.98 (0.67-1.41)	1.31 (1.05-1.64)	1.42 (1.07-1.88)	VD	1 (0.88-1.14)	0.91 (0.79-1.06)	0.94 (0.83-1.06)
1.52 (1.18-1.95)	0.99 (0.8-1.23)	0.83 (0.58-1.18)	1.4 (1.09-1.78)	0.81 (0.57-1.16)	1.93 (1.66-2.24)	1.45 (1.17-1.8)	1.29 (1.08-1.55)	0.98 (0.69-1.38)	1.31 (1.1-1.57)	1.42 (1.11-1.82)	1 (0.88-1.14)	VMP	0.91 (0.85-0.98)	0.94 (0.86-1.03)
1.66 (1.28-2.15)	1.09 (0.87-1.36)	0.91 (0.63-1.31)	1.53 (1.18-1.98)	0.89 (0.62-1.28)	2.11 (1.79-2.49)	1.59 (1.27-2)	1.42 (1.16-1.73)	1.07 (0.75-1.52)	1.44 (1.18-1.75)	1.56 (1.2-2.01)	1.1 (0.94-1.27)	1.1 (1.02-1.18)	VMPT-VT	1.03 (0.91-1.16)
1.62 (1.24-2.11)	1.06 (0.84-1.33)	0.88 (0.61-1.28)	1.49 (1.14-1.93)	0.86 (0.6-1.25)	2.05 (1.72-2.44)	1.55 (1.23-1.96)	1.38 (1.12-1.69)	1.04 (0.73-1.49)	1.4 (1.14-1.71)	1.51 (1.16-1.97)	1.07 (0.94-1.21)	1.07 (0.97-1.17)	0.97 (0.87-1.09)	VTD

Supplementary table 10 Sensitive analysis of effect of initial regimens for elderly MM patients on ORR rates. Therapies are reported in alphabetical order. The values in the matrix represent the weighted relative risk (RR) and 95% confidence interval for the row-defining treatment vs. the column-defining treatment.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

CPR	0.94 (0.39-2.28)	1.8 (0.63-5.17)	1.01 (0.6-1.68)	2.57 (0.89-7.4)	1.15 (0.56-2.35)	1.25 (0.72-2.18)	2.03 (0.98-4.17)	1.85 (0.74-4.64)	1.66 (0.79-3.48)	0.88 (0.35-2.23)
1.06 (0.44-2.57)	CTD	1.91 (0.75-4.87)	1.07 (0.44-2.59)	2.73 (1.07-6.97)	1.22 (0.72-2.06)	1.33 (0.67-2.65)	2.15 (1.14-4.07)	1.97 (0.9-4.28)	1.76 (0.97-3.21)	0.94 (0.43-2.06)
0.56 (0.19-1.59)	0.52 (0.21-1.33)	Ld 18 cycles	0.56 (0.19-1.61)	1.43 (0.85-2.41)	0.64 (0.29-1.39)	0.7 (0.28-1.71)	1.13 (0.48-2.65)	1.03 (0.61-1.73)	0.92 (0.4-2.11)	0.49 (0.19-1.3)
0.99 (0.6-1.66)	0.94 (0.39-2.27)	1.79 (0.62-5.14)	Ld 9 cycles	2.56 (0.89-7.36)	1.14 (0.56-2.34)	1.24 (0.71-2.17)	2.01 (0.98-4.14)	1.84 (0.74-4.61)	1.65 (0.79-3.46)	0.88 (0.35-2.22)
0.39 (0.14-1.12)	0.37 (0.14-0.94)	0.7 (0.42-1.18)	0.39 (0.14-1.13)	Ld continuous	0.45 (0.21-0.97)	0.49 (0.2-1.2)	0.79 (0.33-1.86)	0.72 (0.43-1.22)	0.65 (0.28-1.48)	0.34 (0.13-0.91)
0.87 (0.43-1.78)	0.82 (0.49-1.38)	1.57 (0.72-3.4)	0.88 (0.43-1.79)	2.24 (1.03-4.88)	MP	1.09 (0.69-1.71)	1.76 (1.22-2.54)	1.61 (0.91-2.86)	1.45 (1.08-1.93)	0.77 (0.43-1.39)

0.8 (0.46-1.39)	0.75 (0.38-1.5)	1.44 (0.59-3.52)	0.8 (0.46-1.4)	2.05 (0.84-5.05)	0.92 (0.58-1.44)	MPR	1.62 (1.02-2.57)	1.48 (0.71-3.07)	1.33 (0.82-2.16)	0.71 (0.34-1.48)
0.49 (0.24-1.02)	0.47 (0.25-0.88)	0.89 (0.38-2.09)	0.5 (0.24-1.02)	1.27 (0.54-3)	0.57 (0.39-0.82)	0.62 (0.39-0.98)	MPR-R	0.92 (0.46-1.81)	0.82 (0.59-1.14)	0.44 (0.22-0.87)
0.54 (0.22-1.35)	0.51 (0.23-1.11)	0.97 (0.58-1.63)	0.54 (0.22-1.36)	1.39 (0.82-2.35)	0.62 (0.35-1.1)	0.68 (0.33-1.4)	1.09 (0.55-2.16)	MPT	0.9 (0.47-1.71)	0.48 (0.21-1.09)
0.6 (0.29-1.26)	0.57 (0.31-1.03)	1.08 (0.47-2.48)	0.61 (0.29-1.27)	1.55 (0.67-3.55)	0.69 (0.52-0.92)	0.75 (0.46-1.23)	1.22 (0.88-1.69)	1.12 (0.59-2.12)	MPT-T	0.53 (0.28-1.03)
1.13 (0.45-2.86)	1.07 (0.48-2.34)	2.04 (0.77-5.39)	1.14 (0.45-2.88)	2.91 (1.1-7.73)	1.3 (0.72-2.34)	1.42 (0.67-2.98)	2.29 (1.15-4.58)	2.1 (0.92-4.77)	1.88 (0.98-3.62)	TD

Supplementary table 11 Sensitive analysis of effect of initial regimens for elderly MM patients on PFS rates. Therapies are reported in alphabetical order. The values in the matrix represent the weighted relative risk (RR) and 95% confidence interval for the row-defining treatment vs. the column-defining treatment.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

CPR	1.07 (0.6-1.89)	2.01 (1.03-3.93)	0.95 (0.8-1.13)	2.25 (1.15-4.39)	1.2 (0.7-2.05)	1.02 (0.72-1.45)	1.28 (0.76-2.15)	1.76 (0.93-3.34)	1.18 (0.69-2.01)	0.77 (0.4-1.49)	1.37 (0.68-2.74)	1.72 (0.95-3.13)	1.87 (0.83-4.23)	1.38 (0.73-2.64)
0.94 (0.53-1.66)	CTD	1.89 (1.22-2.93)	0.89 (0.5-1.57)	2.11 (1.35-3.28)	1.12 (0.93-1.36)	0.96 (0.61-1.51)	1.2 (0.89-1.61)	1.65 (1.12-2.45)	1.1 (0.86-1.43)	0.72 (0.47-1.11)	1.28 (0.8-2.06)	1.62 (1.17-2.23)	1.76 (0.93-3.33)	1.3 (0.87-1.94)
0.5 (0.25-0.97)	0.53 (0.34-0.82)	Ld 18 cycles	0.47 (0.24-0.92)	1.12 (0.91-1.37)	0.6 (0.4-0.89)	0.51 (0.29-0.9)	0.64 (0.4-1)	0.88 (0.72-1.07)	0.59 (0.38-0.9)	0.38 (0.22-0.67)	0.68 (0.38-1.23)	0.86 (0.53-1.38)	0.93 (0.45-1.93)	0.69 (0.4-1.17)
1.05 (0.88-1.26)	1.12 (0.64-1.98)	2.12 (1.09-4.12)	Ld 9 cycles	2.37 (1.22-4.61)	1.26 (0.74-2.15)	1.08 (0.77-1.52)	1.35 (0.8-2.26)	1.86 (0.98-3.51)	1.24 (0.73-2.11)	0.81 (0.42-1.57)	1.44 (0.72-2.88)	1.82 (1-3.29)	1.98 (0.88-4.44)	1.46 (0.77-2.77)
0.45 (0.23-0.87)	0.47 (0.31-0.74)	0.9 (0.73-1.1)	0.42 (0.22-0.82)	Ld continuous	0.53 (0.36-0.79)	0.46 (0.26-0.81)	0.57 (0.36-0.9)	0.78 (0.64-0.96)	0.52 (0.34-0.81)	0.34 (0.2-0.6)	0.61 (0.34-1.1)	0.77 (0.48-1.23)	0.83 (0.4-1.73)	0.62 (0.36-1.05)
0.83 (0.49-1.43)	0.89 (0.74-1.08)	1.68 (1.13-2.5)	0.79 (0.46-1.35)	1.88 (1.26-2.8)	MP	0.85 (0.57-1.29)	1.07 (0.85-1.34)	1.47 (1.04-2.07)	0.98 (0.83-1.17)	0.65 (0.44-0.94)	1.14 (0.74-1.77)	1.44 (1.11-1.86)	1.56 (0.85-2.88)	1.16 (0.81-1.65)
0.98 (0.69-1.39)	1.04 (0.66-1.64)	1.97 (1.11-3.48)	0.93 (0.66-1.31)	2.2 (1.24-3.89)	1.17 (0.78-1.76)	MPR	1.25 (0.85-1.84)	1.72 (1.01-2.94)	1.15 (0.77-1.73)	0.76 (0.43-1.32)	1.34 (0.74-2.43)	1.69 (1.04-2.74)	1.83 (0.88-3.82)	1.35 (0.79-2.32)
0.78 (0.46-1.32)	0.83 (0.62-1.12)	1.57 (1-2.49)	0.74 (0.44-1.24)	1.76 (1.11-2.79)	0.94 (0.75-1.18)	0.8 (0.54-1.18)	MPR-R	1.38 (0.91-2.08)	0.92 (0.77-1.11)	0.6 (0.39-0.94)	1.07 (0.65-1.75)	1.35 (0.95-1.91)	1.47 (0.76-2.81)	1.08 (0.71-1.65)
0.57 (0.3-1.08)	0.61 (0.41-0.9)	1.14 (0.94-1.39)	0.54 (0.29-1.02)	1.28 (1.04-1.56)	0.68 (0.48-0.96)	0.58 (0.34-0.99)	0.73 (0.48-1.1)	MPT	0.67 (0.46-0.98)	0.44 (0.26-0.73)	0.78 (0.45-1.35)	0.98 (0.64-1.51)	1.06 (0.53-2.14)	0.79 (0.48-1.29)
0.85 (0.5-1.45)	0.91 (0.7-1.17)	1.71 (1.11-2.63)	0.81 (0.47-1.37)	1.91 (1.24-2.95)	1.02 (0.86-1.21)	0.87 (0.58-1.3)	1.09 (0.9-1.31)	1.5 (1.02-2.2)	MP-T	0.66 (0.43-1)	1.16 (0.73-1.86)	1.46 (1.07-2)	1.59 (0.84-3)	1.18 (0.79-1.74)
1.29 (0.67-2.5)	1.38 (0.9-2.11)	2.6 (1.5-4.51)	1.23 (0.64-2.36)	2.91 (1.67-5.05)	1.55 (1.06-2.27)	1.32 (0.76-2.31)	1.65 (1.06-2.58)	2.28 (1.36-3.81)	1.52 (1-2.31)	TD	1.77 (0.99-3.16)	2.23 (1.41-3.53)	2.42 (1.18-4.98)	1.79 (1.06-3.01)
0.73 (0.37-1.46)	0.78 (0.48-1.25)	1.47 (0.81-2.65)	0.69 (0.35-1.38)	1.64 (0.91-2.96)	0.88 (0.57-1.35)	0.75 (0.41-1.36)	0.93 (0.57-1.53)	1.29 (0.74-2.24)	0.86 (0.54-1.37)	0.56 (0.32-1.01)	VD	1.26 (0.89-1.79)	1.37 (0.71-2.63)	1.01 (0.72-1.41)
0.58 (0.32-1.05)	0.62 (0.45-0.85)	1.17 (0.73-1.87)	0.55(0.3-1)	1.3 (0.81-2.1)	0.7 (0.54-0.9)	0.59 (0.37-0.96)	0.74 (0.52-1.05)	1.02 (0.66-1.57)	0.68 (0.5-0.93)	0.45 (0.28-0.71)	0.79 (0.56-1.13)	VMP	1.09 (0.63-1.89)	0.8 (0.63-1.02)

0.53 (0.24-1.2)	0.57 (0.3-1.08)	1.07 (0.52-2.22)	0.51 (0.23-1.14)	1.2 (0.58-2.49)	0.64 (0.35-1.18)	0.55 (0.26-1.14)	0.68 (0.36-1.31)	0.94 (0.47-1.89)	0.63 (0.33-1.18)	0.41 (0.2-0.85)	0.73 (0.38-1.41)	0.92 (0.53-1.6)	VMPT-VT	0.74 (0.4-1.35)
0.72 (0.38-1.38)	0.77 (0.52-1.15)	1.45 (0.85-2.47)	0.69 (0.36-1.3)	1.62 (0.95-2.77)	0.87 (0.61-1.23)	0.74 (0.43-1.27)	0.92 (0.61-1.41)	1.27 (0.78-2.09)	0.85 (0.57-1.26)	0.56 (0.33-0.94)	0.99 (0.71-1.38)	1.25 (0.98-1.58)	1.35 (0.74-2.47)	VTD

Supplementary table 12 Sensitive analysis of effect of initial regimens for elderly MM patients on OS. Therapies are reported in alphabetical order. The values in the matrix represent the weighted relative risk (RR) and 95% confidence interval for the row-defining treatment vs. the column-defining treatment.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; S, siltuximab; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²; Ld continuous, lenalidomide plus dexamethasone in 28-day cycles until disease progression; Ld 18 cycles, lenalidomide plus dexamethasone for 18 cycles; Ld 9 cycles, lenalidomide plus dexamethasone for 9 cycles.

Figure S1 Inconsistency plot for the key endpoints assuming loop-specific heterogeneity estimates using the method of moments estimator. (A) inconsistency plot for CR/nCR, (B) inconsistency plot for ORR, (C) inconsistency plot for PFS, (D) inconsistency plot for OS.

Abbreviations: V, bortezomib; M, melphalan; P, prednisone; T, thalidomide; D, dexamethasone; R/L, lenalidomide; MEL100, reduced-intensity stem cell transplantation using melphalan 100 mg/m²;

