

Doubling in median survival in patients diagnosed with multiple myeloma 2005-2019; a real-world study from the UK's Haematological Malignancy Research Network

Authors

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Supplementary Table 1: Skeletal imaging and CRAB criteria distributed by year of diagnosis: Multiple myeloma, Haematological Malignancy Research Network

		Year of diagnosis				
	Total	2005-07	2008-10	2011-2013	2014-16	2017-19
Total	3720 (100)	637 (100)	740 (100)	775 (100)	755 (100)	813 (100)
Skeletal imaging						
No	308 (8.3)	64 (10.0)	67 (9.1)	52 (6.7)	63 (8.3)	62 (7.6)
Yes ¹	3412 (91.7)	573 (90.0)	673 (90.9)	723 (93.3)	692 (91.7)	751 (92.4)
Plain radiography ²	2958 (86.7)	551 (96.2)	649 (96.4)	693 (95.9)	580 (83.8)	485 (64.6)
Plain radiography only ²	1770 (51.9)	425 (74.2)	447 (66.4)	413 (57.1)	269 (38.9)	216 (28.8)
MRI ^{2,3}	1308 (38.3)	138 (24.1)	213 (31.6)	295 (40.8)	335 (48.4)	327 (43.5)
CT ²	655 (19.2)	27 (4.7)	61 (9.1)	67 (9.3)	178 (25.7)	322 (42.9)
PET-CT ²	158 (4.6)	-	1 (0.1)	6 (0.8)	36 (5.2)	115 (15.3)
CRAB symptoms⁴						
No	926 (27.0)	126 (23.0)	168 (25.1)	215 (29.4)	194 (27.0)	223 (29.3)
Yes	2502 (73.0)	422 (77.0)	502 (74.9)	516 (70.6)	524 (73.0)	538 (70.7)
CRAB components 0	926 (27.0)	126 (23.0)	168 (25.1)	215 (29.4)	194 (27.0)	223 (29.3)
1	1385 (40.4)	236 (43.1)	285 (42.5)	270 (36.9)	299 (41.6)	295 (38.8)
2	754 (22.0)	128 (23.4)	146 (21.8)	163 (22.3)	158 (22.0)	159 (20.9)
3	300 (8.8)	54 (9.9)	61 (9.1)	66 (9.0)	52 (7.2)	67 (8.8)
4	63 (1.8)	4 (0.7)	10 (1.5)	17 (2.3)	15 (2.1)	17 (2.2)
Not known	292	89	70	44	37	52
Hypercalcaemia						
No	2870 (88.4)	378 (90.6)	516 (88.8)	651 (88.1)	661 (90.2)	664 (85.6)
Calcium (mmol/l) Median (IQR)	2.41 (2.33 - 2.50)	2.39 (2.30 - 2.49)	2.42 (2.34 - 2.50)	2.40 (2.31 - 2.50)	2.40 (2.33 - 2.50)	2.43 (2.34 - 2.51)
Yes	376 (11.6)	39 (9.4)	65 (11.2)	88 (11.9)	72 (9.8)	112 (14.4)
Calcium (mmol/l) Median (IQR)	3.04 (2.87 - 3.39)	2.97 (2.85 - 3.39)	3.07 (2.90 - 3.35)	3.02 (2.85 - 3.26)	3.07 (2.86 - 3.42)	3.03 (2.87 - 3.44)
Not known	474	220	159	36	22	37
Renal insufficiency						
No	2992 (82.8)	501 (80.4)	586 (83.1)	611 (82.0)	620 (83.9)	674 (83.9)
Creatinine (µmol/l) median (IQR)	90.0	97.0	98.0	86.0	86.0	84.0

		Year of diagnosis					
		Total	2005-07	2008-10	2011-2013	2014-16	2017-19
Yes		(74.0-110.0)	(83.0-118.0)	(79.0-118.0)	(72.0-106.0)	(71.0-107.0)	(69.0-105.0)
		623 (17.2)	122 (19.6)	119 (16.9)	134 (18.0)	119 (16.1)	129 (16.1)
	Creatinine (μmo/l) median (IQR)	310.0	296.5	284.0	333.0	282.0	333.0
		(224.0-483.0)	(222.0-424.0)	(207.0-423.0)	(233.0-507.0)	(218.0-529.0)	(236.0-560.0)
Not known		105	14	35	30	16	10
Anaemia							
No		2402 (66.0)	407 (65.1)	464 (65.2)	492 (65.6)	498 (66.8)	541 (67.0)
	Haemoglobin (g/dl) median (IQR)	120.0	119.0	119.0	119.0	120.0	120.0
		(109.0 - 132.0)	(109.0 - 130.0)	(109.0 - 131.0)	(109.0 - 131.5)	(110.0 - 134.0)	(110.0 - 132.0)
Yes		1237 (34.0)	218 (34.9)	248 (34.8)	258 (34.4)	247 (33.2)	266 (33.0)
	Haemoglobin (g/dl) median (IQR)	87.0	87.0	87.0	89.0	87.0	87.0
		(80.0 - 94.0)	(81.0 - 94.0)	(78.5 - 94.5)	(82.0 - 94.0)	(78.0 - 93.0)	(79.0 - 93.0)
Not known		81	12	28	25	10	6
Bone Disease							
No		1627 (47.4)	297 (50.5)	321 (46.6)	341 (47.2)	300 (43.3)	368 (49.5)
Yes		1809 (52.6)	291 (49.5)	368 (53.4)	382 (52.8)	393 (56.7)	375 (50.5)
Not known		284	49	51	52	62	70

¹ At least one of: plain radiography, MRI, CT, PET-CT; ²Denominator= Skeletal imaging, Yes. Patients may have had more than one form of imaging; ³Whole spine or whole-body diffusion weighted MRI; ⁴Yes indicates at least one of the following: hypercalcaemia (serum calcium: >0.25 mmol/L higher than the upper limit of normal or >2.75 mmol/L), renal insufficiency (creatinine clearance <40 mL per min or serum creatinine >177 μmol/L), anaemia (haemoglobin >20 g/L below the lower limit of normal or haemoglobin <100 g/L) or bone disease one or more osteolytic lesions on skeletal radiography, CT, or PET-CT, No: all negative; Incomplete: none positive and at least one incomplete data

Supplementary Table 2: First-line management, autologous stem cell transplantation (ASCT), and clinical trial entry by age and year of diagnosis: Multiple myeloma, Haematological Malignancy Research Network

	Total	Year of diagnosis				
		2005-07	2008-10	2011-2013	2014-16	2017-19
All ages	3720 (100)	637 (100)	740 (100)	775 (100)	755 (100)	813 (100)
Chemotherapy	2429 (65.3)	414 (65.0)	460 (62.2)	498 (64.3)	502 (66.5)	555 (68.3)
ASCT – Yes ¹	505 (20.8)	80 (19.3)	92 (20.0)	99 (19.9)	117 (23.3)	117 (21.1)
Clinical trial – Yes ¹	455 (18.7)	112 (27.1)	17 (3.7)	216 (43.4)	106 (21.1)	4 (0.7)
Active monitoring ²	968 (26.0)	157 (24.6)	205 (27.7)	222 (28.6)	197 (26.1)	187 (23.0)
Median years (95% CI) on W&W ³	2.8 (2.5-3.3)	2.7 (1.9-3.6)	3.7 (2.6-4.4)	2.7 (2.0-3.3)	2.0 (1.6-2.5)	2.5 (1.5-NR ²)
Radiotherapy only	45 (1.2)	17 (2.7)	9 (1.2)	7 (0.9)	6 (0.8)	6 (0.7)
Supportive/palliative care only	278 (7.4)	49 (7.7)	65 (8.8)	48 (6.2)	50 (6.6)	65 (8.0)
<70	1515 (100.0)	261 (100.0)	277 (100.0)	297 (100.0)	322 (100.0)	358 (100.0)
Chemotherapy	1103 (72.8)	192 (73.6)	197 (71.1)	217 (73.1)	232 (72.0)	265 (74.0)
ASCT – Yes ¹	495 (44.9)	80 (41.7)	92 (46.7)	97 (44.7)	115 (49.6)	111 (41.9)
Clinical trial – Yes ¹	261 (23.7)	70 (36.5)	12 (6.1)	115 (53.0)	60 (25.9)	4 (1.5)
Active monitoring ²	347 (22.9)	59 (22.6)	69 (24.9)	73 (24.6)	74 (23.0)	72 (20.1)
Median years (95% CI) on W&W ³	4.0 (3.4-4.7)	4.1 (2.2-6.7)	4.2 (2.7-9.3)	4.1 (1.9-8.4)	3.6 (1.8-NR ³)	NR ³
Radiotherapy only	14 (0.9)	3 (1.1)	4 (1.4)	3 (1.0)	3 (0.9)	1 (0.3)
Supportive/palliative care only	51 (3.4)	7 (2.7)	7 (2.5)	4 (1.3)	13 (4.0)	20 (5.6)
70-79	1295 (100.0)	217 (100.0)	255 (100.0)	283 (100.0)	253 (100.0)	287 (100.0)
Chemotherapy	872 (67.3)	142 (65.4)	160 (62.7)	190 (67.1)	181 (71.5)	199 (69.3)
ASCT – Yes ¹	10 (1.1)	-	-	2 (1.1)	2 (1.1)	6 (3.0)
Clinical trial – Yes ¹	159 (18.2)	37 (26.1)	5 (3.1)	80 (42.1)	37 (20.4)	-
Active monitoring ²	333 (25.7)	48 (22.1)	72 (28.2)	82 (29.0)	61 (24.1)	70 (24.4)
Median years (95% CI) on W&W ³	2.7 (2.2- .0)	2.1 (1.5-3.9)	4.3 (2.2-5.8)	2.7 (1.7-4.4)	2.1 (1.6-2.6)	NR ³
Radiotherapy only	19 (1.5)	10 (4.6)	2 (0.8)	1 (0.4)	2 (0.8)	4 (1.4)
Supportive/palliative care only	72 (5.5)	17 (7.8)	22 (8.2)	10 (3.5)	9 (3.6)	14 (4.9)
≥80	910 (100.0)	159 (100.0)	208 (100.0)	195 (100.0)	180 (100.0)	168 (100.0)
Chemotherapy	454 (49.9)	80 (50.3)	103 (49.5)	91 (46.7)	89 (49.4)	91 (54.2)
ASCT – Yes ¹	-	-	-	-	-	-
Clinical trial – Yes ¹	35 (7.7)	5 (6.2)	-	21 (23.1)	9 (10.1)	-
Active monitoring ²	288 (31.6)	50 (31.4)	64 (30.8)	67 (34.4)	62 (34.4)	45 (26.8)
Median years (95% CI) on W&W ³	2.1 (1.8-2.6)	1.9 (1.5-3.0)	2.7 (1.7-4.0)	2.1 (1.5-2.7)	1.6 (1.4-2.1)	1.5 (1.5-NR ³)
Radiotherapy only	12 (1.3)	4 (2.5)	3 (1.4)	3 (1.5)	1 (0.6)	1 (0.6)
Supportive/palliative care only	155 (17.0)	25 (15.7)	37 (17.8)	34 (17.4)	28 (15.6)	31 (18.5)

¹ Denominator = patients receiving chemotherapy; Active monitoring = Watch and Wait (W&W); ³Time from diagnosis to start of chemotherapy or death, otherwise censoring at the last date of follow-up; ³ NR=not reached

Supplementary Table 3: First-line regimen of patients initially treated with chemotherapy by year of diagnosis: Multiple myeloma, Haematological Malignancy Research Network

	Total	Year				
		2005-07	2008-10	2011-13	2014-16	2017-19
Total	2429 (100)	414 (100.0)	460 (100.0)	498 (100.0)	502 (100.0)	555 (100.0)
Clinical trial - Yes¹	455 (18.7)	112 (27.1)	17 (3.7)	216 (43.4)	106 (21.1)	4 (0.7)
Autologous stem cell transplant - Yes	505 (20.8)	80 (19.3)	92 (20.0)	99 (19.9)	117 (23.3)	117 (21.1)
Oral thalidomide based	1013 (41.7)	95 (22.9)	355 (77.2)	282 (56.6)	195 (38.8)	86 (15.5)
CTD (Cyclophosphamide, Thalidomide, Dexamethasone)	357 (14.7)	58 (14.0)	158 (34.3)	92 (18.5)	46 (9.2)	3 (0.5)
CTD attenuated (Cyclophosphamide, Thalidomide, Dexamethasone)	522 (21.5)	31 (7.5)	150 (32.6)	170 (34.1)	124 (24.7)	47 (8.5)
MPT (Melphalan, Prednisolone, Thalidomide)	116 (4.8)	-	37 (8.0)	19 (3.8)	25 (5.0)	35 (6.3)
Thal/Dex (Thalidomide, Dexamethasone)	18 (0.7)	6 (1.4)	10 (2.2)	1 (0.2)	-	1 (0.2)
Parenteral chemotherapy based	122 (5.0)	99 (23.9)	10 (2.2)	5 (1.0)	4 (0.8)	4 (0.7)
PAD (Bortezomib, Doxorubicin, Dexamethasone)	15 (0.6)	-	3 (0.7)	5 (1.0)	4 (0.8)	3 (0.5)
VAD (Vincristine, Doxorubicin, Dexamethasone)	24 (1.0)	22 (5.3)	1 (0.2)	-	-	1 (0.2)
CVAD (Cyclophosphamide, Vincristine, Doxorubicin, Dexamethasone)	83 (3.4)	77 (18.6)	6 (1.3)	-	-	-
Bortezomib based	733 (30.2)	-	3 (0.7)	67 (13.5)	220 (43.8)	443 (79.8)
VCD (Bortezomib, Cyclophosphamide, Dexamethasone)	401 (16.5)	-	-	25 (5.0)	142 (28.3)	234 (42.2)
VMP (Bortezomib, Melphalan, Prednisolone)	41 (1.7)	-	1 (0.2)	6 (1.2)	6 (1.2)	28 (5.0)
Vel/Dex (Bortezomib, Dexamethasone)	123 (5.1)	-	2 (0.4)	36 (7.2)	36 (7.2)	49 (8.8)
VTD (Bortezomib, Thalidomide, Dexamethasone)	168 (6.9)	-	-	-	36 (7.2)	132 (23.8)
Lenalidomide based	178 (7.3)	-	7 (1.5)	110 (22.1)	46 (9.2)	15 (2.7)
RCD (Lenalidomide, Cyclophosphamide, Dexamethasone)	68 (2.8)	-	4 (0.9)	50 (10.0)	14 (2.8)	-
RCD attenuated (Lenalidomide, Cyclophosphamide, Dexamethasone)	93 (3.8)	-	3 (0.7)	60 (12.0)	30 (6.0)	-
REV/DEX (Lenalidomide, Dexamethasone)	16 (0.7)	-	-	-	2 (0.4)	14 (2.5)
VRd (Bortezomib, Lenalidomide, Dexamethasone)	1 (0.0)	-	-	-	-	1 (0.2)
Clinical trial only regimens	32 (1.3)	-	-	-	29 (5.8)	3 (0.5)
CCRD (Carfilzomib, Cyclophosphamide, Lenalidomide, Dexamethasone)	27 (1.1)	-	-	-	27 (5.4)	-
CarCyDex (Carfilzomib, Cyclophosphamide, Dexamethasone)	3 (0.1)	-	-	-	-	3 (0.5)
DRd (Daratumumab, Lenalidomide, Dexamethasone)	2 (0.1)	-	-	-	2 (0.4)	-
Oral chemotherapy based	351 (14.5)	220 (53.1)	85 (18.5)	34 (6.8)	8 (1.6)	4 (0.7)
Melphalan +/- steroids	264 (10.9)	186 (44.9)	54 (11.7)	17 (3.4)	4 (0.8)	3 (0.5)
Cyclophosphamide +/- steroids	81 (3.3)	29 (7.0)	30 (6.5)	17 (3.4)	4 (0.8)	1 (0.2)
C-Z-Dex	6 (0.2)	5 (1.2)	1 (0.2)	-	-	-

¹ Myeloma XI (n=333), Myeloma IX (n=105), MERIT (n=9), Cardamon (n=3), MAIA (n=3), EuLITE (n=2), MUK9b (n=1), PADIMAC (n=1)