
Article:
Cook, G orcid.org/0000-0003-0223-3652, Ashcroft, AJ, Cairns, DA orcid.org/0000-0002-2338-0179 et al. (16 more authors) (2016) The effect of salvage autologous stem-cell transplantation on overall survival in patients with relapsed multiple myeloma (final results from BSBMT/UKMF Myeloma X Relapse [Intensive]): a randomised, open-label, phase 3 trial. The Lancet Haematology, 3 (7). e340-e351.

https://doi.org/10.1016/S2352-3026(16)30049-7

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1 Collaborators

In addition to the authors, the following investigators participated in the study:

Recruiting centre	Principal Investigator	Number of participants registered
Nottingham University Hospital	Dr Cathy Williams	30
University College London Hospital	Dr Kwee Yong	17
Royal Hallamshire Hospital	Dr John Snowden	14
Leeds Teaching Hospitals	Prof Gordon Cook	14
Derriford Hospital	Dr Hannah Hunter	11
Christie Hospital	Dr Jim Cavet	10
St. Bartholomew's Hospital	Dr Heather Oakervee	10
Bristol Haematology & Oncology Centre	Dr Jenny Bird	9
Birmingham Heartlands Hospital	Dr Guy Pratt	8
Gloucestershire Royal Hospital	Dr Sally Chown	8
Glan Clwyd	Dr Earnest Heartin	7
Manchester Royal Infirmary	Dr Eleni Tholouli	7
Addenbrookes Hospital	Dr Jenny Craig	7
Ipswich Hospital	Dr A J Ademokun	7
Royal Derby Hospital	Dr David Allotey	7
Castle Hill Hospital	Dr Haz Sayala	7
Medway Maritime Hospital	Dr Vivienne Andrews	6
Southampton University Hospital	Dr Matthew Jenner	6
Guy's & St Thomas' NHS Foundation Trust	Dr Majid Kazmi	5
Frenchay Hospital	Dr Alastair Whiteway	5
Singleton Hospital	Dr Hamdi Sati	5
Kings College Hospital	Prof Steve Schey	5
Leicester Royal Infirmary	Dr Claire Chapman	5
James Cook Hospital	Dr Angela Wood	4
St Helier & Epsom Hospitals	Dr Simon Stern	4
Queen Elizabeth Hospital, Birmingham	Dr Mark Cook	4
Aberdeen Royal Infirmary	Dr Jane Tighe	4
Colchester Hospital	Dr Gavin Campbell	4
Rotherham General Hospital	Dr Helen Barker	4
Beatson West of Scotland Cancer Centre	Dr Grant McQuaker	4
Belfast City Hospital	Dr Mary Drake	4
Ysbyty Gwynedd	Dr Melinda Hamilton	3
Stafford Hospital	Dr Paul Revell	3
Royal Berkshire NHS Foundation Trust	Dr Henri Grech	3
Chesterfield Royal Hospital	Dr Emma Welch	3
Doncaster Royal Infirmary	Dr Youssef Sorour	3
St Georges Hospital	Dr Fenella Willis	3
Ninewells Hospital	Dr Duncan Gowans	2
Bradford Royal Infirmary	Dr Samuel Ackroyd	2
Crosshouse and Ayr Hospitals	Dr Julie Gillies	2
Norfolk & Norwich Hospital	Dr Martin Auger	2
Diana Princess of Wales Hospital	Dr Susan Levison-Keating	2
Raigmore Hospital	Dr Peter Forsyth	2
Royal Devon & Exeter Hospital	Dr Malcolm Hamilton	2
Sandwell & West Birmingham Hospitals	Dr Farooq Wandroo	2
University Hospital Coventry	Dr Syed Bokhari	2
University Hospital of Wales, Cardiff	Dr Keith Wilson	2
Dorset County Hospital	Dr Akeel Moosa	2
Queens Hospital, Burton	Dr Hamayun Ahmed	2
Torbay Hospital	Dr Deborah Turner	2
Cheltenham General Hospital	Dr Sally Chown	1
The Great Western Hospital, Swindon	Dr Norbert Blesing	1
United Lincolnshire Hospitals	Dr Kandeepan Saravanamuttu	1
Peterborough District Hospital	Dr S Kumar Nagumantry	1

Salisbury Hospital	Dr Jonathan Cullis	1
Mid Yorkshire Hospitals NHS Trust	Dr John Ashcroft	1
Russells Hall Hospital	Dr Savio Fernandes	1
Countess of Chester Hospital	Dr Salaheddin Tueger	1
Royal Oldham Hospital	Dr Vivek Sen	1
Warwick Hospital	Dr Anton Borg	1
Royal Bournemouth Hospital	Dr Helen McCarthy	1

2 Appendix Figures

Figure 1: Trial CONSORT flow diagram.

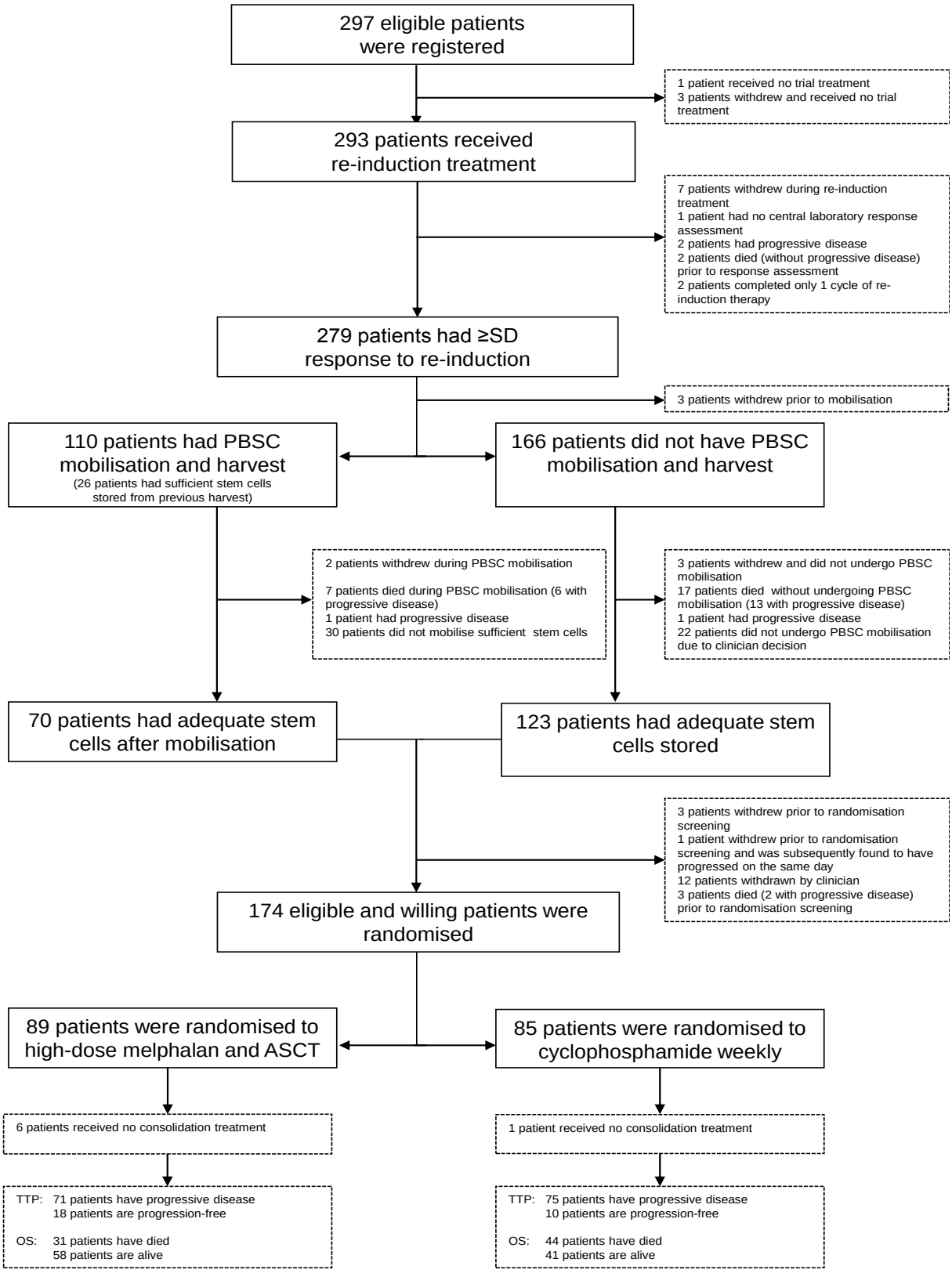
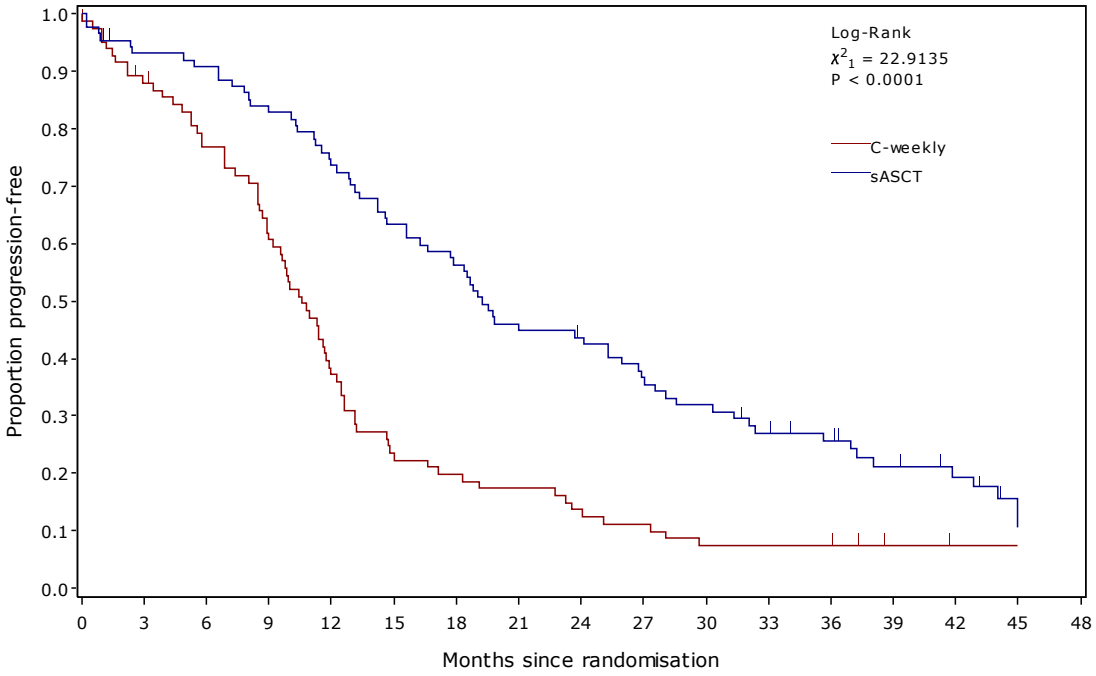
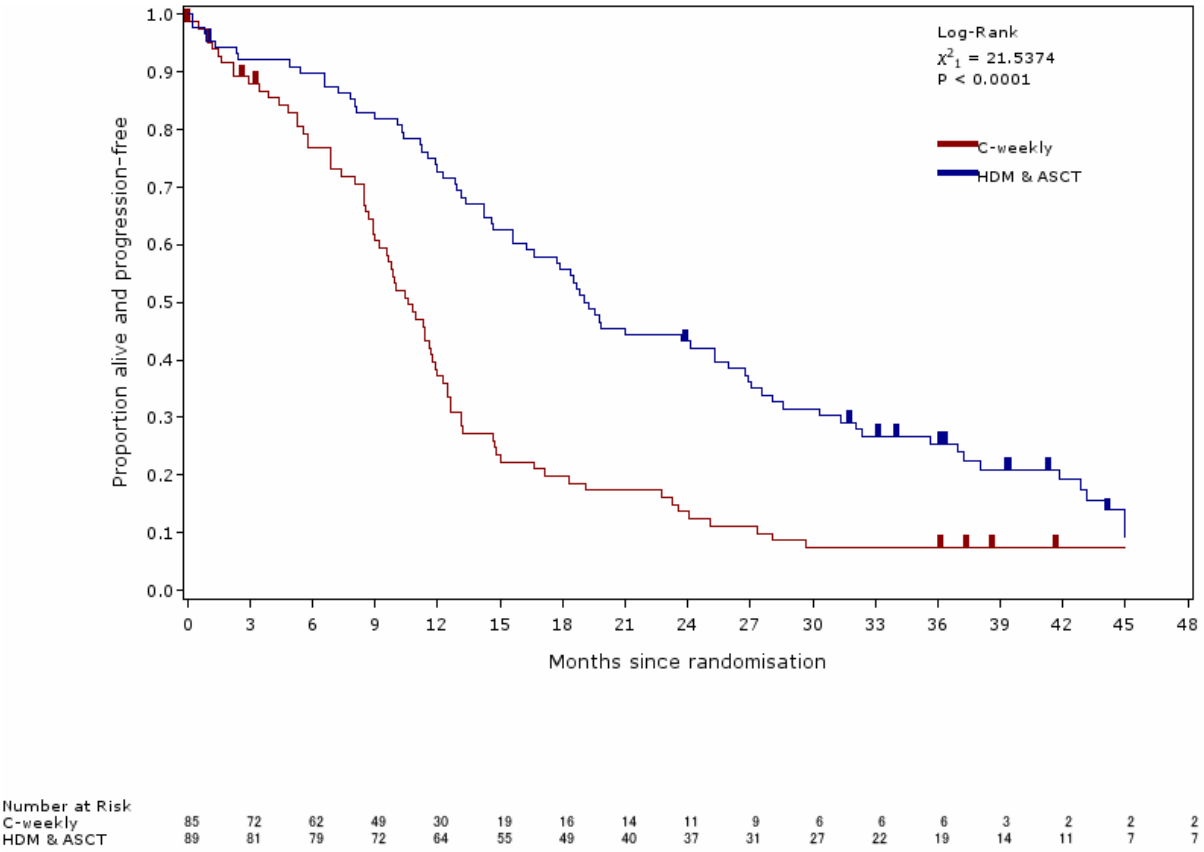


Figure 2: TTP (updated analysis of the trial primary endpoint)



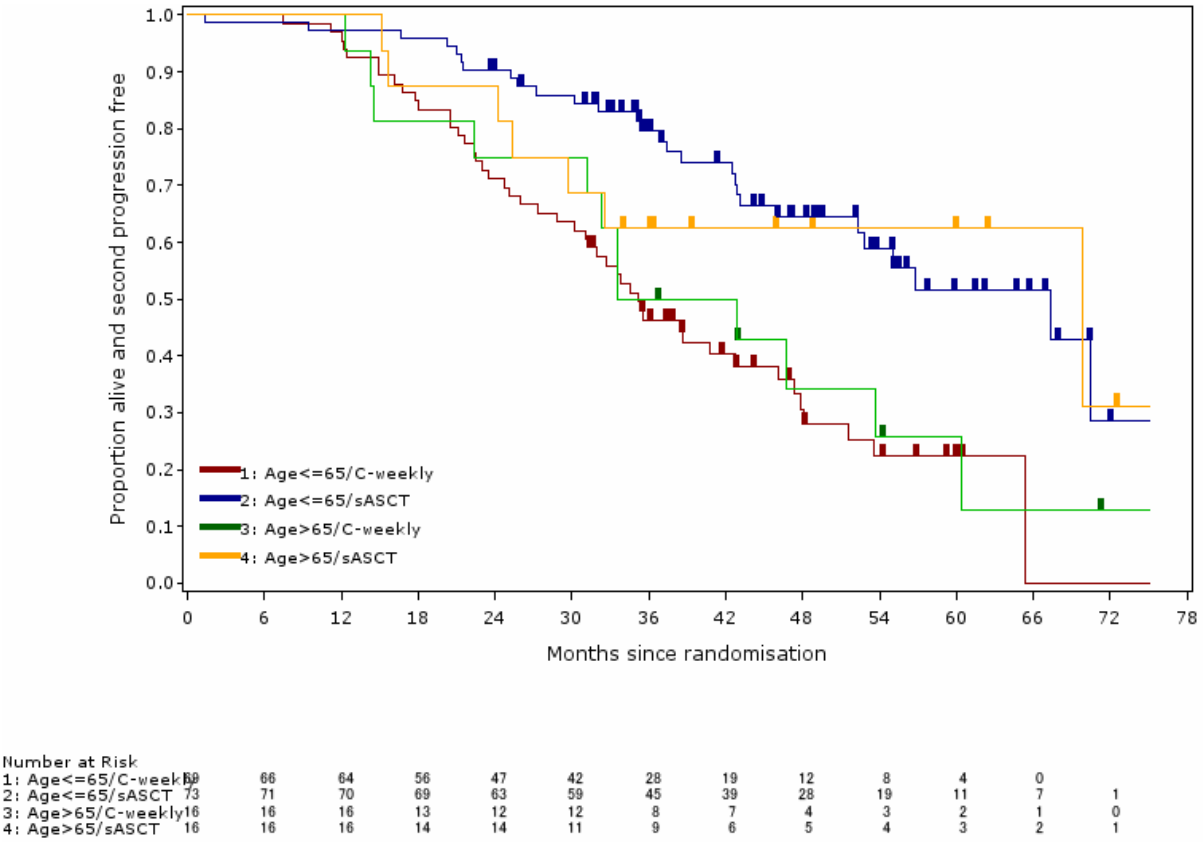
Number at Risk																	
C-weekly	85	72	62	49	30	19	16	14	11	9	6	6	6	3	2	2	2
sASCT	89	81	79	72	64	55	49	40	37	31	27	22	19	14	11	7	7

Figure 3: PFS (updated analysis of the trial secondary endpoint)



Number at Risk																	
C-weekly	85	72	62	49	30	19	16	14	11	9	6	6	6	3	2	2	2
HDM & ASCT	89	81	79	72	64	55	49	40	37	31	27	22	19	14	11	7	7

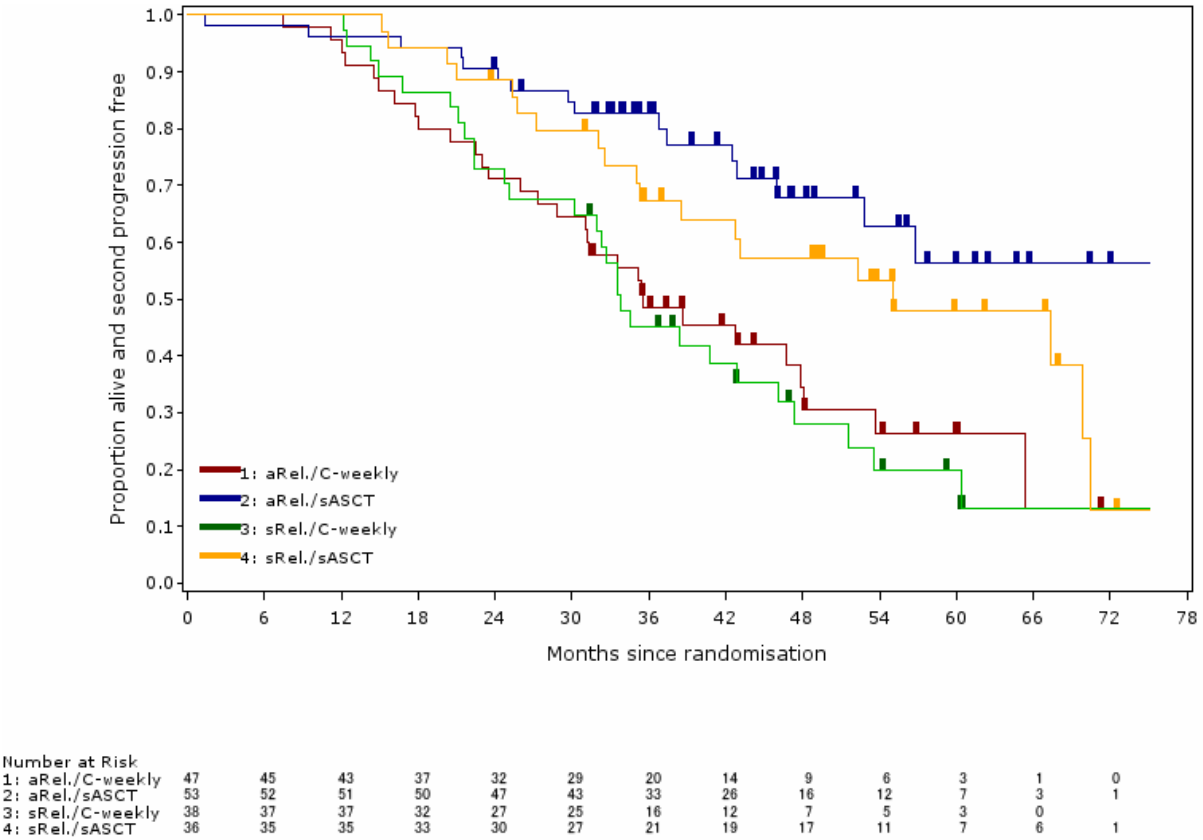
Figure 3: The impact of age on PFS2



Number at Risk

1: Age<=65/C-weekly	89	66	64	56	47	42	28	19	12	8	4	0	
2: Age<=65/sASCT	73	71	70	69	63	59	45	39	28	19	11	7	1
3: Age>65/C-weekly	16	16	16	13	12	12	8	7	4	3	2	1	0
4: Age>65/sASCT	16	16	16	14	14	11	9	6	5	4	3	2	1

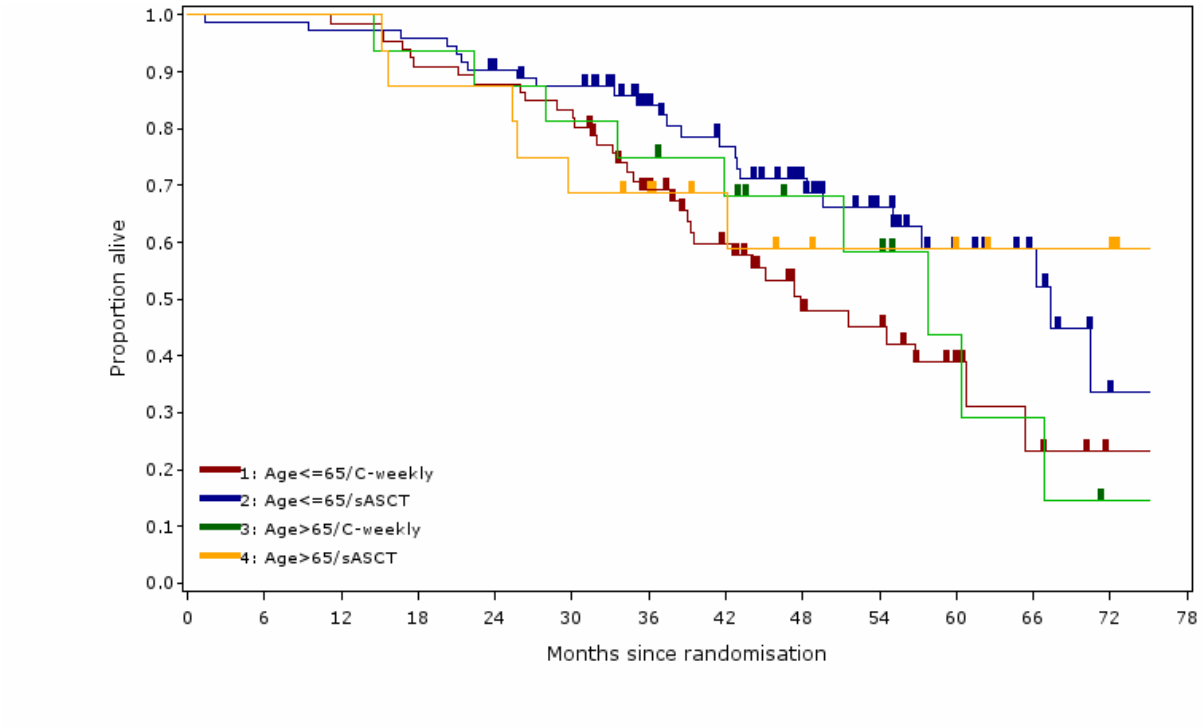
Figure 4: The impact of biochemical vs symptomatic relapse on PFS2



Number at Risk

1: aRel./C-weekly	47	45	43	37	32	29	20	14	9	6	3	1	0
2: aRel./sASCT	53	52	51	50	47	43	33	26	16	12	7	3	1
3: sRel./C-weekly	38	37	37	32	27	25	16	12	7	5	3	0	
4: sRel./sASCT	36	35	35	33	30	27	21	19	17	11	7	6	1

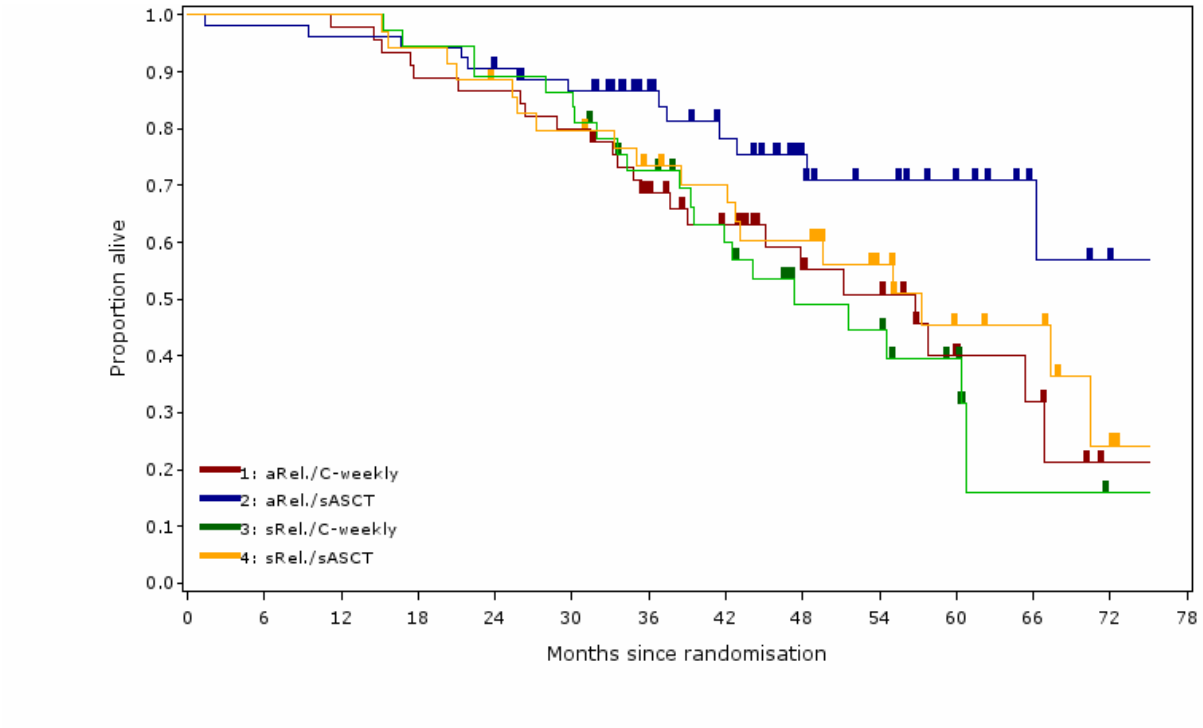
Figure 5: The impact of age on OS



Number at Risk

1: Age<=65/C-weekly	89	66	65	60	58	55	41	30	18	16	9	3	0
2: Age<=65/sASCT	73	71	70	69	63	60	48	41	30	21	13	9	2
3: Age>65/C-weekly	16	16	16	15	14	13	12	10	7	6	3	2	0
4: Age>65/sASCT	16	16	16	14	14	11	10	7	5	4	3	2	2

Figure 6: The impact of biochemical vs. symptomatic relapse on OS



Number at Risk

1: aRel./C-weekly	47	45	44	40	39	36	28	21	14	12	6	4	0
2: aRel./sASCT	53	52	51	50	47	44	35	27	17	13	9	5	2
3: sRel./C-weekly	38	37	37	35	33	32	25	19	11	10	6	1	0
4: sRel./sASCT	36	35	35	33	30	27	23	21	18	12	7	6	2

3 Appendix Tables

Table 1: response to PAD with corresponding 95% confidence intervals for patients in the all registered patients ITT population

	Total (n=297)
Overall response (PAD)	
sCR or CR	49 (16.5%) (12.46 to 21.22)
- sCR	23 (7.7%) (4.97 to 11.39)
- CR	26 (8.8%) (5.80 to 12.56)
VGPR or PR	186 (62.6%) (56.85 to 68.15)
- VGPR	62 (20.9%) (16.40 to 25.95)
- PR	124 (41.8%) (36.08 to 47.59)
SD	44 (14.8%) (10.98 to 19.37)
Progressive disease	2 (0.7%) (0.08 to 2.41)
Early death	2 (0.7%) (0.08 to 2.41)
Missing	10 (3.4%) (1.63 to 6.10)
Patient did not receive any PAD treatment	4 (1.3%) (0.37 to 3.41)

Early death is defined as death between registration and up to and including 21 days post date last PAD cycle started

Table 2: overall response rate following randomised treatments: response following randomised treatments with corresponding 95% confidence intervals for the ITT population

	High-dose melphalan and ASCT (n=89)	Cyclophosphamide weekly (n=85)	Difference
Overall response (randomised treatments)			
sCR or CR	35 (39.3%) (29.13 to 50.25)	19 (22.4%) (14.03 to 32.69)	17.0% (1.88 to 31.24)
- sCR	20 (22.5%) (14.30 to 32.55)	11 (12.9%) (6.64 to 21.98)	9.5% (-5.26 to 24.28)
- CR	15 (16.9%) (9.75 to 26.27)	8 (9.4%) (4.15 to 17.71)	7.4% (-7.51 to 22.18)
VGPR or PR	39 (43.8%) (33.32 to 54.75)	45 (52.9%) (41.81 to 63.87)	-9.1% (-23.87 to 5.99)
- VGPR	18 (20.2%) (12.45 to 30.07)	21 (24.7%) (15.99 to 35.25)	-4.5% (-19.30 to 10.55)
- PR	21 (23.6%) (15.24 to 33.78)	24 (28.2%) (19.00 to 39.04)	-4.6% (-19.54 to 10.33)
SD	4 (4.5%) (1.24 to 11.11)	2 (2.4%) (0.29 to 8.24)	2.1% (-12.89 to 16.96)
Progressive disease	2 (2.2%) (0.27 to 7.88)	15 (17.6%) (10.23 to 27.43)	-15.4% (-29.92 to -0.52)
Early death	1 (1.1%) (0.03 to 6.10)	0 (0.0%) (0.00 to 4.25)	1.1% (-13.86 to 16.05)
Missing	2 (2.2%) (0.27 to 7.88)	3 (3.5%) (0.73 to 9.97)	-1.3% (-16.25 to 13.61)
Patient did not receive any consolidation treatment	6 (6.7%) (2.51 to 14.10)	1 (1.2%) (0.03 to 6.38)	5.6% (-9.51 to 20.29)

Early death is defined as death between randomisation and up to and including 100 days post-randomisation

Table 3: Fine-Gray Competing risks regression analysis for randomised treatment accounting for the stratification factors and whether or not PBSC mobilization and harvest was given.

Parameter	DF	Estimate	Hazard Ratio Estimate (HR)	95% CI for HR	Test Statistic	p-value
Randomisation treatment	1				23.19	<.0001
High Dose Melphalan and ASCT vs. C-weekly	1	-0.86	0.42	[0.30, 0.60]		
Previous treatment response length	2				28.73	<.0001
18 - 24 months vs. > 24 months	1	0.61	1.84	[1.29, 2.63]	11.20	0.0008
<18 months vs. > 24 months	1	1.68	5.38	[2.72, 10.64]	23.33	<.0001
Response to PAD treatment	1				4.45	0.0349
SD vs. More than PR (PR, VGPR, CR or sCR)	1	0.90	2.45	[1.07, 5.64]		
PBSC mobilization and harvest given	2				3.53	0.1715
Missing Data vs. No	1	0.25	1.29	[0.78, 2.12]	1.00	0.3185
Yes vs. No	1	-0.24	0.79	[0.54, 1.15]	1.52	0.2180