

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: James ND, de Bono JS, Spears MR, et al. Abiraterone for prostate cancer not previously treated with hormone therapy. *N Engl J Med*. DOI: 10.1056/NEJMoa1702900

Abiraterone acetate with prednisolone for hormone-naïve prostate cancer: First survival results from the STAMPEDE randomized controlled trial (MRC PR08, CRUK/06/019)

== SUPPLEMENTARY MATERIALS ==

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Previous: Reg Hall, , Chris Williams

Trial Steering Committee

Current: Jonathan Ledermann, Jan Erik Dember, David Kirk, Jim Paul

Previous: John Fitzpatrick,

PARTICIPATING SITE (N1|N2|N3: site PI; other investigators)

Key

N1	Recruited and in comparison
N2	Recruitment while comparison recruited
N3	Recruited to data freeze
PI	Principle Investigator

United Kingdom

- **Aberystwyth, Bronglais General Hospital** (4|4|4: Porfiri; Durrani)
- **Ashford William Harvey Hospital** (1|4|19: Thomas; Mithal)
- **Aylesbury, Stoke Mandeville Hospital** (5|5|14: Sabharwal; Camilleri)
- **Ayr Hospital** (10|20|54: Glen; Ansari)
- **Barnet General Hospital** (11|13|25: McGovern; Eichholz)
- **Basingstoke & N Hampshire Hospital** (3|5|21: Shaffer)
- **Bath, Royal united Hospital** (18|26|70: Frim; Beresford)
- **Belfast City** (48|72|191: O'Sullivan; Mitchell, Stewart, Shum)
- **Birmingham, City Hospital** (10|13|26: Sivoglo; Ford)
- **Birmingham, Good Hope Hospital** (5|10|18: Ford)
- **Birmingham, Heartlands Hospital** (8|14|38: Zarkar)
- **Birmingham, QE** (33|48|180: James; Porfiri, Ford)
- **Blackburn East Lancashire Trust** (34|48|180: Parikh; Charnley)
- **Bolton, Royal Bolton Hospital** (6|8|30: Elliott)
- **Boston, Pilgrim Hospital** (8|8|38: Sreenivasan; Panades)
- **Bournemouth, Royal Bournemouth Hospital** (22|28|100: Brock)
- **Bradford Royal Infirmary** (6|11|36: Brown)
- **Brighton, Royal Sussex County Hospital** (21|31|92: Robinson; Robinson, Bloomfield)
- **Bristol H & O Centre** (22|32|106: Bahl; Herbert, Masson)
- **Burton, Queen's Hospital** (21|28|108: Smith-Howell; Chetiyawardana, Pattu)
- **Bury St Edmunds, West Suffolk Hospital** (3|7|21: Woodward)
- **Cardiff, Velindre** (64|99|341: Lester; Staffurth, Barber, Kumar, Palaniappan, Button, Tanguay)
- **Chelmsford, Broomfield Hospital** (21|28|88: Hamid; Panwar, Leone)
- **Cheltenham General Hospital** (5|6|54: Bowen)
- **Chester, Countess of Chester Hospital** (31|41|79: Ibrahim)
- **Coventry & Warwickshire, University Hospital** (11|15|40: Worliding; Stockdale)
- **Crewe, Leighton Hospital** (18|20|54: Wylie)
- **Cumbria, Cumberland Infirmary** (4|6|18: Kumar)
- **Darlington Memorial Hospital** (9|18|49: Kagzi; Hardman, Peedell)
- **Derby, Royal Derby Hospital** (35|44|130: Chakraborti; Pattu)

- **Devon, North Devon District Hospital** (5|15|33: Sheehan)
- **Doncaster Royal Infirmary** (5|10|35: Bowen; Ferguson)
- **Dorset County Hospital** (9|13|30: Crellin; Afzal, Andrews)
- **Dudley, Russells Hall Hospital** (17|22|81: Keng-Koh; Ramachandra)
- **Durham University Hospital** (2|3|17: Heath; McMenemin)
- **Eastbourne District General Hospital** (16|23|63: McKinna)
- **Edinburgh, Western General** (16|28|112: McLaren)
- **Essex County Hospital** (18|22|58: Muthukumar; Sizer, Kumar)
- **Exeter, RD&E** (29|45|189: Sheehan; Srinivasan)
- **Gillingham, Medway Hospital** (8|11|29: Kumar; Taylor)
- **Glasgow, BOC** (62|95|323: Graham; Venugopal, Wallace, Jones, Lamb, Glen, Russell)
- **Guildford, Royal Surrey County Hospital** (26|44|132: Laing; Khaksar, Wood, Money-Kyrle)
- **Harlow, Princess Alexandra Hospital** (7|10|54: Gupta; Melcher, Melcher)
- **Hereford County Hospital** (12|19|71: Grant; Cook)
- **Huddersfield Royal Infirmary** (21|29|105: Hofmann)
- **Hull, Castle Hill Hospital** (20|33|119: Simms; Hetherington)
- **Inverness, Raigmore Hospital** (28|41|88: McPhail; MacGregor)
- **Ipswich Hospital** (21|32|103: Brierly; Venkitaraman, Scrase)
- **Keighley, Airedale Hospital** (15|22|52: Brown; Crawford)
- **Kent and Canterbury Hospital** (27|35|79: Thomas; Raman, Mithal, Malde)
- **Kent, QE Q Mother Hospital** (5|9|27: Thomas; Raman)
- **Kidderminster General Hospital** (6|10|40: Capaldi; Churn)
- **Larbert, Forth Valley Royal Hospital** (8|13|36: Sidek)
- **Leeds, St James University Hospital** (17|24|94: Cross; Loughrey, Bottomley, Prescott)
- **Lincoln County Hospital** (18|21|50: Sreenivasan; Ballesteros-Quintail, Panades, Baria)
- **Liverpool, Royal Liv University Hospital** (30|40|88: Malik; Robson, Eswar)
- **Liverpool, UH Aintree** (8|9|26: Robson)
- **London, Charing Cross Hospital** (11|13|38: Falconer; Mangar)
- **London, Guy's Hospital** (44|66|161: Chowdhury)
- **London, Hammersmith Hospital** (2|4|4: Falconer; Mangar)
- **London, N Middlesex Hospital** (6|10|24: Gupta; Newby, Thompson)
- **London, Royal Free Hospital** (10|15|44: Vilarino-Varela; Pigott)
- **London, St Georges Hospital** (7|10|35: Pickering)
- **London, St Mary's Hospital** (2|2|8: Falconer; Stewart)
- **London, UCH** (13|17|46: McGovern)
- **Maidstone, Kent Oncology Centre** (17|26|114: Beesley)
- **Manchester Christie Hospital** (27|38|167: Clarke; Elliot, Livsey, Choudhury, Wylie)
- **Manchester Hope Hospital** (12|17|59: Clarke; Elliot)
- **Manchester, Royal Oldham Hospital** (17|25|54: Conroy; Livsey, Choudhury)
- **Manchester, Withington Hospital** (1|2|7: Sangar)
- **Middlesbrough, James Cook UH** (20|31|103: Peedell; Van der Voet, Hardman, Shakespeare)
- **Newcastle, Freeman Hospital** (16|17|92: Azzabi; McMenemin, Frew)
- **North Staffordshire UH** (33|43|80: Adab)
- **Northwood, Mount Vernon Hospital** (22|36|126: Hoskin; Anyamene, Ostler, Alonzi)
- **Nottingham University Hospitals (City Campus)** (20|31|141: Sundar; Mills)
- **Nuneaton, George Eliot Hospital** (7|7|14: Khan; Chan)
- **Oxford, Churchill Hospital** (36|48|165: Protheroe; Cole, Sabharwal, Sugden)
- **Poole Hospital** (18|23|62: Davies)
- **Portsmouth, Q Alexandra Hospital** (49|72|173: Gale)
- **Preston, Royal Preston Hospital** (59|74|221: Birtle; Parikh, Wise)

- **Reading, Royal Berkshire Hospital** (8|11|42: Rogers; O'Donnell, Brown, Brown)
- **Redditch, Alexandra Hospital** (5|6|15: Capaldi; Hamilton)
- **Romford, Queen's Hospital** (23|32|127: Gibbs; Subramaniam)
- **Scarborough General Hospital** (28|35|82: Hingorani)
- **Sheffield, Weston Park** (19|28|142: Ferguson)
- **Shrewsbury, Royal Shrewsbury Hospital** (36|47|192: Srihari)
- **Somerset, Weston General Hospital** (6|9|18: Hilman)
- **Southampton General Hospital** (18|24|75: Jones; Heath, Wheeler, Crabb)
- **Southend University Hospital** (23|31|114: Tsang; Ahmed, Chan)
- **Southport and Formby District GH** (15|18|46: Bhalla; Sivapalasantharam, Sivapalasantharam)
- **St Leonards-on-Sea, Conquest Hospital** (11|20|42: McKinna; Beesley, Lees)
- **Stevenage, Lister Hospital** (10|18|35: Hughes)
- **Stockport, Stepping Hill Hospital** (23|32|106: Logue; Coyle, Coyle)
- **Stockton-on-Tees, UH North Tees** (3|5|28: Leaning; Shakespeare)
- **Sunderland Royal Hospital** (1|2|45: Azzabi)
- **Sutton-in-Ashford, King's Mill Hospital** (15|22|64: Saunders)
- **Sutton-London, RMH** (29|42|162: Dearnaley; Parker, Selvadurai)
- **Swansea, Singleton** (36|57|188: Wagstaff; Phan, Phan)
- **Swindon, Great Western Hospital** (15|22|52: Khan; Cole)
- **Taunton, Musgrove Park Hospital** (30|45|137: Gray; Graham, Varughese, Plataniotis)
- **Torbay District General Hospital** (28|38|135: Lydon; Srinivasan)
- **Tyne & Wear, S Tyneside District Hospital** (1|2|6: Azzabi)
- **Warrington Hospital** (24|33|111: Syndikus; Tolan)
- **Warwick Hospital** (5|5|17: Chan; Stockdale)
- **Wigan, Royal Albert Edward Infirmary** (6|12|37: Tran)
- **Wirral, Clatterbridge Centre for Oncology** (39|55|128: Tolan; Syndikus, Ibrahim, Montazeri, Littler)
- **Wolverhampton, New Cross Hospital** (3|3|53: Gray; Sayers)
- **Woolwich, QE Hospital** (8|11|18: Hughes)
- **Worcestershire Royal Hospital** (8|12|57: Capaldi; Bowen)
- **Worthing Hospital** (20|28|90: Nikapota)
- **Wycombe Hospital** (6|10|52: Sabharwal; Protheroe, Pwint)

Switzerland

- **Basel Universitatsspital** (1|1|5: Rentsch)
- **Berne University Hospital (Inselspital)** (1|1|5: Thalmann)
- **Chur Kantonsspital Graubunden** (5|9|31: Strebel; Cathomas)
- **Kantonsspital St Gallen** (2|2|10: Engeler)
- **Lausanne, Centre Hospital Univ Vaudois** (4|5|7: Berthold; Jichlinski)

Plus all of the local team staff at all of these sites.

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Swiss Group for Cancer Clinical Research

- **Project and Trial Managers** – Corinne Schar, Estelle Cassolly

AUTHOR CONTRIBUTIONS

Name	Initial	Conceived the original MAMS idea	Designed this comparison	Was a grant holder	Collected or collated data	Performed or oversaw statistical analyses	Interpreted data	Wrote critical sections of the report	Reviewed and agreed the report
James, Nick	NDJ		x	x	x		x	x	x
de Bono, Johann	JSdB		x	x	x		x	x	x
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Clarke, Noel	NWC		x	x	x		x	x	x
Mason, Malcolm	MDM		x	x	x		x	x	x
Dearnaley, David	DPD		x		x		x	x	x
Ritchie, Alastair W S	AWSR		x		x		x	x	x
Amos, Claire	CLA		x		x		x		x
Gilson, Clare	CEG				x		x		x
Jones, Rob	RJJ				x		x		x
Matheson, David	DM				x		x		x
Millman, Robin	RMM				x		x		x
Attard, Gerhardt	GA				x		x		x
Chowdhury, Simon	SC				x		x		x
Cross, Bill	WRC				x		x		x
Gillessen, Silke	SG				x		x		x
Parker, Chris	CCP				x		x		x
Russell, Martin	JMR		x		x		x		x
Berthold, Dominik	DB				x		x		x
Brawley, Chris	CB				x	x	x	x	x
Adab, Fawzi	FA				x		x		x
Aung, San	SA				x		x		x
Birtle, Alison	AB				x		x		x
Bowen, Jo	JB				x		x		x
Brock, Sue	SB				x		x		x
Chakraborti, Prabir	PC				x		x		x
Ferguson, Catherine	CF				x		x		x
Gale, Joanna	JG				x		x		x
Gray, Emma	EG				x		x		x
Hingorani, Mohan	MH				x		x		x
Hoskin, Peter	PH				x		x		x
Lester, Jason	JL				x		x		x
Malik, Zafar	ZM				x		x		x
McKinna, Fiona	FM				x		x		x
McPhail, Neil	NM				x		x		x
Money-Kyrle, Julian	JM				x		x		x
O'Sullivan, Joe	JO				x		x		x
Parik, Omi	OP				x		x		x
Protheroe, Andrew	AP				x		x		x
Robinson, Angus	AR				x		x		x
Srihari, Narayanan	NS				x		x		x
Thomas, Carys	CT				x		x		x
Wagstaff, John	JW				x		x		x
Wylie, James	JW				x		x		x
Zarkar, Anjali	AZ				x		x		x
Parmar, Max	MKBP	x	x	x	x	x	x	x	x
Sydes, Matt	MRSy		x	x	x	x	x	x	x

SUPPLEMENTARY FIGURES

Figure S1: Enrolment and Randomization of Patients for the Analysis of Overall Survival

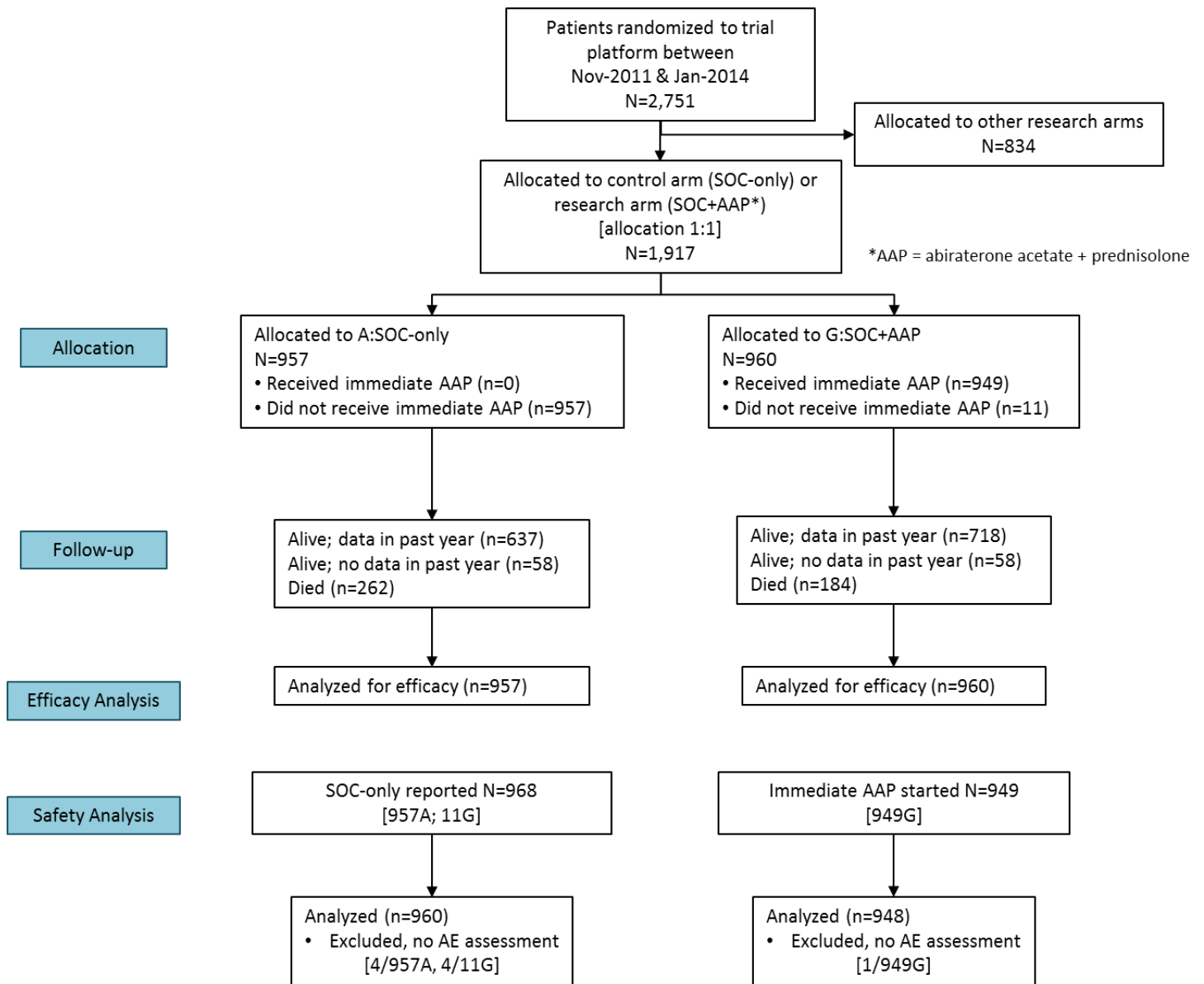
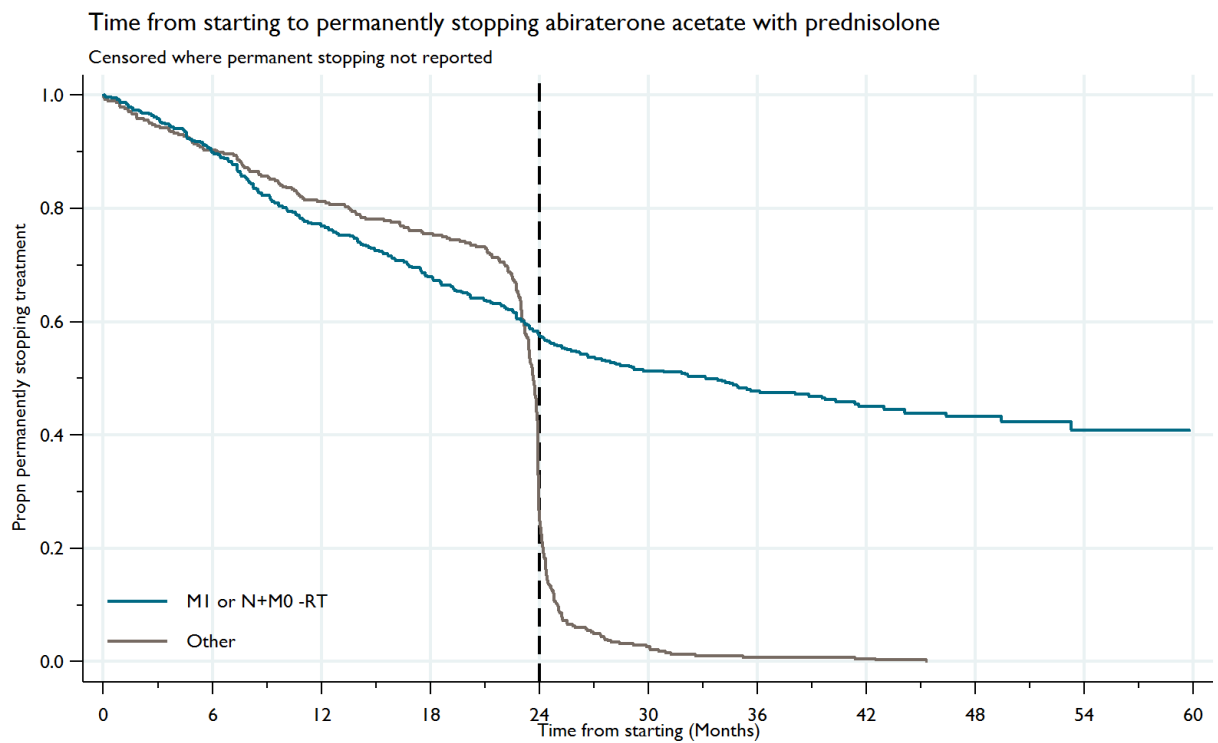


Figure S2: Time on abiraterone acetate with prednisolone



	Number of patients (events)																				
MI or N+M0 -RT	565	(57)	502	(72)	428	(50)	376	(57)	316	(34)	262	(17)	177	(8)	90	(3)	54	(2)	17	(0)	1
Other	384	(37)	347	(35)	312	(22)	290	(188)	102	(92)	10	(7)	3	(1)	2	(2)	0	(0)	0	(0)	0

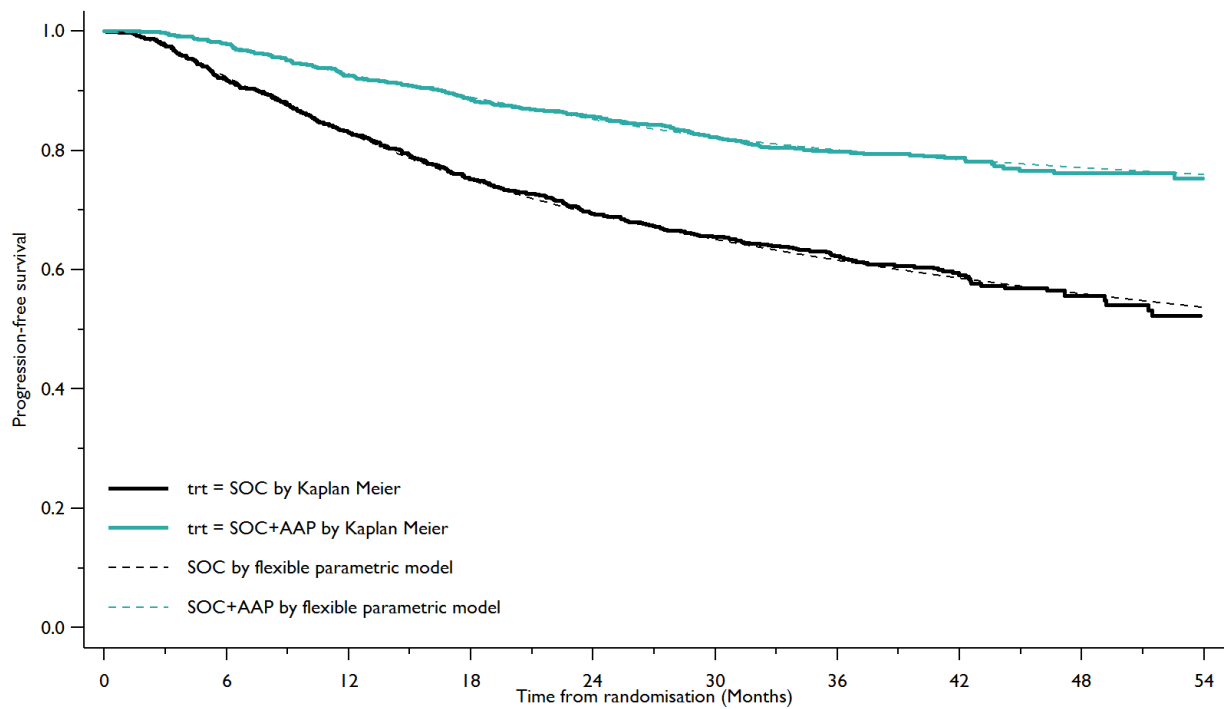
Key:

M1 = Patients with metastatic disease at randomisation

N+M0 -RT = Patients with node positive, non-metastatic disease at randomisation who did not receive radiotherapy

Other = Patients with either node negative, non-metastatic disease at randomisation, or with node positive, non-metastatic disease who received radiotherapy

Figure S3: Time to first Progression-Free Survival Event



Number of patients (events)

SOC	957	(161)	783	(128)	641	(60)	392	(24)	91
SOC+AAP	960	(71)	870	(63)	781	(51)	504	(12)	149

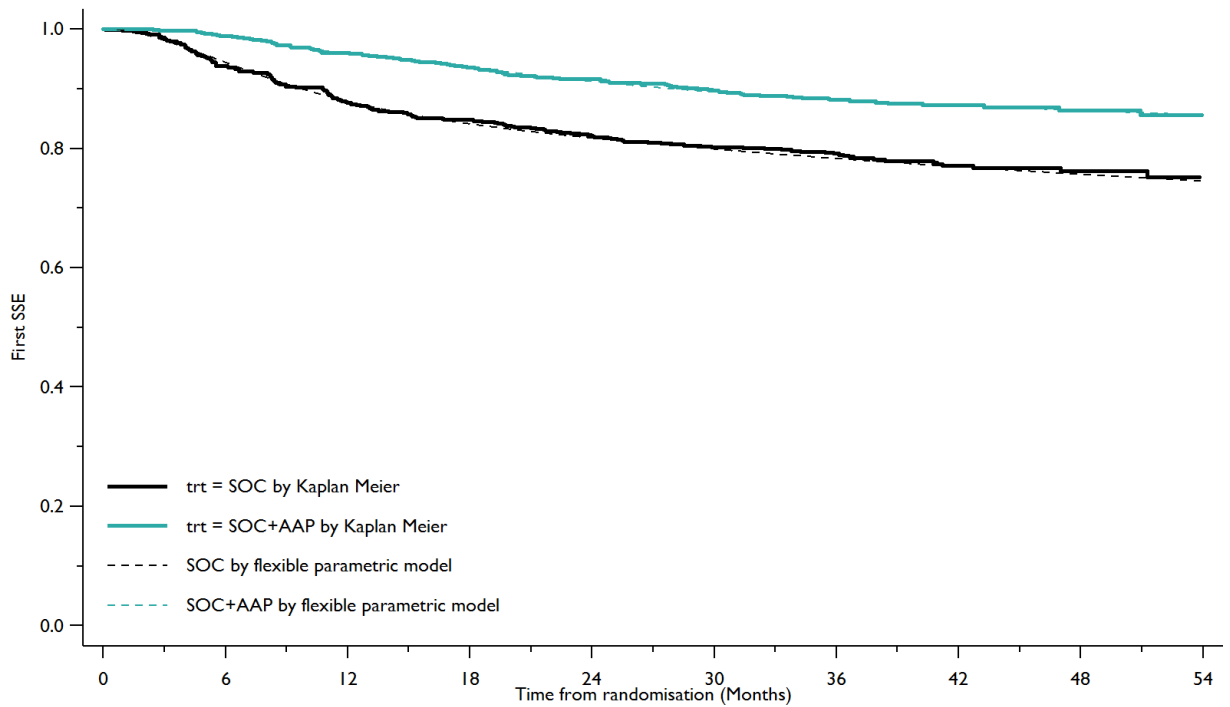
HR 0.40 (95%CI 0.34-0.47; p<0.001)

Key:

SOC = standard-of-care

AAP = abiraterone acetate + prednisolone

Figure S4A: Time to first Symptomatic Skeletal Event



Number of patients (events)

SOC	957	(59)	885	(58)	820	(26)	770	(24)	721	(17)	651	(7)	449	(9)	222	(2)	106	(1)	41
SOC+AAP	960	(11)	936	(27)	894	(22)	848	(17)	805	(17)	732	(12)	517	(4)	286	(2)	154	(1)	49

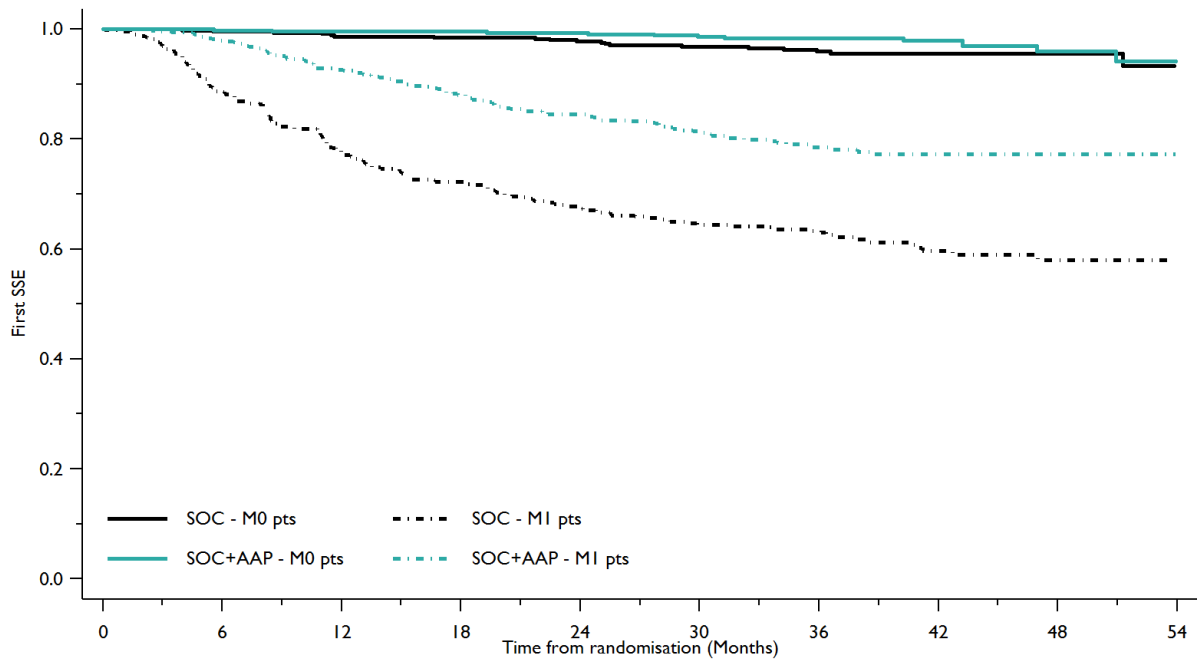
HR 0.46 (95%CI 0.37-0.58; p<0.001)

Key:

SOC = standard-of-care

AAP = abiraterone acetate + prednisolone

Figure S4B: Time to first Symptomatic Skeletal Event by baseline metastasis



	Number of patients (events)																		
SOC - M0 pts	455	(2)	449	(4)	443	(1)	440	(3)	430	(4)	388	(3)	267	(1)	129	(0)	59	(1)	23
SOC+AAP - M0 pts	460	(1)	454	(1)	446	(0)	437	(1)	424	(3)	397	(1)	283	(1)	151	(2)	78	(1)	22
SOC - M1 pts	502	(57)	436	(54)	377	(25)	330	(21)	291	(13)	263	(4)	182	(8)	93	(2)	47	(0)	18
SOC+AAP - M1 pts	500	(10)	482	(26)	448	(22)	411	(16)	381	(14)	335	(11)	234	(3)	135	(0)	76	(0)	27

M0 patients: HR 0.56 (95%CI 0.27-1.18)

M1 patients: HR 0.45 (95%CI 0.36-0.58)

Key:

SOC = standard-of-care

AAP = abiraterone acetate + prednisolone

M0 = non-metastatic patients

M1 = metastatic patients

SUPPLEMENTARY TABLES

Table S1: Full Characteristics of All Patients in the Comparison

		SOC (n=957)	SOC+AAP (n=960)
Age at randomization (years)	Median (IQR)	67 (62-72)	67 (63-72)
	Range	39-84	42-85
PSA pre-ADT (ng/ml)	Median (IQR)	56 (19-165)	51 (19-158)
	Range	0-10530	0-21460
Time from diagnosis (Days)	Median (IQR)	77 (57-101)	79 (57-100)
	Range	0-4866	1-5384
	Missing	2	6
Pain from prostate cancer	Absent	836 (88%)	814 (86%)
	Present	114 (12%)	131 (14%)
	Missing	7	15
WHO Performance Status	0	744 (78%)	745 (78%)
	1-2	213 (22%)	215 (22%)
T-category at randomization	T0	4 (<1%)	3 (<1%)
	T1	13 (1%)	7 (1%)
	T2	78 (8%)	71 (7%)
	T3	642 (67%)	663 (69%)
	T4	176 (18%)	167 (17%)
	TX	44 (5%)	49 (5%)
N-category at randomization	N0	438 (46%)	434 (45%)
	N+	483 (50%)	484 (50%)
	NX	36 (4%)	42 (4%)
Metastases at randomization	None	455 (48%)	460 (48%)
	Any metastases	502 (52%)	500 (52%)
	<i>Bone metastases</i>	448 (47%)	434 (45%)
	<i>Liver metastases</i>	8 (1%)	7 (1%)
	<i>Lung metastases</i>	21 (2%)	21 (2%)
	<i>Nodal metastases</i>	150 (16%)	142 (15%)
	<i>Other metastases</i>	26 (3%)	23 (2%)

		SOC (n=957)	SOC+AAP (n=960)
Broad disease grouping			
	Newly-diagnosed NOM0	256 (27%)	253 (26%)
	Newly-diagnosed N+M0	187 (20%)	182 (19%)
	Newly-diagnosed M1	476 (50%)	465 (48%)
	Previously treated M0	12 (1%)	25 (3%)
	Previously treated M1	26 (3%)	35 (4%)
Gleason sum score			
	<=7	223 (23%)	221 (23%)
	8-10	721 (75%)	715 (74%)
	Unknown	13 (1%)	24 (3%)
Aspirin or NSAID use			
	No	718 (75%)	714 (74%)
	Yes	239 (25%)	246 (26%)
Planned or current long-term ADT			
	Orchidectomy	5 (1%)	3 (<1%)
	Bicalutamide	5 (1%)	5 (1%)
	Dual Androgen Blockade	4 (<1%)	1 (<1%)
	LHRH-based	943 (99%)	951 (99%)
Time to starting ADT from randomization (Days)			
	Median (IQR)	-45 (-67; -23)	-44 (-63; -24)
	Range	-85; 39	-85; 28
	Missing	1	0
Planned anti-androgen use			
	No	50 (5%)	61 (6%)
	Short-term anti-androgen	902 (94%)	895 (93%)
	Long-term anti-androgen	5 (1%)	4 (<1%)
	Missing	0	0
Radiotherapy planned			
	No	561 (59%)	564 (59%)
	Yes	396 (41%)	396 (41%)
Smoker			
	No	829 (88%)	821 (86%)
	Yes	118 (12%)	129 (14%)
	Missing on cardiovascular assessment	9	8
	Cardiovascular assessment not received	1	2

		SOC (n=957)	SOC+AAP (n=960)
Diabetes			
	No	848 (89%)	844 (88%)
	Yes, type 1	34 (4%)	36 (4%)
	Yes, type 2	74 (8%)	78 (8%)
	<i>Missing on cardiovascular assessment</i>	0	0
	<i>Cardiovascular assessment not received</i>	1	2
Myocardial infarction			
	No	912 (95%)	915 (96%)
	Yes, but still fit for trial	44 (5%)	43 (4%)
	<i>Missing on cardiovascular assessment</i>	0	0
	<i>Cardiovascular assessment not received</i>	1	2
Cerebrovascular disease			
	No	941 (98%)	932 (97%)
	Yes, but still fit for trial	15 (2%)	26 (3%)
	<i>Missing on cardiovascular assessment</i>	0	0
	<i>Cardiovascular assessment not received</i>	1	2
Congestive heart failure			
	No	954 (100%)	954 (100%)
	Yes, but still fit for trial	2 (<1%)	4 (<1%)
	<i>Missing on cardiovascular assessment</i>	0	0
	<i>Cardiovascular assessment not received</i>	1	2
Angina			
	No	920 (96%)	924 (96%)
	Yes, but still fit for trial	36 (4%)	34 (4%)
	<i>Missing on cardiovascular assessment</i>	0	0
	<i>Cardiovascular assessment not received</i>	1	2
Hypertension			
	No	571 (60%)	557 (58%)
	Yes, but still fit for trial	385 (40%)	401 (42%)
	<i>Missing on cardiovascular assessment</i>	0	0
	<i>Cardiovascular assessment not received</i>	1	2

Key:

SOC = standard-of-care

AAP = abiraterone acetate + prednisolone

Table S2: Study-Drug Exposure in the Abiraterone Acetate with Prednisolone (AAP) Arm

		G	
		<i>SOC+AAP</i>	
		(n=960)	
Numbers not starting allocated AAP		11 (1%)	
Numbers starting allocated AAP		949 (99%)	
Time from randomization to starting AAP (Weeks); median (IQR)		1.3 (0.7-2.6)	
Time from starting ADT to starting AAP (Weeks); median (IQR)		8.0 (5.0-10.9)	
Time from starting to last administration* (Months); median (IQR)		23.9 (14.9-46.4)	
Breakdown by treatment duration group:			
		M1 or N+M0 -RT	Other**
Total number who started		565	384
Numbers permanently stopping		300	384
Time from starting to last administration* (Months); median (IQR)		33.2 (13.8-NR)	23.7 (18.7-24.0)
Main reasons for stopping AAP:			
Treatment complete		15 (5%)	259 (67%)
Progression		154 (51%)	5 (1%)
Excessive toxicity		61 (20%)	65 (17%)

*Only in patients starting treatment; censored where permanent stopping not reported

**NOM0 or N+M0 receiving RT; duration capped at 24m

Table S3: Summary of relapse therapies

Treatment started since first progression	A SOC	G SOC+AAP
Patients randomized	957	960
Patients with progression	535 (56%)	248 (26%)
Reported new treatment	477 (89%)	196 (79%)
Reported “life-prolonging” treatment	310 (58%)	131 (53%)
Docetaxel	200 (37%)	115 (46%)
Enzalutamide	138 (26%)	25 (10%)
Abiraterone acetate	120 (22%)	8 (3%)
Cabazitaxel	28 (5%)	15 (6%)
Radium-223	24 (4%)	19 (8%)
Other treatments		
Anti-androgens	387 (72%)	83 (33%)
Dexamethasone	113 (21%)	52 (21%)
Zoledronic acid	78 (15%)	40 (16%)
Prednisolone	83 (16%)	33 (13%)
Stilboestrol	14 (3%)	8 (3%)
Other chemotherapy	10 (2%)	11 (4%)
Other bisphosphonate	9 (2%)	4 (2%)
Sr89	2 (<1%)	0 (0%)
Cox-2 inhibition	0 (0%)	1 (<1%)

Key:

SOC = standard-of-care

AAP = abiraterone acetate + prednisolone

The following tables provide a detailed breakdown of worst adverse event (AE) reported over entire time on trial, by treatment received (safety population)

Table S4: Worst AE grade within each category ever (by treatment arm) – Part 1

	A SOC		G SOC+AAP	
	N	%	N	%
Hypersensitivity				
0	926	97%	910	96%
1	26	3%	32	3%
2	6	1%	4	0%
3	0	0%	2	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Blood/bone marrow				
0	587	62%	482	51%
1	324	34%	422	45%
2	27	3%	26	3%
3	11	1%	13	1%
4	4	0%	5	1%
5	0	0%	0	0%
Missing	7	n/a	0	n/a
Cardiovascular disorder				
0	753	78%	541	57%
1	104	11%	190	20%
2	62	6%	125	13%
3	34	4%	80	8%
4	5	1%	12	1%
5	2	0%	0	0%
Missing	0	n/a	0	n/a
Gastrointestinal disorder				
0	445	46%	308	32%
1	347	36%	416	44%
2	126	13%	175	18%
3	34	4%	46	5%
4	6	1%	2	0%
5	0	0%	1	0%
Missing	2	n/a	0	n/a
Endocrine disorder				
0	108	11%	84	9%
1	432	45%	398	42%
2	284	30%	337	36%
3	133	14%	129	14%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	3	n/a	0	n/a
Total	960	100%	948	100%

Blood/bone marrow AEs shown in more detail in Table S8

Cardiovascular disorder AEs shown in more detail in Tables S9-S11

Gastrointestinal disorder AEs shown in more detail in Tables S12-S14

Endocrine disorder AEs shown in more detail in Table S15

Table S5: Worst AE grade within each category ever (by treatment arm) – Part 2

	A SOC		G SOC+AAP	
	N	%	N	%
General disorder				
0	335	35%	221	23%
1	442	46%	446	47%
2	154	16%	236	25%
3	22	2%	36	4%
4	7	1%	8	1%
5	0	0%	1	0%
Missing	0	n/a	0	n/a
Hepatic disorder				
0	781	82%	631	67%
1	144	15%	188	20%
2	17	2%	59	6%
3	11	1%	65	7%
4	1	0%	5	1%
5	0	0%	0	0%
Missing	6	n/a	0	n/a
Lab abnormalities				
0	628	66%	462	49%
1	270	28%	392	41%
2	35	4%	60	6%
3	19	2%	30	3%
4	2	0%	4	0%
5	0	0%	0	0%
Missing	6	n/a	0	n/a
Metabolic & Nutritional				
0	796	83%	782	82%
1	146	15%	139	15%
2	13	1%	22	2%
3	4	0%	5	1%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	1	n/a	0	n/a
Musculoskeletal				
0	309	32%	266	28%
1	417	43%	388	41%
2	187	19%	226	24%
3	44	5%	68	7%
4	2	0%	0	0%
5	0	0%	0	0%
Missing	1	n/a	0	n/a

General disorder AEs shown in more detail in Tables S16-S17

Hepatic disorder AEs shown in more detail in Tables S18-S19

Lab abnormalities AEs shown in more detail in Table S20

Metabolic & nutritional AEs shown in more detail in Table S21

Musculoskeletal AEs shown in more detail in Tables S22-S23

Table S6: Worst AE grade within each category ever (by treatment arm) – Part 3

	A SOC		G SOC+AAP	
	N	%	N	%
Nervous system				
0	705	74%	582	61%
1	200	21%	262	28%
2	35	4%	72	8%
3	15	2%	26	3%
4	3	0%	4	0%
5	0	0%	2	0%
Missing	2	n/a	0	n/a
Ocular disorder				
0	881	92%	816	86%
1	63	7%	105	11%
2	9	1%	10	1%
3	5	1%	17	2%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Psychiatric disorder				
0	631	66%	547	58%
1	246	26%	277	29%
2	71	7%	100	11%
3	10	1%	23	2%
4	0	0%	1	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Renal disorder				
0	284	30%	268	28%
1	381	40%	373	39%
2	263	27%	271	29%
3	28	3%	31	3%
4	3	0%	5	1%
5	0	0%	0	0%
Missing	1	n/a	0	n/a
Respiratory disorder				
0	642	67%	487	51%
1	162	17%	218	23%
2	132	14%	199	21%
3	19	2%	37	4%
4	3	0%	2	0%
5	1	0%	5	1%
Missing	1	n/a	0	n/a
Total	960	100%	948	100%

Nervous system AEs shown in more detail in Table S24

Ocular disorder AEs shown in more detail in Table S25

Psychiatric disorder AEs shown in more detail in Table S26

Renal disorder AEs shown in more detail in Tables S27-S28

Respiratory disorder AEs shown in more detail in Tables S29-S30

Table S7: Worst AE grade within each category ever (by treatment arm) – Part 4

	A SOC		G SOC+AAP	
	N	%	N	%
Skin disorder				
0	731	76%	624	66%
1	178	19%	242	26%
2	41	4%	65	7%
3	8	1%	16	2%
4	0	0%	1	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Total	960	100%	948	100%

Skin disorder AEs shown in more detail in
Table S31

Table S8: Worst blood/bone marrow grade within each category ever (by treatment arm)

	A SOC-only		G SOC+AAP	
	N	%	N	%
Neutropenia (G1-4)				
0	913	96%	875	92%
1	35	4%	58	6%
2	3	0%	5	1%
3	1	0%	8	1%
4	1	0%	2	0%
5	0	0%	0	0%
Missing	7	n/a	0	n/a
Febrile neutropenia (G3-5)				
0	951	100%	944	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	2	0%	4	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	7	n/a	0	n/a
Decreased platelet count (G1-4)				
0	917	96%	897	95%
1	33	3%	45	5%
2	3	0%	4	0%
3	0	0%	1	0%
4	0	0%	1	0%
5	0	0%	0	0%
Missing	7	n/a	0	n/a
Anaemia				
0	618	65%	521	55%
1	301	32%	395	42%
2	22	2%	25	3%
3	9	1%	5	1%
4	3	0%	2	0%
5	0	0%	0	0%
Missing	7	n/a	0	n/a
Total	960	100%	948	100%

Table S9: Worst cardiac disorder grade within each category ever (by treatment arm) – Part 1

	A <i>SOC-only</i>		G <i>SOC+AAP</i>	
	N	%	N	%
Cardiac dysrhythmia				
0	921	96%	893	94%
1	24	3%	27	3%
2	12	1%	14	1%
3	2	0%	12	1%
4	0	0%	2	0%
5	0	0%	0	0%
<i>Missing</i>	<i>1</i>	<i>n/a</i>	<i>0</i>	<i>n/a</i>
Hypertension				
0	828	86%	649	68%
1	71	7%	152	16%
2	47	5%	103	11%
3	13	1%	44	5%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	<i>1</i>	<i>n/a</i>	<i>0</i>	<i>n/a</i>
Hypotension				
0	939	98%	905	95%
1	13	1%	33	3%
2	5	1%	9	1%
3	2	0%	1	0%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	<i>1</i>	<i>n/a</i>	<i>0</i>	<i>n/a</i>
Acute coronary syndrome incl. MI				
0	950	99%	934	99%
1	0	0%	4	0%
2	0	0%	0	0%
3	3	0%	5	1%
4	4	0%	5	1%
5	2	0%	0	0%
<i>Missing</i>	<i>1</i>	<i>n/a</i>	<i>0</i>	<i>n/a</i>
Heart failure				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	<i>629</i>	<i>n/a</i>	<i>489</i>	<i>n/a</i>
Total	960	100%	948	100%

Table S10: Worst cardiac disorder grade within each category ever (by treatment arm) – Part 2

	A <i>SOC-only</i>		G <i>SOC+AAP</i>	
	N	%	N	%
Stroke				
0	330	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	1	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	629	<i>n/a</i>	489	<i>n/a</i>
TIA (G1-2)				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	629	<i>n/a</i>	489	<i>n/a</i>
Thromboembolic event				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	629	<i>n/a</i>	489	<i>n/a</i>
Other cardiac disorder				
0	902	94%	849	90%
1	29	3%	49	5%
2	11	1%	17	2%
3	17	2%	28	3%
4	1	0%	5	1%
5	0	0%	0	0%
<i>Missing</i>	0	<i>n/a</i>	0	<i>n/a</i>
Total	960	100%	948	100%

Table S11: Worst hypertension toxicity reported ever, split by hypertensive status at baseline (by treatment arm)

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Non-hypertensive	0	518	91%	380	69%
	1	27	5%	88	16%
	2	21	4%	67	12%
	3	6	1%	17	3%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	1	<i>n/a</i>	0	<i>n/a</i>
Hypertensive	0	310	80%	269	68%
	1	44	11%	63	16%
	2	25	6%	36	9%
	3	7	2%	27	7%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	1	<i>n/a</i>	0	<i>n/a</i>
<i>Missing hypertensive status</i>	1	<i>n/a</i>	1	<i>n/a</i>	
Total		960	100%	948	100%

Table S12: Worst gastrointestinal disorder grade within each category ever (by treatment arm) – Part 1

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Abdominal pain (G1-3)	0	834	87%	771	81%
	1	89	9%	134	14%
	2	27	3%	34	4%
	3	8	1%	9	1%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Constipation	0	740	77%	660	70%
	1	173	18%	238	25%
	2	36	4%	45	5%
	3	9	1%	5	1%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Diarrhoea	0	714	75%	653	69%
	1	194	20%	229	24%
	2	42	4%	53	6%
	3	8	1%	13	1%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Indigestion (Dyspepsia; G1-3)	0	859	90%	793	84%
	1	85	9%	129	14%
	2	14	1%	25	3%
	3	0	0%	1	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Flatulence (G1-2)	0	827	86%	807	85%
	1	104	11%	119	13%
	2	27	3%	22	2%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Total		960	100%	948	100%

Table S13: Worst ever gastrointestinal disorder grade (by treatment arm) – Part 2

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
GI haemorrhage (CTCAE V3)					
	0	887	93%	879	93%
	1	51	5%	57	6%
	2	14	1%	12	1%
	3	5	1%	0	0%
	4	1	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Upper GI haemorrhage					
	0	331	100%	459	100%
	1	0	0%	0	0%
	2	0	0%	0	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	629	<i>n/a</i>	489	<i>n/a</i>
Lower GI haemorrhage					
	0	331	100%	459	100%
	1	0	0%	0	0%
	2	0	0%	1	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	629	<i>n/a</i>	489	<i>n/a</i>
Nausea (G1-3)					
	0	866	90%	797	84%
	1	81	8%	132	14%
	2	10	1%	18	2%
	3	1	0%	1	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Vomiting					
	0	919	96%	863	91%
	1	34	4%	63	7%
	2	3	0%	18	2%
	3	1	0%	4	0%
	4	1	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Total		960	100%	948	100%

Table S14: Worst ever gastrointestinal disorder grade (by treatment arm) – Part 3

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Mucositis (Stomatitis)	0	938	98%	915	97%
	1	19	2%	27	3%
	2	1	0%	5	1%
	3	0	0%	1	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Other gastrointestinal disorder	0	804	84%	730	77%
	1	111	12%	154	16%
	2	27	3%	39	4%
	3	12	1%	22	2%
	4	4	0%	2	0%
	5	0	0%	1	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Total		960	100%	948	100%

Table S15: Worst endocrine disorder grade within each category ever (by treatment arm)

	A <i>SOC-only</i>		G <i>SOC+AAP</i>	
	N	%	N	%
Hot flashes (G1-3)				
0	145	15%	116	12%
1	510	53%	496	52%
2	263	27%	295	31%
3	39	4%	41	4%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	3	<i>n/a</i>	0	<i>n/a</i>
Impotence (G1-3)				
0	455	48%	428	45%
1	262	28%	262	28%
2	128	13%	160	17%
3	105	11%	97	10%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	10	<i>n/a</i>	1	<i>n/a</i>
Gynaecomastia (G1-3)				
0	756	86%	795	86%
1	118	13%	124	13%
2	9	1%	4	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	77	<i>n/a</i>	25	<i>n/a</i>
Glucose intolerance				
0	828	94%	823	89%
1	28	3%	56	6%
2	23	3%	38	4%
3	2	0%	6	1%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	79	<i>n/a</i>	25	<i>n/a</i>
Other endocrine disorder				
0	916	96%	914	96%
1	26	3%	30	3%
2	13	1%	3	0%
3	1	0%	1	0%
4	0	0%	0	0%
5	0	0%	0	0%
<i>Missing</i>	4	<i>n/a</i>	0	<i>n/a</i>
Total	960	100%	948	100%

Table S16: Worst general disorder grade within each category ever (by treatment arm) – Part 1

	A SOC-only		G SOC+AAP	
	N	%	N	%
Fever				
0	932	97%	907	96%
1	22	2%	30	3%
2	2	0%	9	1%
3	2	0%	2	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Flu-like symptoms (G1-3)				
0	901	94%	844	89%
1	49	5%	90	9%
2	8	1%	12	1%
3	0	0%	2	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Oral candidiasis (CTCAE V3)				
0	953	99%	927	98%
1	4	0%	11	1%
2	1	0%	9	1%
3	0	0%	1	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Fatigue (G1-3)				
0	408	43%	300	32%
1	400	42%	424	45%
2	136	14%	203	21%
3	15	2%	21	2%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	1	n/a	0	n/a
Falls (G1-3)				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	629	n/a	489	n/a
Total	960	100%	948	100%

Table S17: Worst general disorder grade within each category ever (by treatment arm) – Part 2

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Oedema (G1-3)	0	812	85%	738	78%
	1	134	14%	176	19%
	2	12	1%	29	3%
	3	0	0%	5	1%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Other general disorder	0	881	92%	823	87%
	1	51	5%	71	7%
	2	13	1%	32	3%
	3	6	1%	13	1%
	4	7	1%	8	1%
	5	0	0%	1	0%
	Missing	2	n/a	0	n/a
Total		960	100%	948	100%

Table S18: Worst hepatic disorder grade within each category ever (by treatment arm) – Part 1

	A SOC-only		G SOC+AAP	
	N	%	N	%
Abnormal hepatic function (CTCAE V3)				
0	902	95%	835	88%
1	42	4%	75	8%
2	7	1%	21	2%
3	2	0%	15	2%
4	1	0%	2	0%
5	0	0%	0	0%
Missing	6	n/a	0	n/a
Bilirubin increase (G1-4)				
0	952	100%	939	99%
1	0	0%	0	0%
2	0	0%	0	0%
3	2	0%	9	1%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	6	n/a	0	n/a
Increased AST (G1-4)				
0	924	97%	879	93%
1	26	3%	45	5%
2	1	0%	14	1%
3	2	0%	9	1%
4	0	0%	1	0%
5	0	0%	0	0%
Missing	7	n/a	0	n/a
Increased ALT (G1-4)				
0	828	87%	710	75%
1	112	12%	142	15%
2	10	1%	43	5%
3	4	0%	50	5%
4	0	0%	3	0%
5	0	0%	0	0%
Missing	6	n/a	0	n/a
Hypoalbuminaemia				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	629	n/a	489	n/a
Total	960	100%	948	100%

Table S19: Worst hepatic disorder grade within each category ever (by treatment arm) – Part 2

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Other hepatic disorder	0	927	97%	901	95%
	1	21	2%	38	4%
	2	4	0%	5	1%
	3	2	0%	4	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	6	n/a	0	n/a
Total		960	100%	948	100%

Table S20: Worst lab abnormalities grade within each category ever (by treatment arm)

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Hypocalcaemia	0	925	97%	892	94%
	1	27	3%	54	6%
	2	2	0%	2	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	6	n/a	0	n/a
Hypokalaemia	0	932	98%	832	88%
	1	19	2%	104	11%
	2	2	0%	11	1%
	3	0	0%	0	0%
	4	1	0%	1	0%
	5	0	0%	0	0%
	Missing	6	n/a	0	n/a
Elevated ALP (G1-4)	0	331	100%	459	100%
	1	0	0%	0	0%
	2	0	0%	0	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	629	n/a	489	n/a
Hypophosphataemia (CTCAE V3)	0	937	98%	903	95%
	1	14	1%	31	3%
	2	3	0%	13	1%
	3	0	0%	0	0%
	4	0	0%	1	0%
	5	0	0%	0	0%
	Missing	6	n/a	0	n/a
Other lab abnormalities	0	650	68%	546	58%
	1	253	27%	331	35%
	2	33	3%	50	5%
	3	17	2%	19	2%
	4	1	0%	2	0%
	5	0	0%	0	0%
	Missing	6	n/a	0	n/a
Total		960	100%	948	100%

Table S21: Worst metabolic & nutritional grade within each category ever (by treatment arm)

	A SOC-only		G SOC+only	
	N	%	N	%
Anorexia				
0	895	93%	860	91%
1	54	6%	72	8%
2	7	1%	13	1%
3	3	0%	3	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	1	n/a	0	n/a
Weight gain (G1-3)				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	629	n/a	489	n/a
High cholesterol (G1-4)				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	629	n/a	489	n/a
Hypertriglyceridaemia				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	629	n/a	489	n/a
Other metabolic & nutritional				
0	853	89%	852	90%
1	98	10%	83	9%
2	7	1%	11	1%
3	1	0%	2	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	1	n/a	0	n/a
Total	960	100%	948	100%

Table S22: Worst musculoskeletal disorder grade within each category ever (by treatment arm) – Part 1

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Backpain (G1-3)					
	0	331	100%	458	100%
	1	0	0%	0	0%
	2	0	0%	0	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	629	n/a	489	n/a
Muscle pain (Myalgia; G1-3)					
	0	825	86%	806	85%
	1	107	11%	116	12%
	2	26	3%	23	2%
	3	0	0%	3	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Joint pain (Arthralgia; G1-3)					
	0	746	78%	717	76%
	1	161	17%	171	18%
	2	46	5%	48	5%
	3	5	1%	12	1%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Other bone pain (G1-3)					
	0	663	69%	675	71%
	1	200	21%	171	18%
	2	74	8%	81	9%
	3	21	2%	21	2%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Osteoporosis (G1-3)					
	0	331	100%	458	100%
	1	0	0%	0	0%
	2	0	0%	0	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	629	n/a	489	n/a
Total		960	100%	948	100%

Table S23: Worst musculoskeletal disorder grade within each category ever (by treatment arm) – Part 2

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Fracture	0	331	100%	458	100%
	1	0	0%	0	0%
	2	0	0%	0	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	629	n/a	489	n/a
Generalised pain (G1-3)	0	672	70%	627	66%
	1	226	24%	244	26%
	2	54	6%	67	7%
	3	6	1%	10	1%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Other musculoskeletal disorder	0	604	63%	542	57%
	1	248	26%	249	26%
	2	86	9%	118	12%
	3	18	2%	39	4%
	4	2	0%	0	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Total		960	100%	948	100%

Table S24: Worst nervous system grade within each category ever (by treatment arm)

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Dizziness (G1-3)					
	0	854	89%	786	83%
	1	91	9%	132	14%
	2	13	1%	27	3%
	3	0	0%	3	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Headache (G1-3)					
	0	849	89%	782	82%
	1	99	10%	137	14%
	2	9	1%	24	3%
	3	1	0%	5	1%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Seizure					
	0	951	100%	944	100%
	1	0	0%	0	0%
	2	3	0%	3	0%
	3	0	0%	0	0%
	4	0	0%	1	0%
	5	0	0%	0	0%
	Missing	6	n/a	0	n/a
Cognitive disturbance (G1-3)					
	0	918	96%	887	94%
	1	28	3%	44	5%
	2	6	1%	13	1%
	3	2	0%	4	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	6	n/a	0	n/a
Other nervous system					
	0	865	90%	814	86%
	1	60	6%	86	9%
	2	17	2%	27	3%
	3	13	1%	15	2%
	4	3	0%	4	0%
	5	0	0%	2	0%
	Missing	2	n/a	0	n/a
Total		960	100%	948	100%

Table S25: Worst ocular disorder grade within each category ever (by treatment arm)

	A SOC-only		G SOC+AAP	
	N	%	N	%
Blurred vision (G1-3)				
0	924	96%	893	94%
1	31	3%	49	5%
2	2	0%	3	0%
3	1	0%	3	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Cataracts (G1-4)				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	629	n/a	489	n/a
Conjunctivitis (CTCAE V3; G1-3)				
0	952	99%	941	99%
1	5	1%	5	1%
2	1	0%	1	0%
3	0	0%	1	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Other ocular disorder				
0	906	95%	859	91%
1	42	4%	68	7%
2	6	1%	7	1%
3	4	0%	14	1%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Total	960	100%	948	100%

Table S26: Worst psychiatric disorder grade within each category ever (by treatment arm)

	A SOC-only		G SOC+AAP	
	N	%	N	%
Insomnia (G1-3)				
0	720	75%	651	69%
1	180	19%	222	23%
2	52	5%	61	6%
3	6	1%	14	1%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Depression				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	629	n/a	489	n/a
Anxiety				
0	331	100%	459	100%
1	0	0%	0	0%
2	0	0%	0	0%
3	0	0%	0	0%
4	0	0%	0	0%
5	0	0%	0	0%
Missing	629	n/a	489	n/a
Other psychiatric disorder				
0	782	82%	716	76%
1	145	15%	166	18%
2	26	3%	56	6%
3	5	1%	9	1%
4	0	0%	1	0%
5	0	0%	0	0%
Missing	2	n/a	0	n/a
Total	960	100%	948	100%

Table S27: Worst renal disorder grade within each category ever (by treatment arm) – Part 1

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Acute kidney injury	0	953	99%	941	99%
	1	1	0%	2	0%
	2	0	0%	1	0%
	3	4	0%	2	0%
	4	1	0%	2	0%
	5	0	0%	0	0%
	Missing	1	n/a	0	n/a
Haematuria	0	905	94%	875	92%
	1	37	4%	53	6%
	2	13	1%	16	2%
	3	3	0%	2	0%
	4	0	0%	2	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Chronic kidney disease	0	868	91%	859	91%
	1	73	8%	73	8%
	2	13	1%	12	1%
	3	5	1%	4	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	1	n/a	0	n/a
Urinary tract infection (G2-5)	0	883	92%	866	91%
	1	0	0%	0	0%
	2	68	7%	71	7%
	3	7	1%	9	1%
	4	0	0%	2	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Urinary frequency (G1-2)	0	367	38%	340	36%
	1	386	40%	394	42%
	2	205	21%	214	23%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	2	n/a	0	n/a
Total		960	100%	948	100%

Table S28: Worst renal disorder grade within each category ever (by treatment arm) – Part 2

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Urinary urgency (G1-2)	0	331	100%	459	100%
	1	0	0%	0	0%
	2	0	0%	0	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	629	n/a	489	n/a
Urinary tract obstruction	0	331	100%	459	100%
	1	0	0%	0	0%
	2	0	0%	0	0%
	3	0	0%	1	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	Missing	629	n/a	489	n/a
Other renal disorder	0	739	78%	765	81%
	1	137	15%	112	12%
	2	50	5%	47	5%
	3	16	2%	21	2%
	4	2	0%	0	0%
	5	0	0%	0	0%
	Missing	16	n/a	3	n/a
Total		960	100%	948	100%

Table S29: Worst respiratory disorder grade within each category ever (by treatment arm) – Part 1

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Cough (G1-3)					
	0	826	86%	693	73%
	1	122	13%	216	23%
	2	10	1%	34	4%
	3	0	0%	5	1%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Breathlessness (Dyspnoea)					
	0	780	81%	693	73%
	1	136	14%	190	20%
	2	35	4%	47	5%
	3	7	1%	15	2%
	4	0	0%	2	0%
	5	0	0%	1	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Allergic rhinitis (G1-2)					
	0	921	96%	878	93%
	1	35	4%	66	7%
	2	2	0%	4	0%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Sinusitis (G2-5)					
	0	936	98%	915	97%
	1	0	0%	0	0%
	2	22	2%	32	3%
	3	0	0%	1	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Upper respiratory tract infection (G2-5)					
	0	871	91%	803	85%
	1	0	0%	0	0%
	2	85	9%	141	15%
	3	2	0%	4	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Total		960	100%	948	100%

Table S30: Worst respiratory disorder grade within each category ever (by treatment arm) – Part 2

		A		G	
		SOC-only		SOC+AAP	
		N	%	N	%
Lower respiratory tract infection (G2-5)					
	0	331	100%	456	99%
	1	0	0%	0	0%
	2	0	0%	1	0%
	3	0	0%	1	0%
	4	0	0%	0	0%
	5	0	0%	1	0%
	<i>Missing</i>	629	<i>n/a</i>	489	<i>n/a</i>
Other respiratory disorder					
	0	890	93%	797	84%
	1	40	4%	78	8%
	2	14	1%	45	5%
	3	11	1%	24	3%
	4	3	0%	1	0%
	5	1	0%	3	0%
	<i>Missing</i>	1	<i>n/a</i>	0	<i>n/a</i>
Total		960	100%	948	100%

Table S31: Worst skin disorder grade within each category ever (by treatment arm)

		A		G	
		SOC-only		SOC+only	
		N	%	N	%
Nail loss/discolouration (G1-2)					
	0	913	95%	887	94%
	1	43	4%	55	6%
	2	2	0%	6	1%
	3	0	0%	0	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Rash maculo-papular (G1-3)					
	0	873	91%	813	86%
	1	66	7%	103	11%
	2	18	2%	30	3%
	3	1	0%	2	0%
	4	0	0%	0	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Other skin disorder					
	0	796	83%	715	75%
	1	131	14%	178	19%
	2	24	3%	40	4%
	3	7	1%	14	1%
	4	0	0%	1	0%
	5	0	0%	0	0%
	<i>Missing</i>	2	<i>n/a</i>	0	<i>n/a</i>
Total		960	100%	948	100%

The following table provide a broad overview of worst toxicity reported over entire time on trial, by treatment received (safety population) within each subgroup of age at randomization, according to the dichotomous stratification factor used at randomization.

Table S32: Worst Adverse Event Grade Reported Over Entire Time on Trial, by stratified age at randomisation

		Under 70		70 or over	
		SOC-only	SOC+AAP	SOC-only	SOC+AAP
Safety population					
Patients included in adverse event analysis		597	596	363	352
Grade 1-5 AE		589 (99%)	593 (100%)	361 (99%)	350 (99%)
Grade 3-5 AE		189 (32%)	274 (46%)	126 (35%)	169 (48%)
Grade 5 AE*		1	3	2	6
Grade 3-5 AEs by toxicity category					
Endocrine disorder (including hot flashes, impotence)		80 (13%)	89 (15%)	53 (15%)	40 (11%)
Cardiovascular disorder	including:	20 (3%)	53 (9%)	21 (6%)	39 (11%)
	<i>Hypertension</i>	8 (1%)	30 (5%)	5 (1%)	14 (4%)
	<i>MI</i>	3 (<1%)	4 (1%)	6 (2%)	6 (2%)
	<i>Cardiac dysrhythmia</i>	1 (<1%)	8 (1%)	1 (<1%)	6 (2%)
Musculoskeletal disorder		31 (5%)	38 (6%)	15 (4%)	30 (9%)
Gastrointestinal disorder		18 (3%)	27 (5%)	22 (6%)	22 (6%)
Hepatic disorder	including:	7 (1%)	51 (9%)	5 (1%)	19 (5%)
	<i>Increased ALT</i>	3 (<1%)	39 (7%)	1 (<1%)	14 (4%)
	<i>Increased AST</i>	1 (<1%)	9 (2%)	1 (<1%)	1 (<1%)
General disorder	including:	14 (2%)	24 (4%)	15 (4%)	21 (6%)
	<i>Fatigue</i>	9 (2%)	9 (2%)	6 (2%)	12 (3%)
	<i>Oedema</i>	0 (0%)	4 (1%)	0 (0%)	1 (<1%)
Respiratory disorder	including:	15 (3%)	21 (4%)	8 (2%)	23 (7%)
	<i>Breathlessness (dyspnoea)</i>	6 (1%)	9 (2%)	1 (<1%)	9 (3%)
Lab abnormalities	including:	15 (3%)	18 (3%)	6 (2%)	16 (5%)
	<i>Hypokalaemia</i>	3 (<1%)	6 (1%)	0 (0%)	6 (2%)

Key:

SOC = standard-of-care

AAP = abiraterone acetate + prednisolone