List of participating sites, with their principal investigators and numbers of patients recruited.

Royal Liverpool University Hospital (Professor Richard E Clark)	39
Hammersmith Hospital, London (Professor Jane F Apperley)	22
Beatson Institute for Cancer Research, Glasgow (Professor Mhairi Copland)	15
East Kent Hospitals, Canterbury (Dr Christopher Pocock)	12
St James University Hospital, Leeds (Dr Katherine Rothwell)	12
Nottingham City Hospital (Dr Jennifer Byrne)	10
King's College Hospital, London (Dr Hugues de Lavallade)	8
Hereford County Hospital (Dr Lisa Robinson)	7
Freeman Hospital, Newcastle-upon-Tyne (Dr Wendy Osborne)	7
Birmingham Heartlands Hospital (Dr Joanne Ewing) ,	6
Royal Devon & Exeter Hospital, Exeter (Dr Jason Coppell)	5
Salisbury District Hospital (Dr Jonathan Cullis)	5
Colchester General Hospital (Dr Gavin Campbell)	5
North Bristol (Southmead) Hospital (Dr Alistair Whiteway)	4
Queen Elizabeth Hospital, Birmingham (Dr Manoj Raghavan)	4
University Hospital of Wales, Cardiff (Dr Andrew Goringe)	4
Churchill Hospital, Oxford (Professor Adam Mead)	3
Aberdeen Royal Infirmary (Dr Dominic Culligan)	3
Manchester Royal Infirmary (Dr Fiona Dignan)	2
Addenbrookes Hospital, Cambridge (Dr Brian Huntly)	1
TOTAL	174.

Supplementary Table 1. Demographic and clinical details of the recruited patients.
IQR = interquartile range. Other abbreviations are as defined in the text.

Patient characteristics at trial entry	**MR4** n = 125	**MMR** n = 49	**Overall** n = 174
Demographic characteristics			
Age (years); median	61	57	59
IQR	51-68	45-66	50-68
Gender; male [n (%)]	73 (58%)	25 (51%)	98 (56%)
Physical findings			
0 - Fully Active	113 (90%)	42 (86%)	155 (89%)
1 - Work Able	10 (8%)	7 (14%)	17 (9%)
2 - Not Work Able	1 (1%)	-	1 (1%)
3 - Limited Self Care	1 (1%)	-	1 (1%)
4 - Completely Disabled	-	-	-
Clinical characteristics			
BCR-ABL1 % at trial entry: median	0.001	0.0047	0.001
IQR	0.0003- 0.002	0.002- 0.009	0.0006- 0.003
Treatment history			
Duration of TKI (years): median	6.5	7.7	6.9
IQR	4.8- 10.2	5.1- 10.7	4.8- 10.2
Missing	-	1	1
Medication			
Imatinib n (%)	105 (84%)	43 (88%)	148 (85%)
Nilotinib n (%)	14 (11%)	2 (4%)	16 (9%)
Dasatinib n (%)	6 (5%)	4 (8%)	10 (6%)

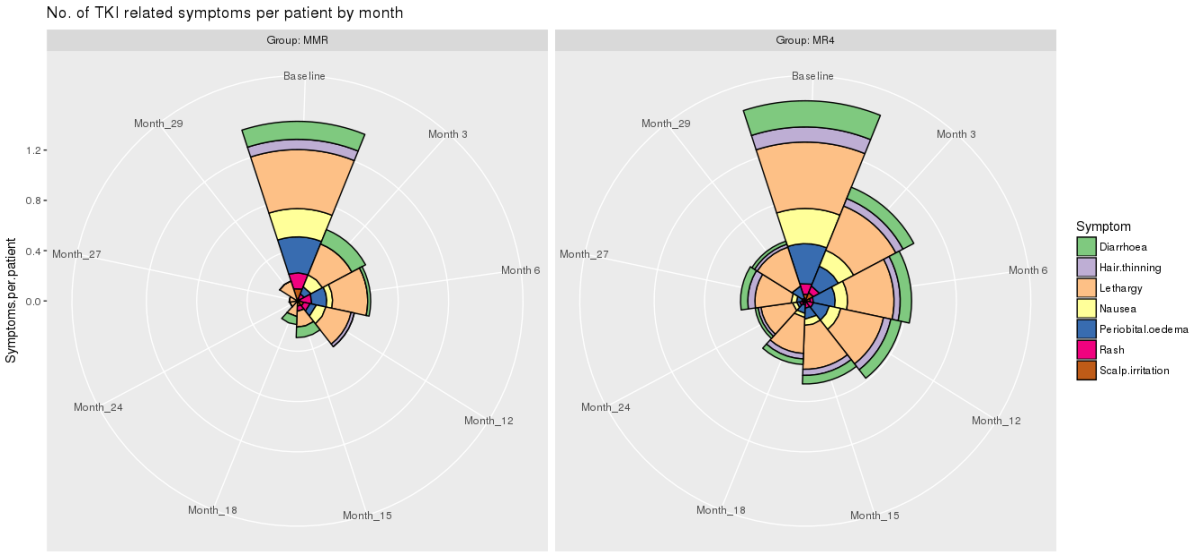
Supplementary Table 2. Endpoint outcomes. Figures in parentheses are 95% confidence limits. Results are at 36 months. The following secondary endpoints have already been reported, as detailed in the Outcomes section in the main text: Health Economic Assessment, Quality of Life and laboratory studies to identify subsets of patients who are more likely to relapse on de-escalation / cessation.

Endpoint	Definition	Group	Result	Further details
Primary:				
Molecular recurrence-free survival (RFS)	Time from commencing de-escalation to the date of confirmed loss of MMR (two consecutive BCR-ABL >0.1% IS)	MR4	72% (64-80%)	Main Figure 2 and Results section
		MMR	36% (25-53%	Main Figure 2 and Results section
Secondary:				
Overall survival	Event = death from any cause	MR4	98% (96-100%)	Supplementary Figure 2
		MMR	100%	Supplementary Figure 2
Progression-free survival	Event = progression to advanced phase; death from any cause.	MR4	98% (96-100%)	Supplementary Figure 2
		MMR	100%	Supplementary Figure 2
Event-free survival	Event = molecular recurrence, progression to advanced phase; death from any cause.	MR4	70% (62-79%)	Supplementary Figure 2
		MMR	36% (25-53%)	Supplementary Figure 2
In patients who lose MMR, the proportion who regain MMR on TKI resumption.	Time to MMR recovery (TTR) = the time from the date of confirmed loss of MMR to the date of MMR recovery).	MR4 and MMR	100% of those assessable in each group	Main Figure 4 and Results section. TTR is shown in Main Figure 4.
In patients who successfully de-escalate, the proportion who lose MMR on TKI cessation		MR4	27% (proportion successfully de-escalating = 98%)	Main Figure 2 and Results section
		MMR	56% (proportion successfully de-escalating = 81%)	Main Figure 2 and Results section
The proportion of MR4.5 patients at entry	Note; some patients were not assessable for this endpoint as there were insufficient (< 31,623) control transcripts.	MR4	87/108 (81%)	Main Figure 3 and Results section
		MMR	9/41 (22%)	Main Figure 3 and Results section

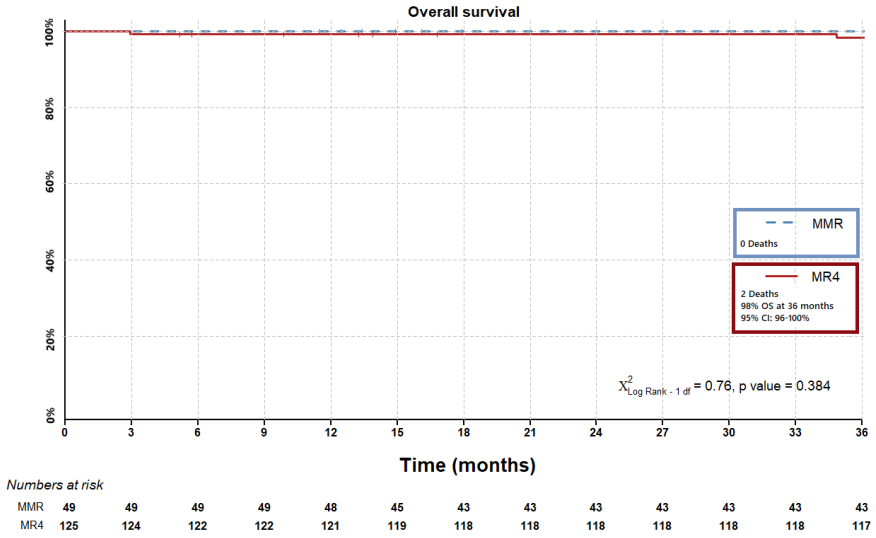
Supplementary Table 3. Molecular recurrence according to diagnostic prognostic score (citations to each in the text). Data were available for 74 patients. Four scoring systems are presented as mentioned in the text; in each case the recurrence rate in the high scoring group is compared to that in the low (and intermediate where relevant) scoring group. CI = confidence intervals.

CHARACTERISTIC	HAZARD RATIO	95% CI	p-value
Sokal: High	1.03	0.24 – 4.39	0.97
EURO (Hasford) : High	0.94	0.13 – 6.96	0.95
EUTOS: High	0.98	0.45 – 2.11	0.95
ELTS: High	1.07	0.44 – 3.31	0.87

Supplementary Figure 1. Radial plot of TKI related symptoms over time. The number of patients reporting individual side effects (lethargy, diarrhoea, rash, nausea, periorbital oedema, hair thinning) is shown according to time from trial entry, for the MMR group (left) and MR4 group (right).

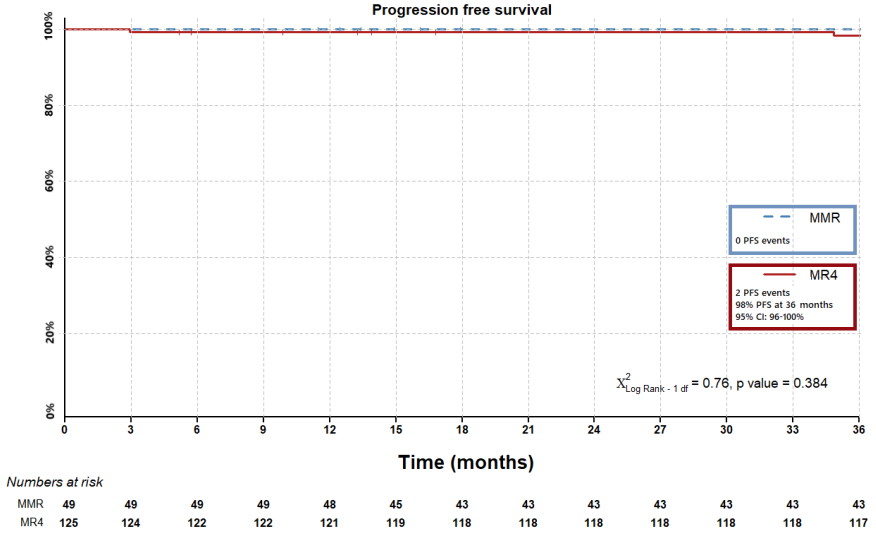


Supplementary Figure 2. Overall survival (OS), Progression free survival (PFS) and Event free survival (EFS).



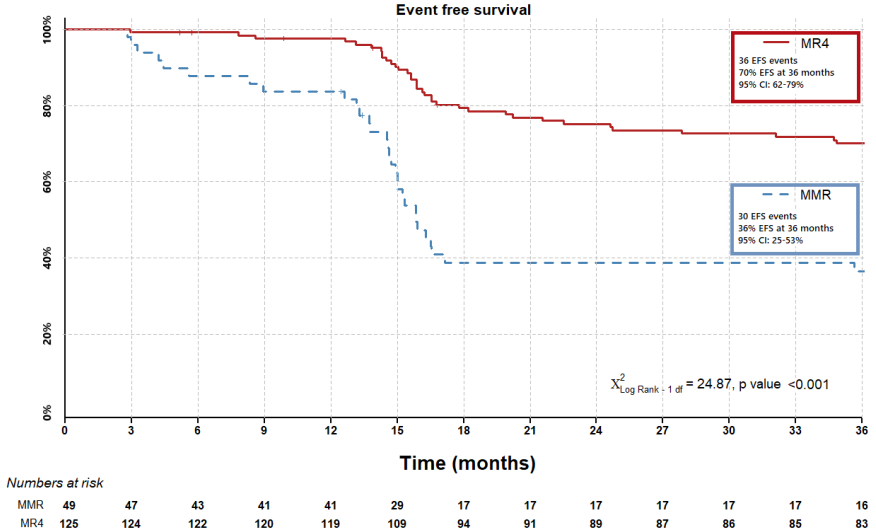
Numbers at risk

MMR	49	49	49	49	48	45	43	43	43	43	43	43	43
MR4	125	124	122	122	121	119	118	118	118	118	118	118	117



Numbers at risk

MMR	49	49	49	49	48	45	43	43	43	43	43	43	43
MR4	125	124	122	122	121	119	118	118	118	118	118	118	117



Numbers at risk

MMR	49	47	43	41	41	29	17	17	17	17	17	17	16
MR4	125	124	122	120	119	109	94	91	89	87	86	85	83