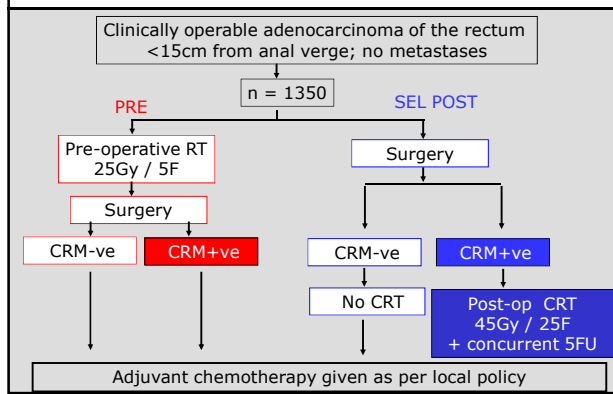


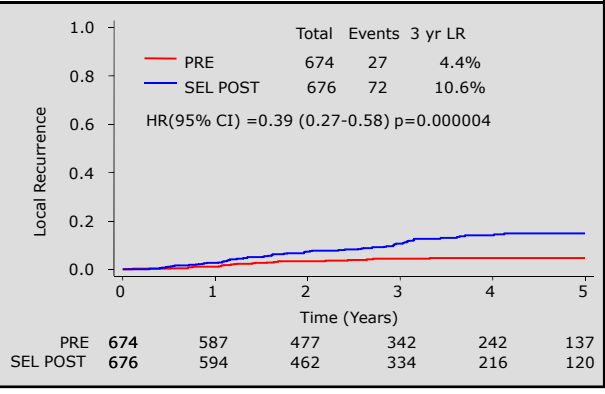
### Factors influencing the risk of local recurrence and the impact of treatment. Subset analyses from the MRC CR07 NCIC CO16 trial

**David Sebag-Montefiore**  
 Bob Steele, John Monson, Bob Grieve, Subhash Khanna,  
 Sun Myint, Eric Bessell, Catherine de Metz, Jean Couture, Lindsay  
 Thompson, Richard Stephens and Phil Quirke

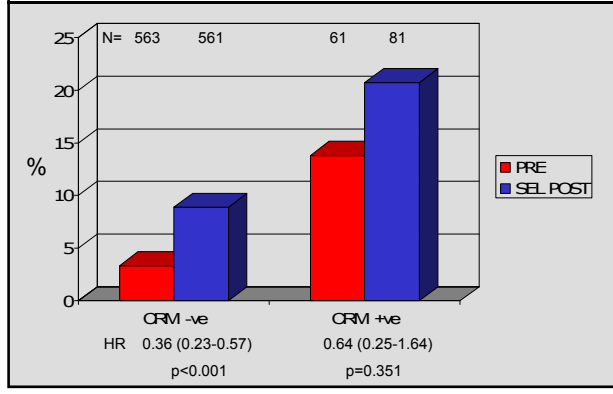
### Trial design (Recruitment 1998-2005)



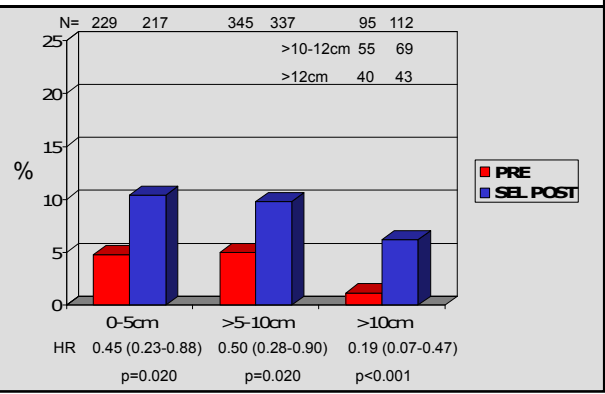
### Local recurrence (ITT) - med FU 4 yrs



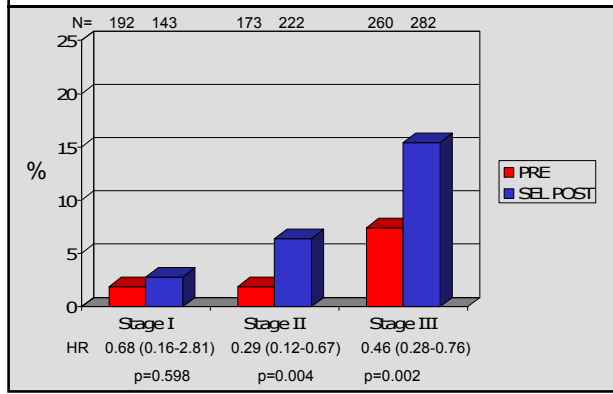
### 3 year LR by CRM status

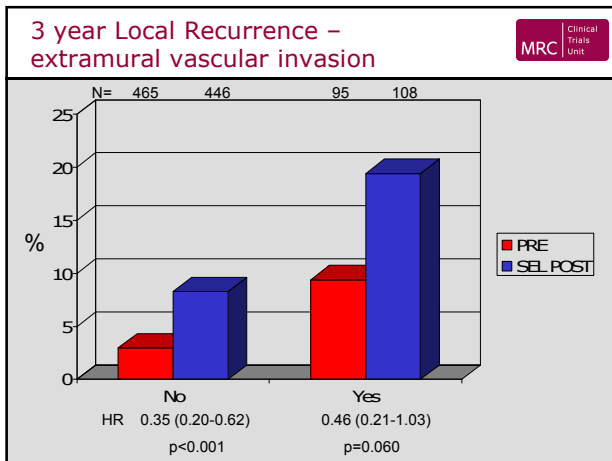
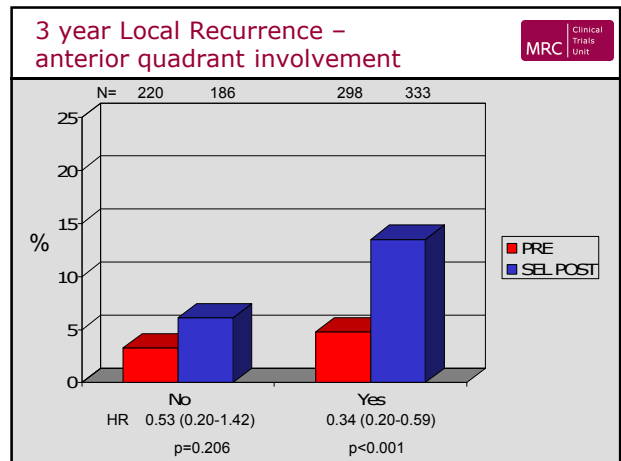
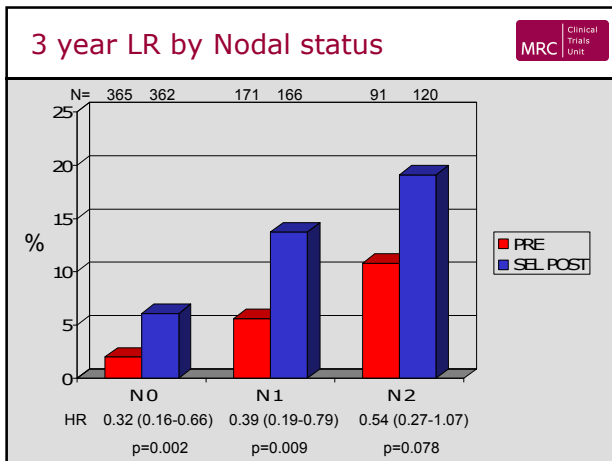


### 3 year LR by tumour position

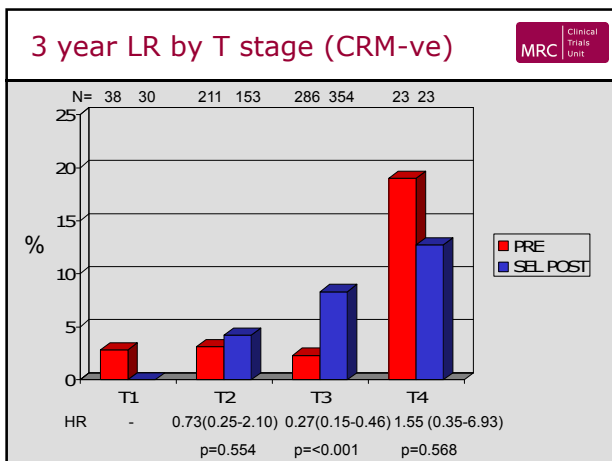


### 3 year LR by TNM stage





- ### Subset analysis of CRM-ve pts
- 89% of patients CRM -ve
  - Pure comparison of SCPRT + S versus S alone
  - MRI staging
    - Can identify this group
    - Accurate in T staging
    - Can subdivide T3 by measurement of extramural spread

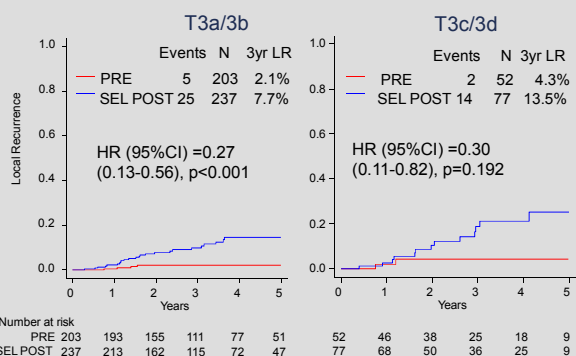


### LR by T3 tumour stage – 3 yr rates (1)

T3 stage	No	CRM -ve subset		Absolute difference	HR (95% CI)
		PRE	S alone		
T3a <1mm	171	3.0%	6.0%	3%	0.49 (0.12-2.00)
T3b 1-5mm	271	1.7%	8.0%	6.3%	0.20 (0.09-0.47)
T3c >5-15mm	104	5.2%	16.3%	11.1%	0.30 (0.10-0.86)
T3d* >15mm	25	-	12.5%	-	-

\*No events in the PRE arm therefore non-estimable

### 3 year LR for T3a/b and T3c/d tumours



### Risk factors of LR



- Aim : to examine the association between LR and clinical, surgical and pathological factors
- Model: Cox proportional hazards
- Outcome: Time to LR
- Analysis: Univariate and Multivariate

### Univariate analysis



- Univariate analysis carried out to see which factors alone have an effect on the risk of LR
- Factors included were:
 

Age	T stage
Sex,	N stage
WHO PS status,	number +ve nodes
Distal extent,	CRM
Operation performed,	EMVI
Anterior quadrant	Plane of surgery

### Univariate Results



Variable	N	LR	HR (95%CI)	p-value
APER No	740	40	1.00	-
APER Yes	322	33	1.74 (1.10-2.77)	0.018
CRM -ve	943	60	1.00	-
CRM +ve	119	13	2.07 (1.13-3.77)	0.018
T Stage 1	53	0	non-estimable	-
T Stage 2	311	12	1.00	-
T Stage 3	631	52	2.34 (1.25-4.38)	0.008
T Stage 4	67	9	5.34 (2.24-12.73)	<0.001
N Stage 0	606	23	1.00	-
N Stage 1	284	26	2.54 (1.45-4.46)	0.001
N Stage 2	172	24	4.42 (2.49-7.83)	<0.001
Extramural vascular invasion No	839	48	1.00	-
Extramural vascular invasion Yes	223	25	2.40 (1.47-3.90)	<0.001
Tumour involving anterior quadrant No	400	16	1.00	-
Tumour involving anterior quadrant Yes	223	57	2.23 (1.28-3.89)	<0.001
Plane of surgery Mesorectal	550	29	1.00	-
Plane of surgery Intramesorectal	370	26	1.33 (0.78-2.25)	0.297
Plane of surgery Muscularis Propria	142	18	2.52 (1.40-4.53)	0.002

### Multivariate Results



Variable	HR (95%CI)	p-value
APER No	1.00	-
APER Yes	1.61 (1.00-2.57)	0.048
T Stage 1	-	-
T Stage 2	1.00	-
T Stage 3	2.07 (1.08-3.99)	0.029
T Stage 4	3.08 (1.22-7.82)	0.018
N Stage 0	1.00	-
N Stage 1	2.01 (1.13-3.57)	0.018
N Stage 2	3.00 (1.62-5.54)	<0.001
Tumour involving anterior quadrant No	1.00	-
Tumour involving anterior quadrant Yes	1.89 (1.08-3.32)	0.026
Plane of surgery Mesorectal	1.00	-
Plane of surgery Intramesorectal	1.13 (0.66-1.95)	0.654
Plane of surgery Muscularis Propria	1.99 (1.16-3.44)	0.013

CRM and EMVI do not have an individual effect on LR

### Conclusions



- Subset analyses
- Multivariate Cox regression analysis shows that APER, muscularis plane, T stage, N stage and anterior tumour position are all risk factors for LR
- There is an observed increase in event rate and absolute benefit within T3 disease
- Thank you to patients, investigators, TMG TSC DMEC.