

Rectal Cancer Update: Current standards and new trends

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OUTLINE

- RT with optimized surgery?
- Neoadjuvant or adjuvant RT?
- 5x5 Gy or long-course RCT?
- RT with new agents?

TME-Trial: RT+TME vs. TME



Local Failure Rate at 5 years:

5x5 Gy+TME: 5.6%
vs.
TME alone: 10.9%
p<0.001

*Kapiteijn E et al., N Engl J Med 2001
Peeters K et al., Ann Surg 2007*

TME - TRIAL



5-year Results	5x5 Gy+TME n=873	TME n=875	P
UICC I	0.4%	1,7%	0.09
UICC II	5.3%	7.2%	0.33
UICC III	10.6%	20.6%	<0.001

Peeters K et al., Ann Surg 2007

TME TRIAL



5-year Results	5x5 Gy + TME n=873	TME n=875	P
0-5 cm	10.7%	12%	0.58
> 5-10 cm	3.7%	13.7%	<0.001
> 10 cm	3.7%	6.2%	0.12

Peeters K et al., Ann Surg 2007

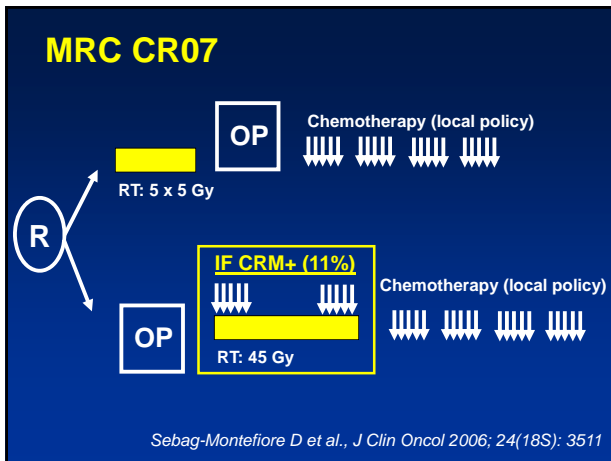
...Lessons from the TME trial:

- Risk reduction at 5y < 2y.
- Only subgroups benefited from RT.
- RT associated with late toxicity.*



Risk-adapted RT ?

** Peeters K et al., J Clin Oncol 2005*

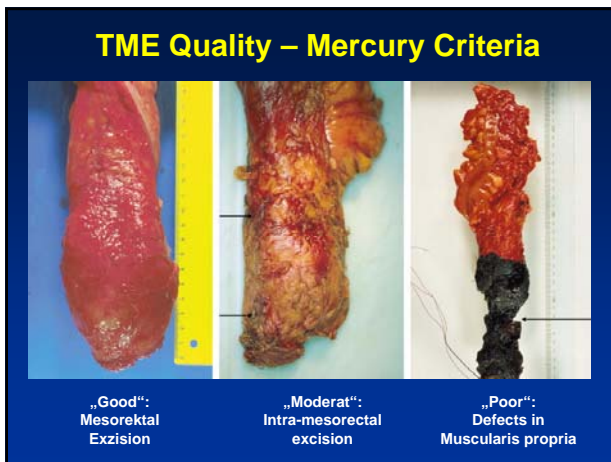


MRC - CR07

5x5Gy +TME ? TME+RCT if CRM+

3-year Results	Preop. RT + TME (n=674)	TME + RCT if CRM + (n=676)	Hazard-Ratio (95%CI)
Local Recurrence	4.7%	11.1%	2.5 (1.61-3.79)
Disease-free Survival	79.5%	74.9%	1.31 (1.02-1.67)
Overall Survival	80.8%	78.7%	1.25 (0.98-1.59)

Sebag-Montefiore D et al., J Clin Oncol 2006; 24(18S): 3511

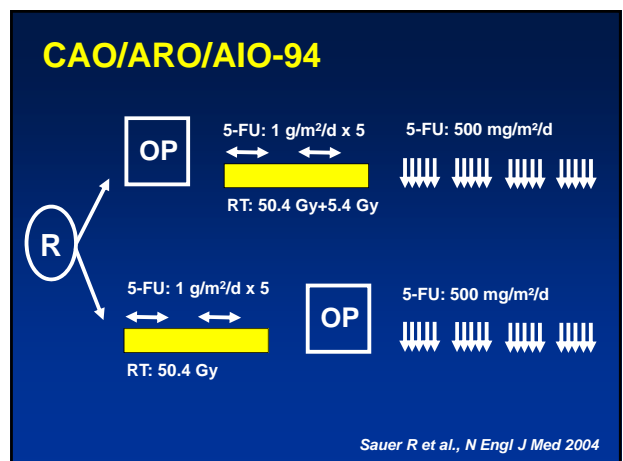


MRC - CR07

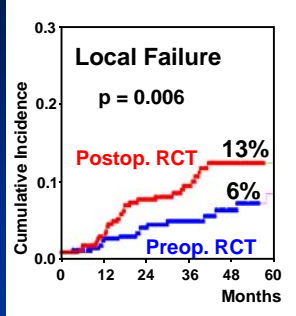
TME-Quality	N	5x5+TME	TME (+RCT if CRM+)	HR
“Poor“: Defects in Muscularis propria	141 (13%)	9%	29%	2.8
“Moderate“: Intra-mesorectal Excision	382 (34%)	6%	12%	2.0
“Good“: Mesorectal Excision	596 (53%)	1%	6%	4.5

Quirke P et al., J Clin Oncol 2006; 24(18S): 3512

- ### OUTLINE
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 - RT with new agents?



CAO/ARO/AIO-94

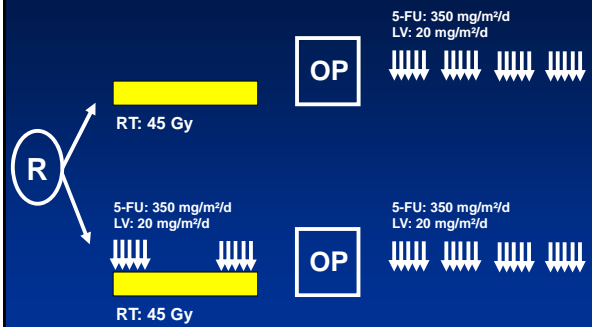


Preop. RCT:

- Local Control +
- Toxicity +
- Compliance +
- Sphincter +
- Risk: overtreatment (UICC I) -

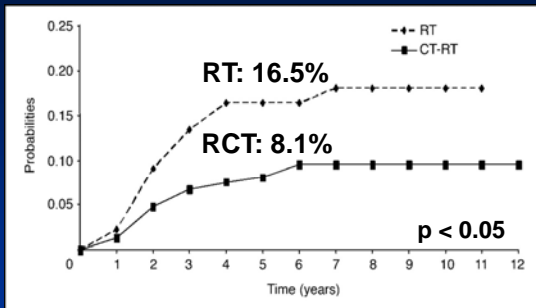
Sauer R et al., N Engl J Med 2004

FFCD 9203



Gérard JP et al, J Clin Oncol 2006

FFCD 9203 – Local Failure



Gérard JP et al, J Clin Oncol 2006

Similar Results:

EORTC 22921: Bosset et al., N Engl J Med 2006

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5x5Gy

?

RCT

POLISH

	Preop. 5 x 5 Gy n=148	Preop. RCT n=138	P-Value
Sphincter Preservation	61%	58%	0.57
T-Category			
ypT0	1%	16%	<0.001
ypT1-2	39%	46%	
ypT3-4	60%	38%	
N-Category			
ypN0	52%	68%	0.007
ypN+	48%	32%	
CRM +	13%	4%	0.017

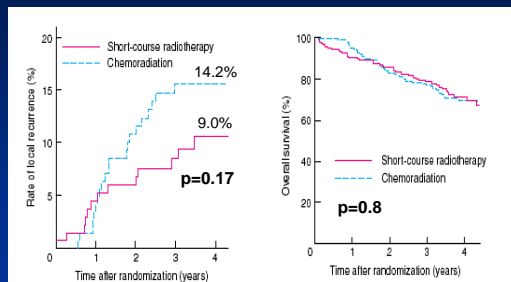
Bujko et al. Radiother Oncol 2004

5x5Gy

?

RCT

POLISH

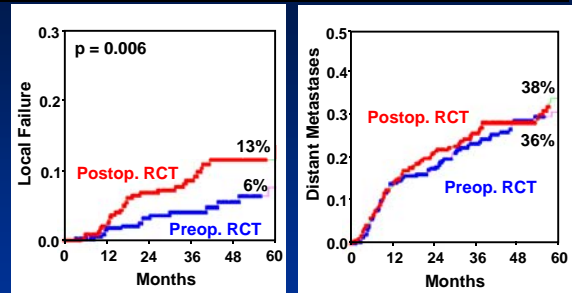


Bujko et al., Br J Surg 2006

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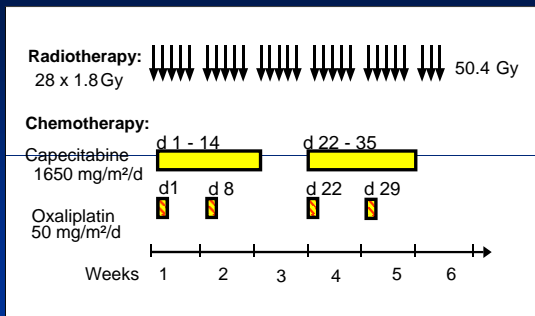
CAO/ARO/AIO-94



Rationale for incorporations of new agents

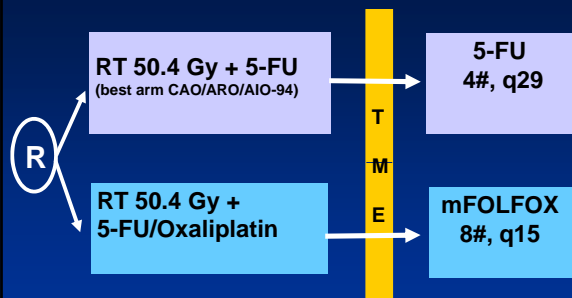
Sauer R et al., N Engl J Med 2004

Phase I/II Studies of RT with new agents



Rödel et al., J Clin Oncol 2003 and J Clin Oncol 2007

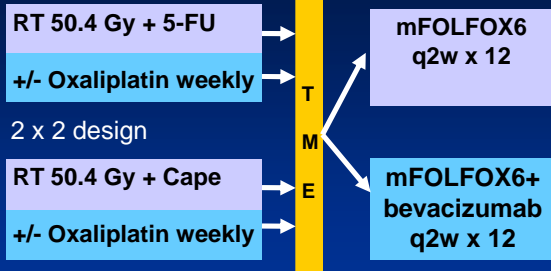
New German Trial: CAO/ARO/AIO-04



Similar Design (Inclusion of Oxaliplatin): ACCORD 12, STAR, CHRONICLE, PETACC 6

NSABP R-04

E5204



Patients can be enrolled in both NSABP-R04 and E5204

SUMMARY

- RT with TME surgery?
YES! Some subgroups may not benefit
- Neoadjuvant or adjuvant RT?
Neoadjuvant! Need for improved staging (MRI)
- 5 x 5 Gy or long-course RCT?
Risk-adapted! If downsizing required: RCT
- RT with new drugs?
Promising! Phase III trials needed