

RECTAL CANCER CLINICAL CASE DISCUSSION

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CLINICAL PRACTICE GUIDELINES

Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[†]

R. Glynne-Jones¹, L. Wyrwicz², E. Tiret^{3,4}, G. Brown⁵, C. Rödel⁶, A. Cervantes⁷ & D. Arnold⁸, on behalf of the ESMO Guidelines Committee*

¹Department of Radiotherapy, Mount Vernon Centre for Cancer Treatment, Northwood, London, UK; ²Department of Gastrointestinal Cancer, Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; ³Department of Surgery, Sorbonne Universités, UPMC Univ Paris 06, Paris; ⁴APHP, Hôpital Saint-Antoine, Paris, France; ⁵Department of Radiology, The Imperial College and Royal Marsden Hospital, Sutton, Surrey, UK; ⁶Department of Radiotherapy and Oncology, University of Frankfurt, Frankfurt, Germany; ⁷CIBERONC, Medical Oncology Department, INCLIVA University of Valencia, Valencia, Spain; ⁸Instituto CUF de Oncologia (I.C.O.), Lisbon, Portugal

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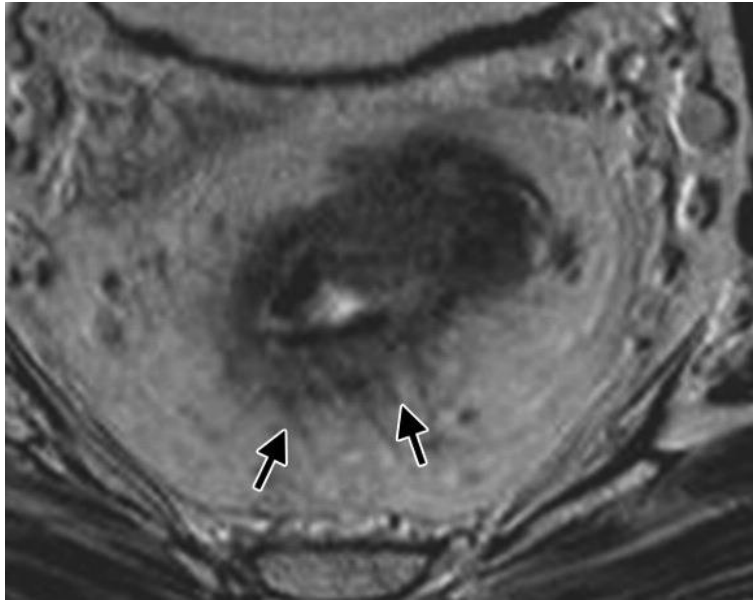
[†]Approved by the ESMO Guidelines Committee: August 2002, last update May 2017. This publication supersedes the previously published version—*Ann Oncol* 2013; 24 (Suppl. 6): vi81–vi88.

BASIS FOR RECTAL CANCER STAGING AND THERAPY

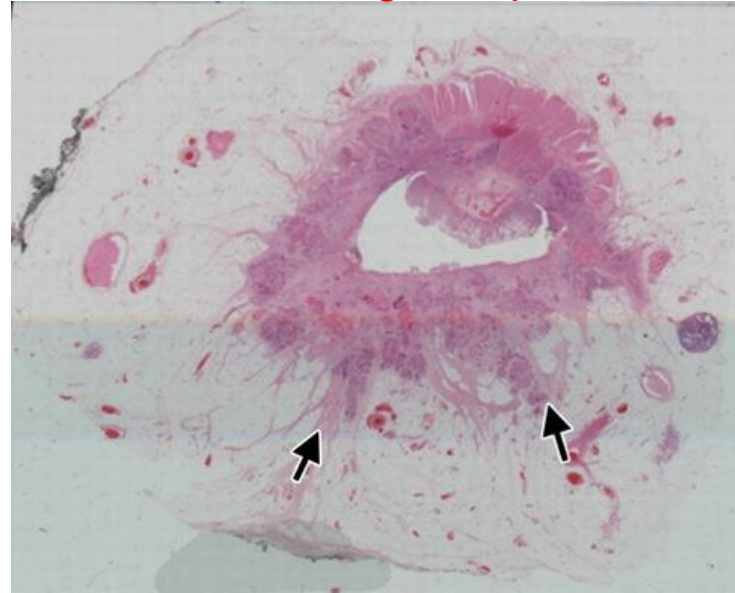
Integration of knowledge in a multidisciplinary team
Optimal staging by MRI
Selective preoperative radiation or chemoradiation
TME surgery
Pathological assessment of the quality of surgery
Non surgical approach for some pCR
Adjuvant chemotherapy for high risk

MERCURY Study Group

MRI before TME



Histopathological assessment
of the surgical specimen



Mean extramural spread

2.8mm

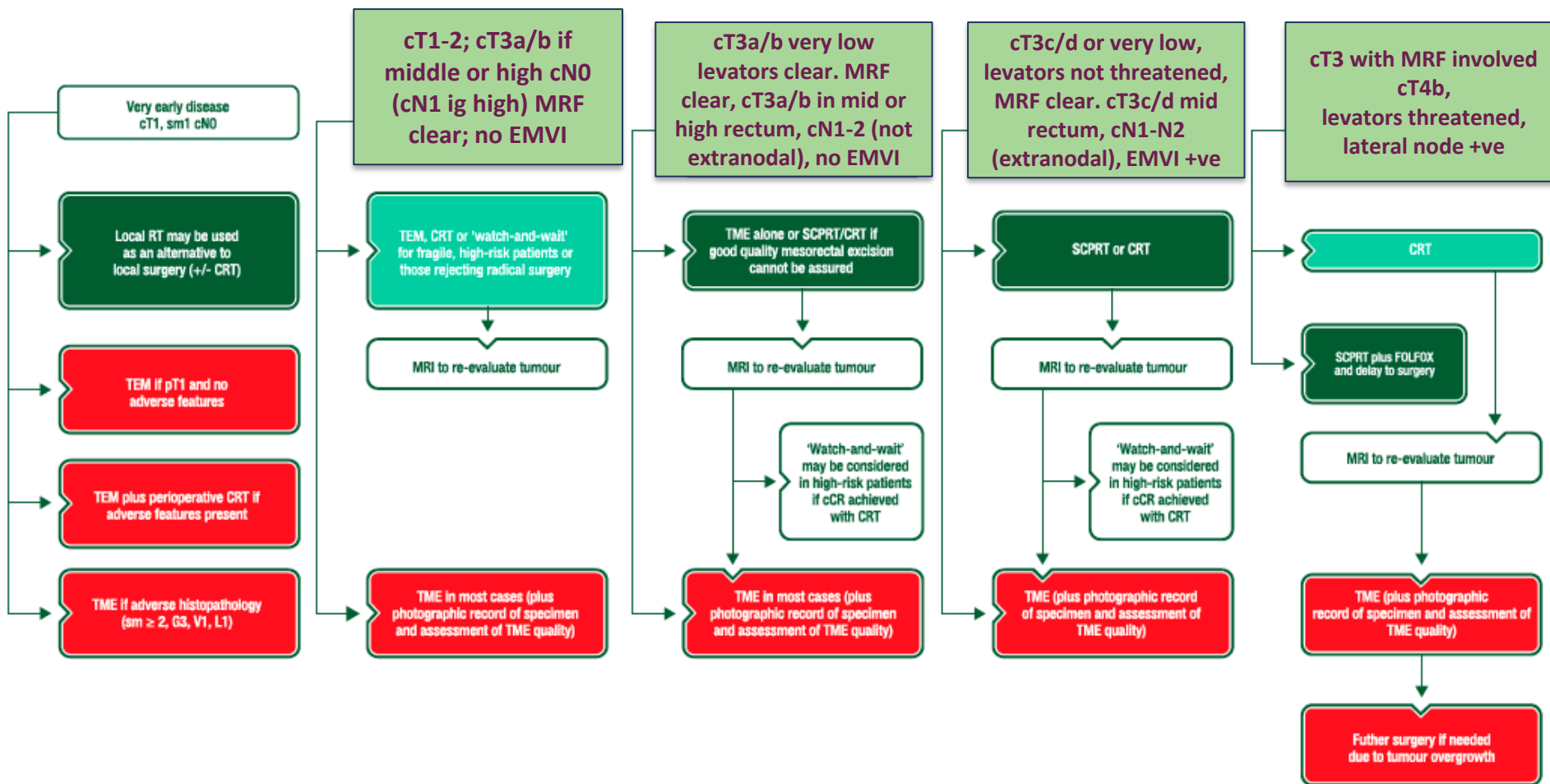
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2.81mm

ESMO Guidelines statement

Rectal MRI for all tumours, including the earliest ones, is required in order to select patients for preoperative treatment and extent of surgery.

ESMO Rectal Cancer Guidelines: Staging



Key Messages

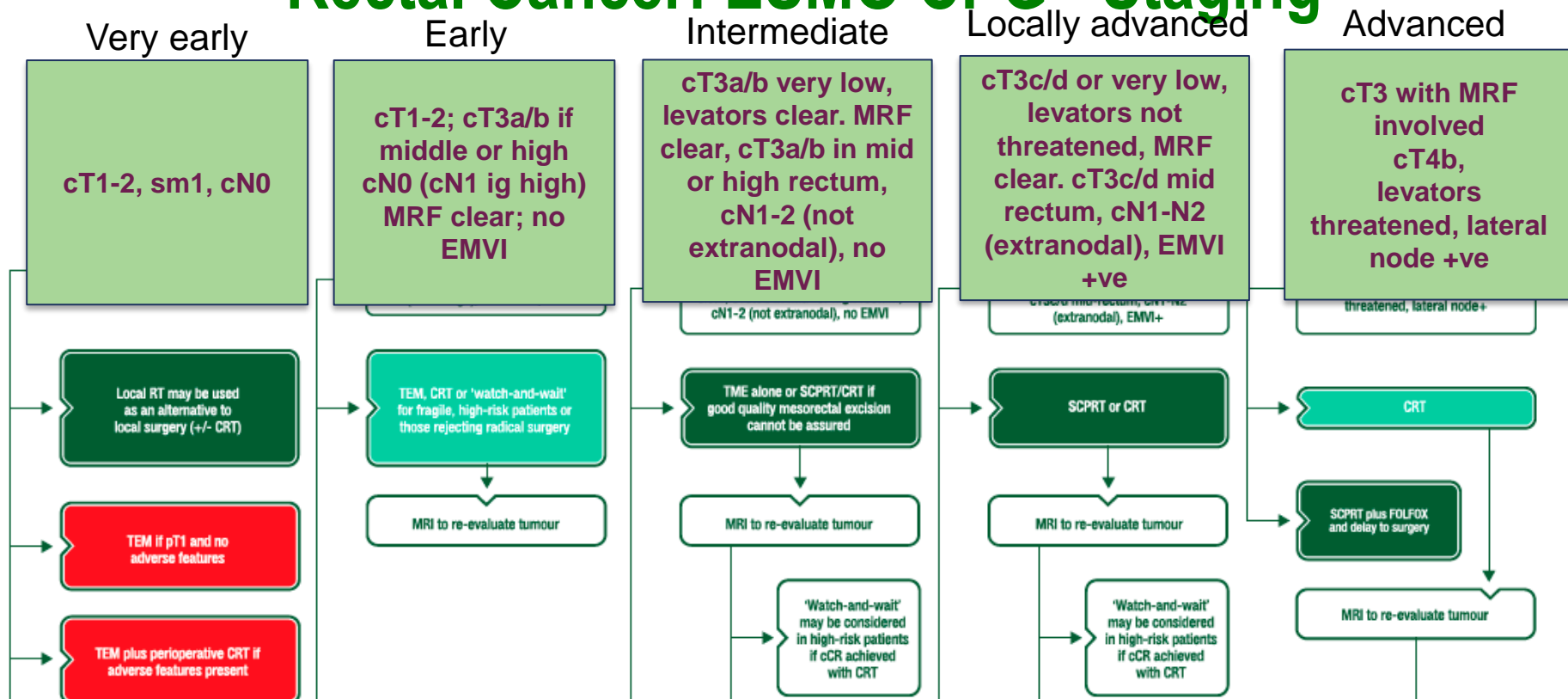
SoC
TME alone
AVOID RT

TME alone if
high quality or
plus
SCPRT/CRT

SCPRT
or
CRT
Then TME

CRT or
SCPRT +
FOLFOX
then TME

Rectal Cancer: ESMO CPG - Staging



Key Messages

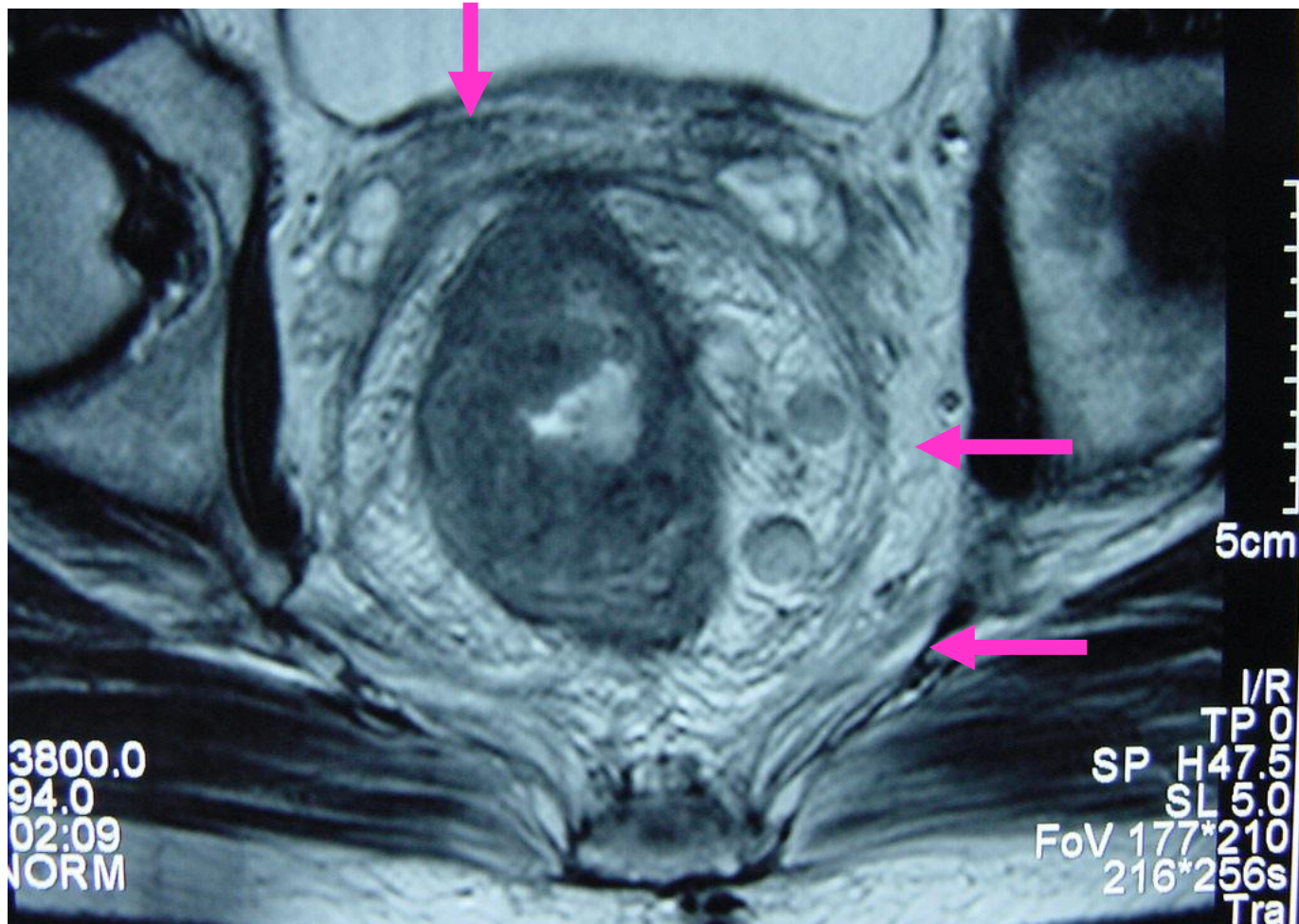
SoC
 TME alone
 Avoid RT

TME alone if
 high quality
 or plus
 SCPRT/CRT

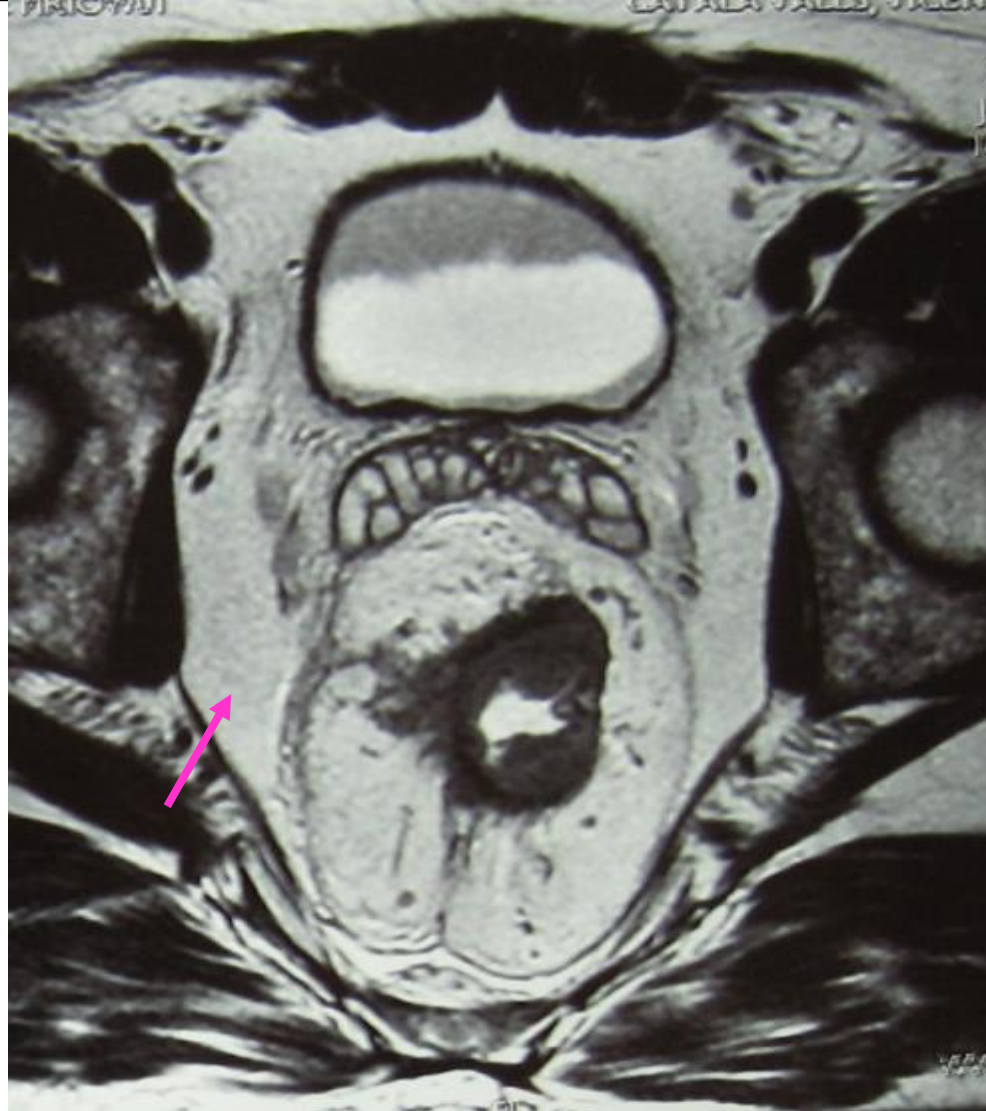
SCPRT
 or
 CRT
 then TME

CRT or
 SCPRT +
 FOLFOX
 then TME

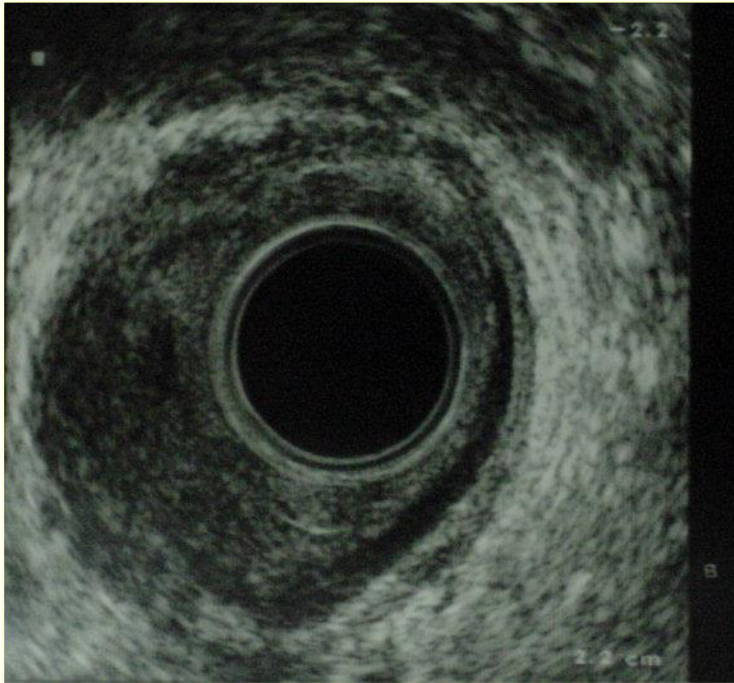
Involvement of mesorectal fascia



Extramural vein invasion



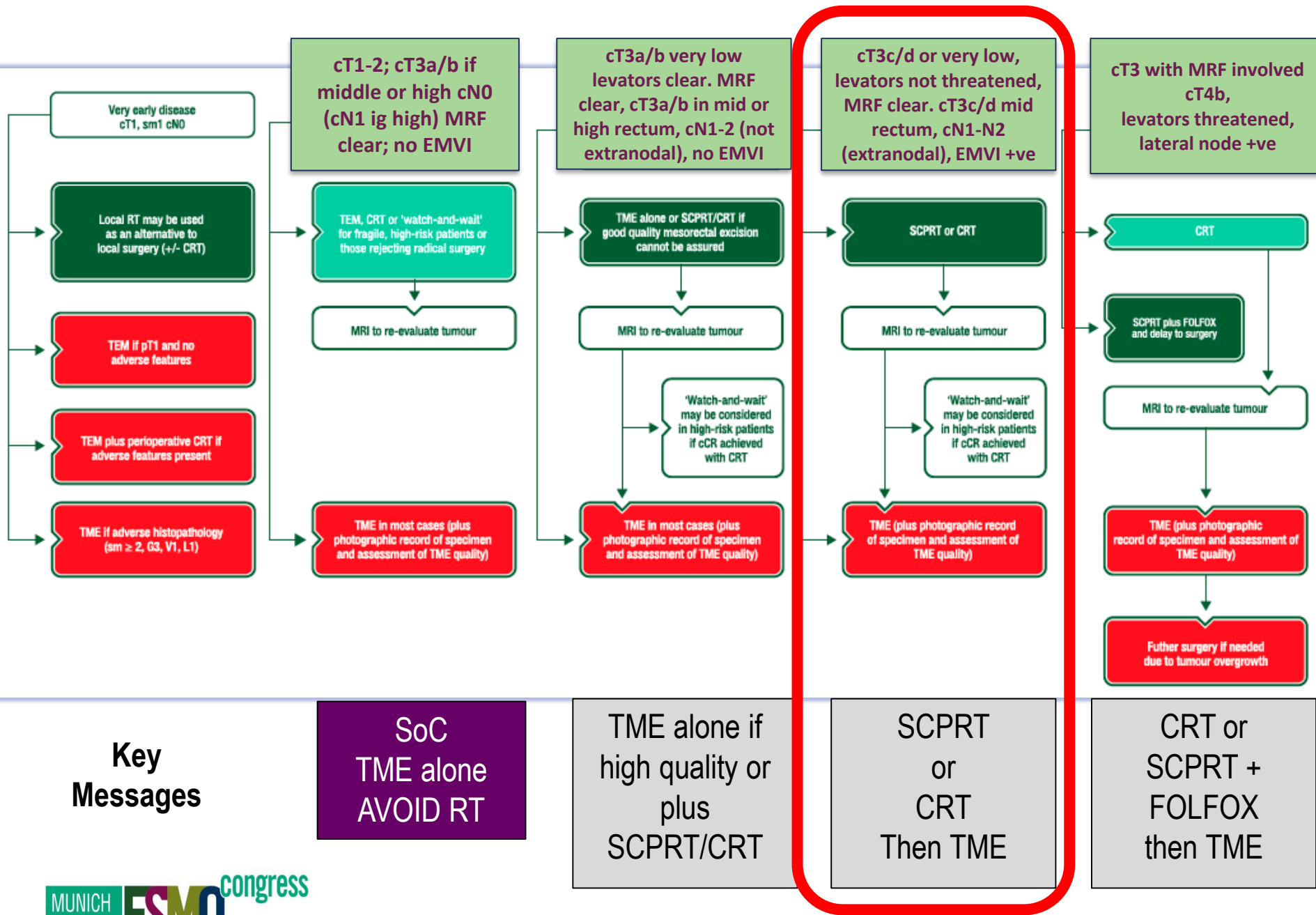
Involvement of puborectal sphincter

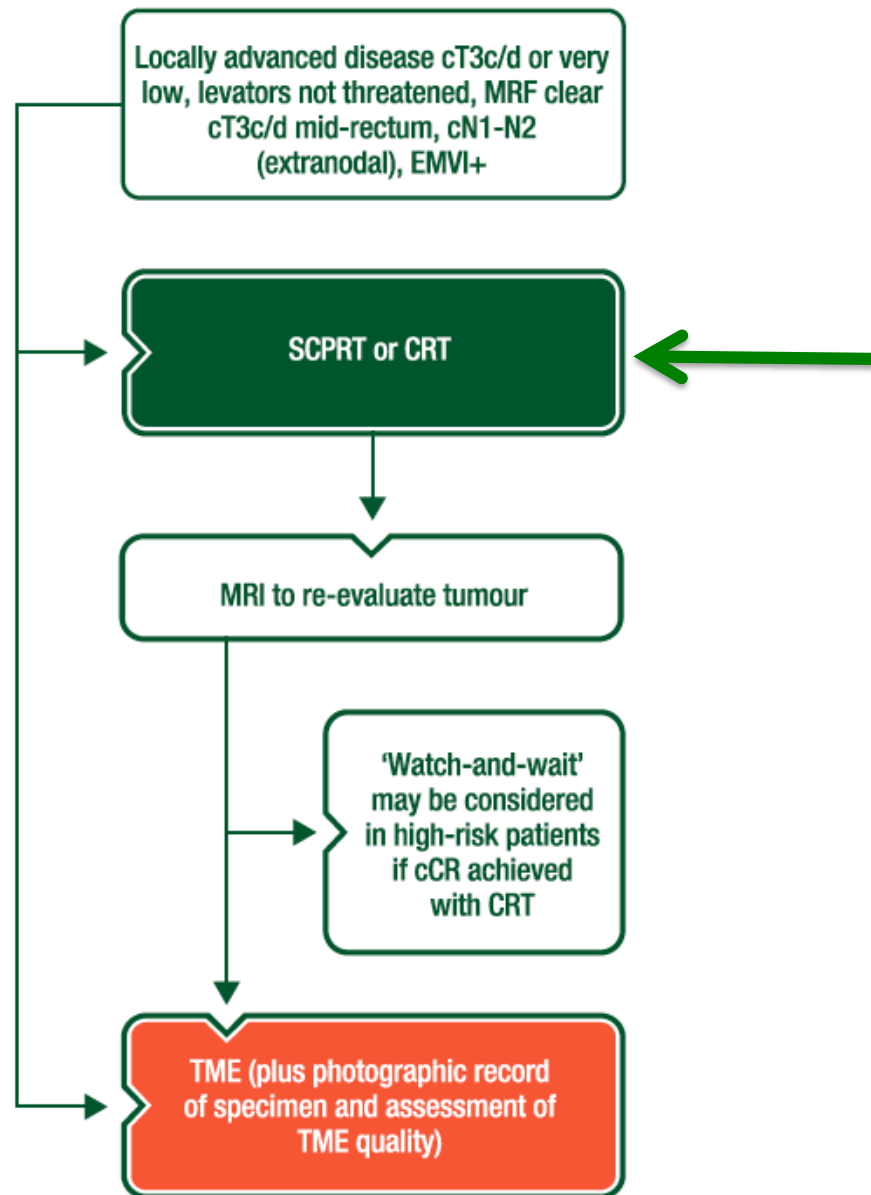


High risk features in our case

- Tumour of the upper rectum (11-16 cm from the a.v.)
- **Extramural spread: 13 mm T3c**
- **> 4 heterogeneous/irregular border lymph nodes**
- **EMVI positive** (left middle rectal vein)
 - No MRF involvement
 - No extramural disease
 - No lateral nodes

Stage: cT3cN2M0





Glynn-Jones R et al. Ann Oncol 2017

Our case treatment

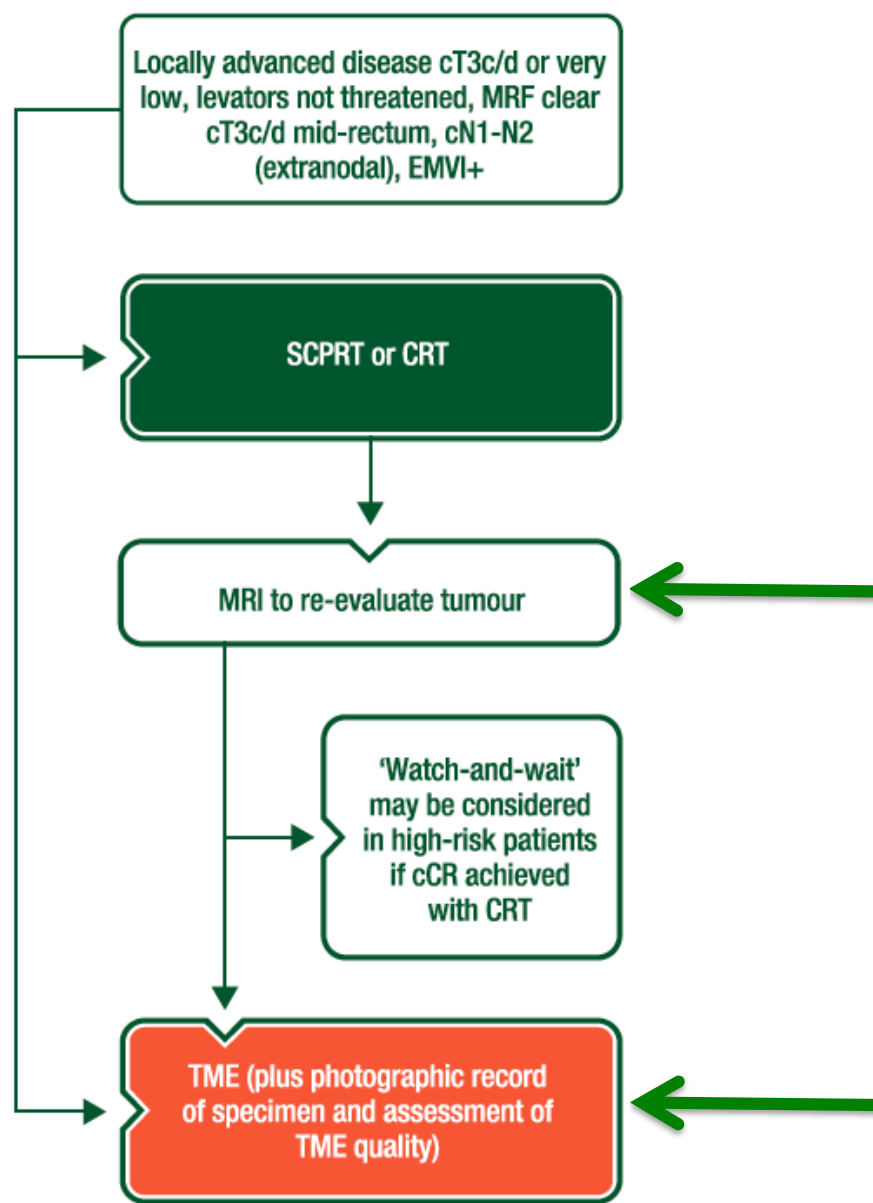
Long-course chemo-radiotherapy

45 Gy in 25 fractions + 9 Gy boost in 5 fractions

Concurrent capecitabine (825 mg/m² twice daily continuously)

Rectal cancer with pre-operative Chemo-RT: OXALIPLATIN NOT RECOMMENDED

Study	Patients	ChemoRT Regimen	ypCR Rate (%)
ACCORD 12 (JCO 2010)	291	Cape+RT	14
	293	Cape + Oxali 50mg/m ² wkly+RT	19 (p=0.09)
STAR-01 (JCO 2011)	379	FU CI+RT	16
	368	FU CI + Oxali 60mg/m ² wkly+RT	16
German AIO-04 (Lancet 2012)	623	FU CI+RT	13
	613	FU CI + Oxali 50mg/m ² wkly+RT	17 (p=0.038)
PETAAC-6 (PASCO, 2013)	547	Cape+RT	11
	547	Cape + Oxali 50mg/m ² wkly+RT	13 (p=0.031)
NSABP R-04 (PASCO, 2012)	636	FU/Cape+RT	18
	640	FU/Cape + Oxali 50mg/m ² wkly+RT	20 (p=0.42)



Glynn-Jones R et al. Ann Oncol 2017

Our case surgery & pathology

Low anterior resection according to the TME principles

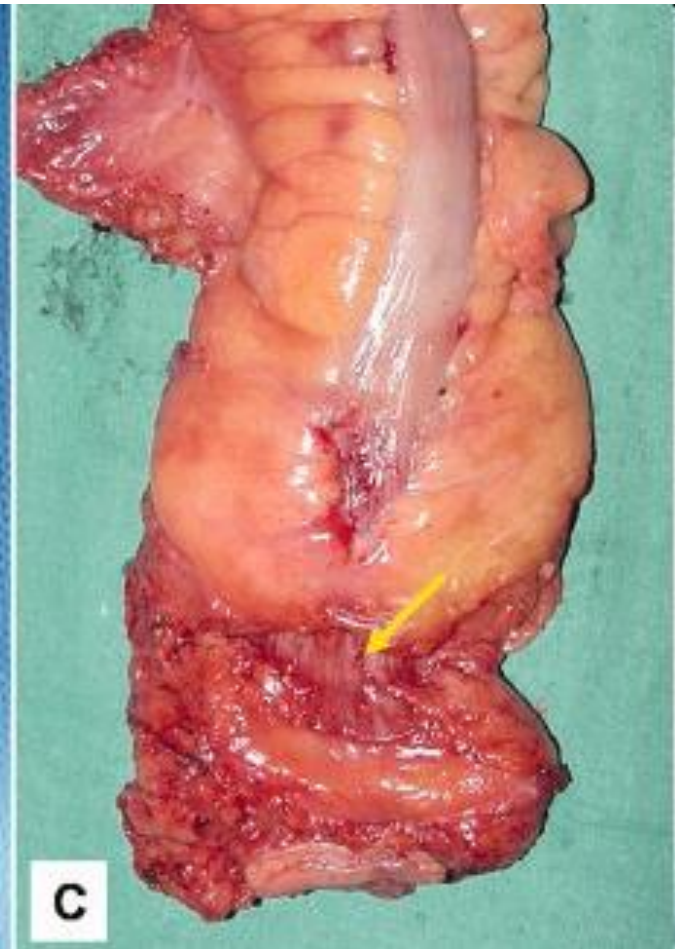
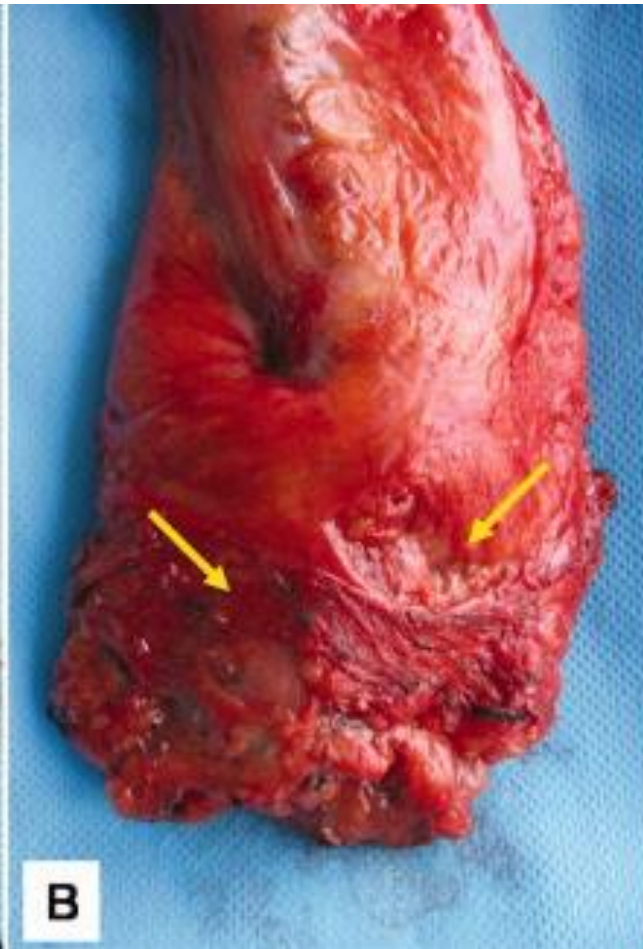
and loop ileostomy performed 8 weeks after completion of CRT

No post-operative complications.

Histology

- Resection in the mesorectal plane
- Scanty residual moderately differentiated adenocarcinoma (Dworak's TRG 3)
- ypT3N0 (0/45)
- No lymphatic or venous invasion

Macroscopic assessment of mesorectal excision



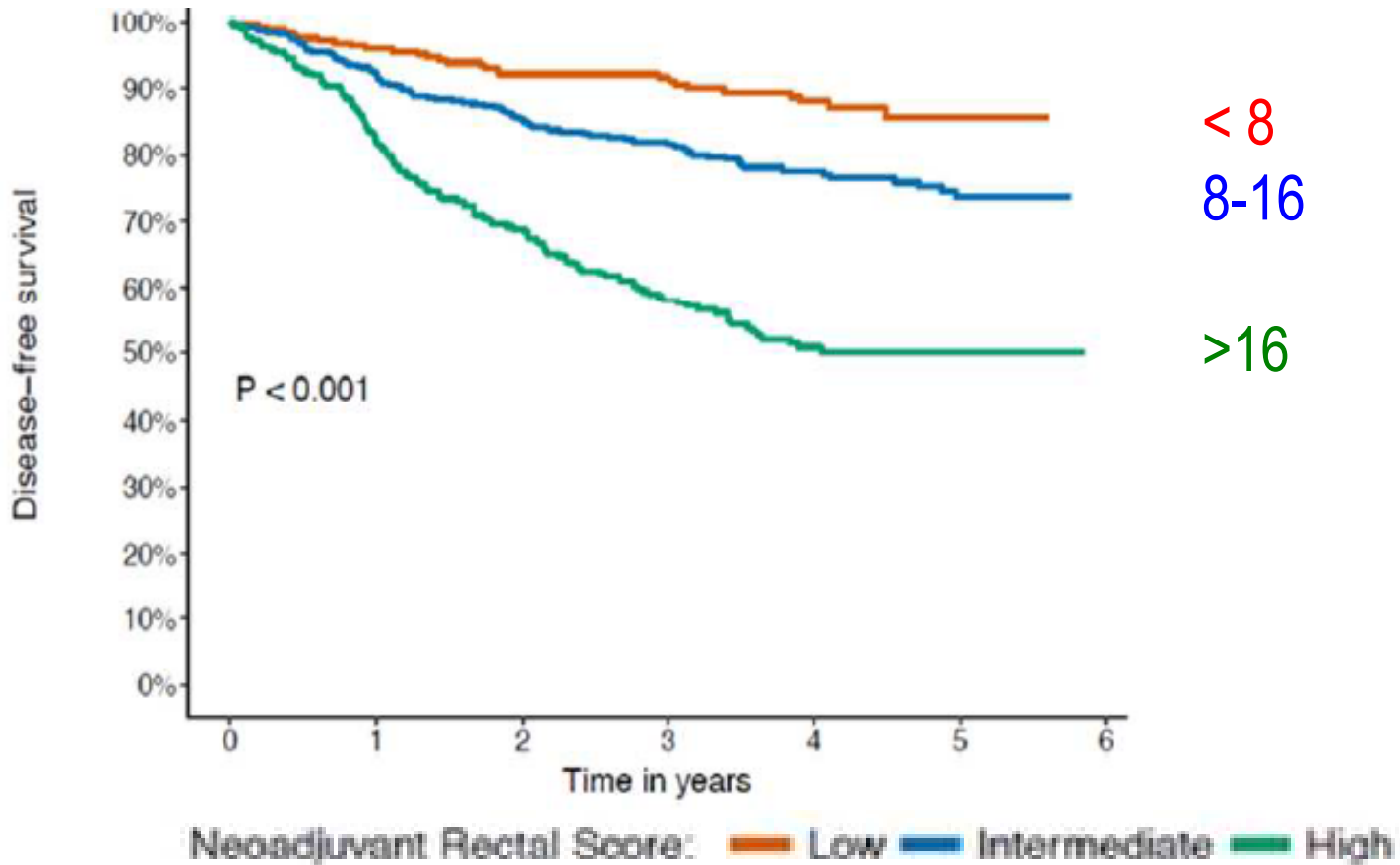
Downstaging after neoadjuvant treatment : neoadjuvant rectal score

$$NAR = \frac{[5 pN - 3(cT - pT) + 12]^2}{9.61}$$

Our patient NAR score: 14,95

George TG , et al. Curr Colorectal Cancer Rep 2015

Neoadjuvant rectal score in CAO/ARO/AIO04 trial



Our cases decision on adjuvant chemotherapy

**4 months (i.e. 6 cycles) of adjuvant chemotherapy
with single agent capecitabine**

Adding Oxaliplatin to 5-FU based adjuvant therapy in localised colon/rectal cancer

Trial	N	Control	Exp.	Stage	DFS HR P value	OS HR P value	Absolute Gain in OS	G3 Neuro Tox
MOSAIC ¹	2246	FULV2	FOLFOX4	II/III	0.80 0.003	0.84 0.046	4,2% at 6 y stage III	12%
NSABP-C07 ²	2407	FULV Roswell	FLOX	II/III	0.80 0.0034	0.82 0.002	2,7 at 5 y Stage III	8,2%
XELOXA ³	1886	FULV Mayo	CAPEOX	III	0.80 0.0038	0.83 0.04	6 % at 7 y	11%

¹André T et al. J Clin Oncol 2007

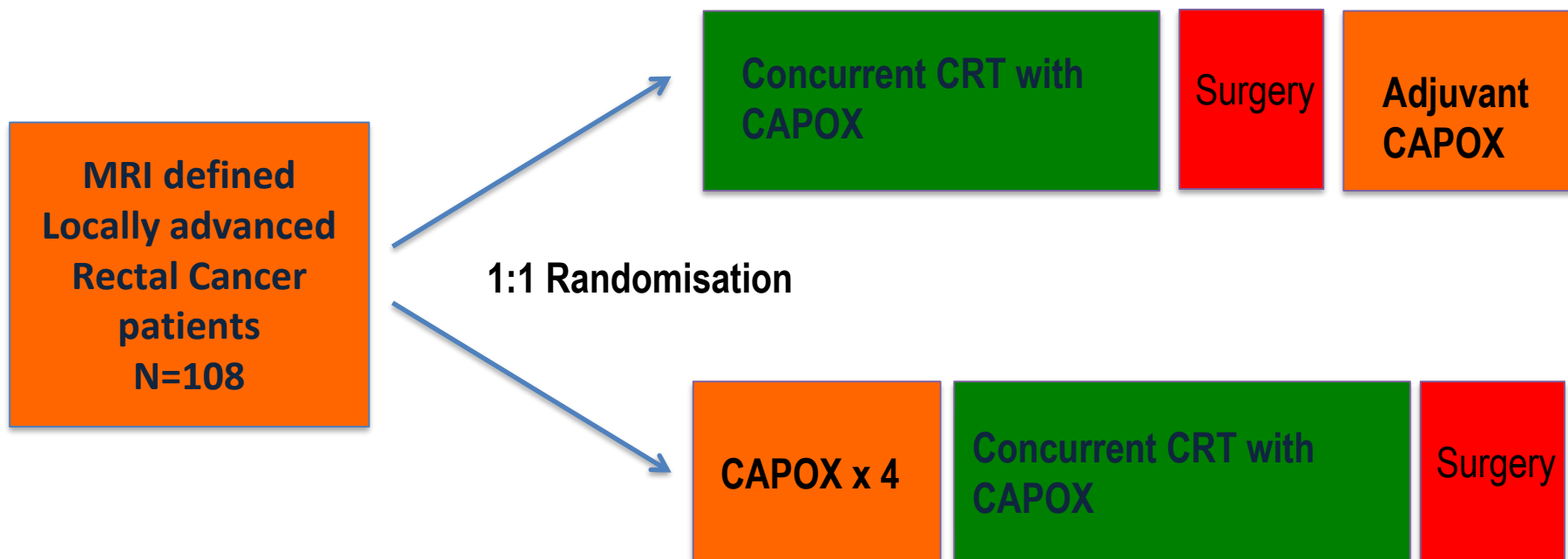
²Kuebler JP et al. J Clin Oncol 2007

³Schmoll HJ et al. J Clin Oncol 2015

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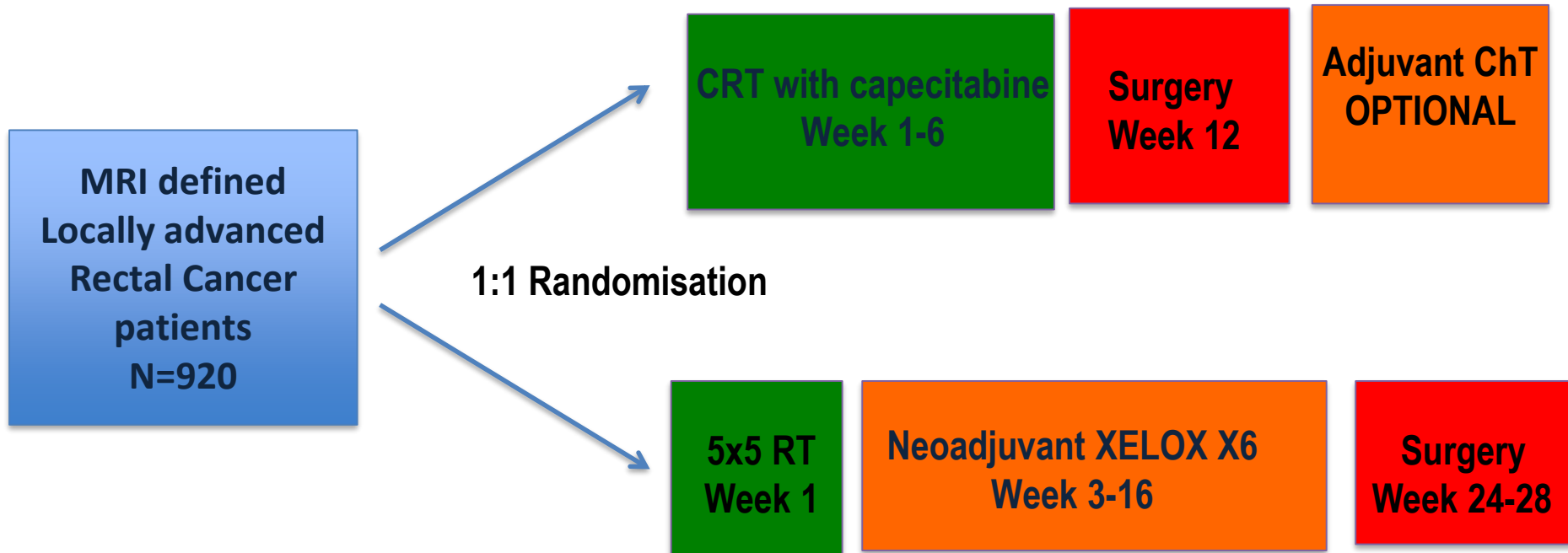
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AIO04 ⁴	1233	FU	mFOLFOX	II/III	0.79 0.030	0.96 NS	0.7 at 3 y	9%
NSABP R04 ⁵	1284	FU/Cape	+ Oxali	II/III	0.94 NS	0.94 NS	NR	6%
PETACC6 ⁶	898	Cape	+ Oxali	II/III	1.04 NS	NR	NR	8%

Neoadjuvant ChT plus chemo-RT versus chemo-RT followed by surgery and adjuvant ChT in MRI defined high risk rectal cancer: the Phase II randomised valencian experience



Fernández-Martos et al. Ann Oncol 2015

THE WAY FORWARD: THE PHASE III RANDOMIZED RAPIDO TRIAL



DFS at 3 years improved by 10% from 50% to 60%

PI: Prof. C. van de Velde

Conclusions

Integration of knowledge in a multidisciplinary team

LoE: IV GoR: A

Optimal staging by MRI LoE: III GoR: A

Selective preoperative radiation or chemoradiation

LoE: I GoR: A

TME surgery LoE: II GoR: A

Adjuvant chemotherapy for high risk patients: LoE II GoR:B

THANKS