The surgeon´s point of view

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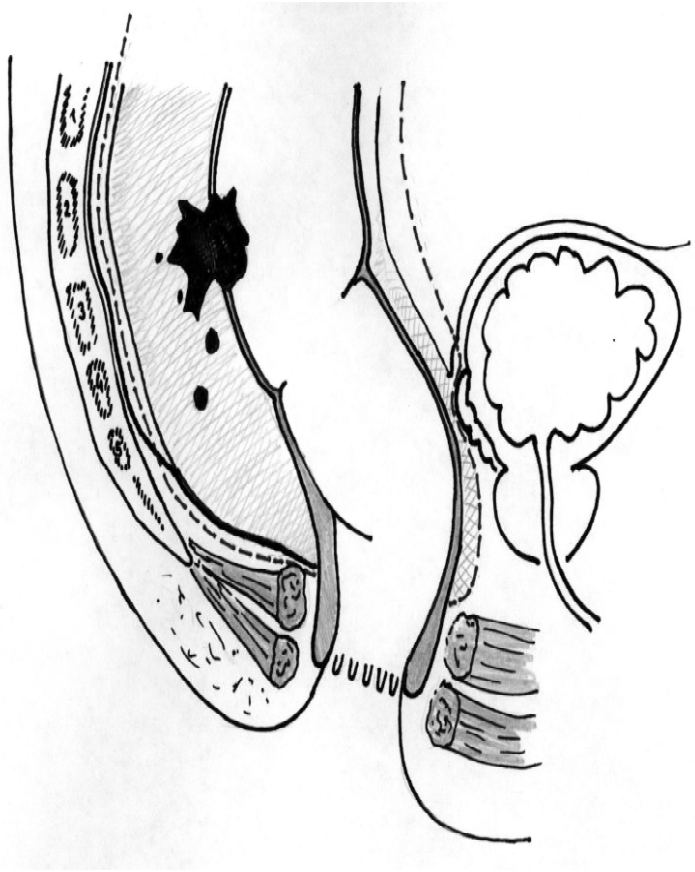
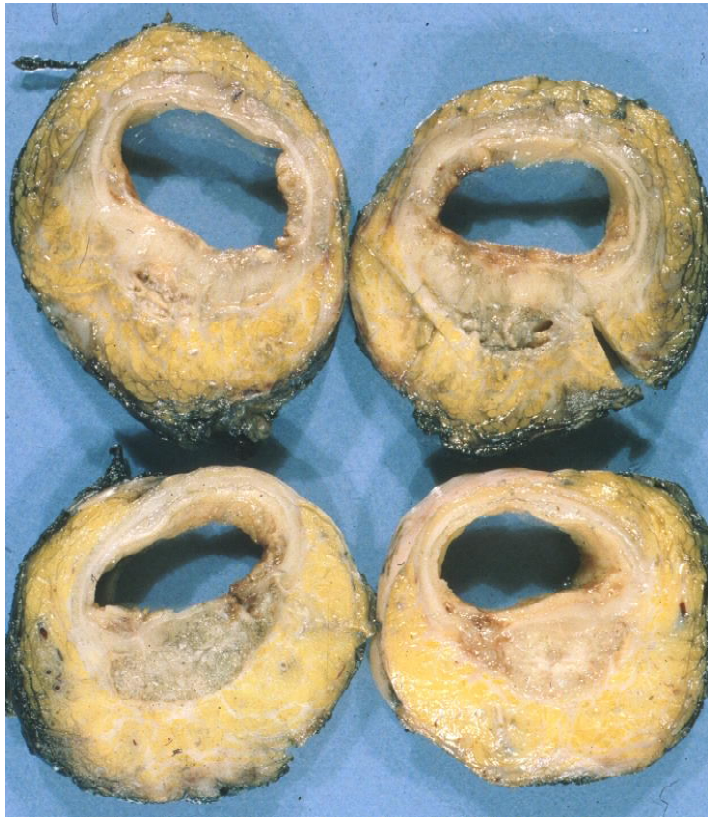
Cancer of the mid/upper rectum
T3 EMVI +, CRM-, N+: treatment options

- Surgery
- Chemoradiation
- Chemotherapy

Cancer of the mid/upper rectum
T3 EMVI+, CRM -, N+

- **Total mesorectal excision (TME)**



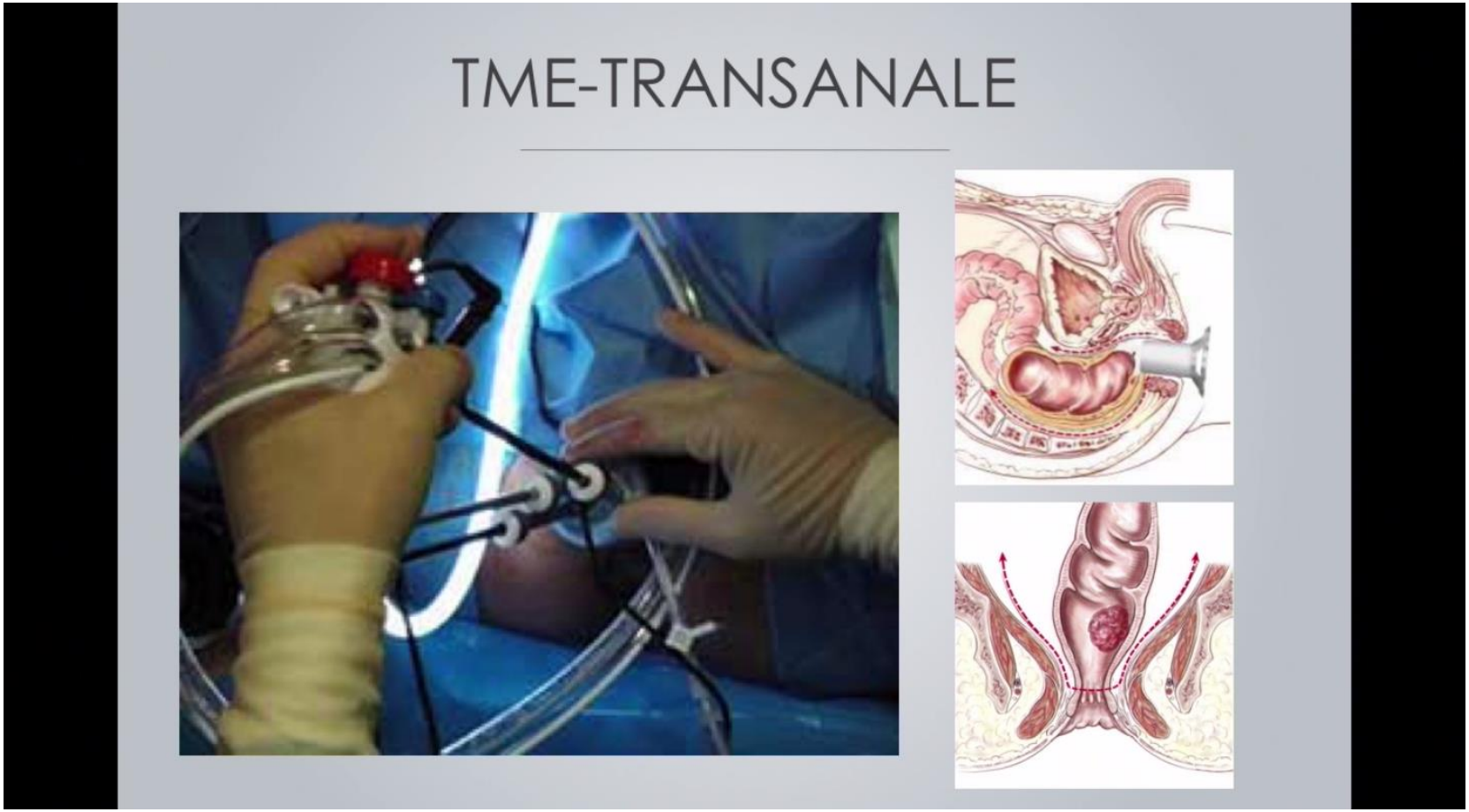


Laparoscopic surgery for rectal cancer ?

- shorter incision
- becoming the reference treatment but need for specific surgical expertise
- hospital stay 1 day shorter…. (8 vs 9 days)*
- restoration of bowel function faster… (2vs3d)*
- surgical morbidity similar*
- long term oncologic results similar: COLOR II * COREAN**

* Bonjer et al. NEJM , 2015; ** Park et al. ASCO 2017 abst 3518;

The future? Trans anal TME



From L. Maggiori

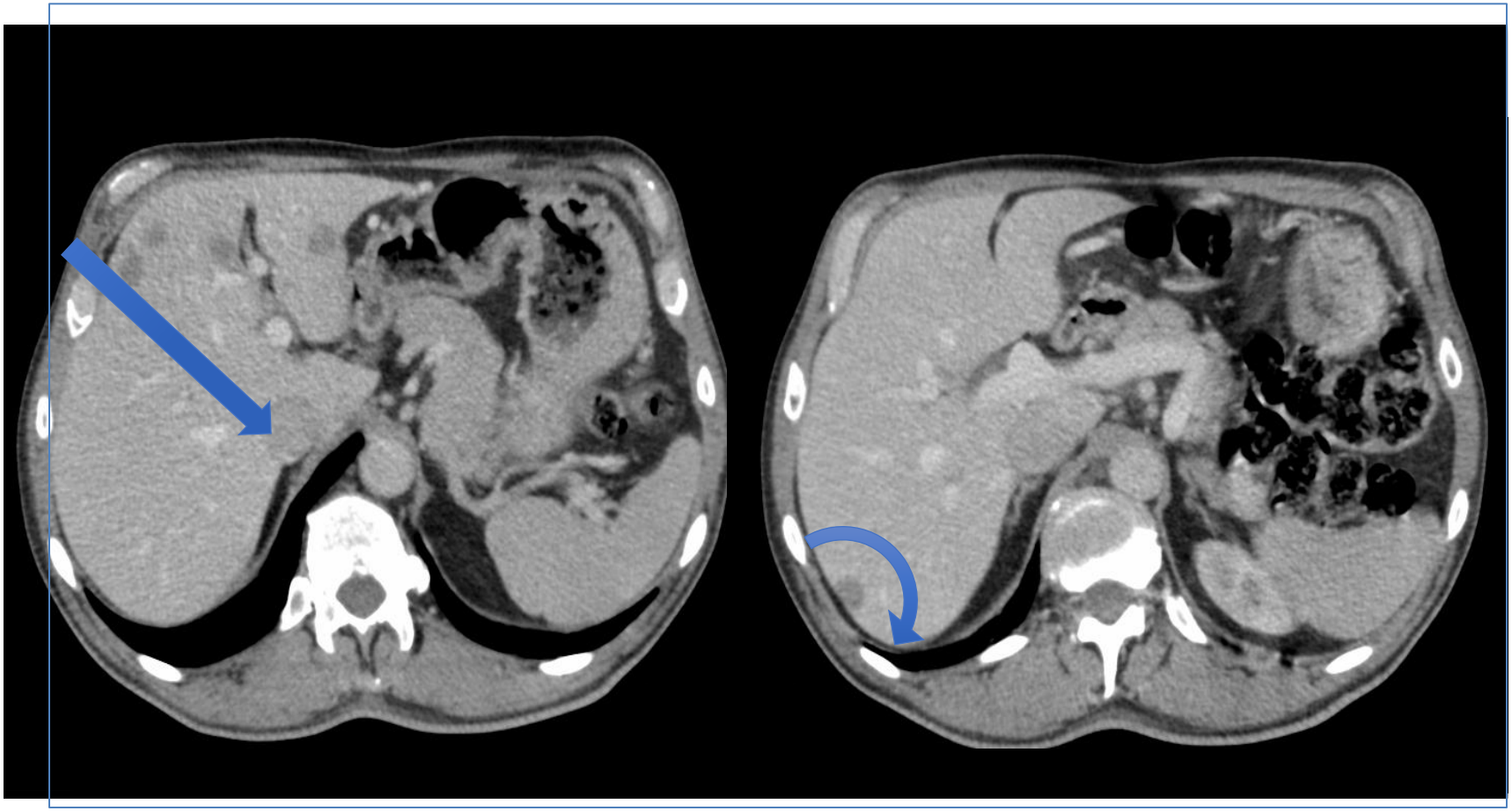
Surgery for resectable CRC liver metastases

- Surgery alone:

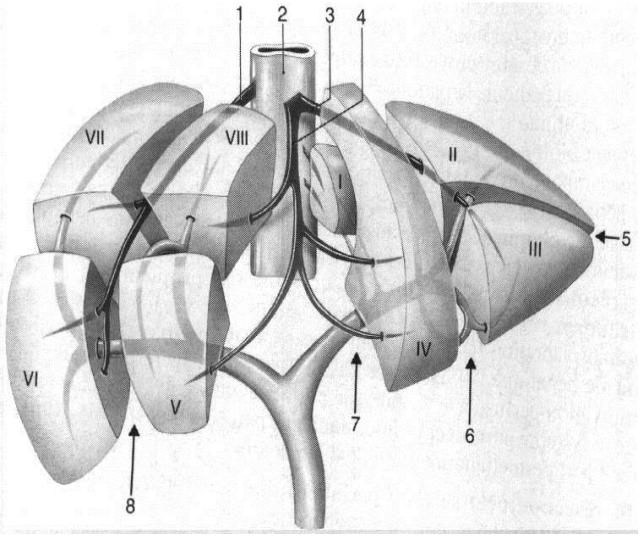
  - 5 y OS: 30 – 50 % according to risk factors,
  - 50% (EORTC 40983)
  - Cancer relapses: 2/3 patients (EORTC 40983)

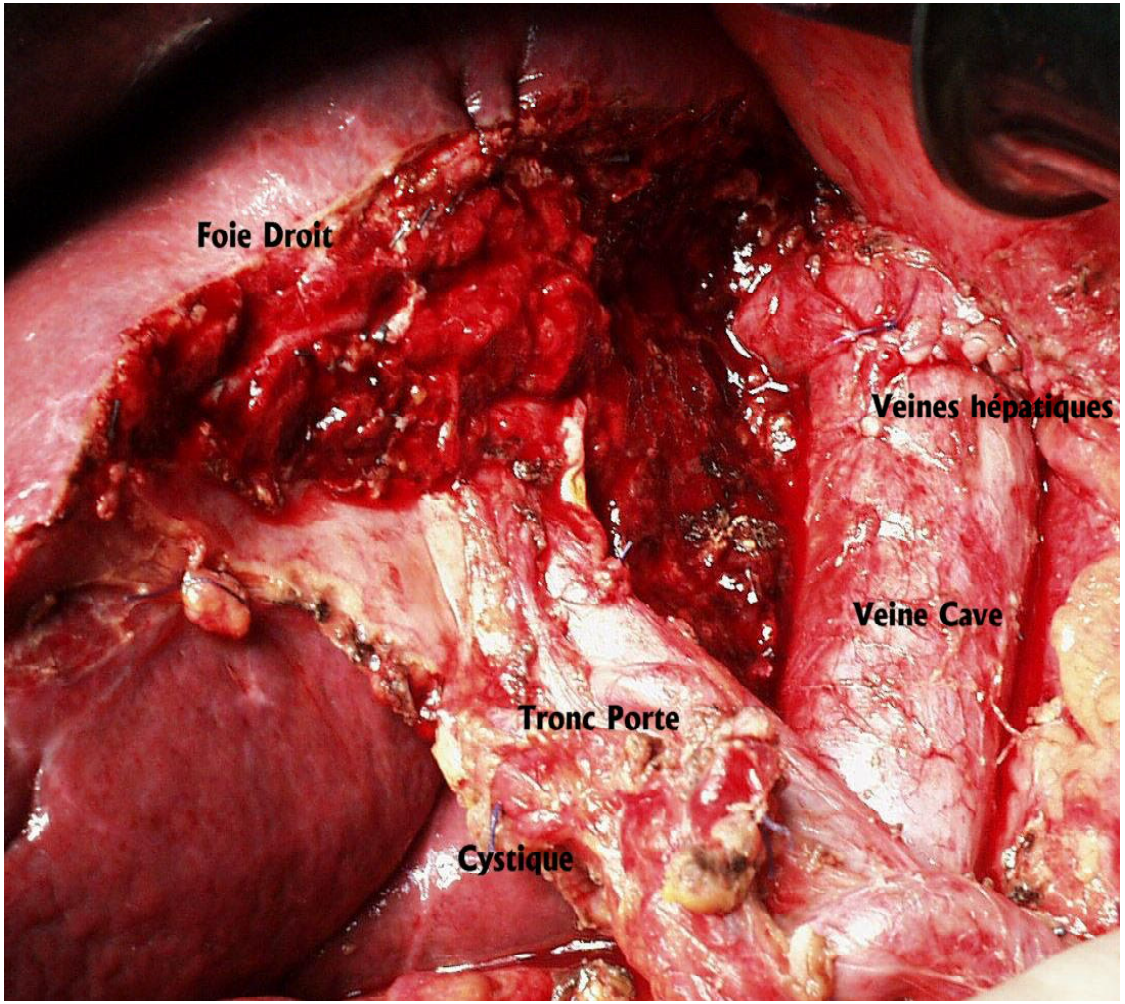
- Nordlinger et al. Lancet 2008f Lancet

Clinical Case:
left lobectomy, right wedge resection

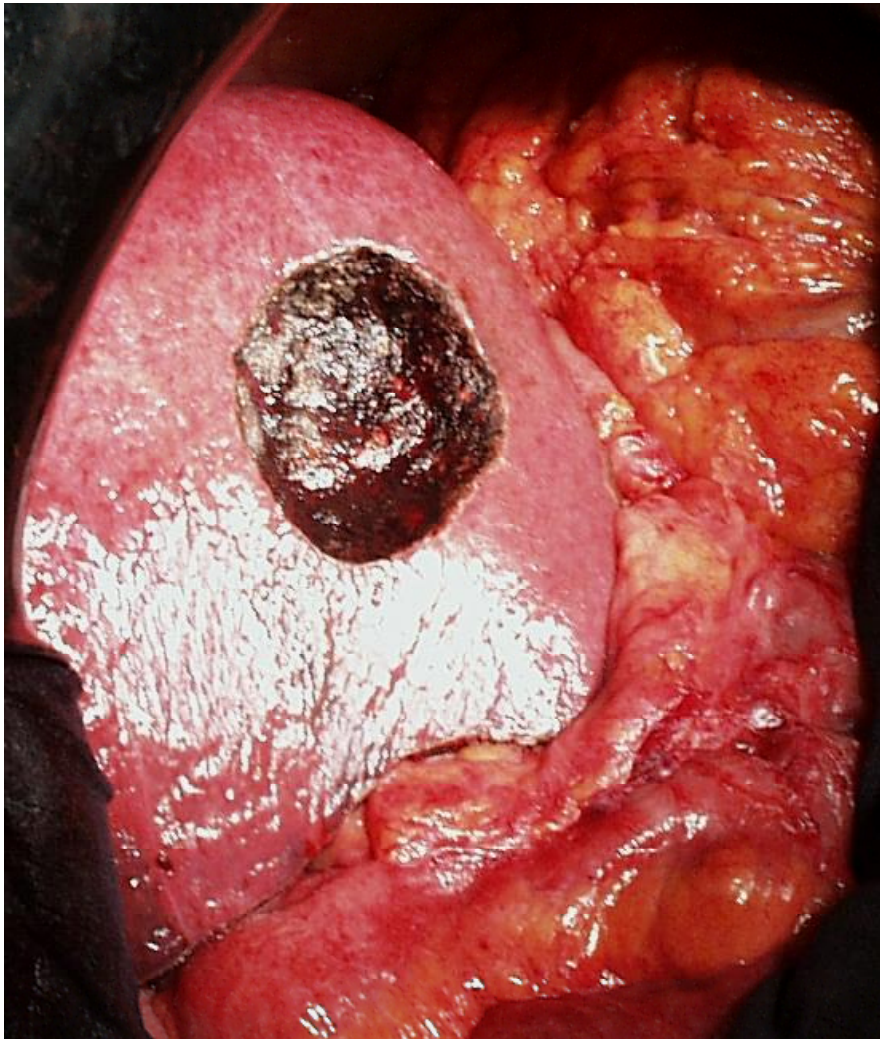


Left lobectomy





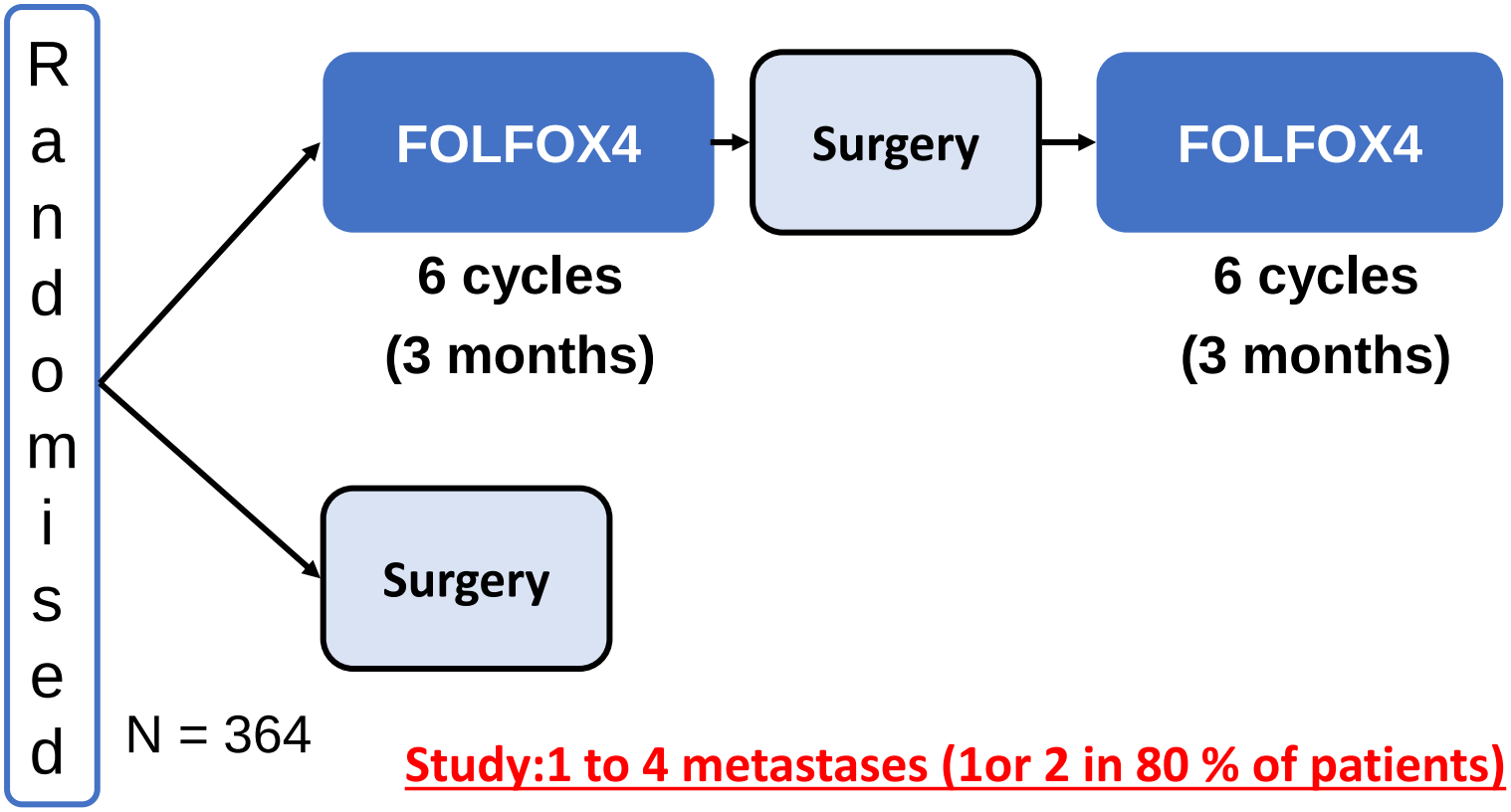
Wedge resection



Peri-operative Chemotherapy for CRC resectable liver metastases

EORTC 40983

Peri-operative chemotherapy vs surgery alone

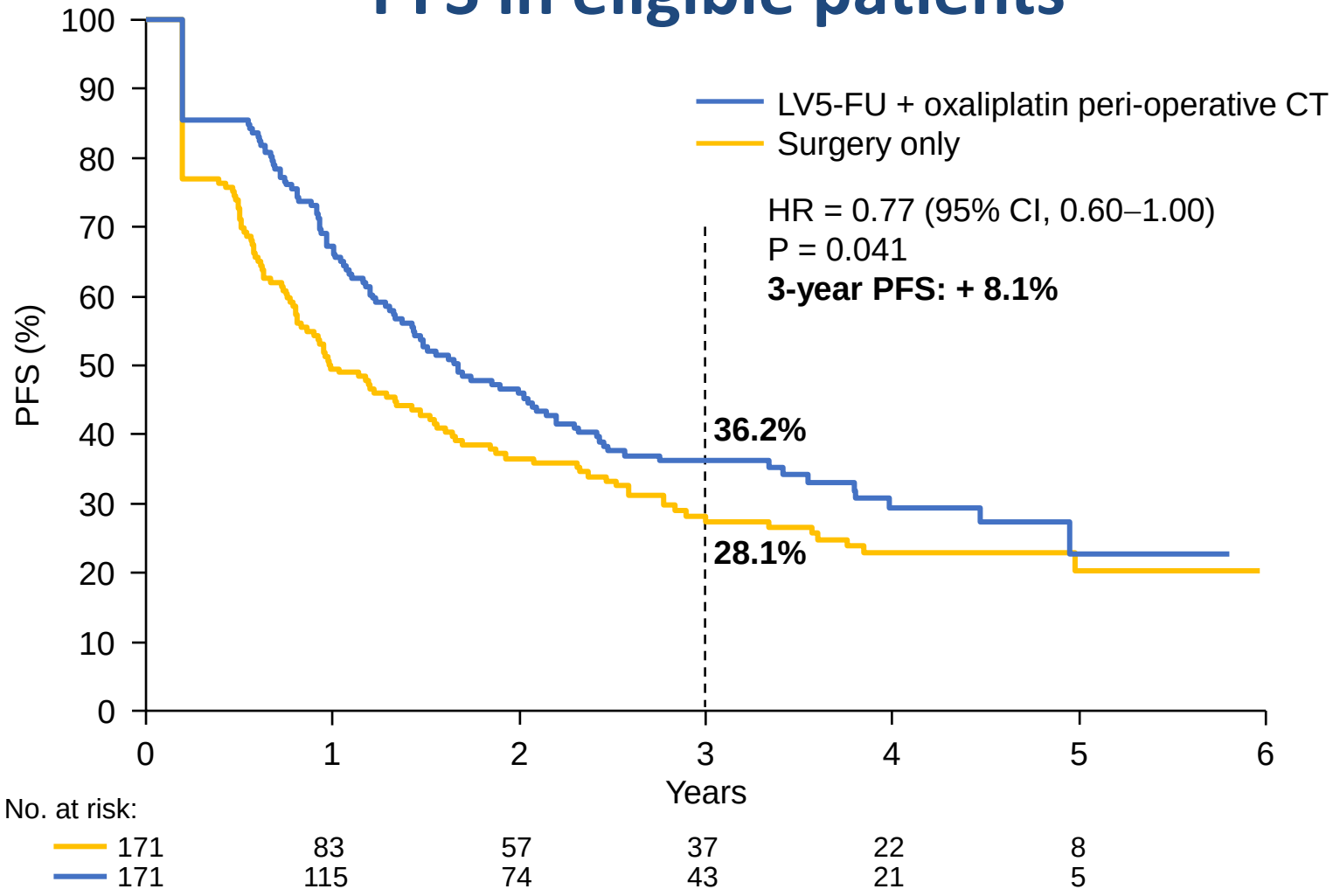


Study:1 to 4 metastases (1or 2 in 80 % of patients)

With CR UK, ALM CAO, AGITG, FFCD

ClinicalTrials.gov identifier: NCT00006479;
Nordlinger B, et al. Lancet 2008;371:1007–16; Nordlinger B, et al. Lancet 2013;14:1208–14.

EORTC 40983 Peri-operative chemotherapy FOLFOX
PFS in eligible patients

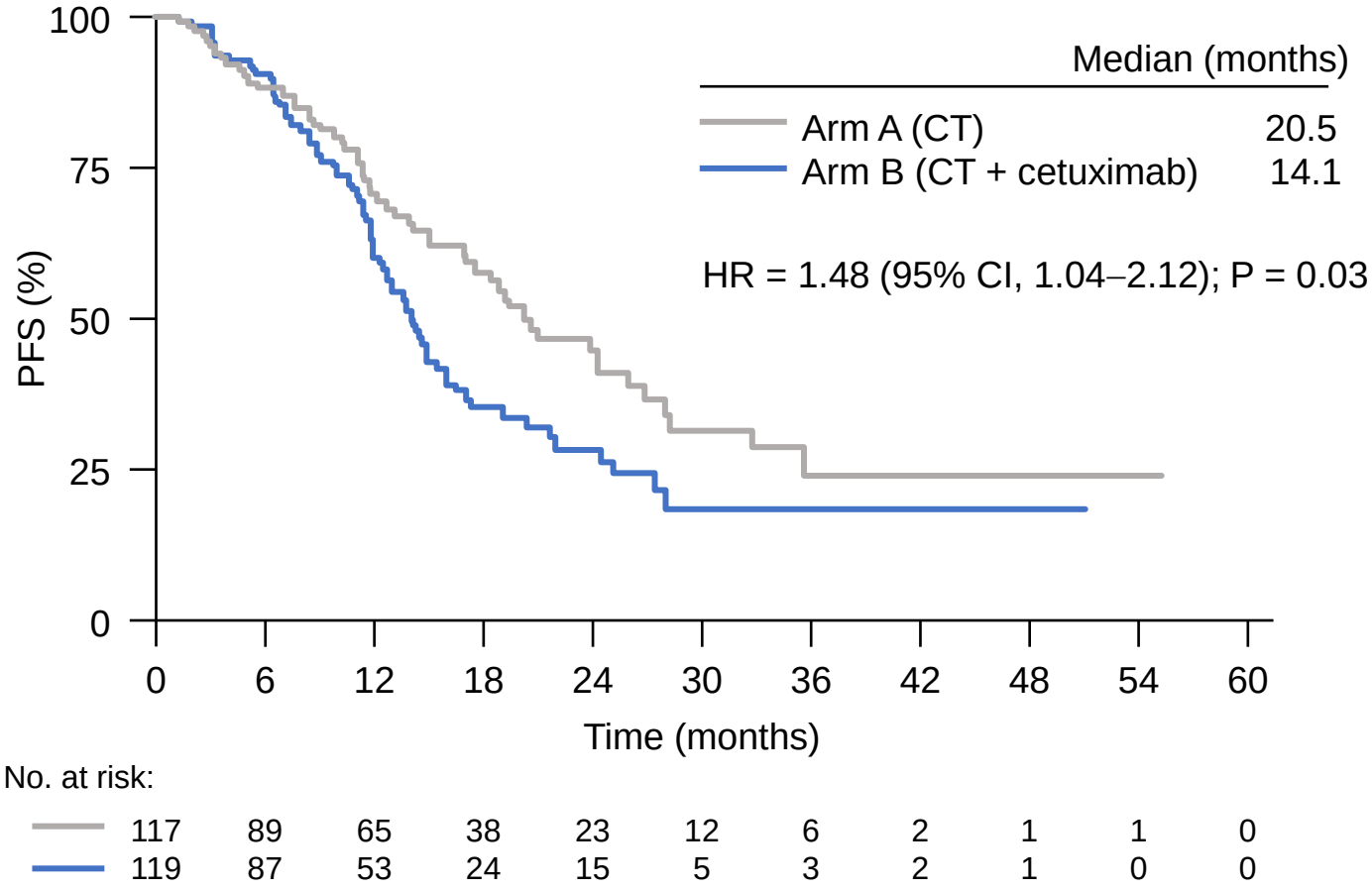


Nordlinger B, et al. Lancet 2008;371:1007–16.

CT, chemotherapy.

New EPOC

PFS of all randomised WT *KRAS* patients (primary analysis)



Primrose J, et al. Lancet Oncol 2014;15:601–11.

Peri-operative chemotherapy

- EORTC 40983 is the only positive trial which demonstrates the superiority of combined treatment over surgery alone in resectable metastases
- Peri-operative FOLFOX is the reference treatment
- The benefit of combining biologics not demonstrated in this indication
- New trials are eagerly awaited, particularly for high risk metastases

High risk resectable metastases: new studies

- Adjuvant IV vs IA :(PACHA 01: ph II III;France) *
  - high risk resectable metastases:
  - IV FOLFOX vs LV5FU 2+ IA FOLFOX *
- Peri-op vs post-op(PEPCORLI China) **
  - resectable liver metastases
  - XELOX: 2 cycles before S + 4 after vs 6 cycles after S**
- Pre-op chemo+ surgery vs surgery alone: (CHARISMA, the Netherlands***
  - in high-risk resectable liver metastases

* ClinicalTrials.gov NCT02494973; ** ClinicalTrials.gov NCT02912052 ** BMC Cancer. 2015 Mar 26

**;

Combining the options for our clinical case with synchronous metastases

Surgical options and the synchronous presentation

- **Rectum first (after chemo-radiation)**:

  - pro: ideal for rectum

  - risk: metastases progress ➔ unresectable

- **Liver first (after pre-op chemo):**

  - pro: ideal for liver metastases

  - risk: delays treatment of rectum, but primary T can also respond to FOLFOX

- **Simultaneous resections of rectum and liver**

  - pro: avoids delays

  - risk: increased morbidity if two simultaneous major resections; requires double expertise

Reddy et al. Ann Surg Oncol 2007, De Santibanes et al. J Am Coll Surg 2003, Fujita et al, Jpn J Clin Oncol 2000, Tocchi et al, Int J Colorectal Dis 2004; Adam et al.Br J Surg 2010

Rectum first

- - RCT(50 Gy) xeloda➔S rectum➔chemo➔S liver

  - RCT(50 Gy) FOLFOX➔S rectum➔chemo➔S liver

  - RT(5x5 Gy) ➔S rectum➔chemo➔S liver

  -FOLFOX + RT(5x5 Gy) ➔S rectum➔chemo➔S liv.

  - FOLFOX + CRT (50 Gy) xeloda ➔S rectum➔chemo➔S liv.

Primary tumor resection first: studies

- Studies concern patients with **unresectable** metastases
- Some retrospective studies suggest a benefit of resecting primary colon or rectal first
- Ongoing Ph III trials:CLIMAT-PRODIGE 30 (France),

  CAIRO 4 (The Netherlands), SYNCHRONOUS (Germany)

Liver first ” the reverse approach” *

-Chemo ➔S. liver➔RCT (50Gys+ xel)➔S rect.

-Chemo ➔S. liver➔RCT (50Gys+ FOLFOX) ➔S rect.

-Chemo ➔S. liver➔ RCT (5x5 Gys+ FOLFOX) ➔S rect.

-Chemo ➔S. liver➔ CT➔S rect.

* Mentha G et al. *Br J Surg* 2006

Simultaneous resections of liver and rectum

-FOLFOX ➔combined surgery.

-RCT (50Gys+ FOLFOX) ➔combined surgery.

-RCT (5x5 Gys+ FOLFOX) ➔combined surgery

- not advisable in this clinical case: combined major liver and intestinal resections induce increased surgical morbidity) *,**

*Nordlinger, Jaeck , Cancer 1996; **Reddy SK et al. Ann SurgOncol 2007

Surgery for synchronous colorectal liver metastases and primary tumor

Approach	No Pts	Tumors No.	Mortality %	Cumulative Morbidity %	5y OS
Primary first	**72**	**3**	**3**	**51**	**48%**
Combined	**43**	**1**	**5**	**47**	**55%**
Liver first	**27**	**4**	**0**	**31**	**39%**
P value		.01, .001	NS	NS	NS

the different approaches appear similar for postoperative morbidity and control of cancer

Brouquet et al.(M. D. Anderson) J Am Coll Surg 2010

Is there a need for adjuvant chemotherapy ?

Decision of the MDT

- **D. Arnold:**

Start with best **chemo** → **consider 5x5** (but likely without RT) → ask the surgeon how to proceed (liver or rectum first) → complete chemo (to 6 mos. total) → observe

- **F. Calvo:**

- **B. Nordlinger:**

start with chemo 3-4 cycles → **CRT** 50Gys + FOLFOX→ **S rectum + wedge** right liver → +/- interval chemo→ **S liver** left lobectomy→ complete chemo