DIALOG

FRENCH COLLABORATIV GROUP
FOR GERIATRIC ONCOLOGY RESEARCH

GERICO

unicancer

SoFOG

SOCIÉTÉ
FRANCOPHONE
D´ONCO-GÉRIATRIE

LA LIGUE

PACAN

Plateforme de recherche clinique
Personnes Agées et CANcer

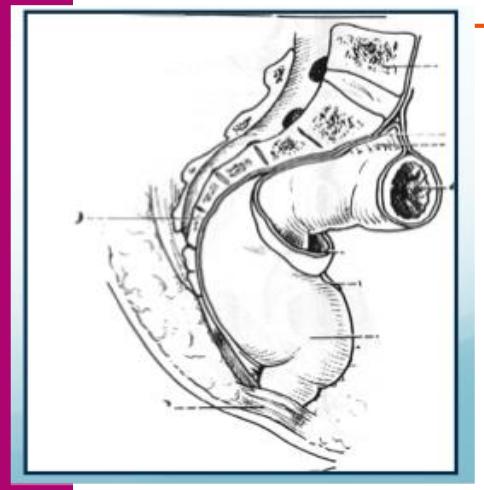
RÉPUBLIQUE
FRANÇAISE

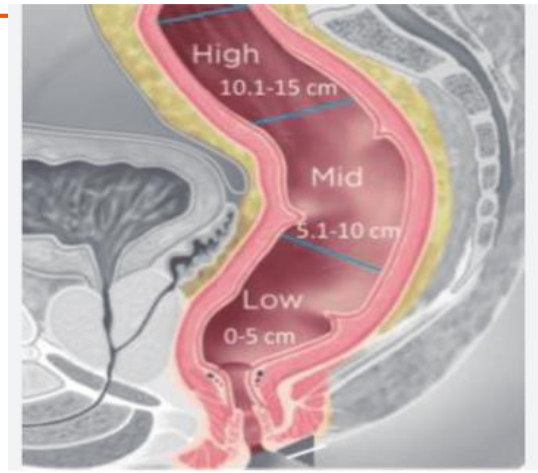
INSTITUT
NATIONAL
DU CANCER

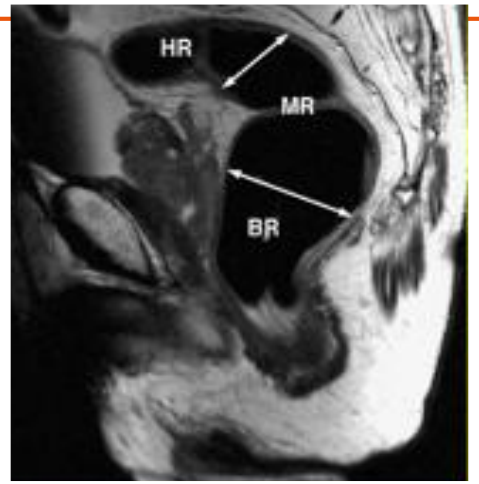
Individualization of surgical approches in the older population with rectal cancer, what can be learned from research?

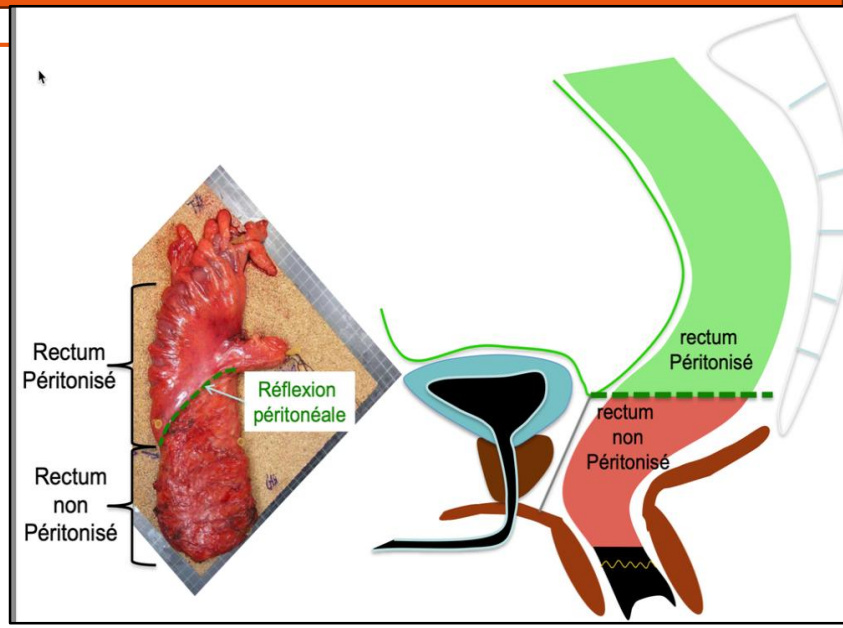
Frédérique PESCHAUD
APHP Ambroise Paré Boulogne

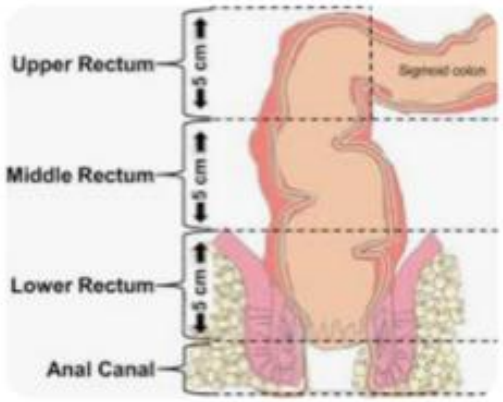
Anatomy of Rectum

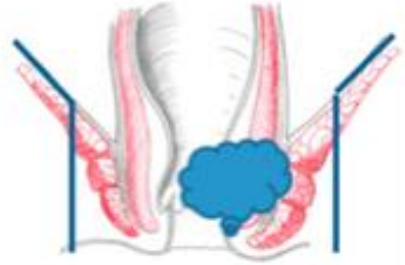












abdominoperineal resection

intersphincterienne resection

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Swedish Rectal Cancer Trial : RT courte pré-op améliore le contrôle local / chirurgie

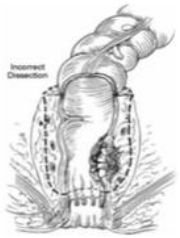
German Trial: Preop RCT améliore le contrôle local / RCT postop

TNT améliore la DFS / RCT Préop (Prodige 23 / RAPIDO)

1990 **2000** **2020**

Dutch trial: Preop RT+ TME vs TME
Améliore le contrôle local

MRC CR07 : Preop RT courte
Améliore le contrôle local et DFS / TTT postop





A Habr Gama

Anterior resection 1970

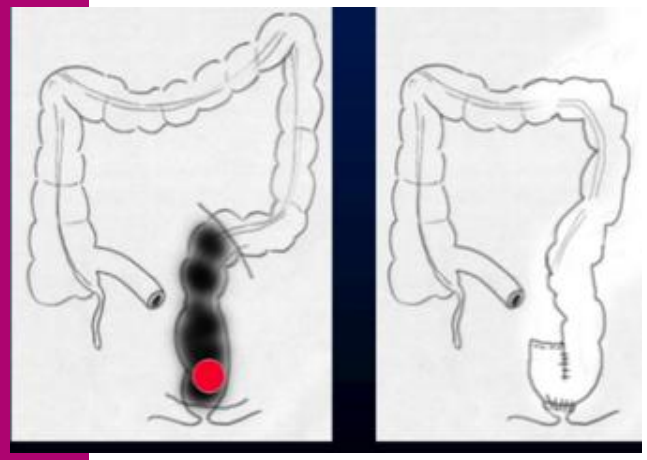
Laparotomy TME 1986
Total Mesorectum Excision

Laparoscopy TME 2000

« Watch and Wait » 2006

Rectal preservation

Morbi-mortality of surgery



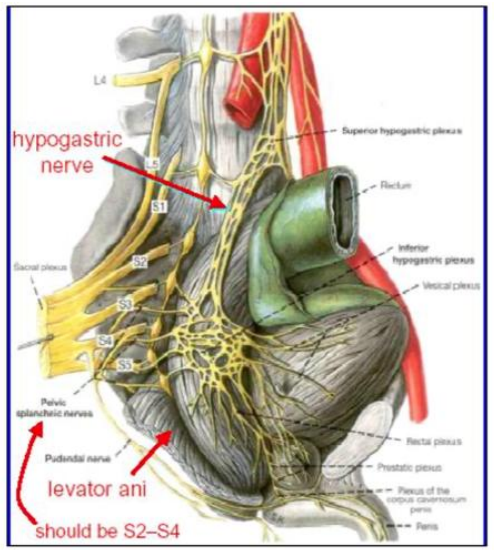


Tableau I. Complications chirurgicales et post-opératoires du cancer colorectal en fonction de l'âge (Adapté de réf.[4]).

Morbidité postopératoire	< 65	65-74	75-84	> 85	P
Complications pulmonaires	5%	10%	12%	15%	<0,0001
Complications cardio-vasculiaires	0,8%	2%	4%	4%	<0,0001
Accident vasculaire cérébral	0,2%	0,6%	1%	1%	<0,001
Accidents thrombo-emboliques	1%	2%	2%	2%	=0,0004
Fistules anastomotiques	4%	5%	4%	3%	=0,2607

Surgery for colorectal cancer in elderly patients: Lancet 2000;356:968-74.

	%
Mortalité	0 - 2%
Morbidité	30 - 40%
Fistule / sepsis pelvien	**15 - 20%**
Stomie définitive	9 - 27%
LARS Sévère (>29)	55 - 60%
Troubles génito-urinaires	40 - 50%

→ 1/3 keep a definitive stomy

Increasing age was only associated with non-surgical complications) not with surgical complications.

Rapport AFC 2009; Color II Trial, N Engl J Med 2015; Alacart trial, JAMA 2016, Jeong, Lancet Oncol 2014; Maggiori, Ann Surg 2017; Chen TY, Clin Colorectal Cancer 2015, Pucciarelli S, Br J Surg 2016; Hupkens Dis Colon Rectum 2017; Wiltink, Eur J Cancer 2015

Geriatric assessment

The Comprehensive Geriatric Assessment (CGA)	identifies frail patients assist in clinical decision-making Correlated with post-therapy morbidity and mortality
The Geriatric score G8	The best screening tools (ss 89%, sp23% in CCR) <14
Prospective GOSAFE study, 1000pts (Geriatric Oncology Surgical Assessment and Functional recovery	Crucial role of frailty assessment to predict postoperative complications and correlate with postoperative quality of life and functional recovery

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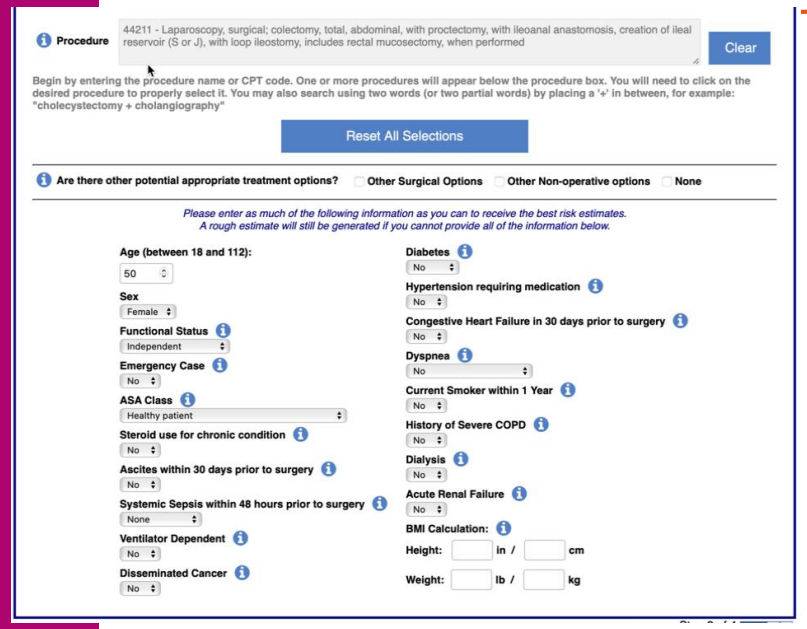
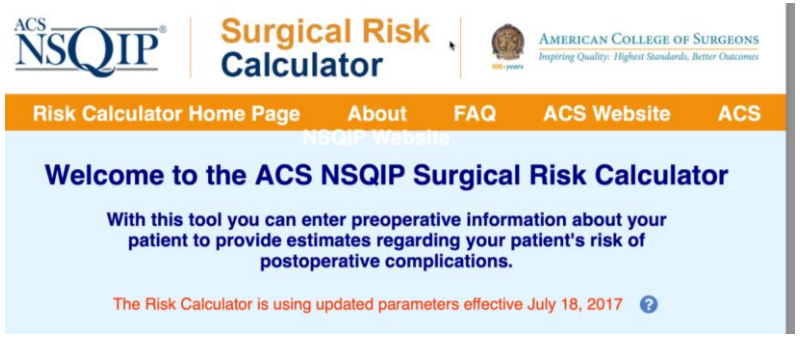
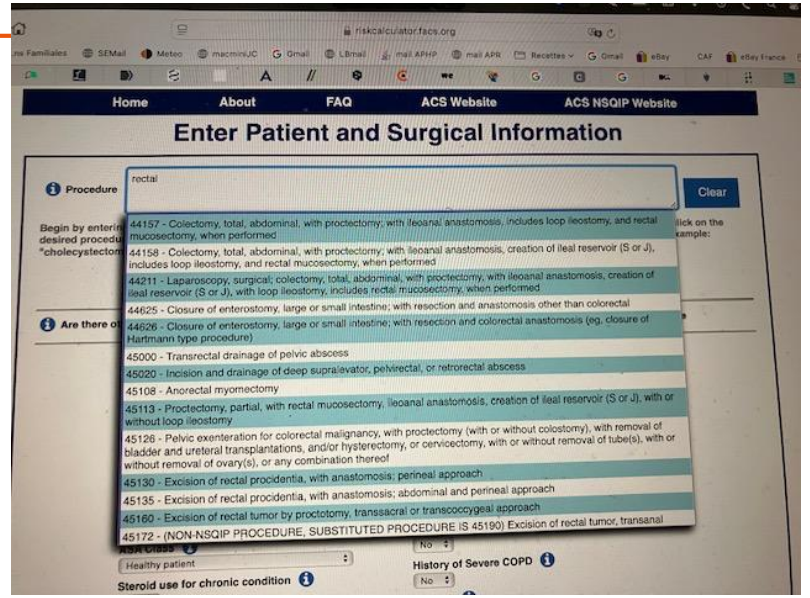
Bellera CA, Ann Oncol 2012, Montroni Gosafe JGO 2020 Soubeyran P, (2014) the ONCODAGE prospective Multicenter Cohort Study.

“Surgery Risk Assessment”







Surgical Risk Calculator

The American College of Surgeons National Surgical Quality Improvement Program
A risk calculator that estimates the chance of an unfavorable outcome (such as a complication or death) within 30 days after surgery

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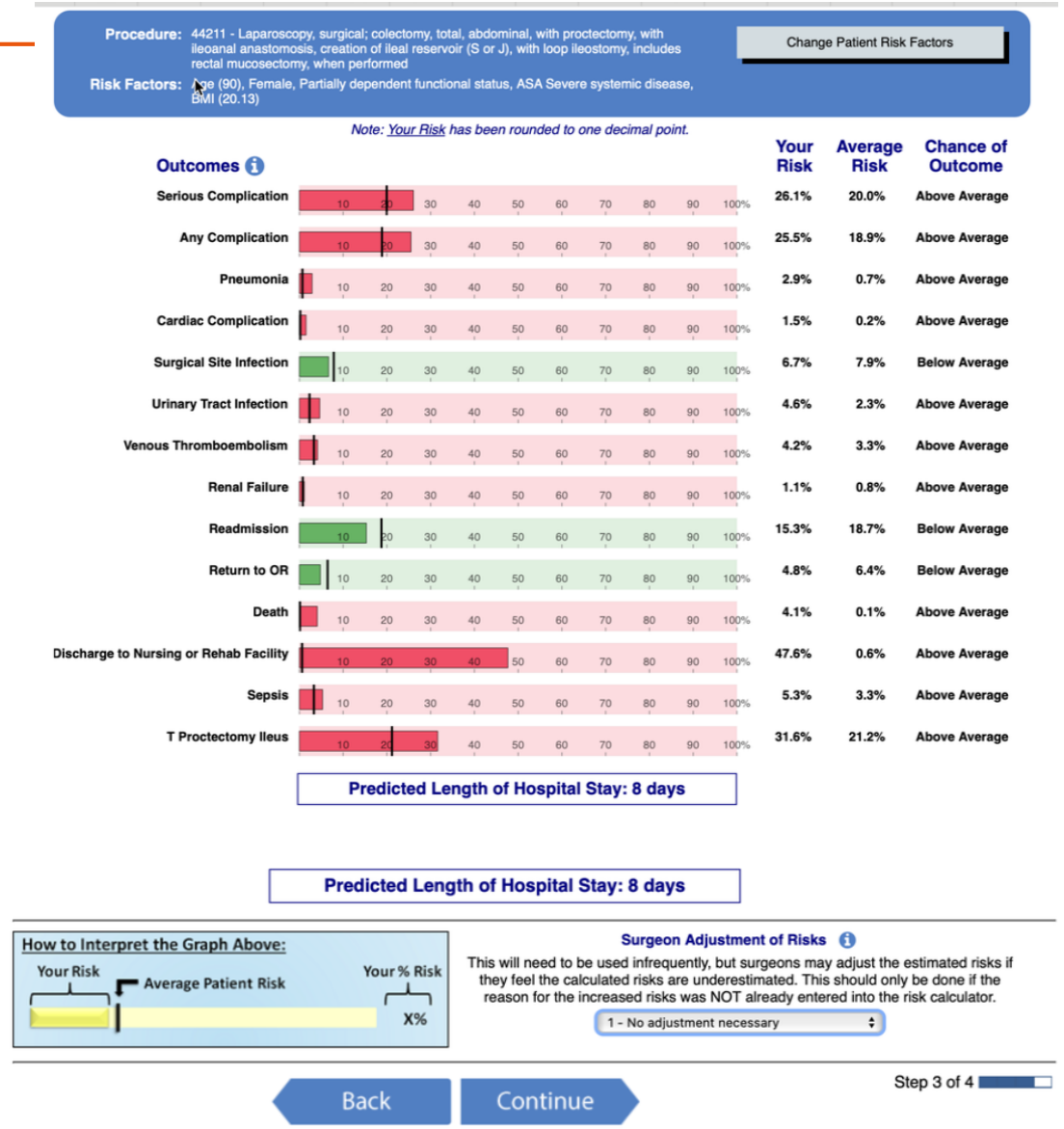
J Am Coll Surg 2020

- The risk calculator is to provide accurate, patient-specific risk information to guide
  - both surgical decision-making and informed consent
  - predict the likelihood of patients having one of 19 different outcomes within 30 days of surgery



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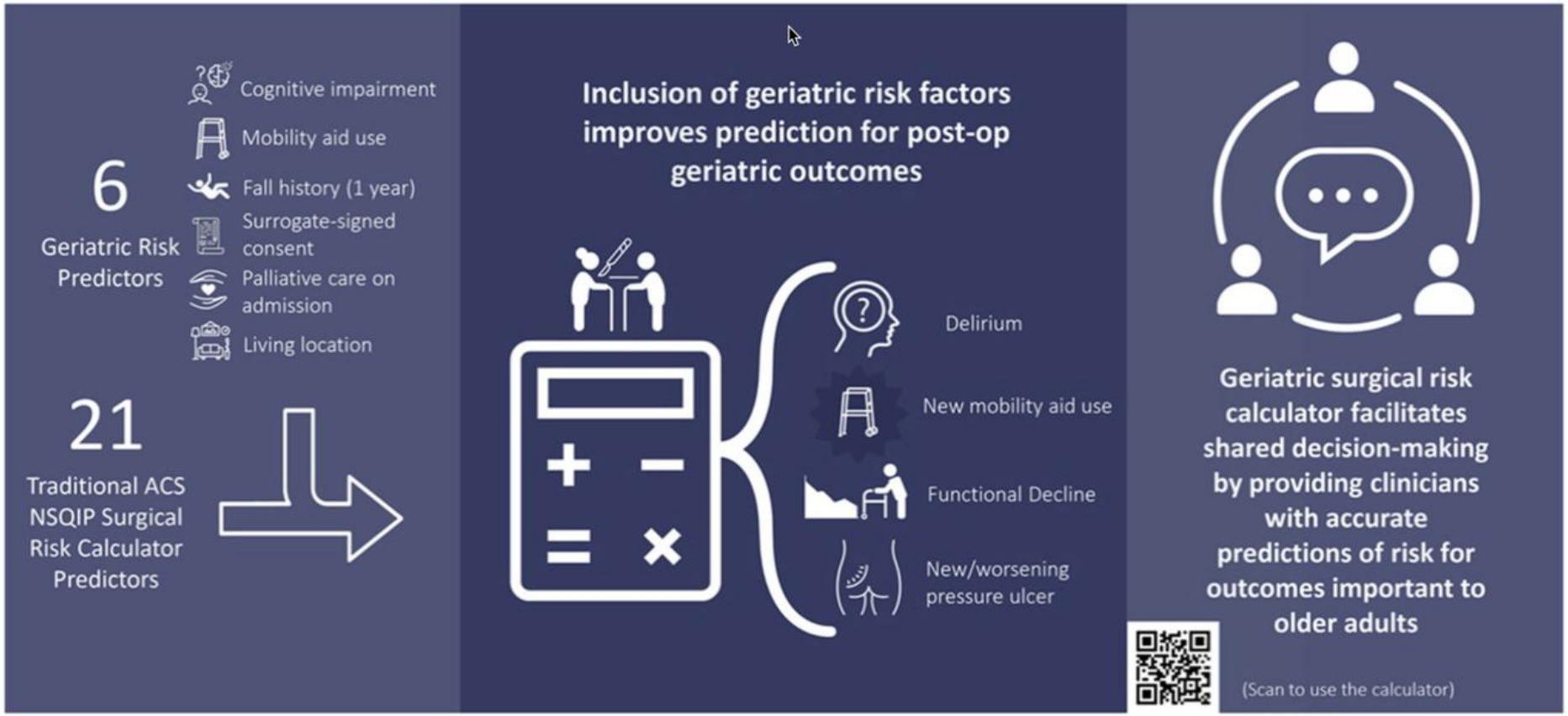
J Am Coll Surg . 2013, Hornor 2020 J Am Surg

Enhancing the ACS NSQIP Surgical Risk Calculator to Predict Geriatric Outcomes



Hornor and Ma et al. J Am Coll Surg, January 2020

JACS

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How to Improve care for elderly patients

Prehabilitation to reduce postoperative complication?
Geriatric co-management: will be the wining solution for patient?

Prehabilitation in older patients and high-risk patients undergoing colorectal cancer surgery

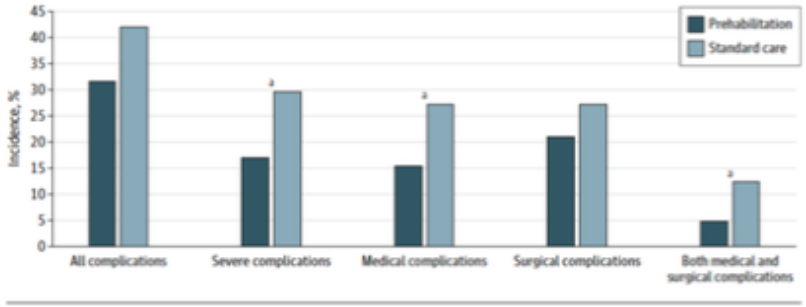
Préhabilitation : Cancer Colorectal

Original Investigation. *JAMA Surg*. 2023 Jun 1;158(6):572–581. doi: 10.1001/jamasurg.2023.0198.

Effect of Multimodal Prehabilitation on Reducing Postoperative Complications and Enhancing Functional Capacity Following Colorectal Cancer Surgery: The PREHAB Randomized Clinical Trial

Charlotte Johanna Laura Molenaar, Enrico Maria Minnella, Miquel Coca-Martinez, David Wouter Gerard Ten Cate, Marta Regis, Rashami Awasthi, Graciela Martínez-Palli, Manuel López-Baamonde, Raquel Sebio-Garcia, Carlo Vittorio Feo, Stefanus Johannes van Rooijen, Jennifer Marijke Janneke Schreinemakers, Rasmus Dahlin Bojesen, Ismail Gögenur, Edwin R van den Heuvel, Francesco Carli, Gerrit Dirk Slooter; PREHAB Study Group

Figure 2. Complications Within 30 Days After Surgery



4-week in-hospital supervised multimodal prehabilitation program:
- high-intensity exercise program 3 times per week,
- nutritional intervention,
- psychological support,
- and a smoking cessation program when needed.

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Age 60-77

Prehabilitation in older patients and high-risk patients undergoing colorectal cancer surgery

Physical intervention: supervised 28 min with oncologic physical therapist and at-home low-intensity

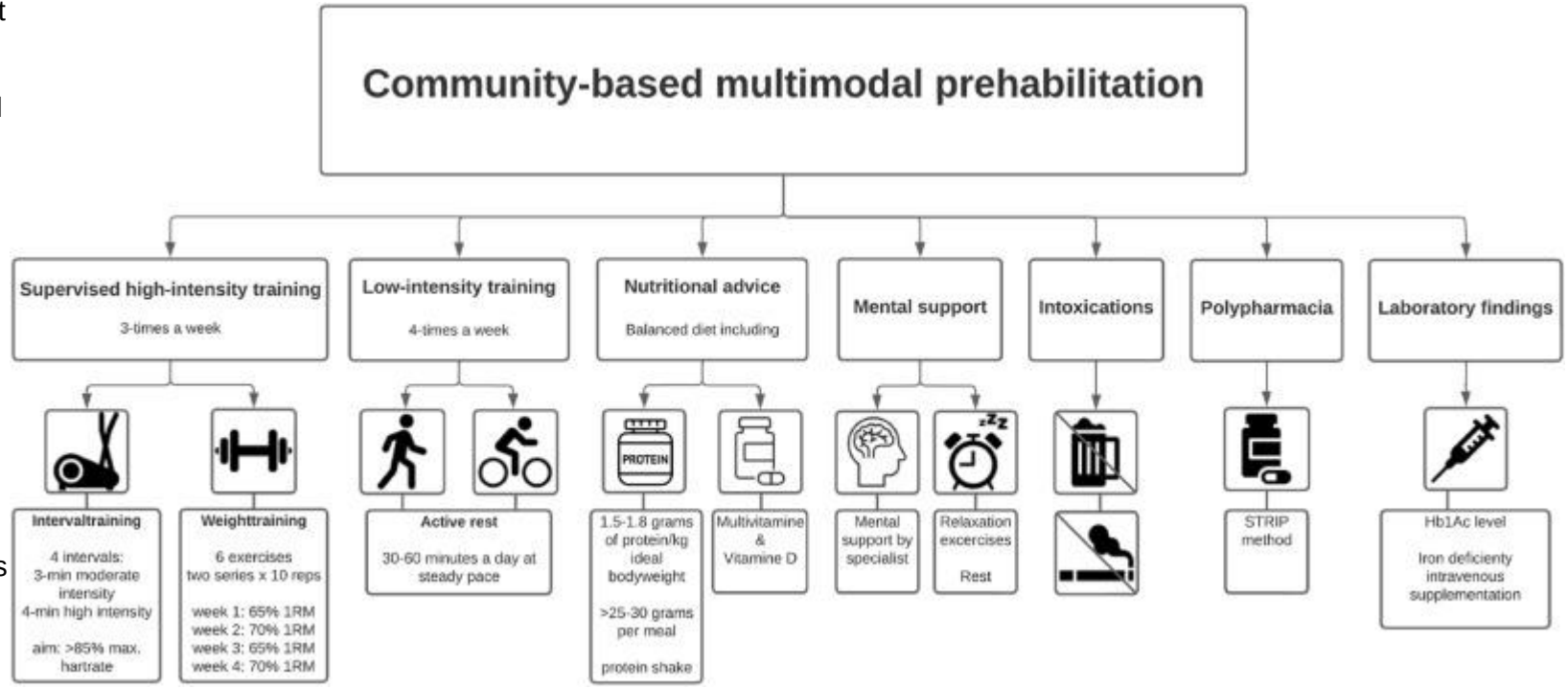
3 weeks

lower readmission rate (p=0,012);

Personalized nutritional 30 g prot 1h the supervised HIT, multivitamin supplement, vit D all follow by a daily logbook

Lower postoperative complication rate (p=0,015)

better functional capacities in all tests (p<0,0 01)



Prehabilitation reduced postoperative complications improved short-term functional outcomes

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Groen 2024 Eur J Surg Oncol

Geriatric co-management: A winning collaboration in Oncology!

Robust group
G8 score ≥ 15

Table 4 Oncologic characteristics and treatments

	Robust Group N=151		Frail Group N=51		p value
	N	%	N	%	
Localisation					
Rectum	52	34.4	16	31.4	0.55
Colon	99	65.6	35	68.6	
Neo-adjuvant treatment					
Preoperative chemo-radiotherapy	24	15.9	12	23.5	0.28
Preoperative chemotherapy	12	8	4	7.8	0.78
Surgical technique					
Robotic	43	28.5	9	18	0,11
Laparoscopy	108	71.5	42	82	
Stade (post-operative)					
Stade I-II	97	64.2	36	70.6	0.44
Stade III-IV	54	35.8	15	29.4	
Including metastasis	14	9.2	3	5.9	0.79
Adjuvant treatment					
Postoperative chemotherapy indication	45	29.8	15	29.4	0.98
Postoperative chemotherapy	40	88.8	9	60	0.02

Frail Group
G8 ≤ 14 with CGA
Older
more comorbidities
Malnutrition 55%
Sarcopenia 47%

One year after surgery: mortality and recurrence rates were similar

Geriatric co-management is feasible and contributes to the reduction of postoperative morbimortality.

Benefit of geriatric co-management, involving G8 screening, CGA, and ERAS, for frail older patients undergoing surgery for CRC.

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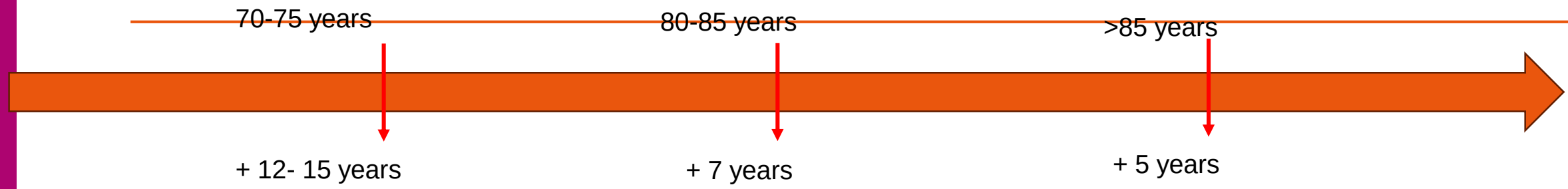
Guidelines J Am Coll Surg 2016 JACS, Pille Aging Clin Exp res 2024

What are the Questions?



Can all tumors be treated in the same way?

NO

Less present family
Isolated person
elderly couples : consider taking care of the spouse
compliance with the decision

What is the background of the elderly person?

Can all patients be treated in the same way?

NO

Mobility
Return home
Go shopping alone

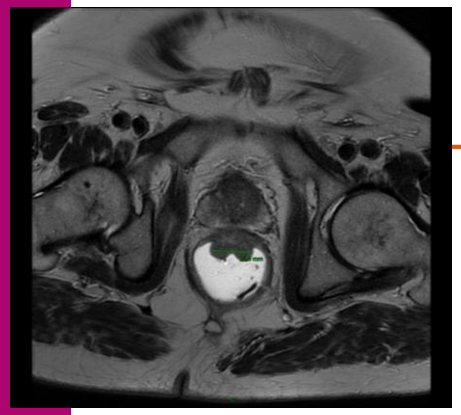
What are the specific expectations of elderly patients?

How to reduce morbidity without oncological risks?

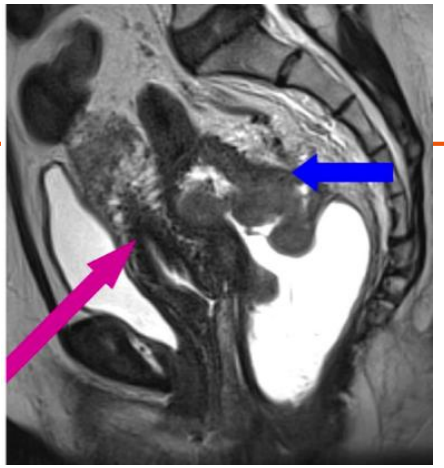
First concept to de-escalation strategies.

Avoid surgery if very good respons to neoadjuvant therapy?

Avoid radiotherapy?



Middle-Low rectal cancer M0



« small » cancers
cT2-T3 ≤4-5cm
N0-N1 avec gg ≤8mm, EMVI-

Locally advanced cancer
cT3Nx **CRM +**, cT4,
EMVI+, SE +

Cancers medium
cT2N+, T3 > 4 CM
a/b/c/d Nx,
CRM-, EMVI+

- **Surgery alone**
- **RTCT**
  - Greccar 2
  - Tautem
  - Opera
- **CT**
  - Neo
  - Prospect
  - Convert
- **RT**

Rectal preservation

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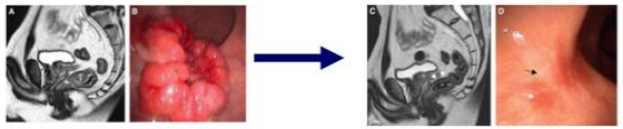


Middle-Low rectal cancer M0

« small tumors »
cT2-T3 ≤4-5cm
N0-N1 avec gg ≤8mm, EMVI-

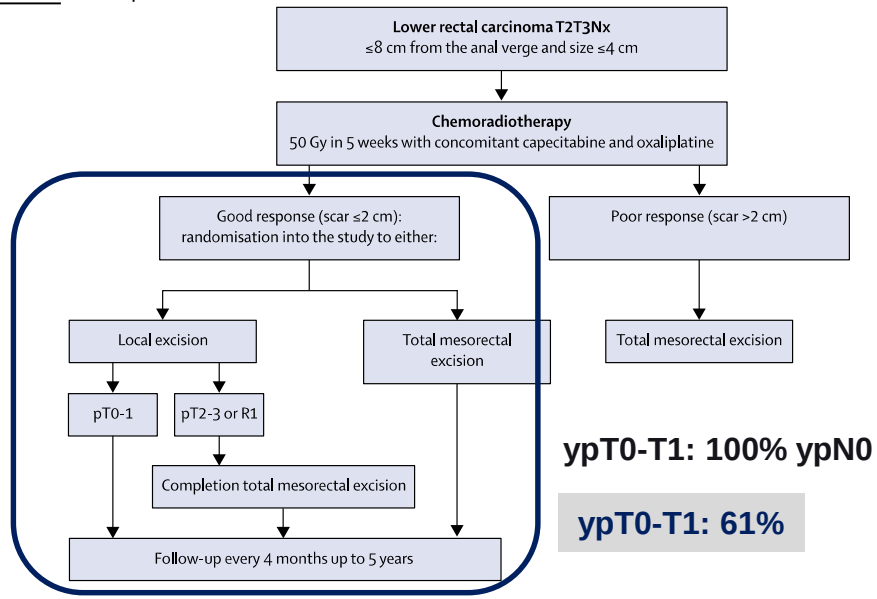
Rectal preservation

GRECCAR 2:
CAP50

CAP50 and tumorectomy
if good responders

Good responders 75%

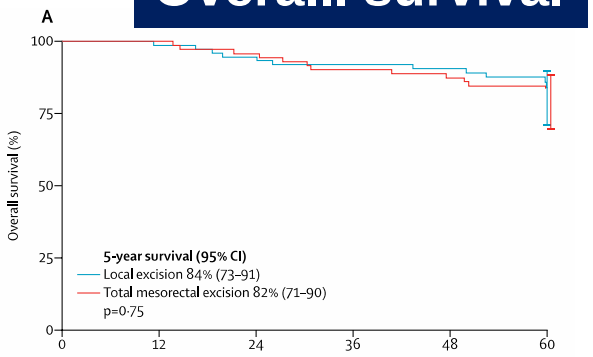
Organe Preservation 46%



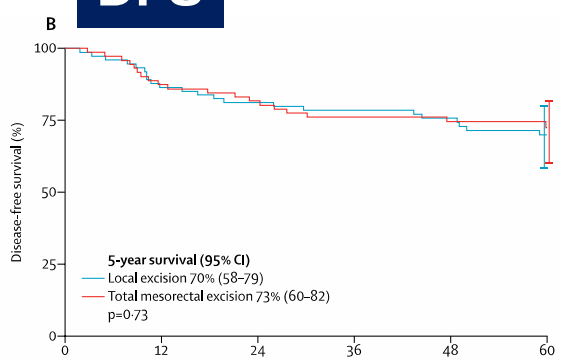
ypT0-T1: 100% ypN0

ypT0-T1: 61%

Overalll survival



DFS



Médiane de suivi : 60 month

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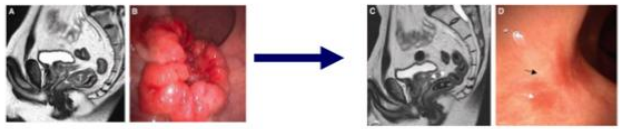
Lancet 2017, Ann Oncol 2023



Middle-Low rectal cancer M0

no elderly patients included

« small tumors »
cT2-T3 ≤4-5cm
N0-N1 avec gg ≤8mm, EMVI-

Rectal preservation

GRECCAR 2:
CAP50

TAU- TEM T2-T3abN0M0
Randomised phase III

Surgery with TME

CAP50 and *Transanal Endoscopic Microsurgery*

Phase III multicentric
Complete response: 44% after RTTEM
Compliance 98%
lower morbidity with organ preservation.

Local recurrence rates are expected soon to confirm the validity of this approach

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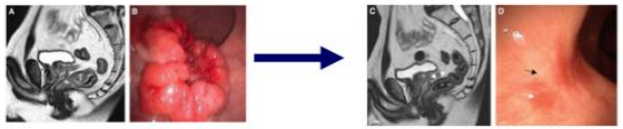
Xavier Serra-Aracil et al., ASCO22, Abs 35



Middle-Low rectal cancer M0

« small tumors »
cT2-T3 ≤4-5cm
N0-N1 avec gg ≤8mm, EMVI-

Rectal preservation

R

RTE 45 Gy + 9 Gy RTE boost
Xeloda

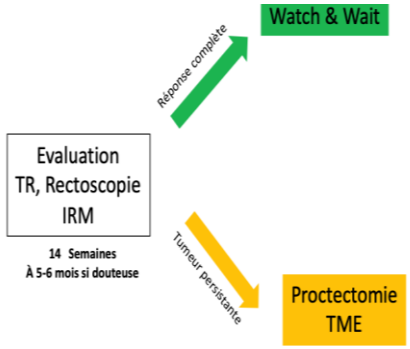
RTE 45 Gy + 3x30 Gy contacthérapie
Xeloda

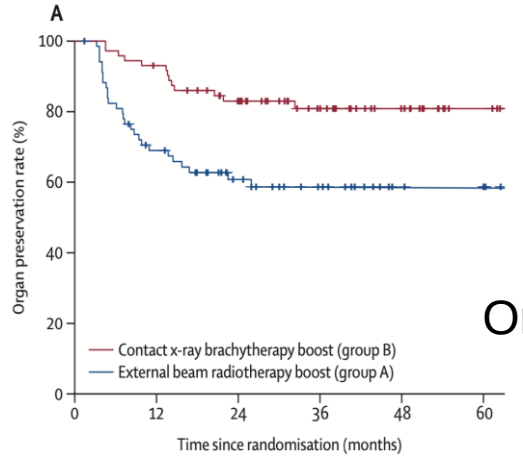
OPERA:
CAP50
+ contacthérapie

RLR à 5 ans et SG idem

Contactherapie
Nice, Lyon, Mâcon, IGR

OPERA: contacthérapie 90Gy + CAP 50

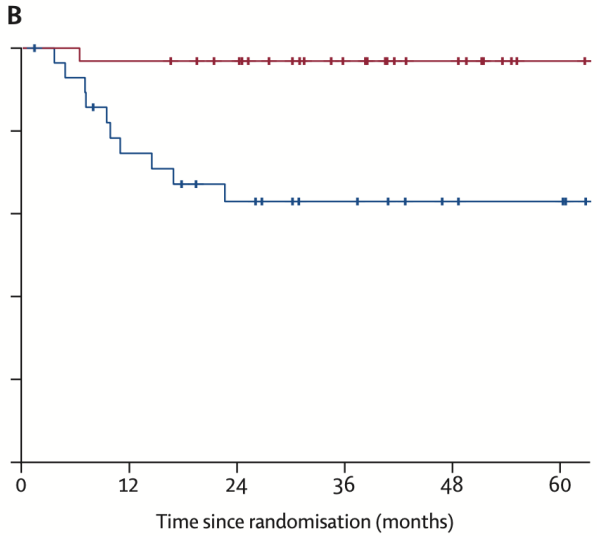




81%

59%

Organe preservation



Tumeurs <3cm: n=61

93%

Organe preservation

54%

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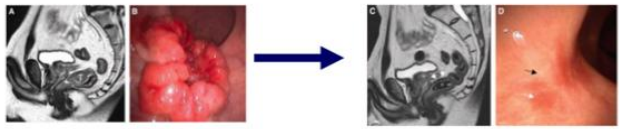
JP Gerard et al. Lancet Gastroenterol Hepatol 2023 D Baron Ann Oncol 2025



Middle-Low rectal cancer M0

Age: range 31- 83 years

« small tumors »
cT2-T3 ≤4-5cm
N0-N1 avec gg ≤8mm, EMVI-

rectal preservation planned

NEO cT1-T3a,bN0
Phase II
58 pts Chemotherapy without RT
6 Folfox ou 4 Capox

Good respondeurs IRM 96%

Local exerese pT0-1: 57%
(54% in Greccar 2 with RTCT)

Caution: Short Follow up

SSR 2 ans for organ preservation 90%

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Hagen F Kennecke JCO 222

« Petits » cancers cT2-T3 ≤4-5cm N0-N1 avec gg ≤8mm, EMVI-

TRESOR: T2T3N0/1 <6cm

Assess potential benefit of intensification of neoadjuvant CT with Folfirinox and contact therapy for organ preservation.

+

GRECCAR 12: T2T3N1 <4cm

Evaluer benefice potentiel intensification par CT neoadjuvante la possibilité de conservation d'organes

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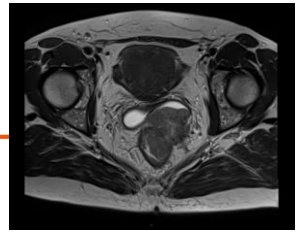
Mid and low M0
Locally Advanced Rectal Cancer



Medium cancers
cT2N+, T3 > 4 CM a/b/c/d
Nx,
CRM-, EMVI+

Locally advanced cancer
cT3Nx **CRM +**, cT4,
EMVI+**,** SE +

Younger

Elderly frailtly

STELLAR
Max 70 years

Elderly frailtly

TNT
PRODIGE 23:
FOLFIRINOX x 6
+ CAP50

PROSPECT:
FOLFOX x 6

TNT
RAPIDO:
5x5 Gy
+ CAPOX x 6/FOLFOX x 9

- Stockholm III
- NACRE
5x5 Gy -> Chir à 7 S
Peu de patients
interrompue

Place CAP 50

NORAD01
Désescalade **avant** ttt
mFOLFIRINOX seul x 6

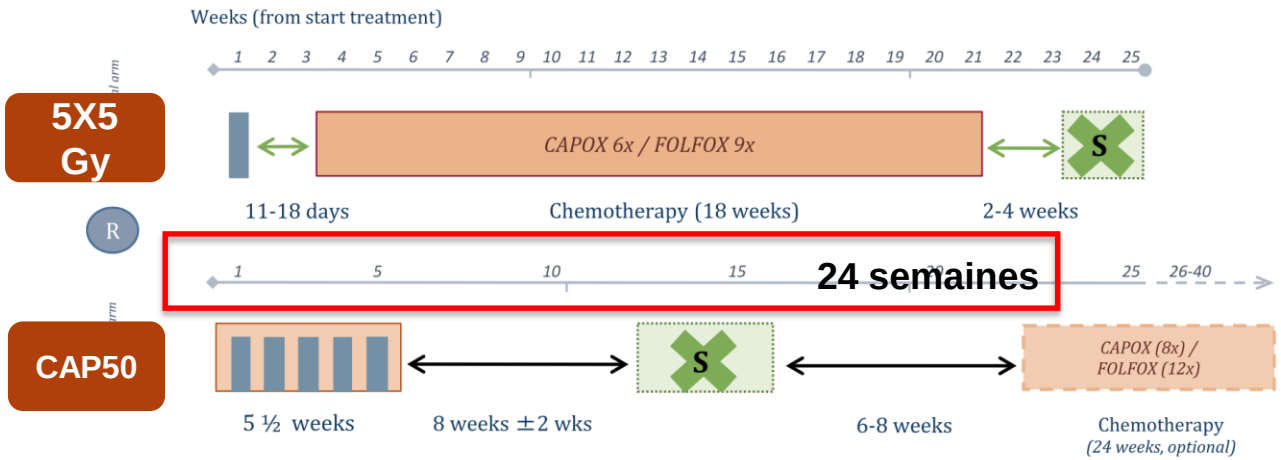
CONVERT
CAPOX x 4

DIALOG

TNT
RAPIDO: 5x Gy + CAPOX/FOLFOX

Medium cancers
cT2N+, T3 > 4 CM a/b/c/d
Nx,
CRM-, EMVI+

Locally advanced cancer
cT3Nx **CRM +**, cT4,
EMVI+, SE +



Phase III supériorité
ADK rectum, ≤ 15 cm de la MA
cT4a/b
cN2
CRM ≤ 1 mm
Ganglions latéro-pelviens cN+
OMS 0 ou 1

	RCT	RT + CT	p
Récidive locorégionale	6%	**10%**	**0,027**

Age: range 31- 84 years
40%> 65 years

Follow up 5 years

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EA Dijkstra et al. Ann Surg 2023.

STELLAR: short RT + CT followed by surgery

Locally advanced cancer
cT3Nx **CRM +**, cT4,
EMVI+**,** SE +

Etude STELLAR

Critères inclusion
- Age 18-70 ans
- Adénocarcinome bas ou moyen rectum
- T_3 -T_4 et/ou N+ évalué en IRM
- ECOG PS 0-1

R 1:1 — 599 pts

CRT → 6-8 sem → TME → 4-6 sem → CAPOX 6 cycles

SCRT → 1 sem → CAPOX 4 cycles, → 4-6 sem → TME → 4-6 sem → CAPOX 2 cycles

SCRT : 25 gy/5 Gy
CRT : 50 Gy/2.0 Gy, capécitabine orale synchrone 1650 mg/m²/j
CAPOX : capécitabine 1000 mg/m² 2 x/j, J1-14 associé avec oxaliplatine 130 mg/m² toutes les 3 semaines.

Critère principal :
→ Survie sans Maladie (SSM)

Critères secondaires :
→ SG, contrôle local, métastases à distance, complications chirurgicales, toxicités liées à la radiothérapie ou à la CT, QdV

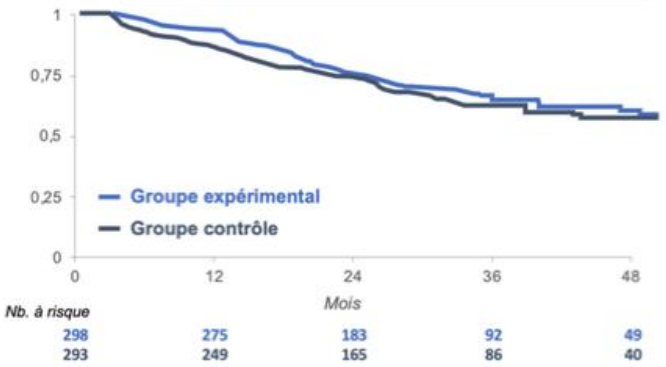
- Pas de différence de survie sans métastases ni de survie sans récidive locorégionale

- Toxicités de grade III/IV plus fréquentes dans le bras expérimental (26,5% versus 12,6%, p<0,001))

- Taux de complications post opératoires similaires

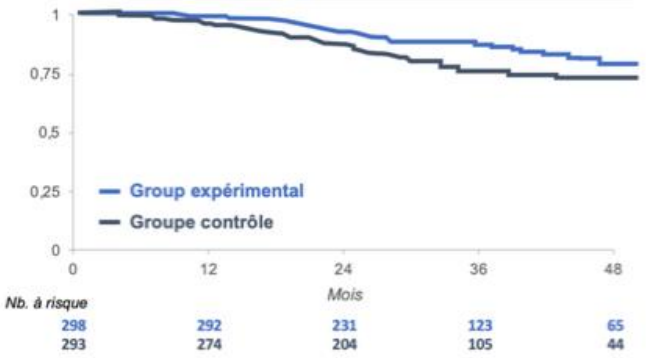
Survie sans maladie

	Groupe expérimental (n=298)	Groupe contrôle (n=293)
SSM à 3 ans (IC 95%)	**64,5%** (58,6 - 71,0)	**62,3%** (56,5 - 68,8)
HR (IC 90%)	**0,88** (0,70 - 1,13)	
Test de non-infériorité	***p*<0,001**	



Survie globale

	Groupe expérimental (n=298)	Groupe contrôle (n=293)
SG à 3 ans (IC 95%)	**86,5%** (82,3 - 90,9)	**75,1%** (69,6 - 81,0)
HR (IC 95%)	**0,67** (0,46 - 0,97)	
Log-rank test	***p*=0,036**	



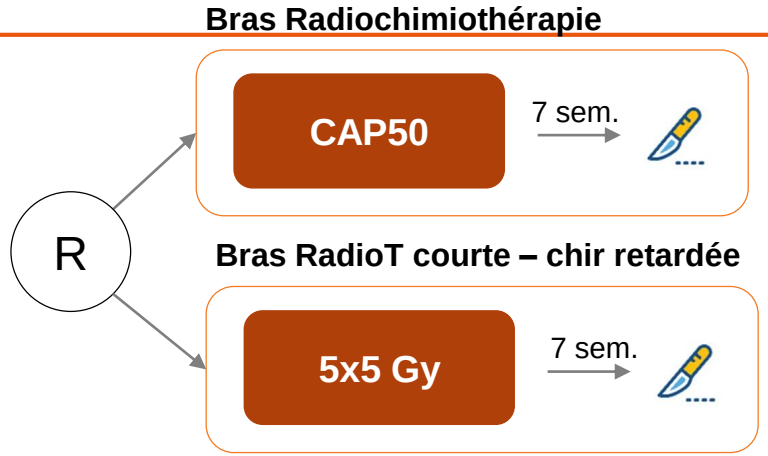
Jin et al., JCO, 2021

Short-term radiotherapy with preoperative chemotherapy followed by surgery was efficacious with acceptable toxicity and could be used as an alternative to CRT for locally advanced rectal cancer.

NACRE: RT courte + chir retardée chez patients >75 ans

Phase III non-infériorité
> 75 ans OMS 0-2
cT3-T4NxM0
cT2 bas rectum

(2016-2019: n = 101)
Major lack of inclusion
100 included instead of 400



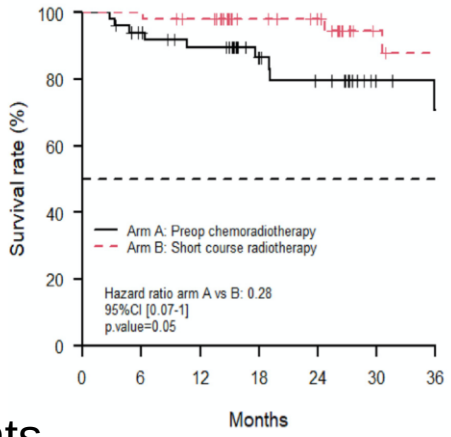
De-escalation
To avoid chemotherapy

The R0 resection rate and the preservation of autonomy were the two co-primaries

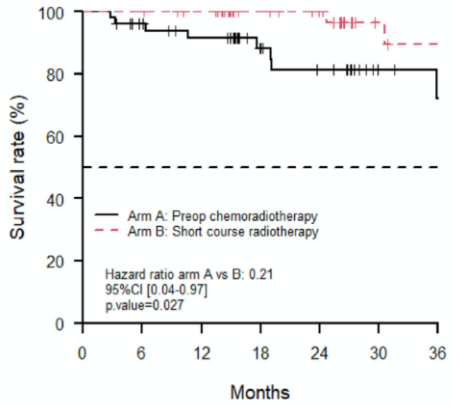
Better tolerance for short course
Better compliance
Better overall survival and specific cancer survival
Identical R0
Faster return to independence
100% of patients complete the 5x5 vs. 86%

FEW PATIENTS

Overall Survival



Specific cancer survival



Short-course RT is a perfectly valid option in elderly patients since it does not compromise surgical resection or local control of the disease,

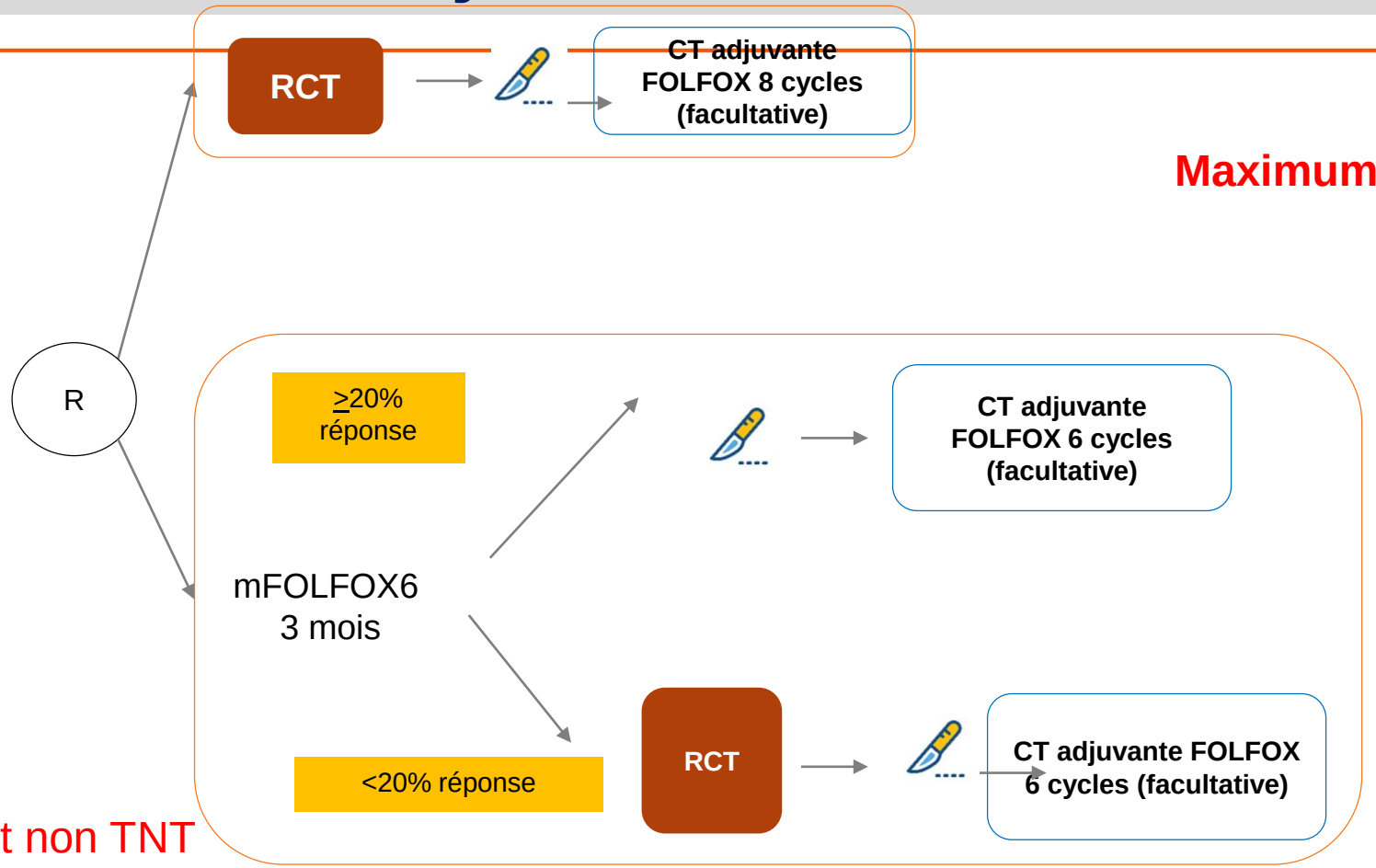
DIALOG

E François et al. Eur J Cancer 2023.

PROSPECT: CT néoadjuvante avec RCT sélective

De-escalation
To avoid radiotherapy

Phase III non-infériorité
ADK rectum T2N+, cT3N0-N1
CRM >3mm



Maximum age 67

Attention : No T4
Control arm: CAP 50 et non TNT

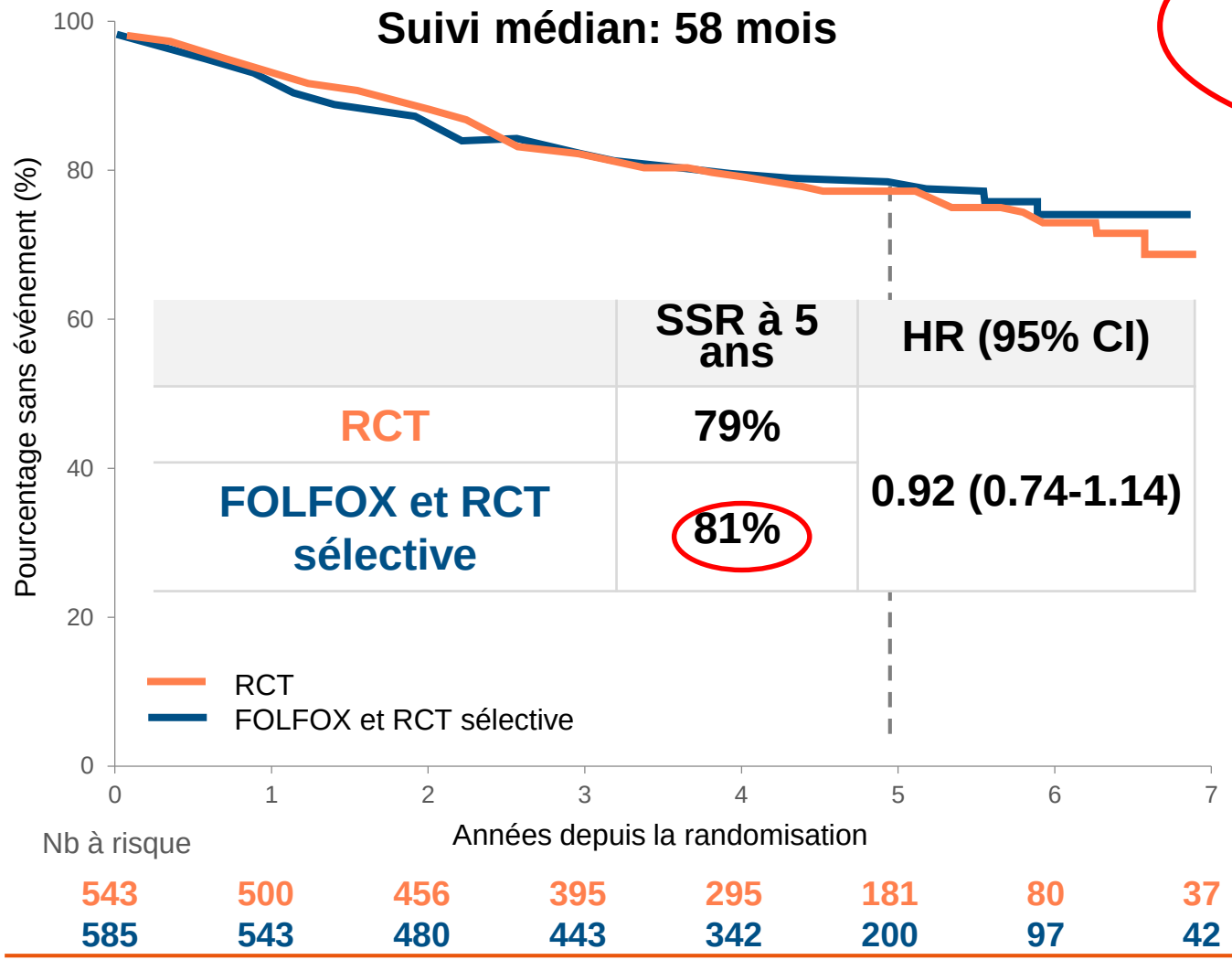
The North American study aimed to reduce sequelae by evaluating the possibility of not using radiotherapy for rectal tumors with a good prognosis

Primary endpoint: 5-year recurrence-free survival

D Schrag et al., ASCO 2023, NEJM 2023.

PROSPECT: CT néoadjuvante avec RCT sélective

DFS
FOLFOX preop without RT
is not lower than CAP50



	RCT	FOLFOX +/- RCT
ypT0N0	24%	22%
Résection R1	2,7%	1,1%

DIALOG

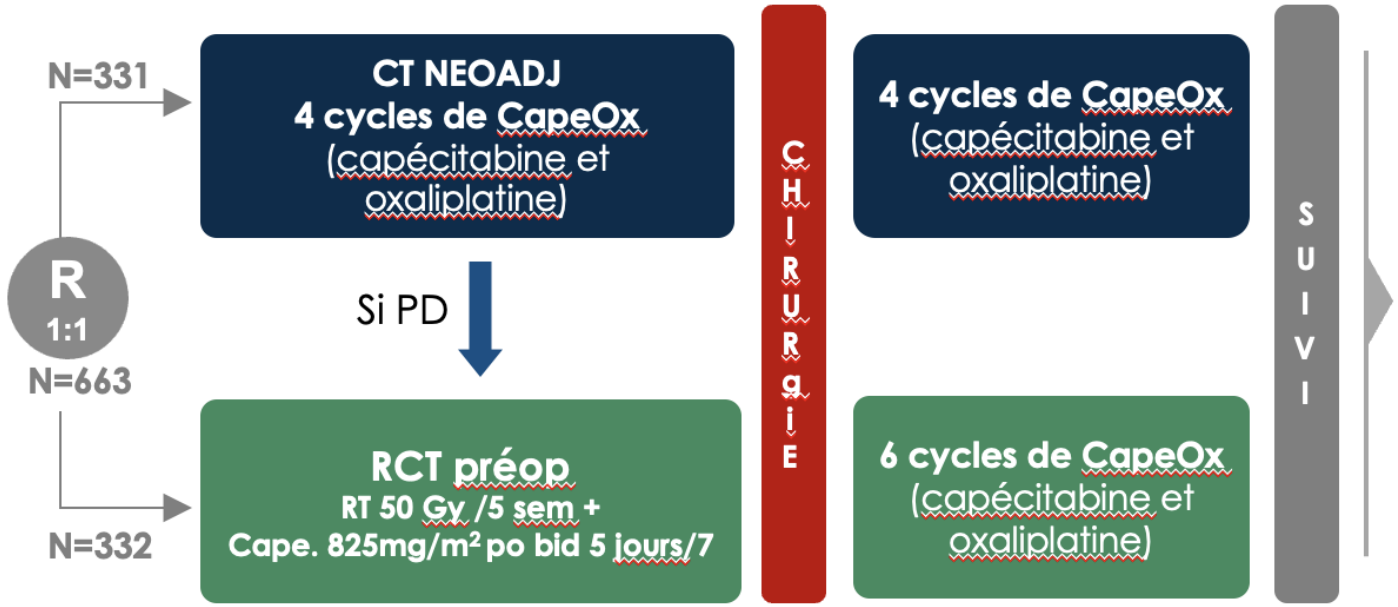
D Schrag et al., ASCO 2023, NEJM 2023.

CONVERT: CT periop without RT

De-escalation
To avoid radiotherapy

Phase III non-infériorité
ADK rectum T2N+, cT3N0-N1
CRM >1mm

Older patients
18-75 years



Main objective
DFS 3 years

Low loco-regional resurrence free survival: 2,6% and 3,7% respectively
DFS similar
Rate complete resection R0 was 99% in two groups
Progression-free survival at 3 years and overall survival at 3 years were similar.

Long-term follow-up is needed to confirm these results.

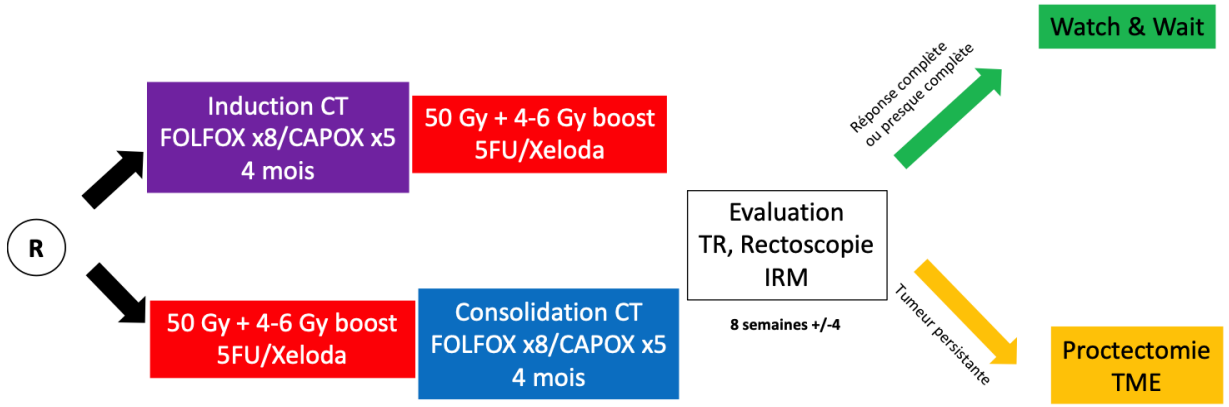
DIALOG

Locally advanced cancer
cT3Nx **CRM +**, cT4,
EMVI+, SE +

OPRA: Phase II

Verheij JCO: 2024

De-escalation
To avoid surgery



	Induction	Consolidation	p
Survie sans récidive à 3 ans	76%	76%	
Récidive locale 5 ans	69%	6%	
Survie sans chirurgie rectale à 3 ans	41%	**53%**	p=0,01
Survie sans métastases à 3 a 5 ans	84%	82%	
TME après bilan évaluation réponse	28%	24%	
Repousse tumorale dans W&W	40%	**27%**	p=0,02
Conservation rectale actualisée	44%	29%	p=0,02

Rectal preservation for one-third of patients with large tumors in complete response after TNT,

→ local recurrence in 30% of cases where the organ is preserved
→ More metastases if local recurrence

Although there are no elderly patients, this strategy should be maintained
in cases of large tumors if organ preservation is desired even if the main problem is a high recurrence rate.

DIALOG

IMPROVED

Implementation of coMplex PeRi-OperatiVe intervEntion in olDer patients with cancer: a multicenter randomized controlled trial

Investigateur coordonnateur : Pr Elena PAILLAUD LAURENT PUIG
Co investigateur coordonnateur : Pr Frédérique PESCHAUD

Promoteur : AP-HP – DRCI,

Unité de Recherche Clinique :
Pr Florence Canoui-Poitrine

IMPROVED Implementation of coMplex PeRi-OperatiVe intervEntion in olDer patients with cancer: a multicenter randomized controlled trial

- The study was of an open-label, national multicenter, randomized, and parallel-group design
- **25 centers**
- Number of patients: 630
- **inclusion criteria :**
  - Over 75 ans
  - Stomac cancer, pancreas, colorectal with surgery: Gastrectomy, Duodenopancreatectomy, left Pancréatectomy, colectomy, rectal surgery, hepatectomy > 3 segments
  - Social security
  - signed consent

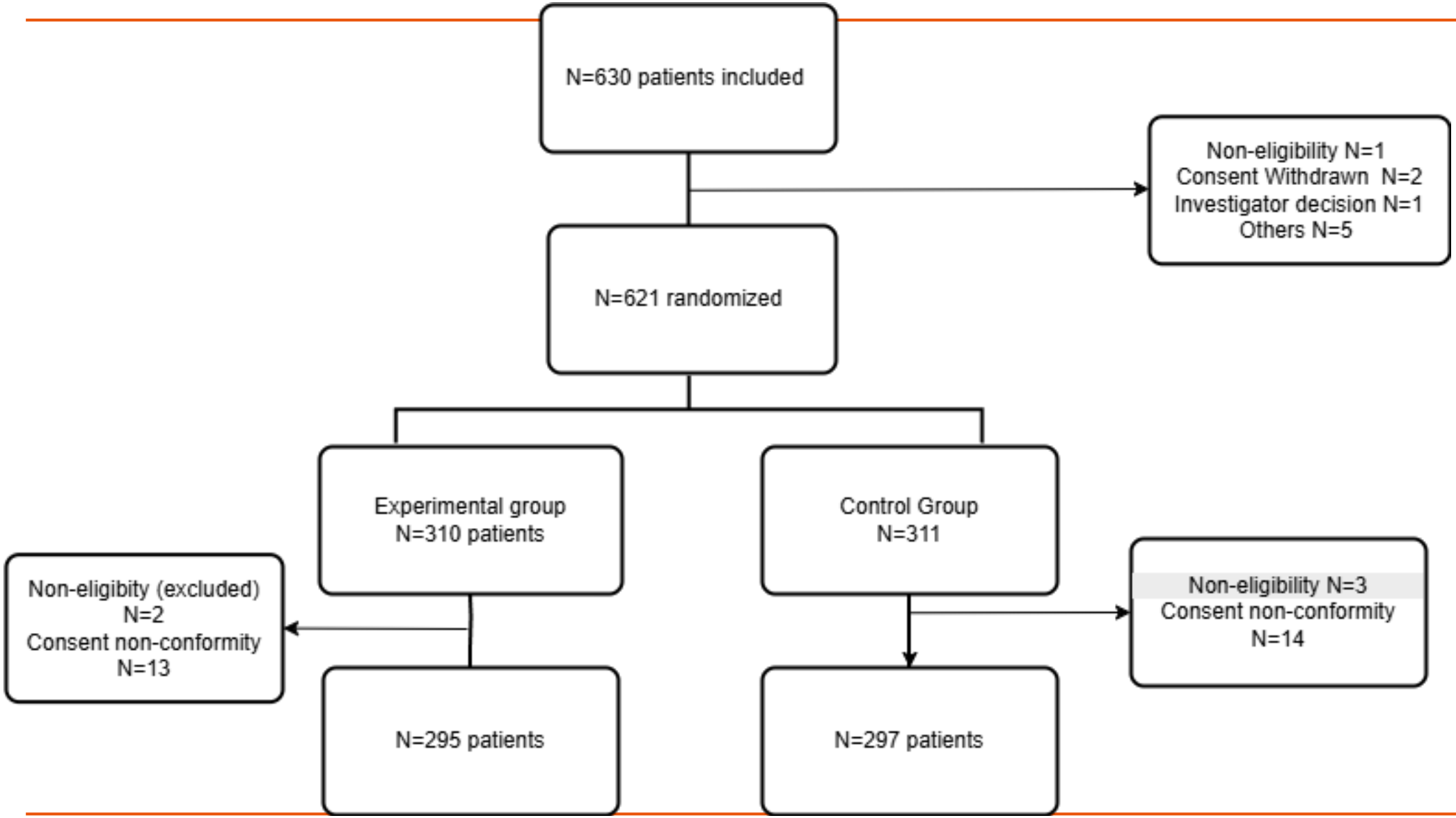
IMPROVED

Main objective

- Evaluate the benefit of personalized, intensive geriatric care during the perioperative period versus standard care on major morbidity at 30 days in patients over 75 years of age with digestive cancer requiring surgery and at risk of postoperative complications

Secondary objective

- Overall survival, different types of severity of postoperative complications, home care, length of stay in the surgical ward, total length of hospital stay, care pathway (transfers to intensive care or rehabilitation, delays and length of hospital stay)


N=630 patients included
Non-eligibility N=1
Consent Withdrawn N=2
Investigator decision N=1
Others N=5
N=621 randomized
Experimental group
N=310 patients
Control Group
N=311
Non-eligibity (excluded)
N=2
Consent non-conformity
N=13
Non-eligibility N=3
Consent non-conformity
N=14
N=295 patients
N=297 patients

Baseline characteristics of participants to the IMPROVED randomized clinical trial

		Total		GROUP			
				CONTROL		ExPerimental	
		N=592		N=297		N=295	
Baseline characteristics		N	n(%) or med(Q1-Q3)	N	n(%) or med(Q1-Q3)	N	n(%) or med(Q1-Q3)
Age, year, median (Q1-Q3)		592	81 (78-86)	297	81 (77-86)	295	81 (78-85)
Female, n(%)		268	45,0%	130	44,0%	138	47,0%
Live alone		216	40,4%	103	38,9%	113	42,0%
No Care Giver		114	21,6%	50	19,0%	64	24,2%
Tumor location	Colon	347	58,7%	172	57,9%	175	59,5%
	Rectum	79	13,4%	42	14,1%	37	12,6%
	Pancreas	124	21,0%	61	20,5%	63	21,4%
	Stomach	41	6,9%	22	7,4%	19	6,5%
Metastatis	Yes	58	9,8%	28	9,4%	30	10,2%
Planned surgery	Colectomy	328	55,4%	164	55,2%	164	55,6%
	Proctectomy	76	12,8%	38	12,8%	38	12,9%
	Pancreatectomy	125	21,1%	61	20,5%	64	21,7%
	Hepatectomy	22	3,7%	12	4,0%	10	3,4%
	Gastrectomy	41	6,9%	22	7,4%	19	6,4%
ECOG-PS	0	233	42,0%	127	45,8%	106	38,1%
	1	207	37,3%	93	33,6%	114	41,0%
	2	91	16,4%	43	15,5%	48	17,3%
	3	21	3,8%	11	4,0%	10	3,6%
	4	3	0,5%	3	1,1%	0	0,0%
G8 score (/14)		534	12 (10-14)	266	12 (10-14)	268	12(10-14)
G8 <14, n(%)		433	81,1%	213	80,1%	220	82,1%
BMI, kg/m², median (Q1-Q3)		549	24 (21-26)	276	24(21-27)	273	24(21-26)
10% Unintentional Weight loss		289	53,0%	143	52,4%	146	53,7%
ADL_SCORE (/6)		551	6 (5.5-6)	277	6 (5.5-6)	274	6(5.5-6)
IADL_SCORE (/4)		542	4 (4-4)	273	4(4-4)	269	4(3-4)
Charlson comorbidity score (/24)		522	2(0-3)	260	2(0-3)	262	2(0-2)
Altered Mini-COG (<4/5)	1	96	26,2%	48	25,9%	48	26,4%
Altered mini GDS (>=1/4)	1	178	33,7%	84	31,6%	94	35,9%
Altered TGUG (>20s)	1	58	20,8%	27	19,7%	31	21,8%

CONCLUSIONS

Rectal surgery has a high morbidity rate compared to colon surgery
The risk of permanent stoma is 30% in elderly patients, is poorly accepted, and leads to a loss of independence
Now, during every multidisciplinary team meeting, we must ask ourselves whether surgery can be avoided and the rectum preserved, and determine the therapeutic objective for an elderly patient based on their condition
Perhaps we need to accept a higher risk of recidivism or poorer local control?

CONCLUSIONS

Different protocols exist

- For small tumors, CAP 50 is preferred
- For large tumors, short RT with Folfox or Capox chemotherapy which does not compromise potential organ preservation

And, above all, working together with surgeons and geriatricians from the onset of the disease to choose the most appropriate strategy and support patients in terms of nutrition and physical activity

Thank you for your attention