Evidence and practice changing treatments in gastro-intestinal tumors

Maria Antonietta Gambacorta

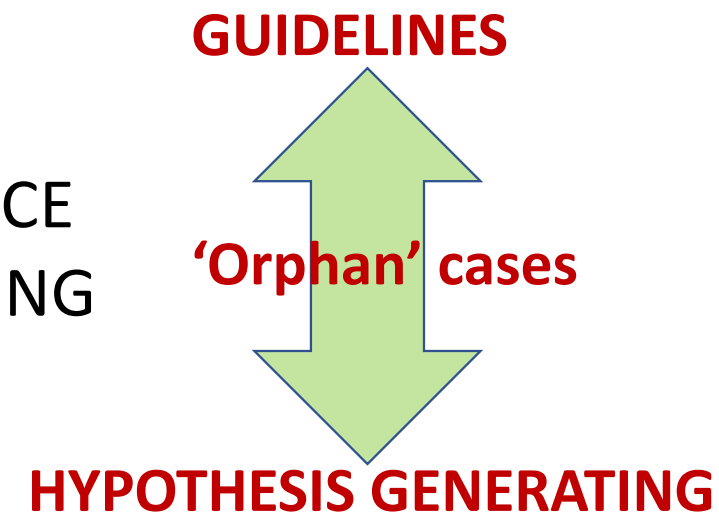
Fondazione Policlinico Universitario A. Gemelli IRCCS

I don’t have conflict of interest
Except that Rectal Cancer is my favourite

Gastro-intestinal

- Stomaco
- Pancreas
- Colon-Retto

EVIDENCES → PRACTICE CHANGING



Gastro-intestinal

2022 ASCO®
ANNUAL MEETING
ADVANCING EQUITABLE CANCER CARE THROUGH INNOVATION

AI & EI: CARING FOR THE PATIENT
IN A WIRELESS WORLD
ASTRO
ANNUAL 2022 MEETING

Gastro-intestinal

- Stomaco
- Pancreas
- Colon-Retto

Marcel Verheij
Netherlands Cancer Institute, Amsterdam/
Radboud university medical center, Nijmegen

Randomized phase 2 trial of pre-operative chemo(radio)therapy in gastric cancer:

CRITICS-II interim results

RT mainly **postoperative**

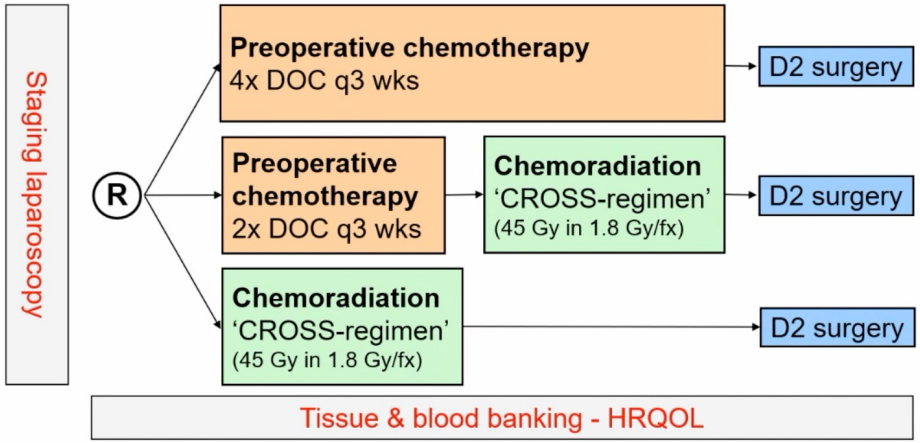
Poor **compliance** ∼ 50% completed post-RT

Increase **compliance** ∼ 70% completed pre-RT

Increase **tumor response**

Overall	*19 - 43 pts*	*40 - 45 Gy*	*5FU / cis- / carboplatin / paclitaxel*	*D2*	*R0: 70 - 100%* *pCR: 11 - 26%*

Pre-operative chemoradiotherapy:
CRITICS-II study



https://clinicaltrials.gov/ct2/show/NCT02931890

- Inclusion per May 1st, 2022: 153 (74% of required 207)
- Planned interim analysis 23 July 2021:
  - N=119; median follow up 14 months
  - Main findings (1): Baseline characteristics
    - No major differences between 3 arms

Gender %		Age Yrs; median (range)	Histology %		Location %		Stage %		Charlson score >2 %	
Male	59	69 (38-82)	Intestinal	52	Gastric	75	0	1	No	64
Female	41		Diffuse	20	GEJ	11	I	10	Yes	36
			Unclass.	28	Other	2	II	40		
					Missing	13	III	30		
							Missing	19		

Main findings (2): Comp

- Arm 1 (chemotherapy):
- Arm 2 (chemotherapy +
- Arm 3 (chemoradiothera

- Total:

- Surgery in 92%
  - Curative intent in 99%
  - Type of resection: total 51%;
  - D2 in 93%
  - Re-intervention in 13%
  - In-hospital mortality: 6%
- Completion according to proto
  - Main reasons: disease progre

Main findings (4): Complications and toxicity

- Complications:
  - General: 23%
  - Infectious: 16%
  - Surgical: 18% (anastomotic leakage n=7)
- Toxicity:
  - Incidence grade >2 any toxicity at 12 months: 60.5
  - Grade 5 toxicity: 7.6% (infectious: n=5; pulmonary:

- Main findings (5): Pathology

Radicality of resection (%)	pT stage (%)	pN stage (%)	Total number of lymph nodes
R0: 95	pT0: 18	pN0: 57	Median (Q1,Q3): 22
R1: 5	pTis: 2	pN1: 26	Q1,Q2: 17, 23
R2: 0	pT1: 14	pN2: 15	Min - Max: 0 - 83
	pT2: 13	pN3: 3	
	pT3: 45		
	pT4: 8		

Randomized phase 2 trial of pre-operative chemo(radio)therapy in gastric cancer:

CRITICS-II interim results

Summary

- Current standard of care for resectable, locally advanced gastric cancer is FLOT-based peri-operative chemotherapy
- Post-operative chemoradiotherapy (without pre-operative chemotherapy) reduces local regional recurrences and improves survival
- Treatment in the post-operative setting is associated with poor patient compliance
- Phase I-II studies show feasibility, safety and efficacy of pre-operative chemoradiotherapy
- Ongoing trials (TOPGEAR, CRITICS-II) evaluate optimal schedules and survival benefit of pre-operative chemoradiotherapy

Gastro-intestinal

- Stomaco → Guidelines; Orphan Cases
- Pancreas
- Colon-Retto

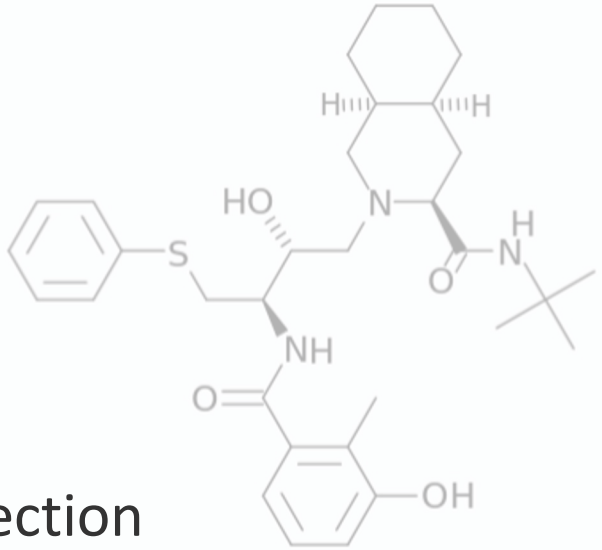
Gastro-intestinal

- Stomaco
- Pancreas
- Colon-Retto

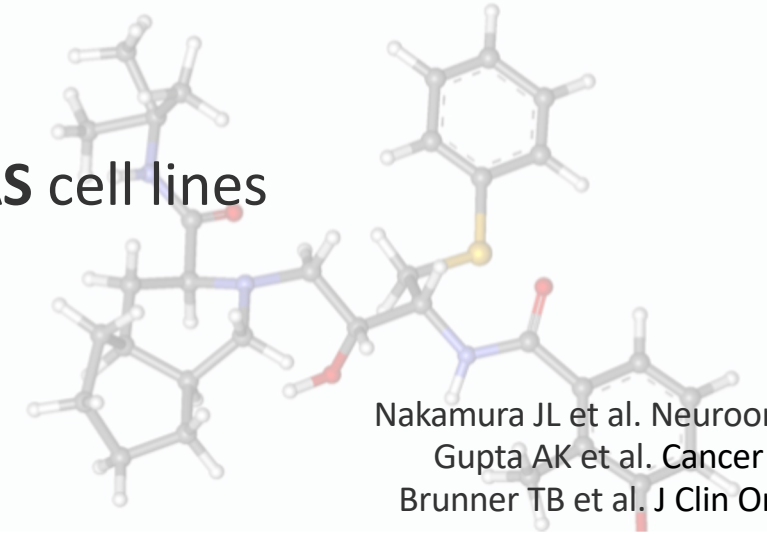
‘NEW’ DRUGS - CRT

Drug abscopal effect

Nelfinavir



- **ANTI-RETROVIRAL** protease inhibitor: HIV infection
- **RADIOSENSITIZING PROPERTIES**
- Head-and-neck, lung carcinoma, **PANCREAS** cell lines
- Therapeutic doses **SAME** for HIV infection



Nakamura JL et al. Neurooncol 2005
Gupta AK et al. Cancer Res 2005
Brunner TB et al. J Clin Oncol 2008

UNIVERSITY OF OXFORD
OCTRU Oxford Clinical Trials Research Unit
CSM
octo Oncology Clinical Trials Office
CANCER RESEARCH UK
Celgene

SCALOP-2

A multi-centre randomised phase II study of induction chemotherapy followed by capecitabine (+/-nelfinavir) with high or standard dose radiotherapy for locally advanced non-metastatic pancreatic cancer

S Mukherjee, C Qi, R Shaw, JA Bridgewater, G Radhakrishna, N Patel, B Tranter, P Parsons, S Falk, HS Wasan, D Holyoake, R Roy, M Scott-Brown, C Hurt, D Sebag-Montefiore, TS Maughan, MA Hawkins, PG Corrie

SCALOP²

ISRCTN: 50083238
ClinicalTrials.gov: NCT02024009
CRUK: C28958/A17139

ESTRO 2022

Somnath MUKHERJEE
(UNITED KINGDOM)

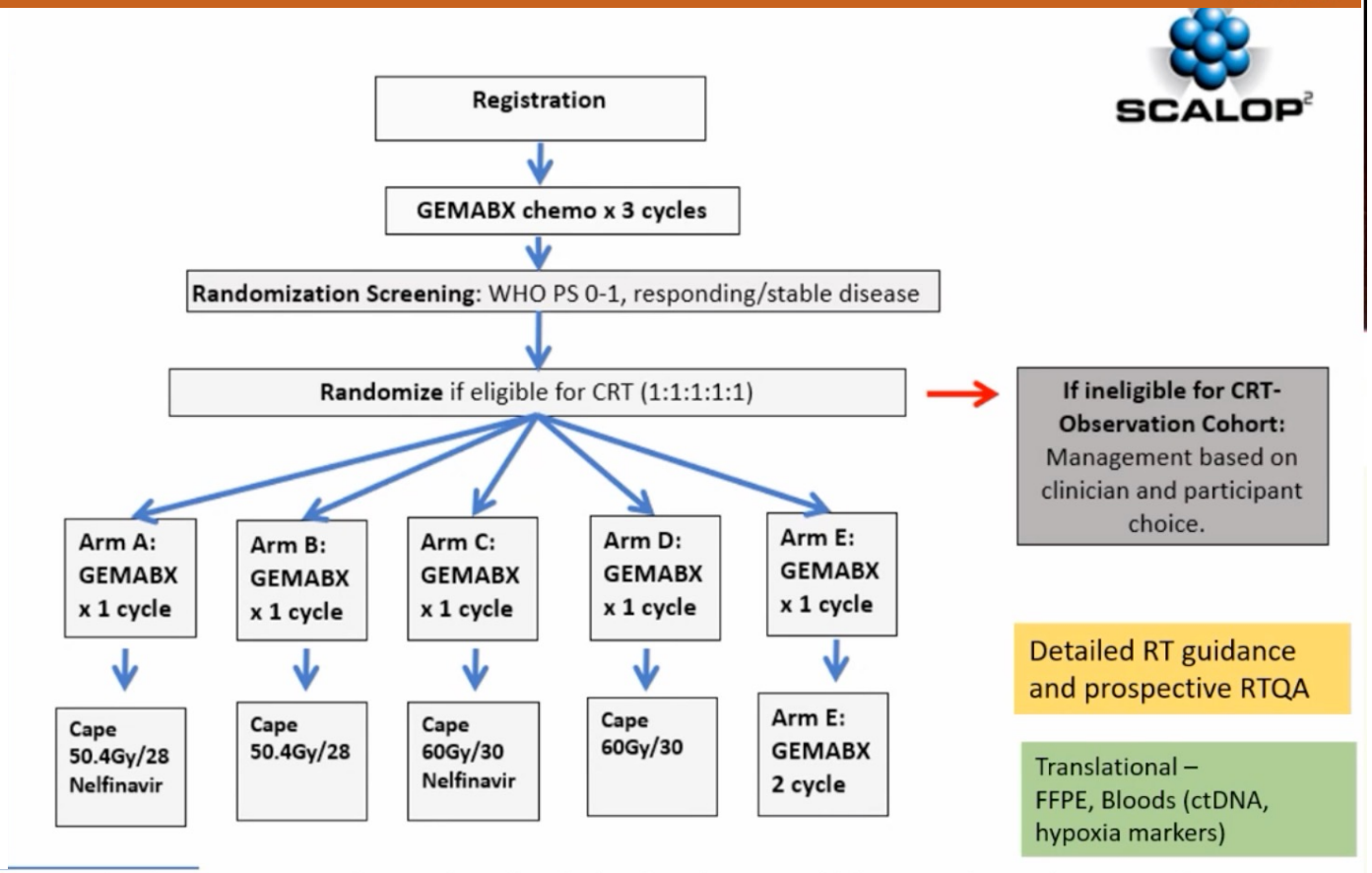
Primary endpoints:

OS

PFS

Secondary endpoints:

1. Safety
2. QoL
3. Ca 19.9 levels
4. ……..



168 patients needed to be recruited to ensure ~65% retention after induction therapy which approximated to **96 patients randomised to arms A to D**. This would be sufficient to detect a **hazard ratio (HR) of ≤0.65 with 80% power and one-sided alpha=0.2**, accounting for 10% loss to follow-up

106 pts RANDOMIZED

COMPLIANCE

Induction CHEMO

- 58-62%
- Completed 100% CT

RADIOTHERAPY

- @50 Gy → 95%
- @ 60 Gy →100% completed RT

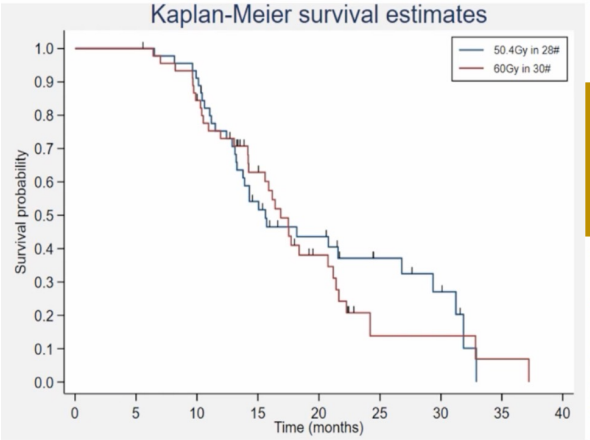
Serious Adverse Events

SCALOP²

	50.4 Gy in 28# (n= 45)	60 Gy in 30# (n= 46)
Induction chemo		
Total no. of patients with grade 1-5 SAEs	20 (44.4)	30 (65.2)
Total no. of patients with SARs/SUSARs	13 (28.9)	22 (47.8)
Patients with grade 3-4 SAEs	13 (28.9)	24 (52.2)
Patients with grade 3-4 SARs/SUSARs	8 (17.8)	16 (34.8)
CRT	(40 started CRT)	(39 started CRT)
Total no. of patients with grade 1-5 SAEs	9 (20)	6 (13)
Total no. of patients with SARs/SUSARs	5 (11.1)	4 (8.7)
Patients with grade 3-4 SAEs	8 (17.8)	6 (13)
Patients with grade 3-4 SARs/SUSARs	**5 (11.1)**	**4 (8.7)**

	CRT without nelfinavir (n= 38)	CRT with nelfinavir (n= 38)
Induction chemo		
Total no. of patients with grade 1-5 SAEs	20 (52.6)	22 (57.9)
Total no. of patients with SARs/SUSARs	13 (34.2)	17 (44.7)
Patients with grade 3-4 SAEs	15 (39.5)	19 (50)
Patients with grade 3-4 SARs/SUSARs	10 (26.3)	13 (34.2)
CRT	(35 started CRT)	(32 started CRT)
Total no. of patients with grade 1-5 SAEs	6 (15.8)	8 (21.1)
Total no. of patients with SARs/SUSARs	4 (10.5)	5 (13.2)
Patients with grade 3-4 SAEs	6 (15.8)	8 (21.1)
Patients with grade 3-4 SARs/SUSARs	**4 (10.5)**	**5 (13.2)**

Overall Survival: 60Gy vs 50.4Gy



	50.4 Gy in 28# Arms A+B (n= 45)	60 Gy in 30# Arms C+D (n= 46)
No. deaths n (%)	31 (68.9)	33 (71.7)
Median overall survival (60% CI)	15.6 (14.3, 18.2)	16.9 (16.2, 17.7)
Log-rank p-value (one-sided)	0.68	
Primary analysis		
[1]Hazard ratio (60% CI)	1.13 (0.91, 1.40)	
[2]Adjusted one-sided p-value	0.68	
[3]Sensitivity analysis with interaction term		
Interaction (80% CI)	1.57 (0.80, 3.09)	
Two-sided p-value	0.39	

[1]adjusted for treatment group (60 Gy vs 50.4 Gy), WHO PS (0 or 1), disease location (head or body/tail) and randomised nelfinavir assignment (arm A/C or B/D)
[2]a p-value of <0.2 is significant
[3]Model covariates were treatment group (60 Gy vs 50.4 Gy), WHO PS (0 or 1), disease location (head or body/tail), randomised nelfinavir assignment (arm A/C or B/D) and an interaction term between treatment group and nelfinavir assignment

12- month Local Progression Rate

Events* within 12 months of registration n (%)	50.4 Gy in 28# Arms A+B (n= 45)	60 Gy in 30# Arms C+D (n= 46)
Local progression (with or without metastasis)	**15 (33.3)**	**11 (23.9)**
Metastasis (no local progression)	**11 (24.4)**	**16 (34.8)**
Deaths	**11 (24.4)**	**12 (26.1)**
Evidence of local progression (with or without metastasis)	**7**	**3**
No local progression	**4**	**9**
Deaths before any known progression	**0**	**0**

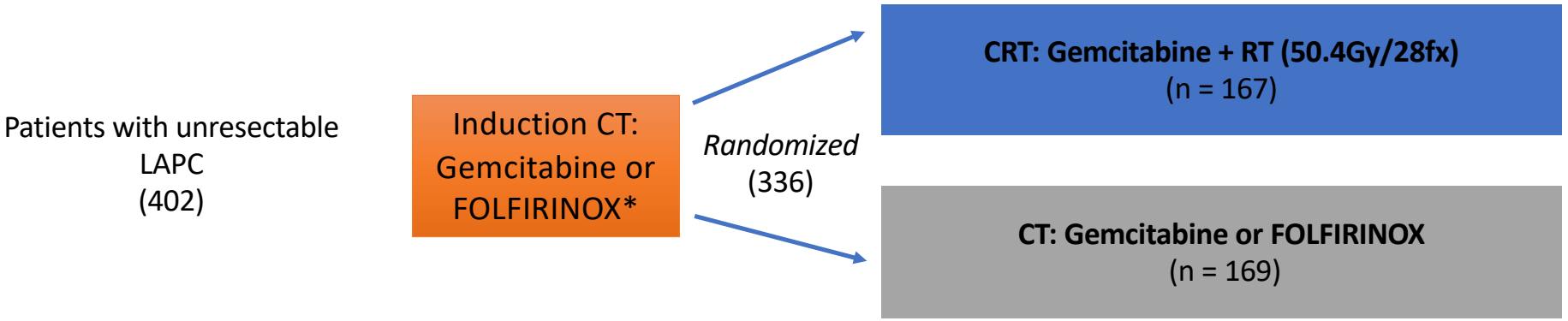
Summary

- NO improvement of OS with NELFINAVIR or RT 60 Gy
- RT 60 Gy + capecitabine well tolerated
- Suggestion of better LOCAL CONTROL with RT 60 Gy

SBRT

CONKO-007: Study Design

Randomized phase III trial of induction chemotherapy followed by chemoradiotherapy or chemotherapy alone for nonresectable locally advanced pancreatic cancer



Primary endpoint: R0 resection rate

Secondary endpoints: OS, DFS, RR, survival following resection

Fietkau. ASCO 2022. and American Society of Clinical Oncology 2022 annual meeting NCT01827553.

CONKO-007: Conclusions

CRT ARM

1. ↑ R0 CRM negative resections (20% vs 9%)
2. Among surgery patients 5-year OS was 27% vs 13%
3. ↑ 2y PFS (24% vs 18%)
4. 5-year OS was doubled (10% vs 4%)

- ↓ R1 resections (3% vs 10%)
- ↑pathologic complete response (pCR) (6% vs 0%)
- No difference in median PFS or OS

Fietkau. ASCO 2022. and American Society of Clinical Oncology 2022 annual meeting

Gastro-intestinal

- Stomaco
- Pancreas
- Colon-Retto

CRT→ guidelines

RT 60 Gy ‘orphan’

nelfinavir hypothesis generating

SBRT→ guidelines

National Comprehensive Cancer Network®

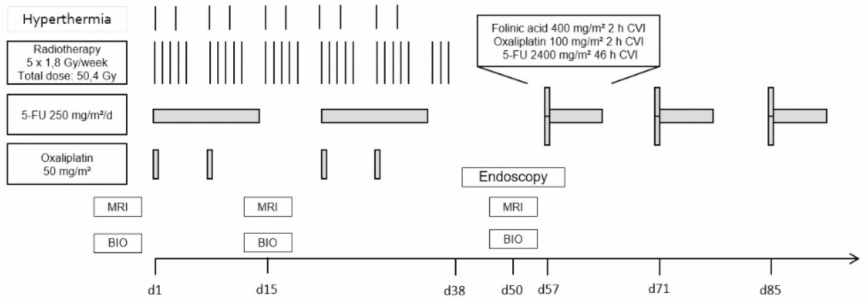
LOCALLY ADVANCED DISEASE	FIRST-LINE THERAPY[o,s]
Good performance status (PS)[r] →	Clinical trial (preferred) or Systemic therapy[t] or Induction chemotherapy[t] (preferably 4–6 mo) followed by chemoradiation[t,u,w,x] or stereotactic body RT (SBRT)[u] in selected patients (locally advanced without systemic metastases[v]) or Chemoradiation[t,u] or SBRT[v] in patients who are not candidates for induction chemotherapy

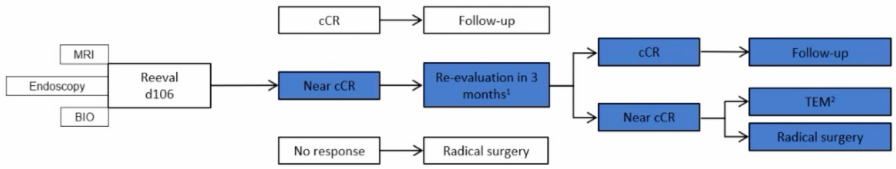
Gastro-intestinal

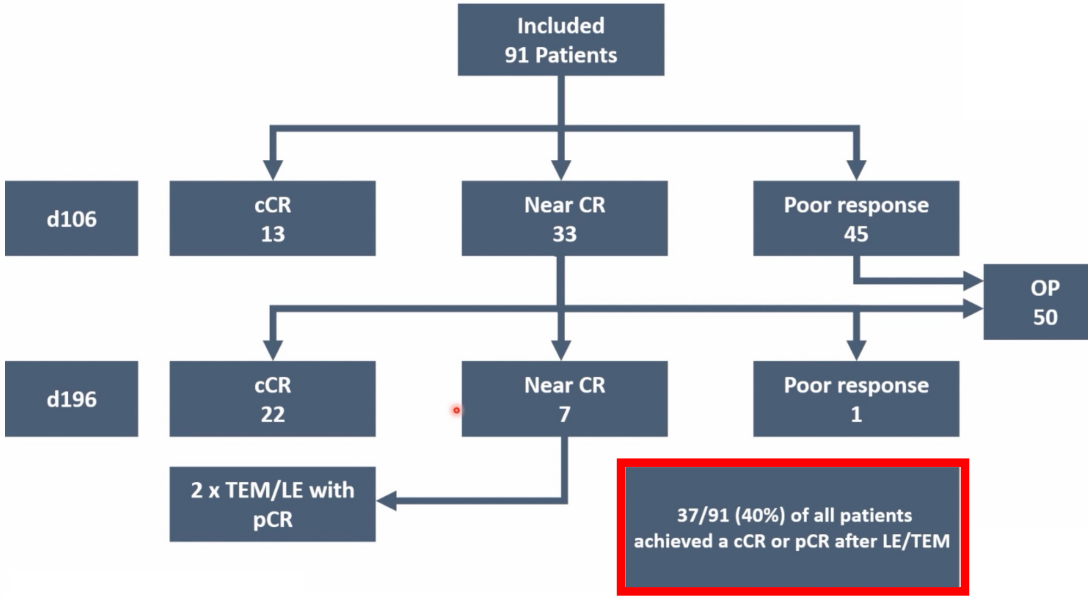
- Stomaco
- Pancreas
- Colon-Retto

LARC

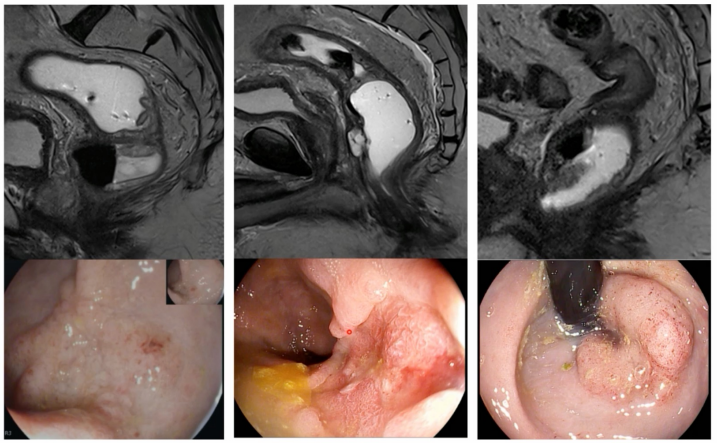
CAO-ARO-AIO-16







Post-OP Pathology in patients without a CR on d106/d196



		n	%
pT-stage	T0	14	28%
	Tis	3	6%
	T1	4	8%
	T2	11	22%
	T3	18	36%
	T4a	0	0%
	T4b	0	0%
pN-stage	N0	42	84%
	N+	8	16%
Regression	Dworak 0	1	2%
	Dworak 1	5	10%
	Dworak 2	15	30%
	Dworak 3	14	28%
	Dworak 4	15	30%

Total Neoadjuvant Therapy

Trial	Endpoint	Stage	Treatment		# patients
			TNT	CRT	
RAPIDO Bahadoer RR Lancet Oncol 2021	3y DRTF	HR (T4, MRF+, mucinous, N extramesorecum)	**Short-TNT** → S	Long CRT → S +/-CT	**912**
PRODIGE 23 Conroy T Lancet Oncol 2021	3y DFS	T3-4 any N	CT + **Long CRT** →S + CT	Long CRT → S + CT	**461**

Total Neoadjuvant Therapy: DM

TRIAL	DRFT/DFS		DM		pCR		LR	
	TNT	CRT	**TNT**	CRT	**TNT**	CRT	TNT	CRT
RAPIDO	**24%**	30%	**20%**	27%	**28%**	14%	8.3%	6%
	p=0.019		**p=0.0048**		p< 0.0001		p=0.12	
PRODIGE 23	**76%**	69%	**17%**	25%	**28%**	12%	4%	6%
	p=0.0034		**p=0.0017**		**p< 0.0001**		p=0.56	

Total Neoadjuvant Therapy: DM

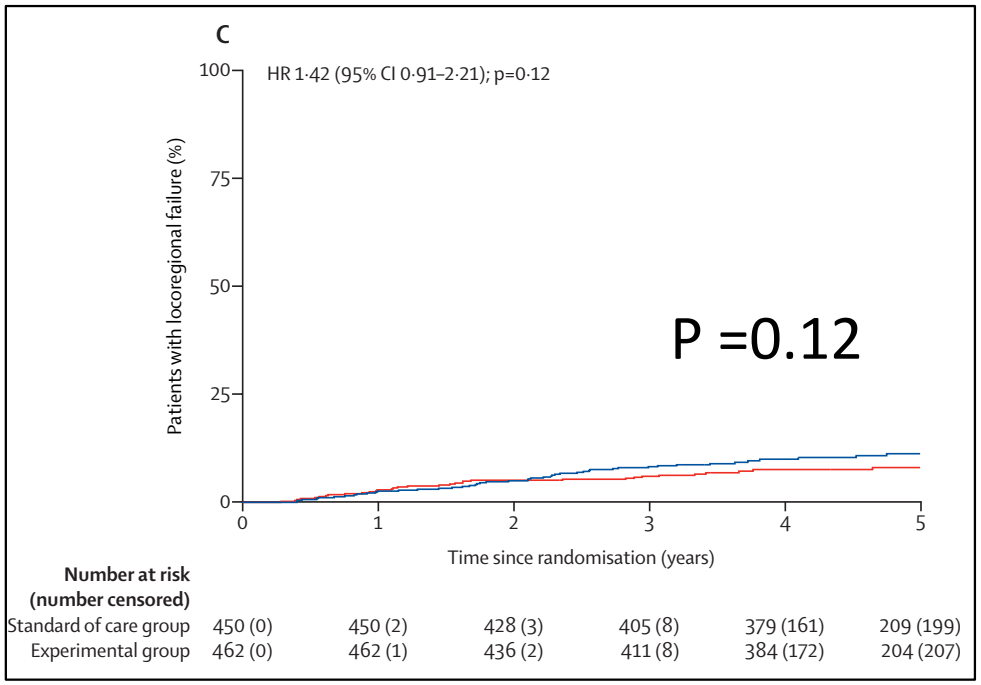
TRIAL	DRFT/DFS		DM		pCR		LR	
	TNT	CRT	**TNT**	CRT	**TNT**	CRT	**TNT**	**CRT**
RAPIDO	**24%**	30%	**20%**	27%	**28%**	14%	**8.3%**	**6%**
	p=0.019		**p=0.0048**		p< 0.0001		**p=0.12**	
PRODIGE 23	**76%**	69%	**17%**	25%	**28%**	12%	**4%**	**6%**
	p=0.0034		**p=0.0017**		**p< 0.0001**		**p=0.56**	

Total Neoadjuvant Therapy

RAPIDO TRIAL

RAPIDO trial

Local Control: RAPIDO data



Bahadoer, Lancet Oncol 2021

Unpublished data ESSO 2021

IMMUNOTHERAPY

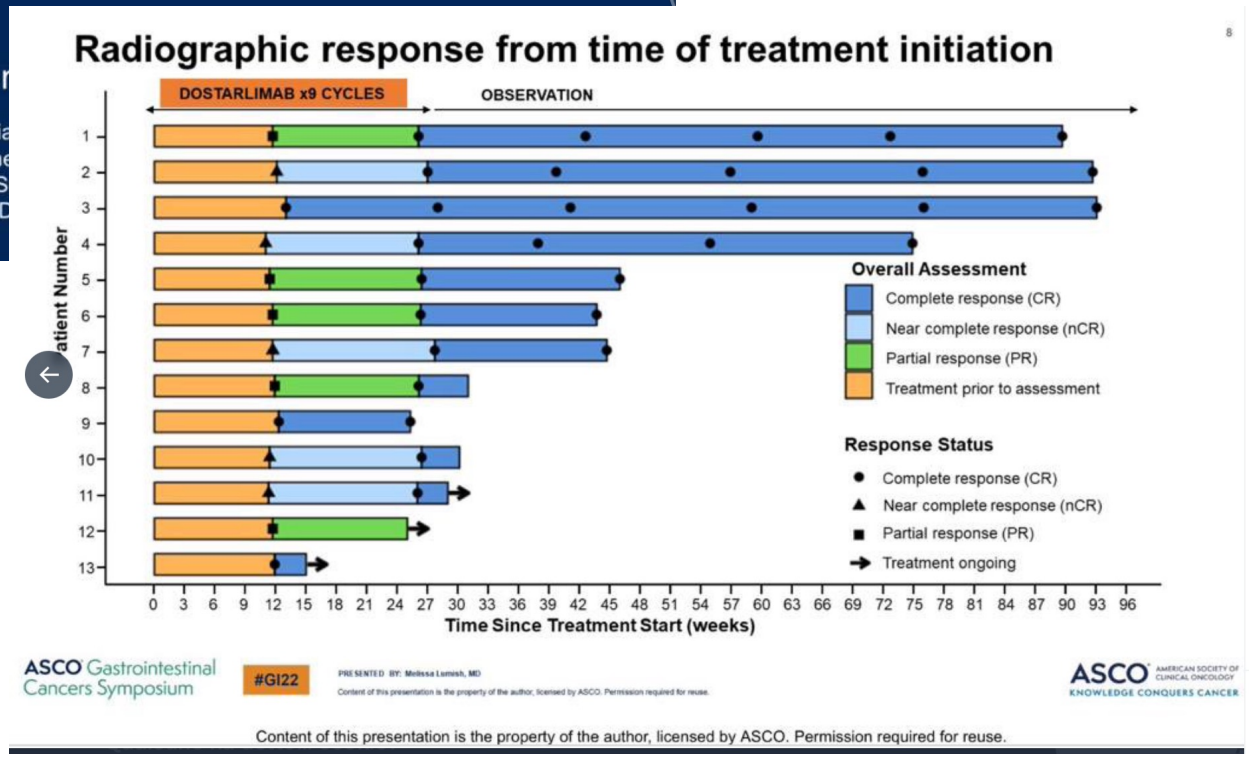
ASCO Gastrointestinal Cancers Symposium

PD-1 Blockade Alone for Mismatch Repair Deficient Locally Advanced Rectal Cancer

Phase II Clinical Trial

Memorial Sloan Kettering Can

Melissa A. Lumish MD, Jenna L. Sinapoli, Zsofia Yaeger MD, Neil Howard Segal MD, PhD, Imane Sugarman MD, Avni Desai MD, Jesse Joshua S PhD, Philip B. Paty MD, Julio Garcia-Aguilar MD



twitter

PD-1 blockade alone (Dostarlimab) for dMMR locally advanced rectal cancer, by Melissa Lumish from @sloan_kettering. #GI22

✅ Clinical Complete Response = 100% (11/11)

💡 interesting results, low numbers, proof of concept.

Traduci il Tweet

2:00 PM · 31 gen 2022 da San Paolo, Brasile

2 Retweet **6** Mi piace

Altri Tweet

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 23, 2022 VOL. 386 NO. 25

PD-1 Blockade in Mismatch Repair–Deficient, Locally Advanced Rectal Cancer

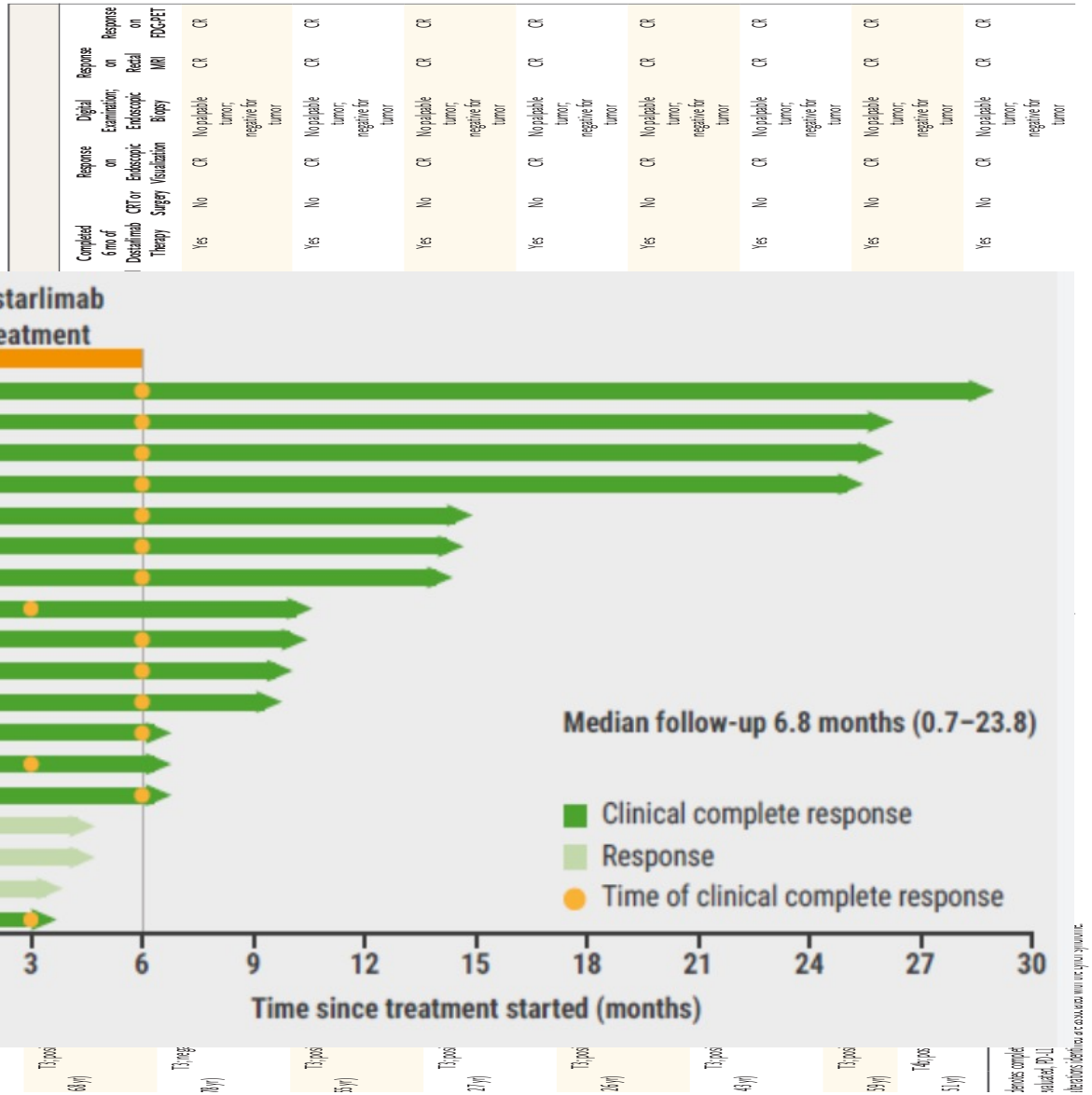
A. Cercek, M. Lumish, J. Sinopoli, J. Weiss, J. Shia, M. Lamendola-Essel, I.H. El Dika, N. Segal, M. Shcherba, R. Sugarman, Z. Stadler, R. Yaeger, J.J. Smith, B. Rousseau, G. Argiles, M. Patel, A. Desai, L.B. Saltz, M. Widmar, K. Iyer, J. Zhang, N. Gianino, C. Crane, P.B. Romesser, E.P. Pappou, P. Paty, J. Garcia-Aguilar, M. Gonen, M. Gollub, M.R. Weiser, K.A. Schalper, and L.A. Diaz, Jr.

MMR deficiency

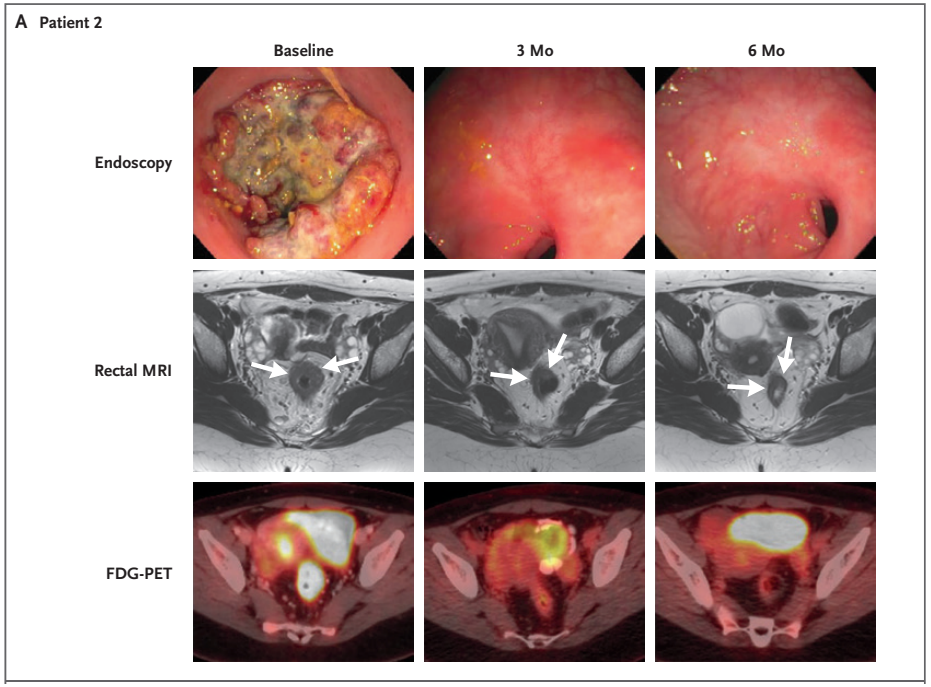
Dostarlimab 6 months every 3 weeks

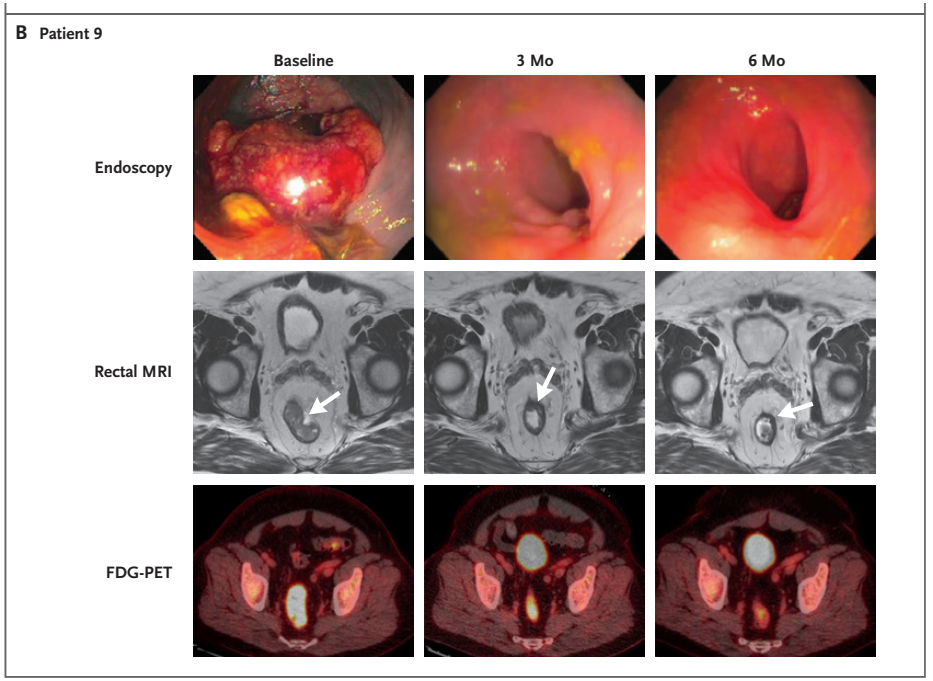
Followed by CRT if not CR

Followed by surgery if not CR



Immune therapy in rectal cancer





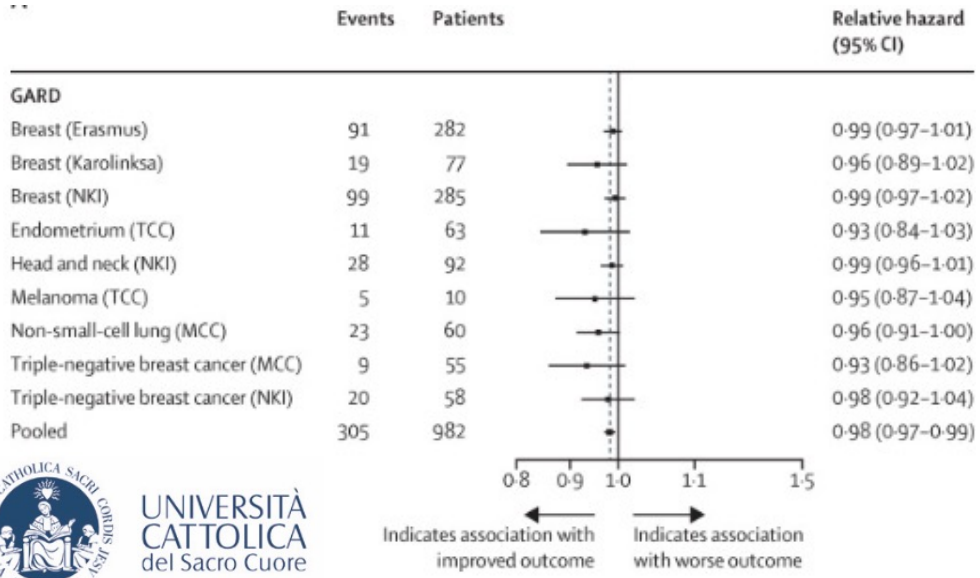
1. Only 3% of all rectal cancer

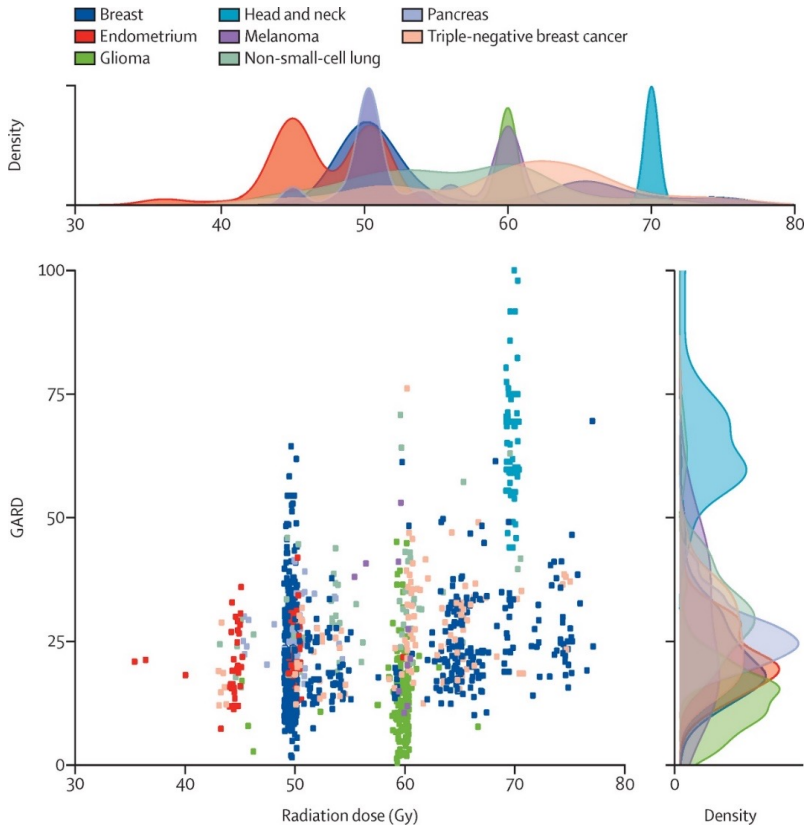
2. MMR/MSI evaluation to ALL patients

Omic guided radioterapy

New radiotherapy dose definition protocols
Genomic-**A**djusted **R**adiation **D**ose (**GARD**)

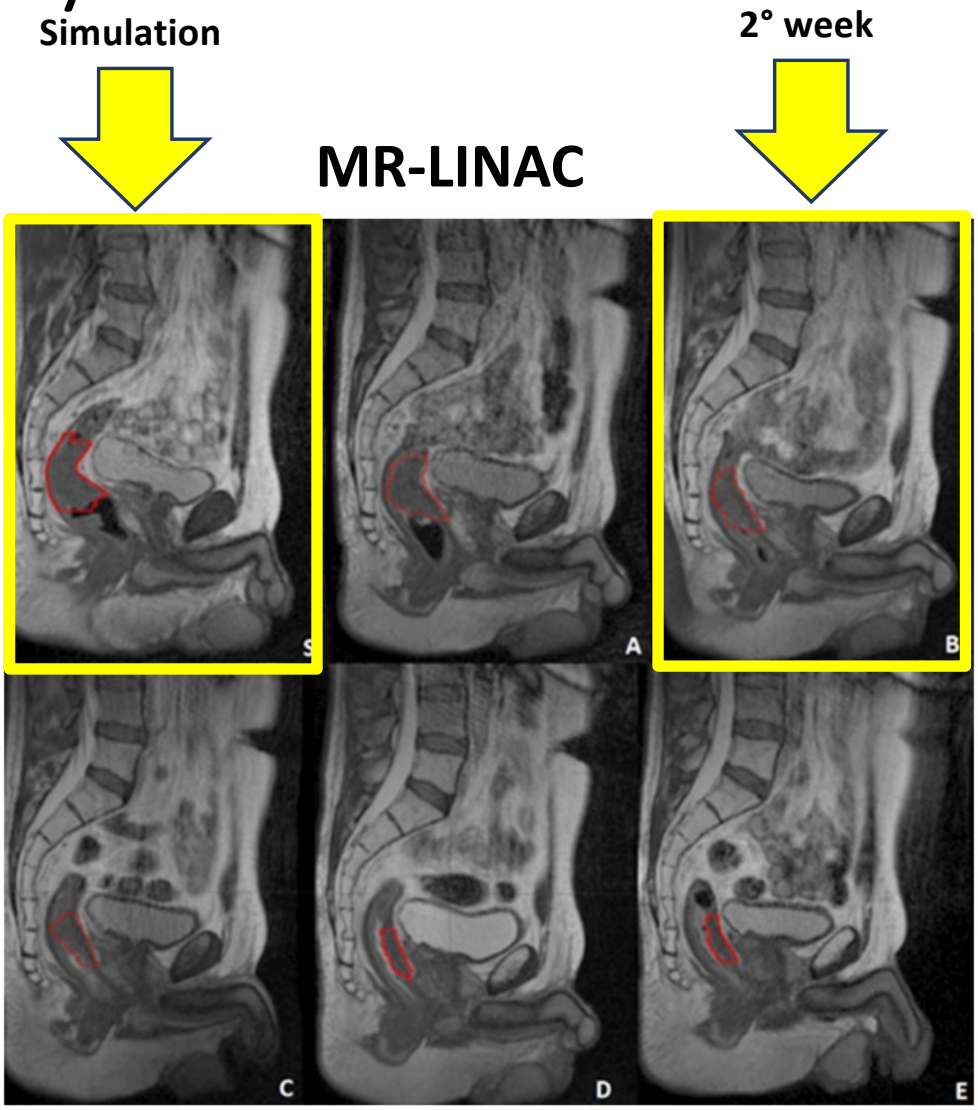
Correlation with time to first recurrence and overall survival



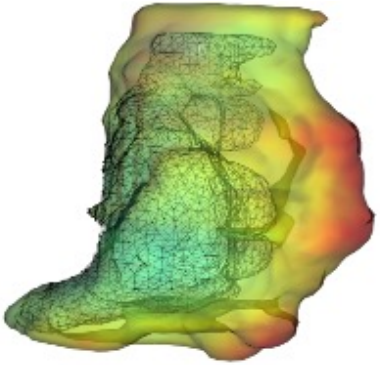


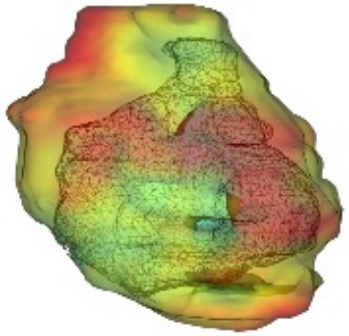
Scott JG et al. Lancet Oncol. 2021 Sep;22(9):1221-1229

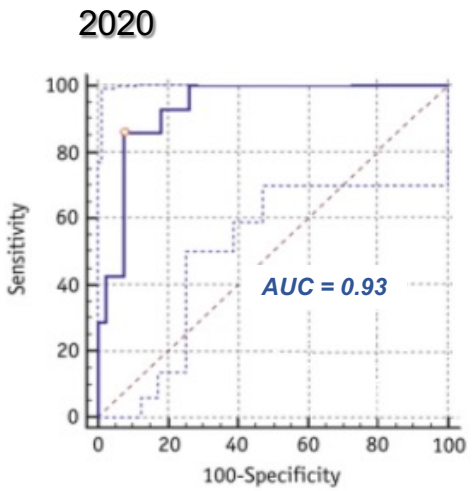
Hybrid machine



pCR prediction during treatment







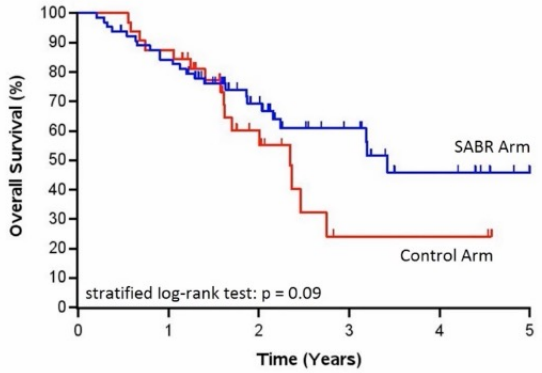
Early regression index

Boldrini et al, La Radiologia Medica 2019

METASTATIC

SABR COMET long term outcomes

SABR-COMET Initial Results: ASTRO 2018



Median OS

Control Arm: 28 months
(95% CI: 19-33 months)

SABR Arm: 41 months
(95% CI: 26 months to 'not reached')

Amended in 2016 to follow patients for 10 years

Western

OICR

ESTRO 2022

David PALMA
(CANADA)

Primary Endpoint

- Overall survival

Secondary endpoints:

- Progression-free survival
- Toxicity (CTC-AE v4.0)
- Quality of life (FACT-G)
- Lesional control rate
- Number of cycles of further systemic therapy
  - Changed to binary variable "Receipt of systemic therapy" (Y/N)

- Number of fractions dependent on tumor size and location
  - Lung: 54/3, 55/5, 60/8
  - Bone: 35/5, 30/3, 16-20/1
  - Brain: SRS (18-24/1) or SABR (40/5), WBRT optional
  - Liver: 45-60 Gy in 3-8
  - Adrenal: 60/8

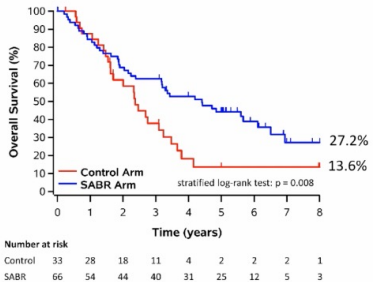
99 pts randomized up to 2016

Characteristic	Arm, No. (%) Control (n = 33)	SABR (n = 66)
Site of original primary tumor		
Breast	5 (15)	13 (20)
Colorectal	9 (27)	9 (14)
Lung	6 (18)	12 (18)
Prostate	2 (6)	14 (21)
Other	11 (33)	18 (27)

SABR COMET long term outcomes

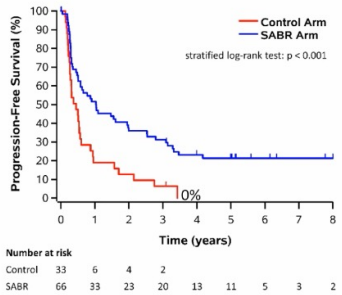
Overall Survival – Median F/U 68 months

Sixty-five OS events (25 control arm, 40 SABR arm)



Progression-Free Survival

Eighty-one PFS events (31 control arm, 50 SABR arm)



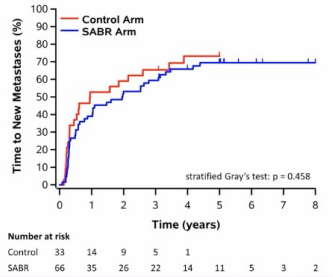
Median PFS

Control Arm: 5.4 months
(95% CI: 3-7 months)

SABR Arm: 12 months
(95% CI: 6-24 months)

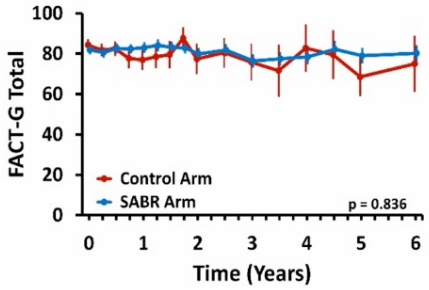
Time to New Metastases

Sixty-seven patients with metastasis events (23 control arm, 44 SABR arm)



QOL and Toxicity

- Rates of all grade ≥2 acute and late toxicities remained higher in the SABR arm (30.3% vs. 9.1%, p=0.019)
- No new grade 3-5 toxicities
- No impact on QOL



Outcomes by Histology

Primary Tumor	OS HR (95% CI)	PFS HR (95% CI)
Breast	0.77 (0.21, 2.88)	0.53 (0.18, 1.59)
Colorectal	0.59 (0.19, 1.80)	0.16 (0.03, 0.76)
Lung	1.17 (0.43, 3.18)	1.15 (0.41, 3.21)
Prostate	Model did not converge	0.09 (0.01, 0.65)
'Other'	0.61 (0.23, 1.59)	0.75 (0.33, 1.71)
All Non-Prostate Primaries	0.62 (0.36, 1.05)	0.59 (0.37, 0.96)

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Clinical and Translational Radiation Oncology

journal homepage: www.sciencedirect.com/journal/clinical-and-translational-radiation-oncology

A predictive model of polymetastatic disease from a multicenter large retrospectIve database on colorectal lung metastases treated with stereotactic ablative radiotherapy: The RED LaIT-SABR study

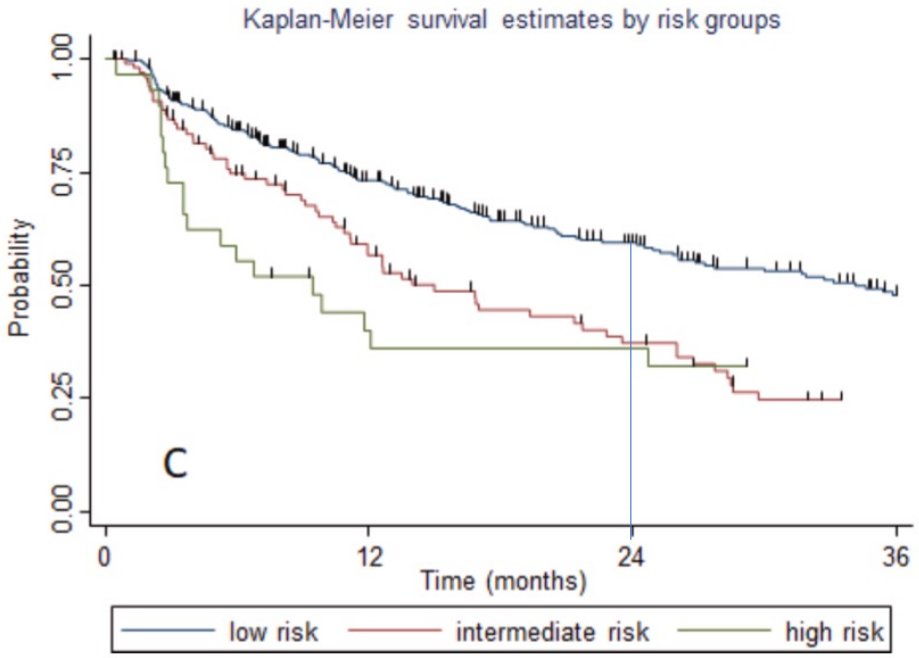
Luca Nicosia [a,*], Davide Franceschini [b], Francesca Perrone-Congedi [c], Alessandro Molinari [d], Marianna Alessandra Gerardi [e], Michele Rigo [a], Rosario Mazzola [a], Marco Perna [f], Vieri Scotti [f], Andrei Fodor [g], Aurelia Iurato [h], Francesco Pasqualetti [i,j], Giovanni Gadducci [i], Silvia Chiesa [k], Rita Marina Niespolo [l], Alessio Bruni [m], Anna Cappelli [m], Elisa D'Angelo [m], Paolo Borghetti [n], Alessandro Di Marzo [o], Andrea Ravasio [p], Berardino De Bari [c] pulcri [r], Dario Aiello [s], Gianluca Mortellaro [t], Claudia Sangalli [u], Marzia Franceschini [u], Giampaolo Montesi [v], Francesco Maria Aquilanti [w], Gianluigi Lunardi [x], Riccardo Valdagni [u,y], Ivan Fazio [s], Giovanni Scarzello [r], Vittorio Vavassori [p], Ernesto Maranzano [o], Stefano Maria Magrini [n], Stefano Arcangeli [l], Maria Antonietta Gambacorta [k,z], Vincenzo Valentini [k,z], Fabiola Paiar [i], Sara Ramella [n], Nadia Gisella Di Muzio [g,aa], Mauro Loi [f], Barbara Alicja Jereczek-Fossa [e,y], Franco Casamassima [d], Mattia Falchetto Osti [c], Marta Scorsetti [b,ab], Filippo Alongi [a,ac]

- International Ethical Committee (Prot. Negrar 2019-ZT)
- 23 Centers
- **450** lung oligometastatic patients from colon and rectum

Table 2
Treatment characteristics (n = 705) (%).

Median lesion diameter (mm) (range)	14 (5–45)
Total treated lesions	
1	301 (42.5)
2	180 (25.5)
3	90 (13)
4	44 (6)
5	90 (13)
Median SUVmax (range)	4.9 (1–28)
Median total dose (Gy) (range)	48 (23–70)
Median dose per fraction (Gy) (range)	12 (5–30)
Median number of fractions (range)	3 (1–10)
Median BED (range)	125 (100–180)
Median GTV volume (cc) (per lesion)	3.07 (0.1–178)
Median cumulative GTV (cc)	4.6 (0.2–255.8)
Mean PTV volume (cc)	13.2 (1.2–113)
Lesion site	
Central	204 (29)
Peripheral	501 (71)

BED: biological effective dose; GTV: gross tumor volume; PTV: planning target volume



Risk class	Cum GTV	# of mets	tPMD median	tPMD 2 years
Low	< 10 cc	1–3	34.1	58.9 %
Intermediate	> 10 cc	1–3	13.9	38.4 %
High	any	4-5	9.4	35.3 %

Table 3
Analysis of time to polymetastatic conversion.

Covariates	*Median tPMC (months)*	*P*	*Covariates*	*Median tPMC (months)*	*P*
Number of oligometastases			Group 1: 1 oligometastasis and cumGTV < 10 cc	36.1	0.00
1	27.7	0.005	Group 2: 1 oligometastasis and cumGTV > 10 cc	13.9	
2–3	21.3		Group 3: 2–3 oligometastases and cumGTV < 10 cc	31.9	0.058
4–5	9.1		Group 4: 2–3 oligometastases and cumGTV > 10 cc	14.9	
			Group 5: 4–5 oligometastases and cumGTV < 10 cc	6.7	0.85
cumGTV			Group 6: 4–5 oligometastase and cumGTV > 10 cc	9.4	
<10 cc	33.1	0.00			
>10 cc	13.5				

tPMC: time ti polymetastatic conversion; cumGTV: cumulative gross tumor volume

Summary

- The number of lesions cannot predict alone OMD → PMD
- Cumulative VOLUME highly predicts OMD→PMD
- PM may be used to design studies on SABR
- Other factors (radiomics) may add info for prognosis/prediction

PATIENT

PREDICTIVE AND PROGNOSTIC VALUE OF **INFLAMMATORY MARKERS** IN **LARC PATIENTS** UNDERGOING NEOADJUVANT CHEMORADIOTHERAPY –A RETROSPECTIVE MULTICENTRIC ANALYSIS BY AIRO GASTROINTESTINAL STUDY GROUP

AIRO Gastrointestinal Study Group - 9 centers

808 patients
out of 1262

Multivariate analysis

pCR

Variable	Value	OR (95% IC)	p value
SII	>500	0.53 (0.37-0.75)	p<0.0001

DFS

Variable	Value	HR (95% IC)	p value
AGE, years	≥65	1.50 (1.16-1.94)	p=0.002
N extra	yes	1.41 (1.06-1.88)	p=0.02
RT dose, Gy	≥55	1.43 (1.07-1.90)	p=0.015
HEI	3	1.39 (1.00-1.96)	p=0.05
MLR	>0.18	1.49 (1.03-2.14)	p=0.03

OS

Variable	Value	HR (95% IC)	p value
AGE, years	≥65	2.00 (1.46-2.75)	p<0.001
RT dose, Gy	≥55	0.73 (0.53-0.99)	p=0.04
MLR	>0.35	1.49 (1.08-2.06)	p=0.01

LEGEND
Hemo-eosinophils inflammation index (**HEI**)
Neutrophil to lymphocyte ratio (**NLR**)
Systemic index of inflammation (**SII**)
Platelet to lymphocyte ratio (**PLR**)

Mariani S et al. AIRO 2022
ctRO in press

Summary

Baseline inflammatory markers do have some predictive and prognostic role in LARC

Baseline inflammatory markers are inexpensive and easy to obtain

Available data are not univocal and are all retrospective in nature (confounding factors?)

Immune response may change over the course of the disease, also as a result of treatments

Prospective studies evaluating pre- and post-treatment inflammation markers may be the key to getting to the point of **including these parameters in the therapeutic work-up of LARC patients**

Mariani S et al. AIRO 2022
ctRO in press

TECHNICAL

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journal homepage: www.thegreenjournal.com

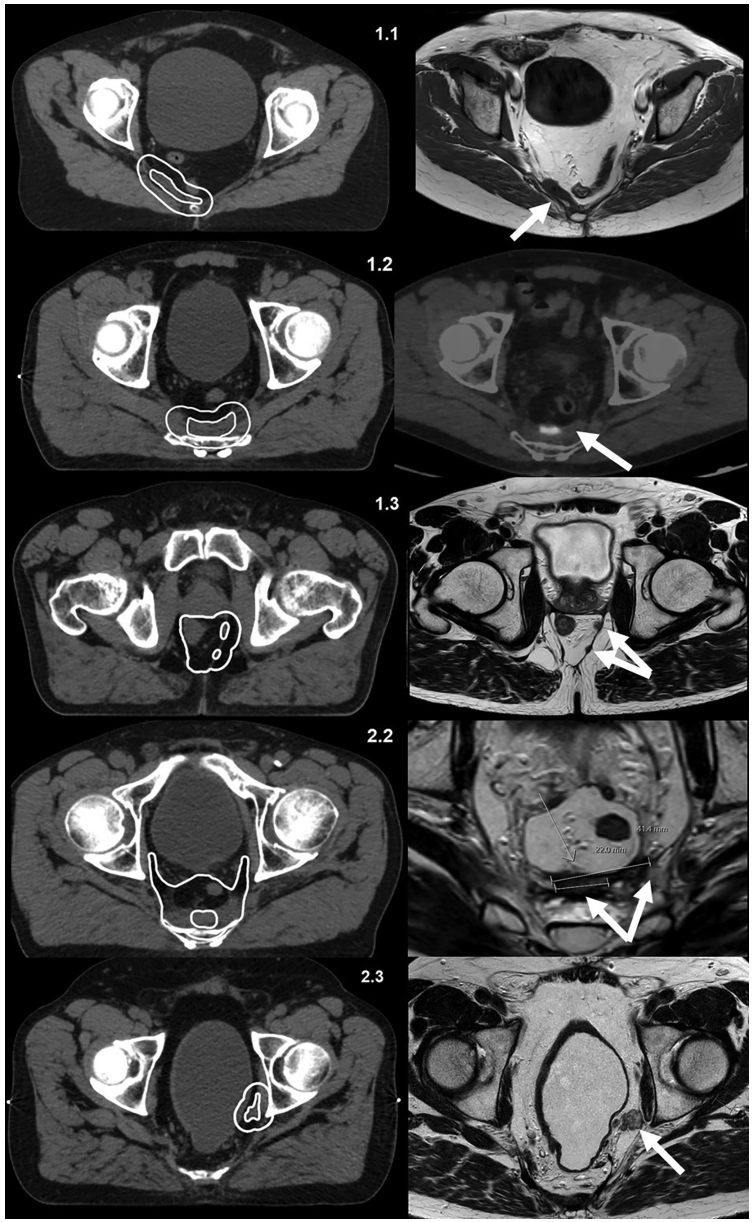
Original Article

Development of a consensus-based delineation guideline for locally recurrent rectal cancer

Floor Piqeur [a,b,c,1], Britt J.P. Hupkens [a,d,1], Stefi Nordkamp [e], Marnix G. Witte [b], Philip Meijnen [f], Heleen M. Ceha [g], Maaike Berbee [d], Margriet Dieters [h], Sofia Heyman [i], Alexander Valdman [j], Martin P. Nilsson [k], Joost Nederend [l], Harm J.T. Rutten [e,m], Jacobus W.A. Burger [e], Corrie A.M. Marijnen [b,c], Heike M.U. Peulen [a,*]

Table 1
Summary of case characteristics, representing diverse disease presentation in LRRC.

	Meeting	Prior radiotherapy	Radiotherapy naïve	Location **
Case 1.1	1	X		Lateral, near the pelvic wall
Case 1.2*	1	X		Posterior
Case 1.3	1	X		Axial/central
Case 2.1*	2	X		Posterior
Case 2.2*	2		X	Posterior
Case 2.3	2	X		Lateral, obturator loge



Gastro-intestinal

- Stomaco
- Pancreas
- Colon-Retto

TNT→ guidelines
TNT→ Do not renounce to RT
IMMUNE→ 'Orphan'

METASTATIC→ SABR guidelines
BLOOD MARKERS → Hypothesis generatimg

DELINEATION GUIDELINES

GRUPPO DI STUDIO PER LE NEOPLASIE GASTROINTESTINALI

PATOLOGIA	Titolo del progetto/studio	Referente
RETTO intermediate	Bridge I – studio prospettico randomizzato volto a valutare l'allungamento del tempo alla chirurgia dopo RT-CT nel tumore del retto	Prof.ssa Maria Antonietta Gambacorta mariaantonietta.gambacorta@policlinicogemelli.it
RETTO advanced	Bridge 2 – studio prospettico di fase II su TNT nel tumore del retto alto rischio	Dr.ssa Elisa Palazzari elisa.palazzari@cro.it
RETTO retreatment	RETRY – Radioterapia e Total Neoadjuvant Therapy nei pazienti con recidiva di carcinoma del retto precedentemente irradiati	Prof.ssa Maria Antonietta Gambacorta mariaantonietta.gambacorta@policlinicogemelli.it
ANO	Validazione multicentrica di un modello predittivo di risposta tumorale basato su MRI diagnostica pre-trattamento nel carcinoma squamocellulare del canale anale	Dott. Marco L. Bonù marco.bonu@unibs.it
PANCREAS	Studio di fase II, multicentrico, della radioterapia stereotassica in pazienti affetti da adenocarcinoma localmente avanzato del pancreas (IRENE)	Dr.ssa Alessandra Arcelli alearceese@hotmail.com
PANCREAS	Studio PAULA (Pooled Analysis Unresectable Locally Advanced): Analisi a lungo termine	Dr.ssa Alessandra Arcelli alearceese@hotmail.com
GIUNZIONE GASTRO-ESOFAGEO	Studio di fase II nelle neoplasie localmente avanzate della giunzione esofago-gastrica	Dr.ssa Elisa Palazzari elisa.palazzari@cro.it Dr. Roberto Innocente roberto.innocente@cro.it
ESOFAGO	Studio retrospettivo sul trattamento del cancro dell'esofago	Dr. Nicola Simoni nicolasimoni81@gmail.com Dr.ssa Elisa Palazzari elisa.palazzari@cro.it
STOMACO	Studio retrospettivo sul ruolo della radioterapia emostatica nel carcinoma gastrico	Dott. Marco Lupattelli marco.lupattelli@ospedale.perugia.it

STUDI CLINICI

https://www.radioterapiaitalia.it/soci/gruppi-di-studio/gruppo-gastrointestinale-indice/gruppo-di-studio-gatrointestinale-progetti-ongoing/