CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE

2ª EDIZIONE

Il paziente anziano con mCRC *Caso clinico*

Vincenzo Formica

Medical Oncology

Medicine and Surgery course

School of Medicine

University of Rome Tor Vergata

Università di Roma Tor Vergata

PTV Azienda Ospedaliera Universitaria POLICLINICO TOR VERGATA

Uomo, 1941

- FAMILIRITA' ONCOLOGICA:
  - fratello HCC, 55 aa ; fratello HNSCC, 55 aa (vivente)
- ANAMNESI FISIOLOGICA:
  - fumatore 120 pack/yrs
- ANAMNESI PATOLOGICA REMOTA:
  - BPCO 2000
  - IPB 2006
  - Adenoma pleomorfo parotide 2010, in FU.
  - ernioplastica inguinale 2016
  - Ateromasia arterie iliache alla TC, 2018
  - Trait microcitemico

Storia Oncologica

- ***Esordio clinico***: Febbraio-Marzo 2018 (**77 aa**) dolore addominale ingravescente, il paziente fa accesso al Pronto Soccorso il 16/03/2018 con un quadro di addome acuto (perforazione intestinale)

- Durante il ricovero il paziente riferisce di avere effettuato TC addome (non in visione) con riscontro di lesione del colon destro perforata, si sottopone ad intervento in urgenza di **EMICOLECTOMIA DX in data 4/4/2018**

Storia Oncologica

Es Istologico:

MACRO: riscontrate due neoformazioni, una nel lume cecale che perfora la parete intestinale, distante 3 cm da questa, altra formazione polipoide di 2x1cm.

MICRO: la prima neoformazione repertata corrisponde ad adenocarcinoma G2 infiltrante la parete a tutto spessore perforandola; la seconda neoformazione corrisponde ad adenoma tubulare con displasia di alto grado e con trasformazione adenocarcinomatosa in situ, con peduncolo e base d'impianto liberi da malattia. Si repertano 11 linfonodi esenti da ripetizione neoplastica, margini liberi da infiltrazione. pT4aN0.

Profilo Molecolare: KRAS wt, NRAS wt, BRAF wt, MSS (piroseq)

SNODO DECISIONALE N.1

- TERAPIA ADIUVANTE VS ALTRO?

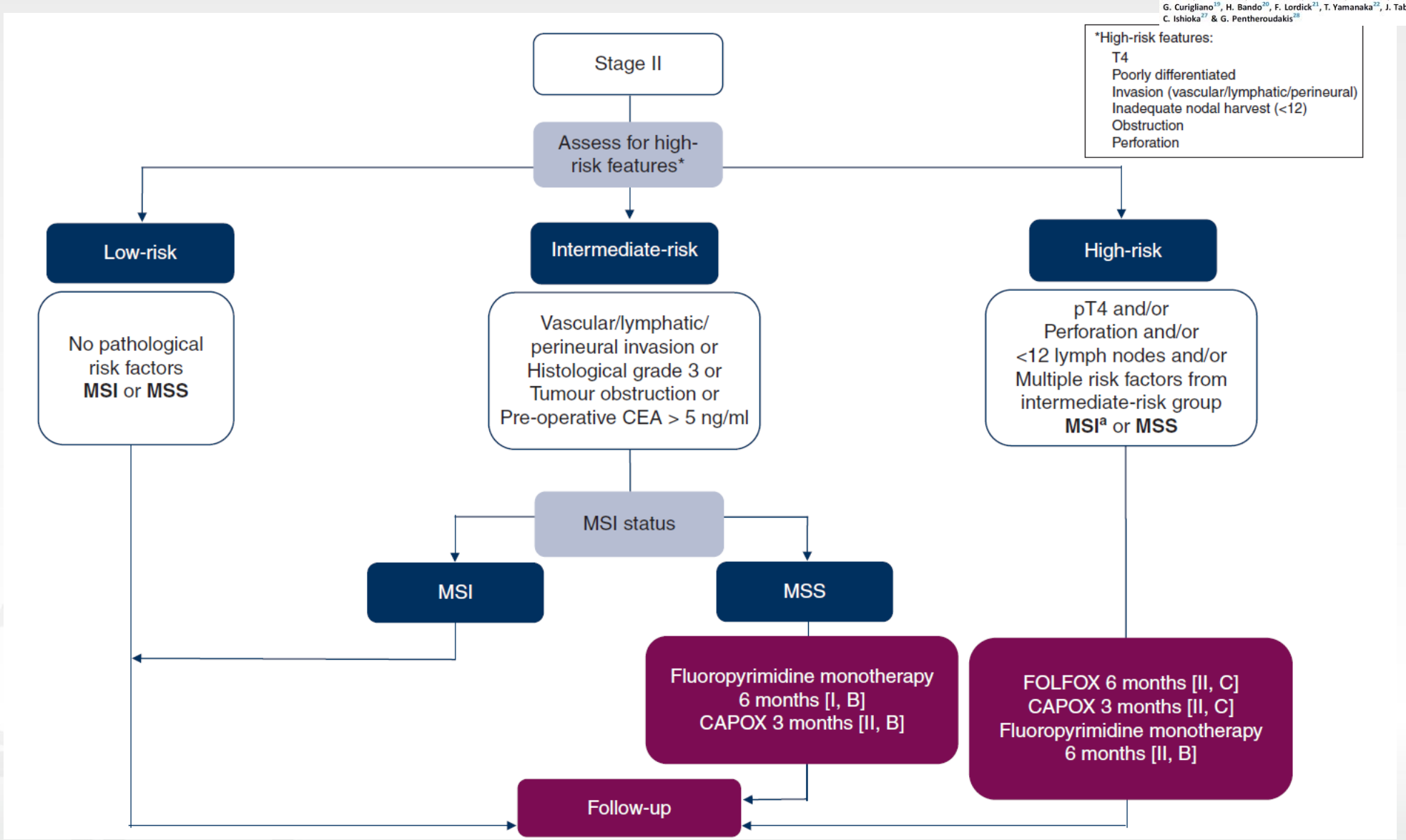
CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE 2ª EDIZIONE

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
Volume 32 ■ Issue 12 ■ 2021
ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Pan-Asian adapted ESMO Clinical Practice Guidelines for the diagnosis treatment and follow-up of patients with localised colon cancer

T. Yoshino[1,*], G. Argilés[2], E. Oki[3], E. Martinelli[4], H. Taniguchi[1], D. Arnold[5], S. Mishima[1], Y. Li[6], B. K. Smruti[7], J. B. Ahn[8], I. Faud[9], C. E. Chee[10], K.-H. Yeh[11,12], P.-C. Lin[13], C. Chua[14], H. H. Hasbullah[15], M. A. Lee[16], A. Sharma[17], Y. Sun[18], G. Curigliano[19], H. Bando[20], F. Lordick[21], T. Yamanaka[22], J. Tabernero[23], E. Baba[24], A. Cervantes[25], A. Ohtsu[1], S. Peters[26], C. Ishioka[27] & G. Pentheroudakis[28]



Adjuvant Therapy for Stage II Colon Cancer: ASCO Guideline Update

Nancy N. Baxter, MD, PhD[1]; Erin B. Kennedy, MHSc[2]; Emily Bergsland, MD[3]; Jordan Berlin, MD[4]; Thomas J. George, MD[5]; Sharlene Gill, MD, MPH, MBA[6]; Philip J. Gold, MD[7]; Alex Hantel, MD[8]; Lee Jones, MBA[9]; Christopher Lieu, MD[10]; Najjia Mahmoud, MD[11]; Arden M. Morris, MD, MPH[12]; Erika Ruiz-Garcia, MD, MS[13]; Y. Nancy You, MD, MHSc[14]; and Jeffrey A. Meyerhardt, MD, MPH[15]

J Clin Oncol 40:892-910. © 2021

Outcome	Results	Absolute Effect Estimates		Quality of Evidence (heterogeneity)	Plain Language Summary
		Surgery Alone	ACT		
OS fewer than 12 sampled lymph nodes	HR: 0.67 (95% CI, 0.57 to 0.77) (6,800 patients in four studies) Follow-up: 5 years	483 deaths per 1,000	357 deaths per 1,000	Low (I^2 = 30%)	ACT probably improves OS for patients with fewer than 12 sampled lymph nodes
		Difference: 126 fewer per 1,000 (95% CI, 170 fewer to 85 fewer)			
DFS/RFS fewer than 12 sampled lymph nodes	HR: 0.71 (95% CI, 0.61 to 0.82) (6,554 patients in three studies) Follow-up: 5 years	541 recurrences/new tumors or deaths per 1,000	425 recurrences/new tumors or deaths per 1,000	Low (I^2 = 0)	ACT probably improves DFS/RFS for patients with fewer than 12 sampled lymph nodes
		Difference: 116 fewer per 1,000 (95% CI, 163 fewer to 69 fewer)			
OS tumor perforation	HR: 0.31 (95% CI, 0.16 to 0.6) (186 patients in two studies) Follow-up: 5 years	483 deaths per 1,000	185 deaths per 1,000	Low (I^2 = 29%)	ACT probably improves OS for patients with tumor perforation
		Difference: 298 fewer per 1,000 (95% CI, 383 fewer to 156 fewer)			
RFS tumor perforation	HR: 0.48 (95% CI, 0.23 to 1.0) (100 patients in one study) Follow-up: 5 years	541 recurrences per 1,000	312 recurrences per 1,000	Very low[a,b]	The impact of ACT on RFS for patients with tumor perforation is uncertain
		Difference: 229 fewer per 1,000 (95% CI, 377 fewer to 0 fewer)			
OS intestinal obstruction	HR: 0.57 (95% CI, 0.38 to 0.85) (911 patients in three studies) Follow-up: 5 years	199 deaths per 1,000	119 deaths per 1,000	Low (I^2 = 0%)	ACT probably improves OS for patients with intestinal obstruction
		Difference: 80 fewer per 1,000 (95% CI, 118 fewer to 27 fewer)			
DFS or RFS intestinal obstruction	HR: 0.63 (95% CI, 0.44 to 0.89) (796 patients in two studies) Follow-up: 5 years	461 recurrences/new tumors or deaths per 1,000	323 recurrences/new tumors or deaths per 1,000	Low (I^2 = 0%)	ACT probably improves DFS/RFS for patients with intestinal obstruction
		Difference: 138 fewer per 1,000 (95% CI, 223 fewer to 38 fewer)			

VOLUME 31 · NUMBER 20 · JULY 10 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

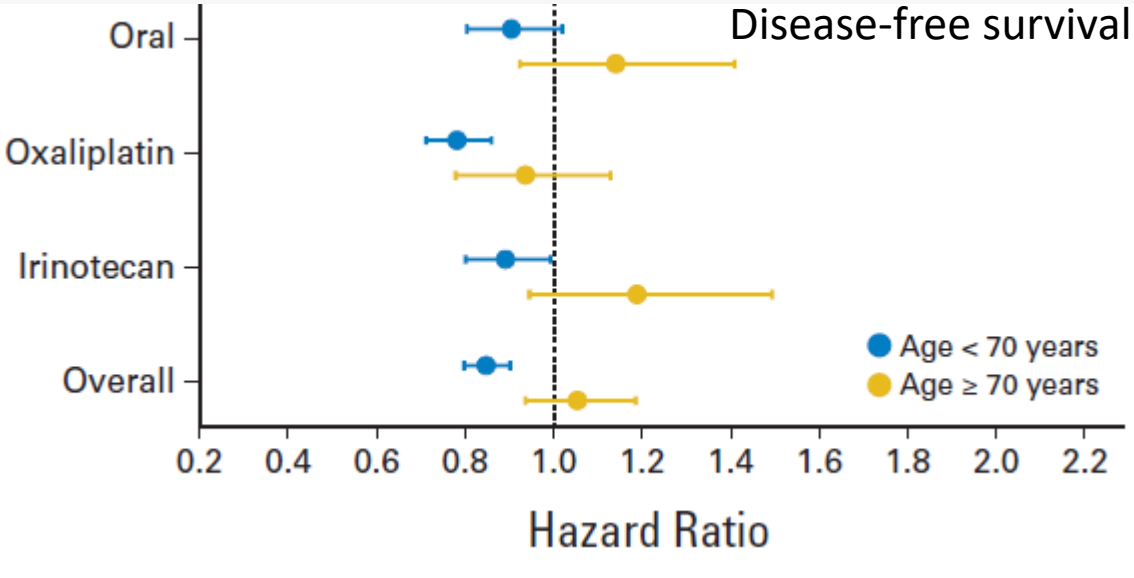
Impact of Age on the Efficacy of Newer Adjuvant Therapies in Patients With Stage II/III Colon Cancer: Findings From the ACCENT Database

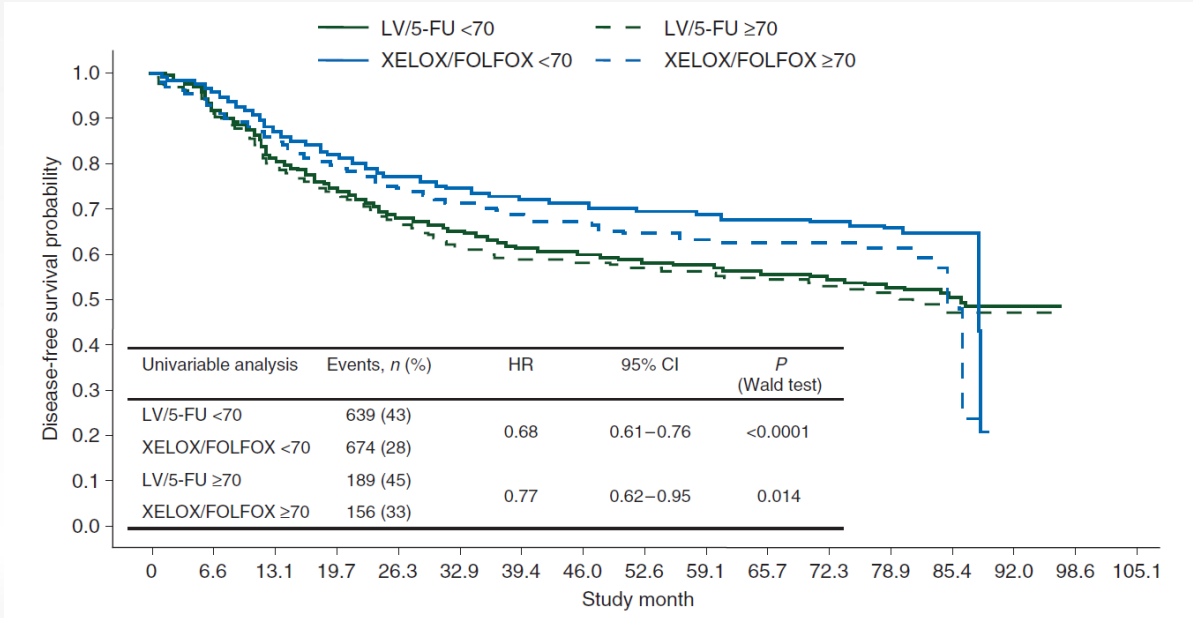
Nadine J. McCleary, Jeffrey A. Meyerhardt, Erin Green, Greg Yothers, Aimery de Gramont, Eric Van Cutsem, Michael O'Connell, Christopher J. Twelves, Leonard B. Saltz, Daniel G. Haller, and Daniel J. Sargent

Impact of age and medical comorbidity on adjuvant treatment outcomes for stage III colon cancer: a pooled analysis of individual patient data from four randomized, controlled trials

D. G. Haller[1*], M. J. O'Connell[2], T. H. Cartwright[3], C. J. Twelves[4], E. F. McKenna[5], W. Sun[6], M. W. Saif[7], S. Lee[5], G. Yothers[8] & H.-J. Schmoll[9]

Annals of Oncology 26: 715–724, 2015





Storia Oncologica

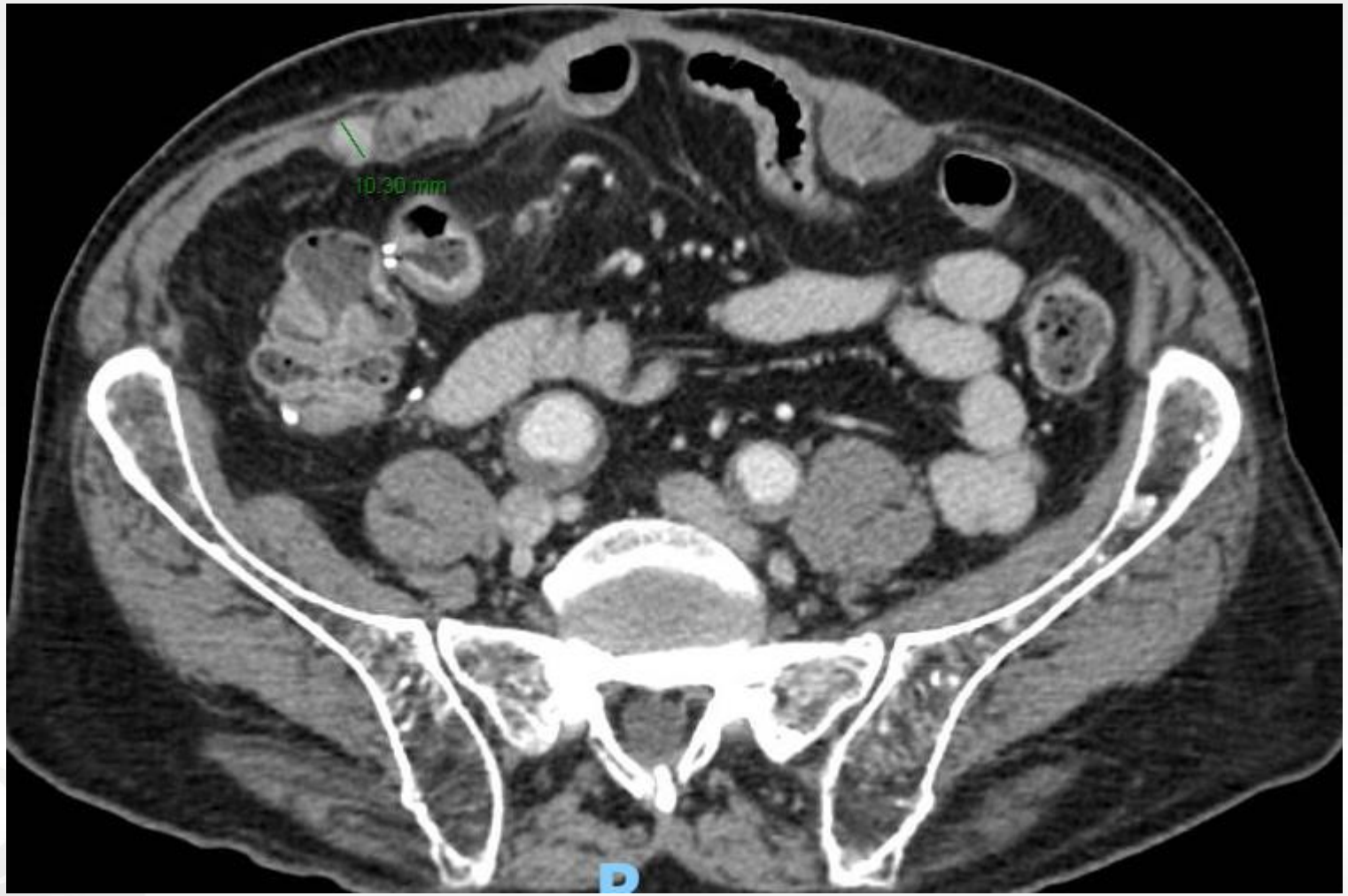
- Intervento chirurgico complicato da deiscenza della ferita ed ascesso della parete addominale nella sede chirurgica.
- 13/04/2018 accesso in PS per sincope, febbre TC 39°C, gemizio purulento in sede chirurgica. TC addome conferma raccolta ascessuale. In data 19/04/2018 drenaggio eco-guidato della raccolta addominale. 04/05/2018 rimosso drenaggio senza complicanze. 10/05/2018 CEA 6.58
- 15/05/2018: condizioni mediocri, KPS 60-70. Si decide di non avviare adiuvante, **avvia follow-up stretto**

Storia Oncologica

- 01/08/2018 PET-TC: area di iperfissazione del tracciante a livello di formazione nodulare dotata di c.e. localizzata in corrispondenza della parete addominale anteriore in fossa iliaca destra (SUVmax 4.1,dtm 10 mm), ulteriori aree più piccole nelle vicinanze della precedente con caratteristiche simili

- 05/09/2018 Biopsia neoformazione in FID: "*infiltrazione neoplastica da adenocarcinoma ampiamente necrotico con aspetti morfologici di tipo intestinale*" – RAS/BRAF wt, MSS

- KPS 90, G8: 16


10.30 mm
R

Geriatric-8 screening tool

Items	Possible answers	Score
Food intake in the last 3 months	**0**: severe reduction in food intake **1**: moderate reduction in food intake **2**: normal food intake	.....
Weight loss during the last 3 months	**0**: weight loss >3kg **1**: does not know **2**: weight loss between 1 and 3 kg **3**: no weight loss	.....
Mobility	**0**: bed/chair bound **1**: able to get out of bed/chair but does not go out **2**: goes out	.....
Neuropsychological problems	**0**: severe dementia or depression **1**: mild dementia or depression **2**: no psychological problems	.....
Body Mass Index (BMI)	**0**: BMI <19 **1**: BMI 19 to <21 **2**: BMI 21 to <23 **3**: BMI 23 or greater	.....
Takes more than 3 medications per day	**0**: yes **1**: no	.....
Self-rated health status (compared to other people of the same age)	**0**: not as good **0.5**: does not know **1**: as good **2**: better	.....
Age	**0**: >85 **1**: 80-85 **2**: <80	.....
Total score (0-17) [Cut-off ≤ 14 indicating impairment]		.....

SNODO DECISIONALE N.2

- Quale terapia?
  - 1° line vs local therapy vs other

Storia Oncologica

- Il pz rifiuta chirurgia + possibile sottostima del carico di malattia. Discussione multidisciplinare: si decide di avviare prima linea

- 04/10/2018 avvia protocollo PANDA

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ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

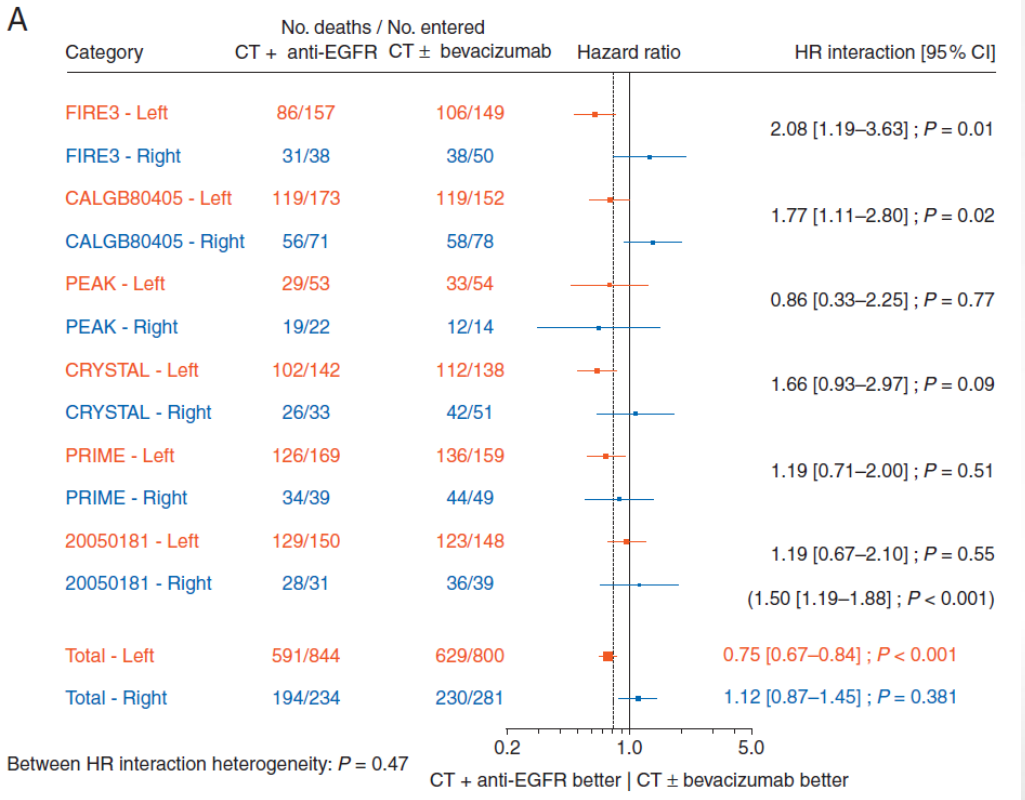
Annals of Oncology 28: 1713–1729, 2017
doi:10.1093/annonc/mdx175
Published online 12 April 2017

SPECIAL ARTICLE

Prognostic and predictive value of primary tumour side in patients with *RAS* wild-type metastatic colorectal cancer treated with chemotherapy and EGFR directed antibodies in six randomized trials†

D. Arnold[1], B. Lueza[2], J.-Y. Douillard[3], M. Peeters[4], H.-J. Lenz[5], A. Venook[6], V. Heinemann[7], E. Van Cutsem[8], J.-P. Pignon[2], J. Tabernero[9], A. Cervantes[10,11] & F. Ciardiello[12]*

OS



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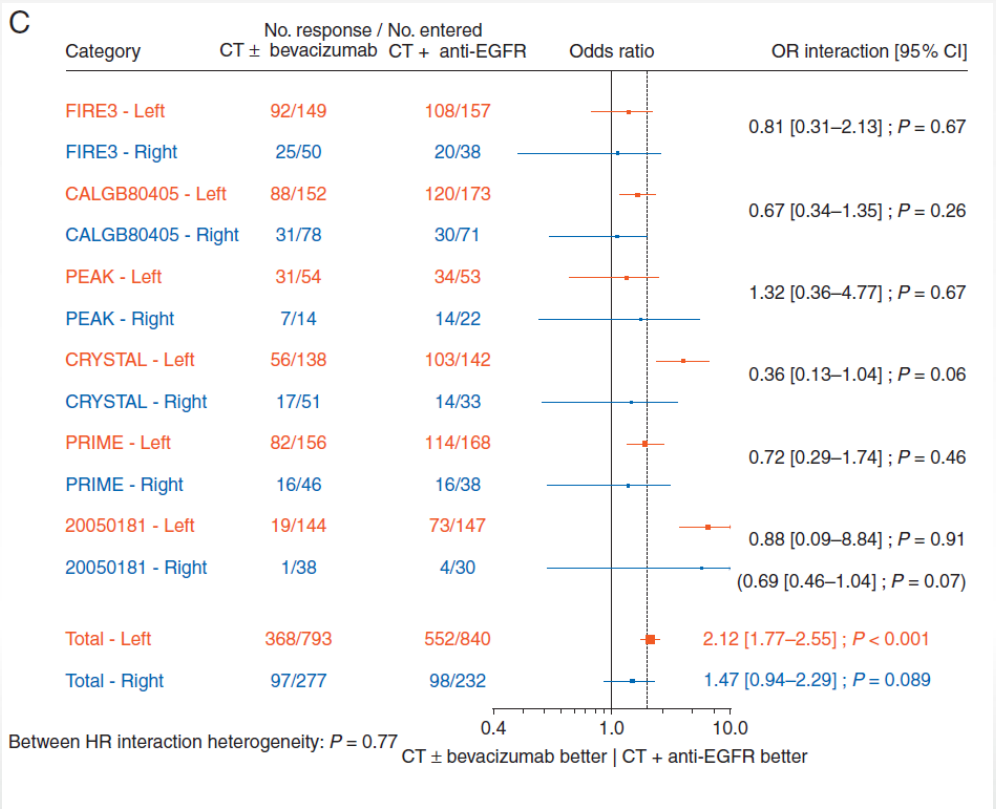

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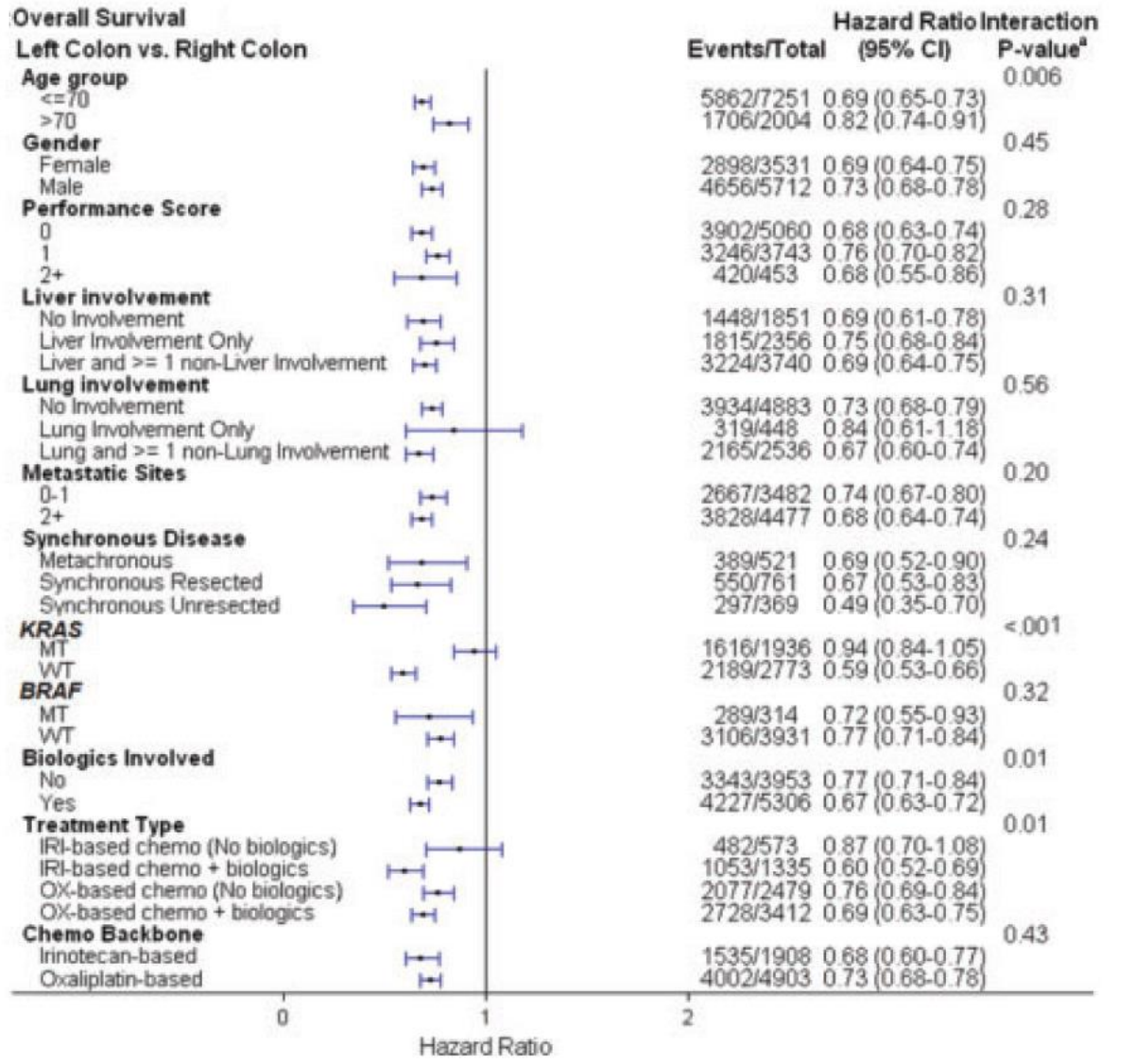


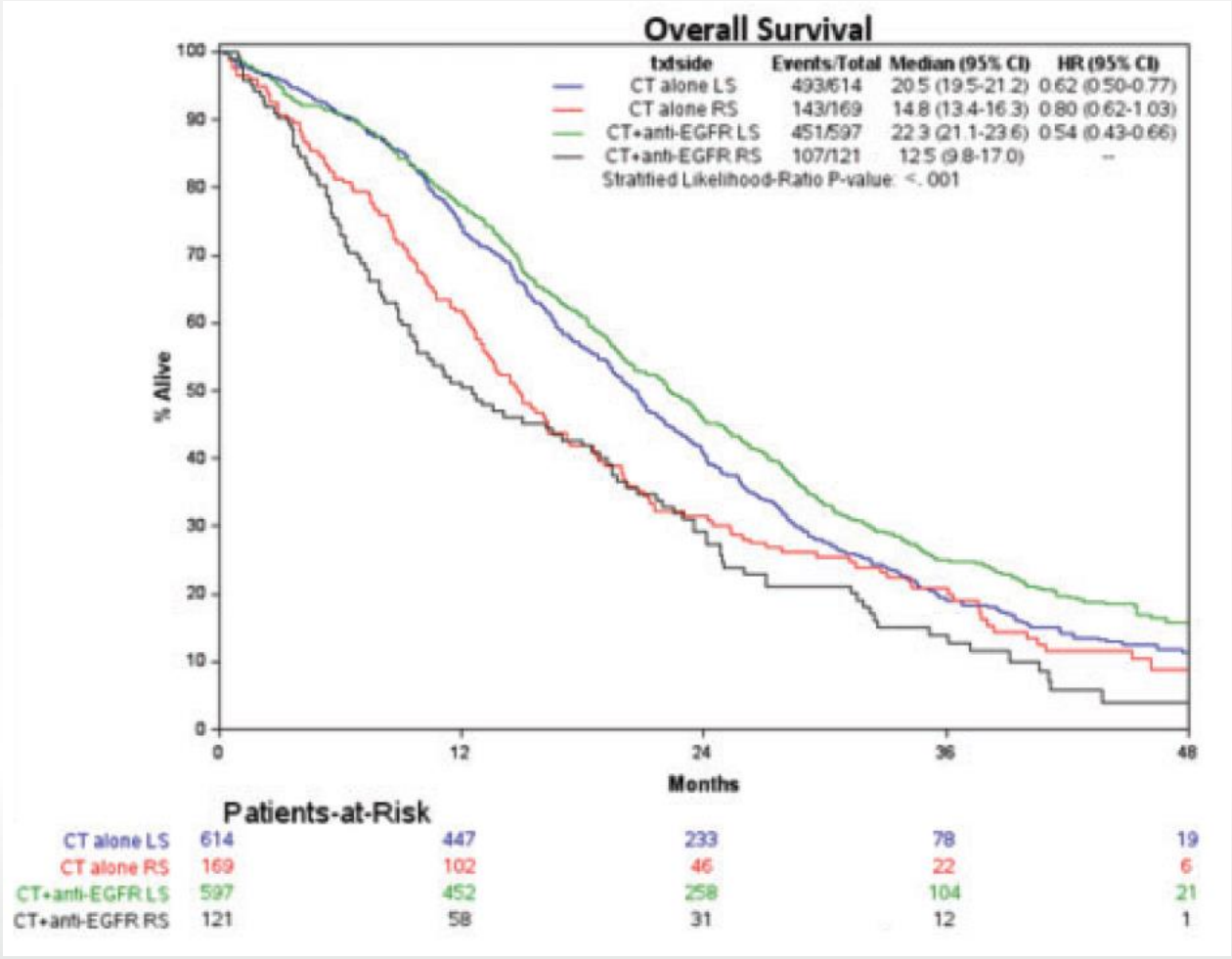
OXFORD

JNCI J Natl Cancer Inst (2021) 113(12): djab112

doi: 10.1093/jnci/djab112
First published online June 1, 2021
Article

Prognostic and Predictive Impact of Primary Tumor Sidedness for Previously Untreated Advanced Colorectal Cancer

Jun Yin, PhD,[1,*] Romain Cohen, MD,[2] Zhaohui Jin, MD,[3] Heshan Liu, MS,[1] Levi Pederson, MS,[1] Richard Adams, MD,[4] Axel Grothey, MD,[5] Timothy S. Maughan, MD,[6,7] Alan Venook, MD,[8] Eric Van Cutsem, MD,[9] Cornelis Punt, MD,[10] Miriam Koopman, MD,[11] Alfredo Falcone, MD,[12] Niall C. Tebbutt, MD,[13] Matthew T. Seymour, MD,[14] Carsten Bokemeyer, MD,[15] Eduardo Diaz Rubio, MD,[16] Richard Kaplan, MD,[17] Volker Heinemann, PhD,[18] Benoist Chibaudel, MD,[19] Takayuki Yoshino, MD, PhD,[20] John Zalcberg, MBBS, PhD,[21] Thierry Andre, MD,[22] Aimery De Gramont, MD,[23] Qian Shi, PhD,[1] Heinz-Josef Lenz, MD[24]



CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE 2ª EDIZIONE

OXFORD

JNCI J Natl Cancer Inst (2021) 113(12): djab112

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Prognostic and Predictive Impact of Primary Tumor Sidedness for Previously Untreated Advanced Colorectal Cancer

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Table 4. Propensity score analyses of treatment effect of CT + cetuximab vs CT + bevacizumab

Variable	No.	Cetuximab + CT median (range), mo	Bevacizumab + CT median (range), mo	HR_{adj} (95% CI)	P[a]	$P_{interaction}$
Overall survival						
KRAS WT						
Left-sided	255	25.5 (22.0-28.4)	24.6 (17.7-29.2)	1.10 (0.77 to 1.56)	.61	.005
Right-sided	300	12.5 (9.4-16.4)	26.0 (22.7-34.4)	1.89 (1.33 to 2.67)	<.001	
KRAS MT						
Left-sided	199	13.1 (10.8-15.4)	24.8 (17.9-28.4)	2.09 (1.40 to 3.12)	<.001	.56
Right-sided	323	15.9 (11.5-19.1)	26.1 (21.5-30.8)	1.84 (1.37 to 2.47)	<.001	
Progression-free survival						
KRAS WT						
Left-sided	254	9.0 (8.5-11.1)	11.7 (9.6-13.7)	1.23 (0.89 to 1.70)	.21	.05
Right-sided	300	6.7 (5.1-8.2)	10.7 (9.8-11.6)	1.84 (1.31 to 2.57)	<.001	
KRAS MT						
Left-sided	198	6.4 (5.7-7.4)	13.1 (9.8-14.7)	3.16 (2.11 to 4.71)	<.001	.07
Right-sided	322	7.0 (6.3-8.2)	10.9 (9.5-11.9)	1.77 (1.35 to 2.33)	<.001	

[a] Two-sided Wald test P values. CI = confidence interval; CT = chemotherapy; HR_{adj} = adjusted hazard ratio; MT = mutant; WT = wild-type.

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cancers

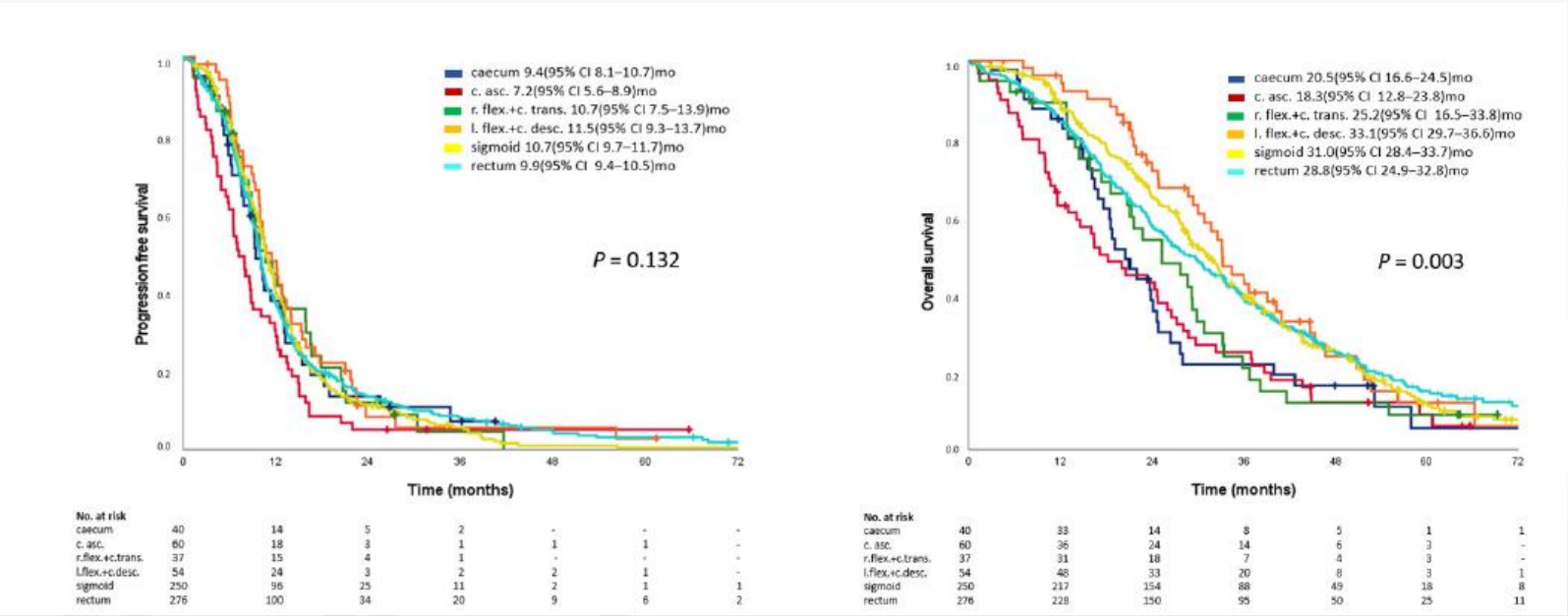
MDPI

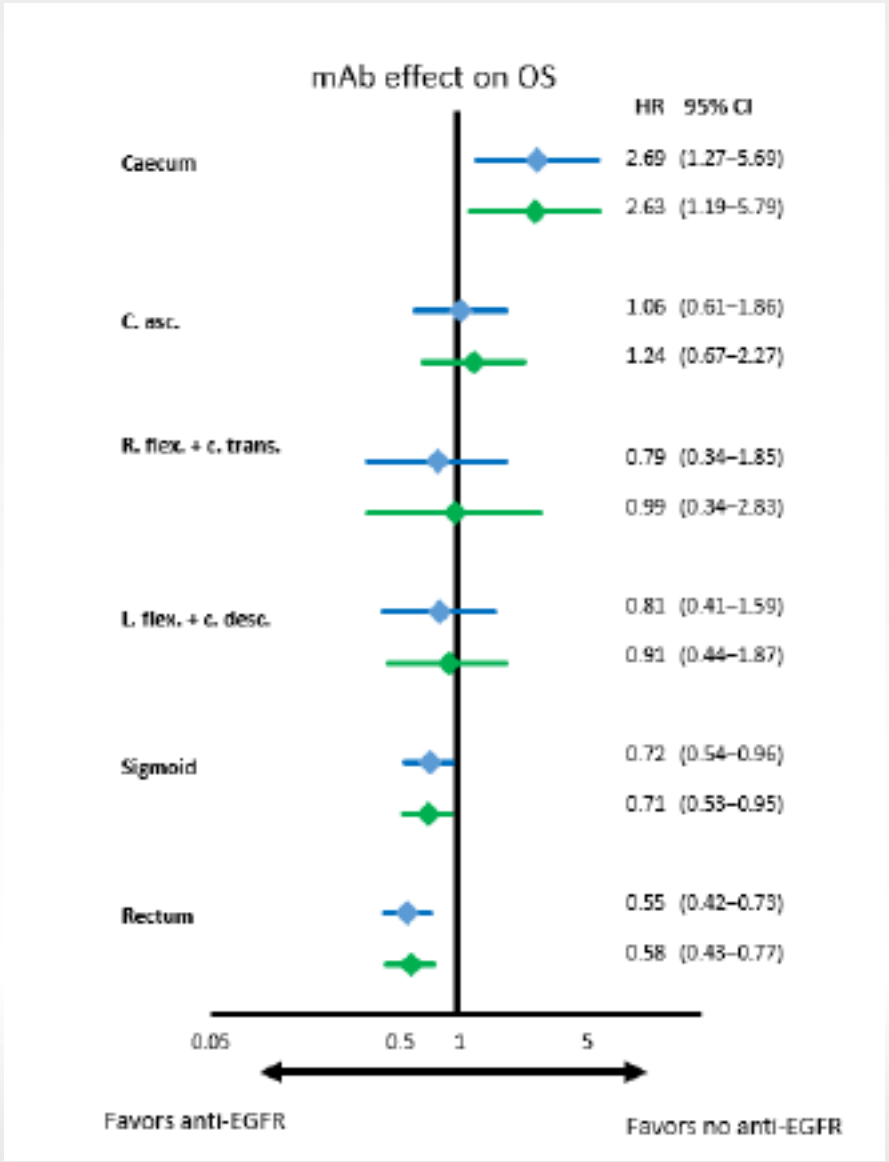
Article

Exact Primary Tumor Location in mCRC: Prognostic Value and Predictive Impact on Anti-EGFR mAb Efficacy

Annabel H. S. Alig [1], Volker Heinemann [2,3], Michael Geissler [4], Ludwig Fischer von Weikersthal [5], Thomas Decker [6], Kathrin Heinrich [2], Swantje Held [7], Lena Weiss [2], Laura E. Fischer [2], Nicolas Moosmann [8], Arndt Stahler [1], Ivan Jelas [1], Annika Kurreck [1], Jobst C. von Einem [1], Anke C. Reinacher-Schick [9], Andrea Tannapfel [10], Clemens Giessen-Jung [2], Sebastian Stintzing [1] and Dominik P. Modest [1,*]

Cancers 2022, *14*, 526. https://doi.org/10.3390/cancers14030526



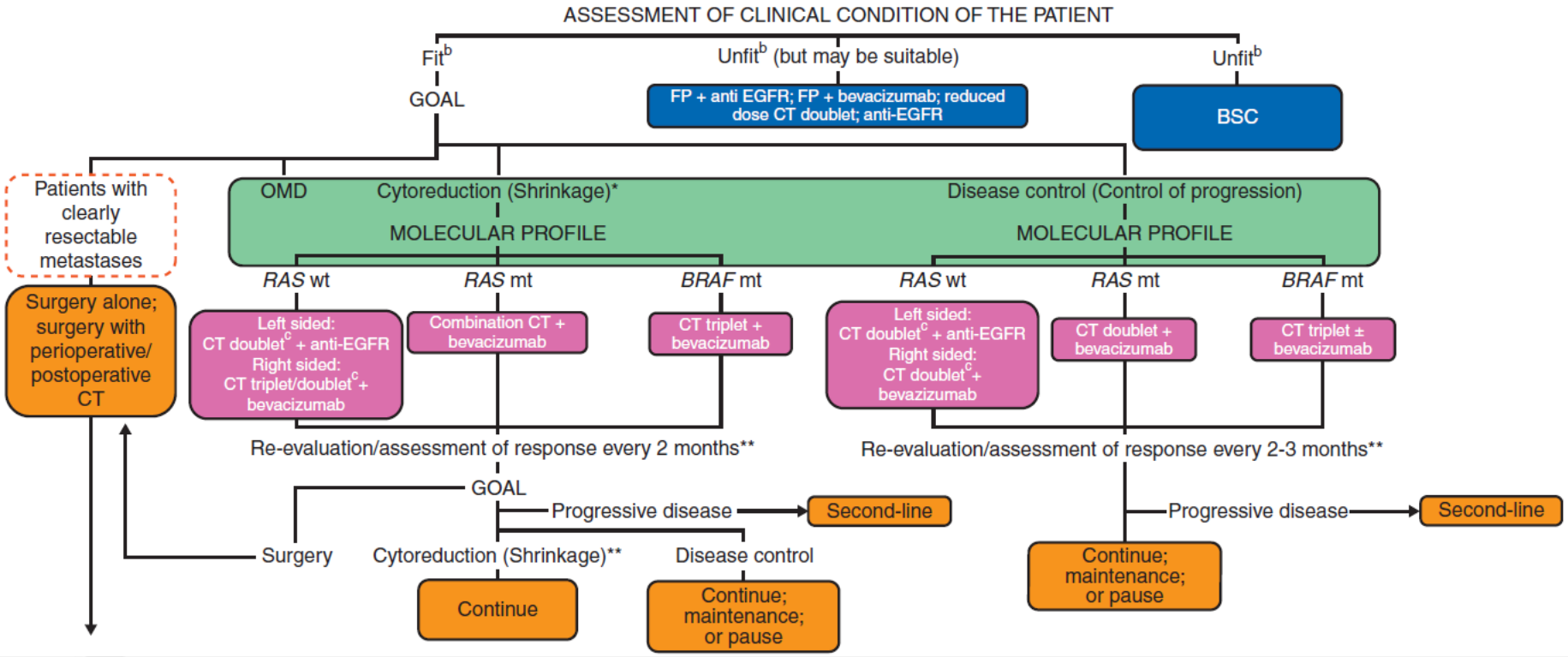


CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE 2ª EDIZIONE

Pan-Asian adapted ESMO consensus guidelines for the management of patients with metastatic colorectal cancer: a JSMO–ESMO initiative endorsed by CSCO, KACO, MOS, SSO and TOS

T. Yoshino[1*], D. Arnold[2], H. Taniguchi[3], G. Pentheroudakis[4], K. Yamazaki[5], R.-H. Xu[6], T. W. Kim[7], F. Ismail[8], I. B. Tan[9], K.-H. Yeh[10], A. Grothey[11], S. Zhang[12], J. B. Ahn[13], M. Y. Mastura[14], D. Chong[15], L.-T. Chen[16], S. Kopetz[17], T. Eguchi-Nakajima[18], H. Ebi[19], A. Ohtsu[20], A. Cervantes[21], K. Muro[22], J. Tabernero[23], H. Minami[24], F. Ciardiello[25] & J.-Y. Douillard[26]

Annals of Oncology 29: 44–70, 2018



CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE 2ª EDIZIONE

Istituto Oncologico Veneto I.R.C.C.S. | OECI Comprehensive Cancer Centre | FONDAZIONE GONO Gruppo Oncologico del Nord Ovest

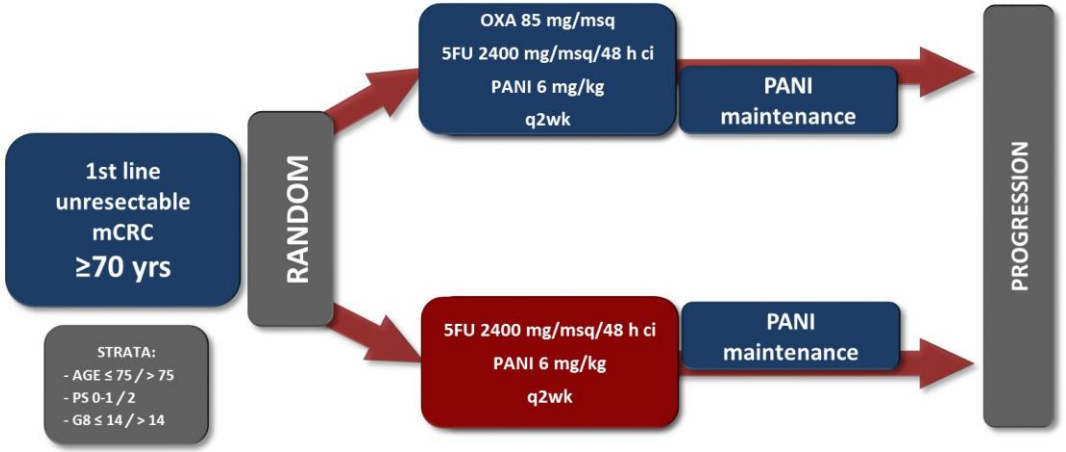
ASCO20 Virtual Meeting
May 29th-31st, 2020

First-line FOLFOX plus panitumumab versus 5FU plus panitumumab in RAS-BRAF wild-type metastatic colorectal cancer elderly patients: the PANDA study

Sara Lonardi, Marta Schirripa, Federica Buggin, Lorenzo Antonuzzo, Barbara Merelli, Giorgia Boscolo, Saverio Cinieri, Samantha Di Donato, Riccardo Lobefaro, Roberto Moretto, Vincenzo Formica, Alessandro Passardi, Vincenzo Ricci, Nicoletta Pella, Mario Scartozzi, Fable Zustovich, Vittorina Zagonel, Matteo Fassan, Luca Boni, Fotios Loupakis

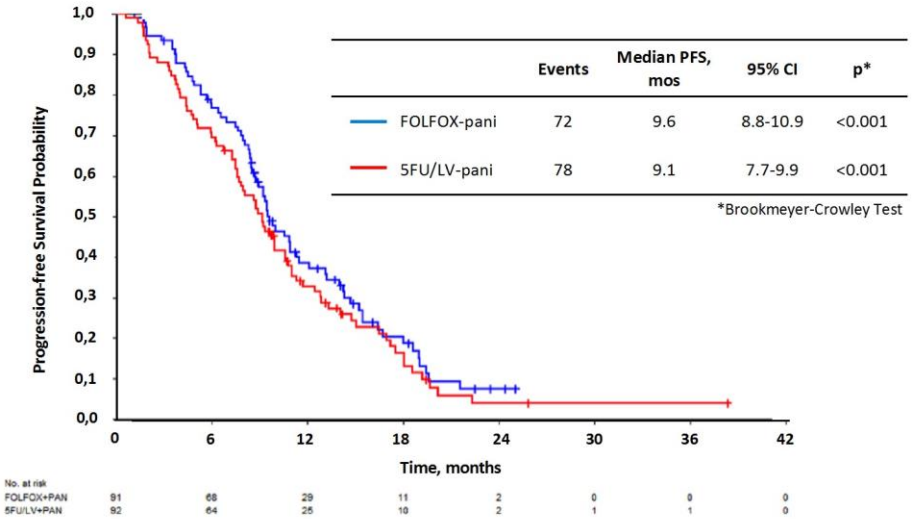
on behalf of the GONO Investigators

Study design



Primary Endpoint: Progression-free Survival

Median follow up: 20.5 mos (Data Cutoff: 04 Feb 2020)



	Events	Median PFS, mos	95% CI	p*
FOLFOX-pani	72	9.6	8.8-10.9	<0.001
5FU/LV-pani	78	9.1	7.7-9.9	<0.001

*Brookmeyer-Crowley Test

Digestive and Liver Disease 52 (2020) 493–505

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Guidelines

Treatment guidelines of metastatic colorectal cancer in older patients from the French Society of Geriatric Oncology (SoFOG)

Thomas Aparicio[a,*], Florence Canouï-Poitrine[b], Philippe Caillet[c], Eric François[d], Tristan Cudennec[e], Elisabeth Carola[f], Gilles Albrand[g], Anne-Marie Bouvier[h], Camille Petri[b], Bérengère Couturier[b], Jean-Marc Phelip[i], Leila Bengrine-Lefevre[j], Elena Paillaud[c]

- *chemotherapy indicated regardless of age*
- *geriatric assessmentis recommended if screening for frailty (G8 score <14) is positive*

- *Omission of chemotherapy should be discussed in patients with severe comorbidities*
- *5FU combined with bevacizumab recommended in patients for whom tumor shrinkage is not the primary objective*
- *doublet chemotherapy (5FU combined with irinotecan or oxaliplatin) combined with bevacizumab or anti-EGFR antibody (cetuximab or panitumumab) in case of a RAS wild type tumor recommended for patients with symptoms related to metastases or if there is a planned metastasis resection*

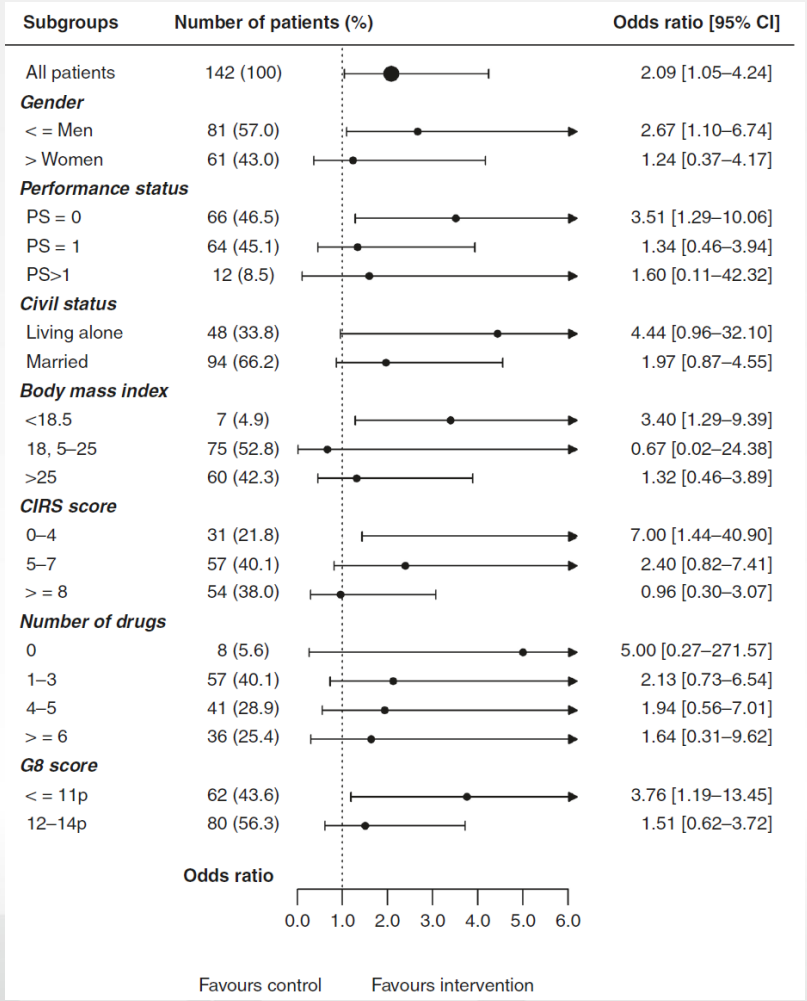
ARTICLE
Clinical Study

BJC British Journal of Cancer

The effect of geriatric intervention in frail older patients receiving chemotherapy for colorectal cancer: a randomised trial (GERICO)

British Journal of Cancer (2021) 124:1949–1958

Cecilia Margareta Lund[1,2,3], Kirsten Kjeldgaard Vistisen[4], Anne Pries Olsen[5], Pernille Bardal[6], Martin Schultz[1,2], Troels Gammeltoft Dolin[1,2], Finn Rønholt[1], Julia Sidenius Johansen[1,3,4] and Dorte Lisbeth Nielsen[3,4]

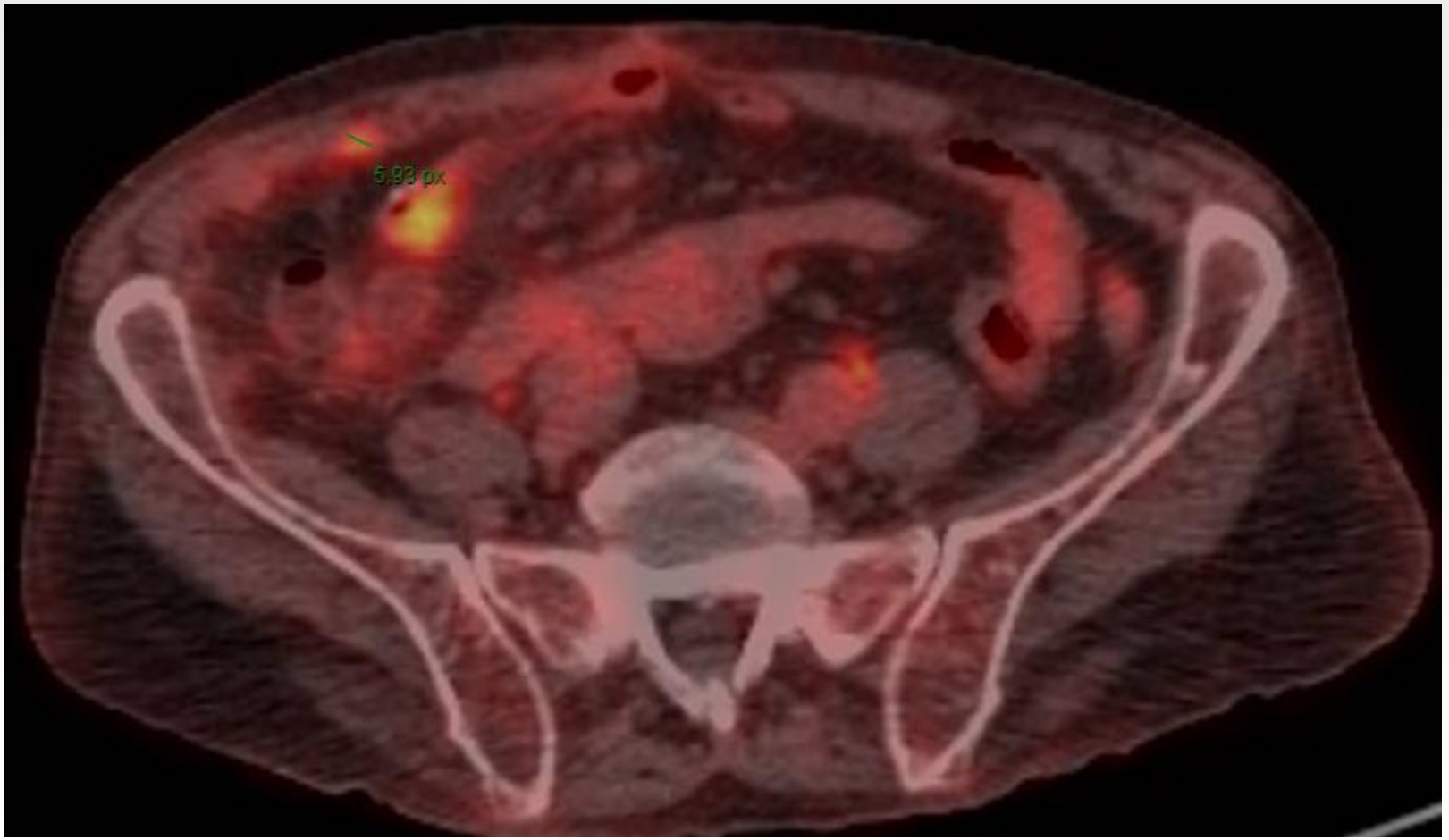


Vulnerable patients (G8 questionnaire ≤14 points) randomised 1:1 to CGA-based interventions VS standard care

Domain	Assessment and screening tool				Possible interventions	Interventions implemented	
		Cut-off	Score	*n* (%)			*n* (%)
Comorbidity	CIRS-G	–	0–4	11 (15)	Optimising treatment	Referrals	23 (32)
			5–7	31 (44)	Referrals to exams/other departments		
	Review of medical records		≥8	29 (41)			
	Clinical examination						
	Patient interview						
Medication review	No. of medications/ polypharmacy	–	0–4	43 (61)	Discontinuation	Changes in medication	44 (62)
			≥5	28 (39)	Prescription		
	START/STOP criteria				Change in dosage		
Cognitive function	MMSE	≤23/30	24–30	71 (100)	Further evaluation	Cognitive evaluation	1 (1.4)
			0–23	0 (0)	Referral/medication		
Psychological function	GDS	≥ 6/ 15	0–5	67 (9)	Assessment of possible depression	Medical treatment	2 (2.8)
			≥6	4 (6)		Referrals	2 (2.8)
Nutritional status	MNA-based local nutritional screening	Weight loss ≥5%	0–5	18 (25)	Nutritional supplements	Referral: GERICO dietitian	36 (51)
			≥5	53 (75)	Referral to dietitian[a]		
Physical function	Gait speed 10 m	>1 m/s	0–1	37 (52)	Referral to the exercise programme[b]	Referral: GERICO exercise programme	28 (39)
			>1	32 (45)			
	Handgrip strength (Jamar Dynamometer)	<♀ 20 kg <♂ 30 kg	below	35 (49)	Referral to the exercise training programme[b]	Referral: GERICO exercise programme	28 (39)
			above	36 (51)			
Functional status	Katz ADL	<6	6	62 (87)	Initiation of home care	Initiation of social support	2 (2.8)
	(In)dependence		0–5.5	9 (13)	Occupational therapy assessment	Occupational therapy	2 (2.8)
	FAQ IADL	>1	0	48 (68)	Initiation of home care	Initiation of home care	2 (2.8)
	(In)dependence		≥1	23 (32)	Transport arrangement		
Laboratory parameters	TSH, cobalamin, folate, albumin, vitamin D	Normative values	Normal	51 (72)	Treat deficiencies/control blood samples	Deficiencies treated	20 (28)
			abnormal	20 (28)			

Storia Oncologica

- Il pz rifiuta chirurgia, possibile sottostima del carico di malattia
- Ottobre 2018 – febbraio 2019: protocollo PANDA: arma A: FOLFOX Panitumumab
- PET-TC feb 2019: risposta di malattia: malattia oligometastatica


6,93 px

SNODO DECISIONALE N.3

- PROSEGUE VS ALTRO?

Storia Oncologica

- MDM: pz rifiuta intervento. Si decide di effettuare crioablazione della lesione.

- Feb 2019: si esegue crioablazione: Buon esito della procedura

Local ablative treatment, including surgery and the management of patients with oligometastatic disease (OMD)

Recommendation 10: OMD

10a. For patients with OMD, systemic therapy is the standard of care and should be considered as the initial part of every treatment strategy (exception: patients with single/few liver or lung lesions, see below).

10b. The best local treatment should be selected from a 'toolbox' of procedures according to disease location, treatment goal ('the more curative the more surgery'/higher importance of local/complete control), treatment-related morbidity and patient-related factors such as comorbidity/ies and age [IV, B].

Recommendation 11: imaging in the identification and management of disease

11a. Imaging should comprise firstly an abdominal/pelvic and thoracic CT scan and, in the case of doubt, a second method such as US (CEUS), MRI or PET/CT scan depending on the location of the metastases. US may be helpful to characterise liver metastases, MRI liver, peritoneal or pelvic metastases and PET/CT extrahepatic disease [IV, B].

11b. A stepwise imaging approach is the recommended policy, in relation to the therapeutic possibilities, rather than the use of all imaging modalities in all patients [V, B].

Recommendation 12 with revision: perioperative treatment

12a. Both, technical criteria for resection and prognostic considerations define the

12b. In patients with clearly resectable disease and favourable prognostic criteria, j justified [I, C; consensus >75%].

12c. In patients with technically resectable disease where the prognosis is unclear (**a fluoropyrimidine plus oxaliplatin**) should be administered [I, B; consen:

12d. Targeted agents should not be used in **patients with** resectable **metastase**

12e. In situations where the criteria for prognosis and resectability are not sharply with synchronous onset of metastases should be allocated to this group and

12f. **In patients who have not received preoperative chemotherapy, with f is no strong evidence to support the use of adjuvant chemotherapy [I [III, B]. Postoperative treatment with a fluoropyrimidine plus oxaliplat**

12h. Decision-making should include patients' characteristics and preferences [A=

Recommendation 13 with revision in consideration of primary tumour location: conversion therapy

13a. In potentially resectable patients (if conversion is the goal), a regimen leading to high response rates and/or a large tumour size reduction (shrinkage) is recommended [II, A].

13b. There is uncertainty surrounding the best combination to use as only a few trials have addressed this specifically:

- In patients with *RAS* wt disease a cytotoxic doublet plus an anti-EGFR antibody seems to have the best benefit risk/ratio, although the combination of FOLFOXIRI plus or minus bevacizumab may also be considered and, to a lesser extent, a cytotoxic doublet plus bevacizumab [II, A]
- In patients with *RAS* mutant disease: a cytotoxic doublet plus bevacizumab or FOLFOXIRI plus or minus bevacizumab [II, A]
- **Consideration needs to be given to new data on the impact of primary tumour location**

13c. Patients must be re-evaluated regularly in order to prevent the overtreatment of resectable patients as the maximal response is expected to be achieved after 12–16 weeks of therapy in most patients.

Recommendation 14: ablative techniques

14. Despite the lack of more available prospective data, this strategic treatment approach should be evaluated and pursued further in suitable patients [II, B].

Recommendation 15: local ablation techniques

15a. In patients with unresectable liver metastases only, or OMD, local ablation techniques such as thermal ablation or high conformal radiation techniques (e.g. SBRT, HDR-brachytherapy) can be considered. The decision should be taken by a MDT based on local experience, tumour characteristics, and patient preference [IV, B].

15b. In patients with lung only or OMD of the lung, ablative high conformal radiation or thermal ablation may be considered if resection is limited by comorbidity, the extent of lung parenchyma resection, or other factors [IV, B].

15c. SBRT is a safe and feasible alternative treatment of oligometastatic colorectal liver and lung metastases in patients not amenable to surgery or other ablative treatments [IV, B].

15d. RFA can be used in addition to surgery with the goal of eradicating all visible metastatic sites [II, B].

T. Yoshino[1*], D. Arnold[2], H. Taniguchi[3], G. Pentheroudakis[4], K. Yamazaki[5], R.-H. Xu[6], T. W. Kim[7], F. Ismail[8], I. B. Tan[9], K.-H. Yeh[10], A. Grothey[11], S. Zhang[12], J. B. Ahn[13], M. Y. Mastura[14], D. Chong[15], L.-T. Chen[16], S. Kopetz[17], T. Eguchi-Nakajima[18], H. Ebi[19], A. Ohtsu[20], A. Cervantes[21], K. Muro[22], J. Tabernero[23], H. Minami[24], F. Ciardiello[25] & J.-Y. Douillard[26]

SNODO DECISIONALE N.4

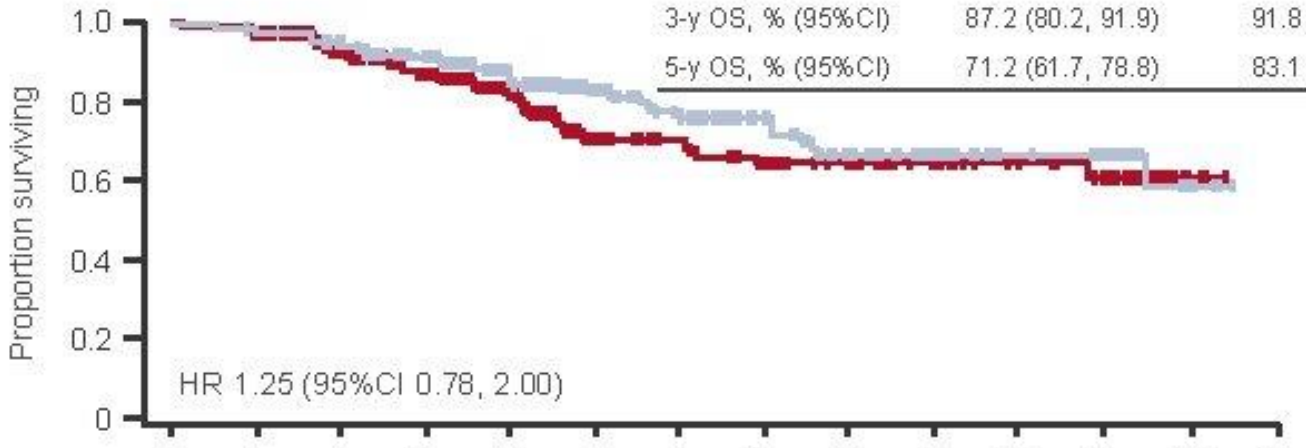
- TX VS FU?

4005: A randomized phase II/III trial comparing hepatectomy followed by mFOLFOX6 with hepatectomy alone for liver metastasis from colorectal cancer: JCOG0603 study – Kanemitsu Y, et al

Key results (cont.)

OS (ITT – updated)

	mFOLFOX6 (n=151)	Surgery alone (n=149)
Events, n (%)	38	32
3-y OS, % (95%CI)	87.2 (80.2, 91.9)	91.8 (85.7, 95.4)
5-y OS, % (95%CI)	71.2 (61.7, 78.8)	83.1 (74.9, 88.9)



No; at risk (No. censored)

mFOLFOX6	151(0)	148(1)	121(18)	102(13)	84(13)	61(12)	55(5)	45(7)	35(10)	24(11)	18(6)	12(5)	2(10)	0(2)
Surgery alone	149(0)	144(3)	124(16)	108(11)	86(15)	71(13)	59(7)	50(9)	33(11)	23(10)	19(4)	13(6)	3(9)	0(3)

*DMC recommended the early termination of the trial based given that the OS curve of adjuvant mFOLFOX6 was below that of surgery alone

Kanemitsu Y, et al. J Clin Oncol 2020;38(suppl);abstr 4005

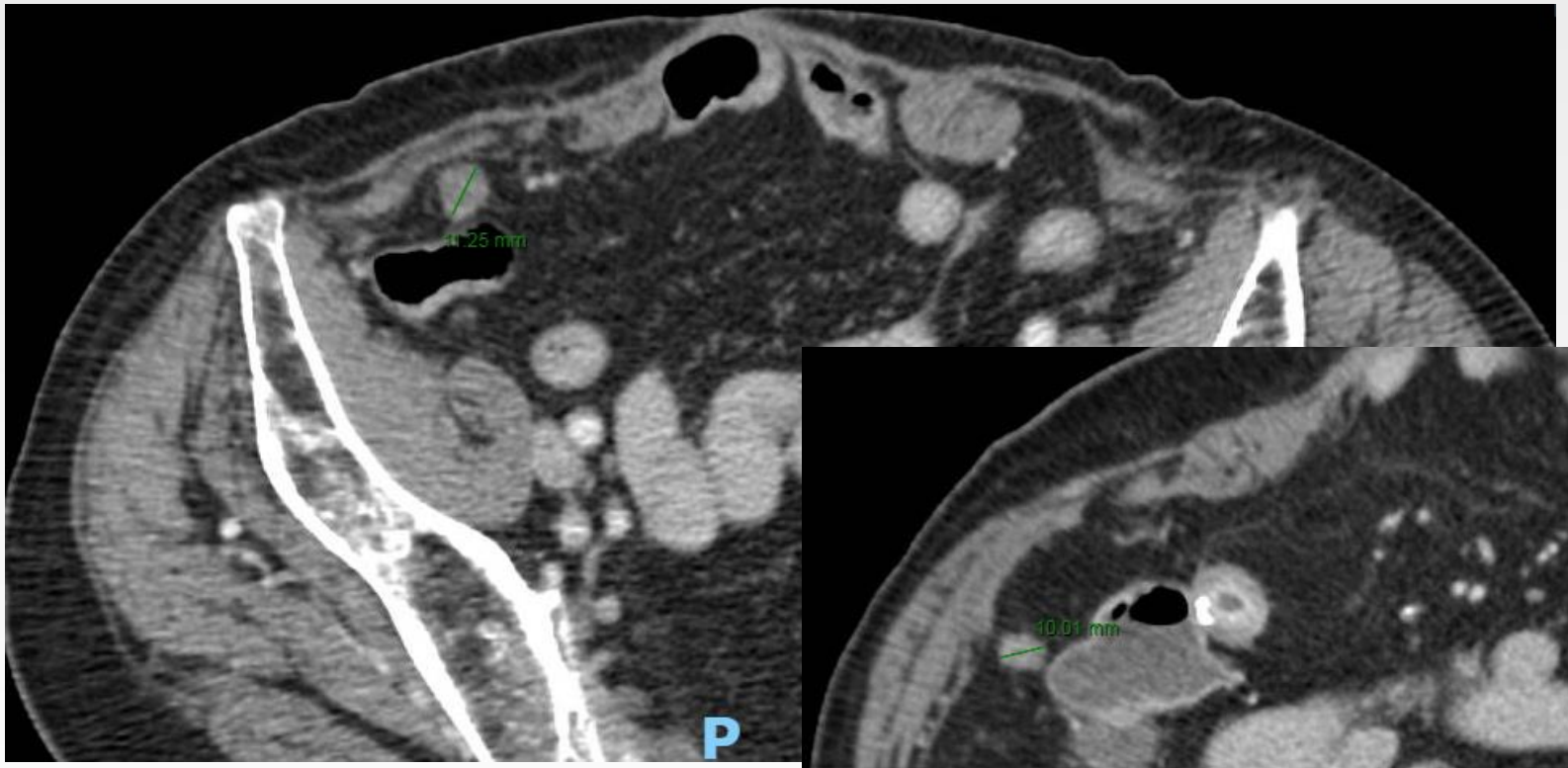
Storia Oncologica

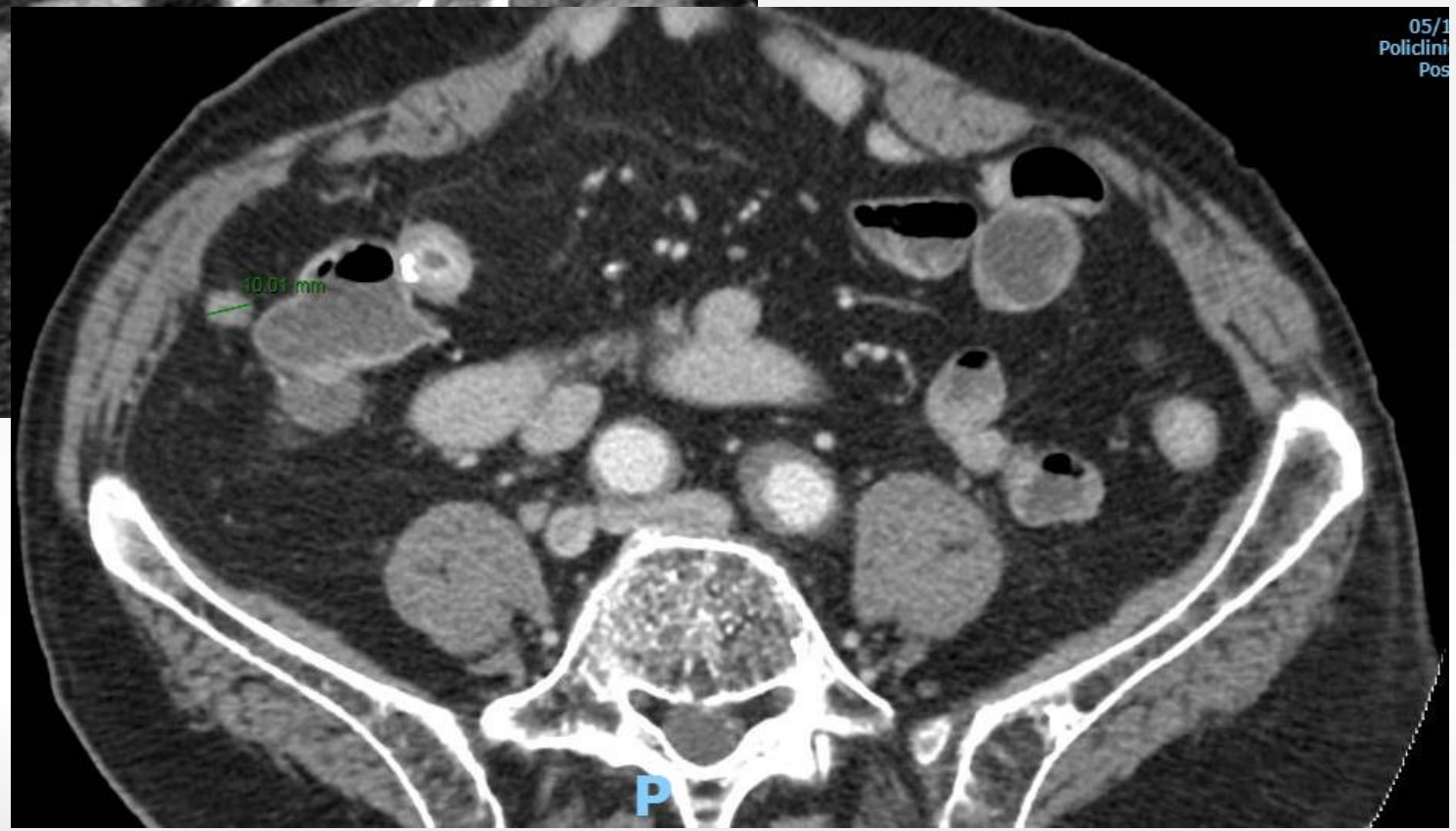
- MDM: avvia fu stretto
- feb 2019: avvio follow-up clinico-strumentale
- Prima tc di rivalutazione a maggio 2019: esiti crioablazione, non altra malattia: prosegue fu

Storia Oncologica

- Nuova TC a Set 2019: PD peritoneale di malattia (7 mesi da ultimo folfox pan)

CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE 2ª EDIZIONE





SNODO DECISIONALE N.5

- Quale terapia?

Storia Oncologica

- MDM: si decide di riavviare folfox panitumumab se bx liquida real-time RAS/BRAF wt
- Bx liquida: (real time easyPGX): RAS/BRAF wt
- Da set 2019 a dic 2019: 6 cicli di folfox-pani. TC di rivalutazione: SD

Phase II study of anti-EGFR rechallenge therapy with panitumumab driven by circulating tumor DNA molecular selection in metastatic colorectal cancer: The CHRONOS trial.

Trial eligibility and study design

- ***RAS/BRAF* WT mCRC on tissue analysis**
- **ECOG PS 0-2**
- **CR/PR to a previous anti-EGFR regimen (any line)**
- **PD at an intervening, anti-EGFR free, therapeutic line**

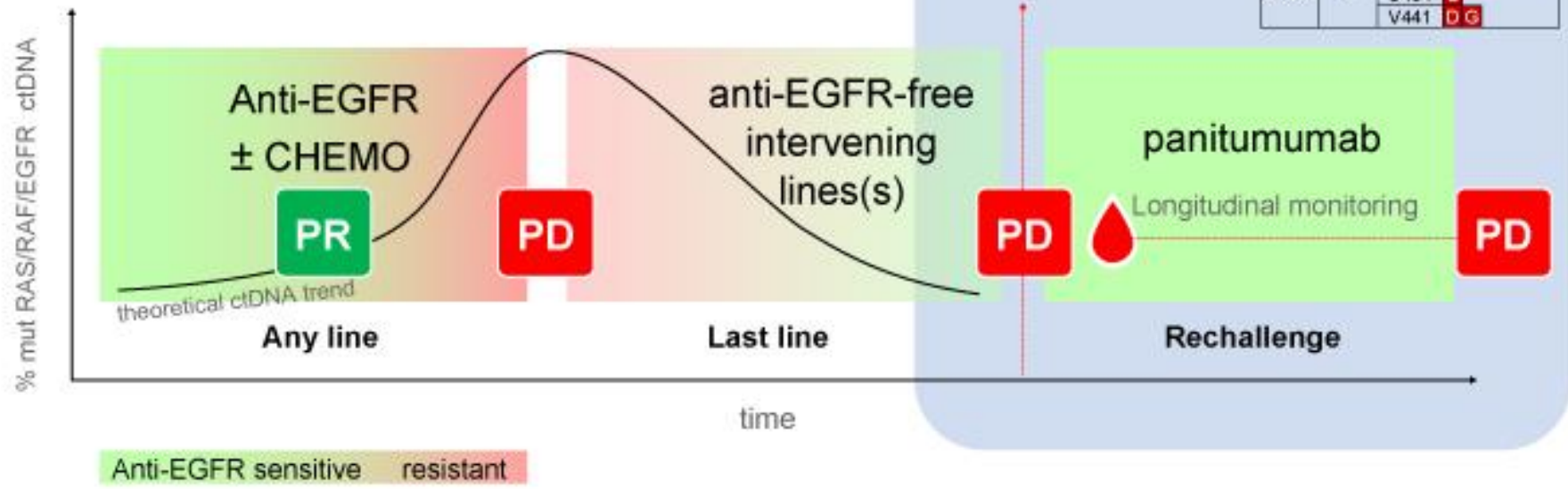
Phase II trial single-stage

ctDNA

RAS, BRAF
EGFR-ECD
wild type

interventional

Gene	Exon	Codon	variations
KRAS	II	G12	D V C S A R
		G13	D
	III	Q61	R K L H P E
NRAS	II	G12	D V C S A R
		G13	D
	III	Q61	R K L H
BRAF	XV	V600	E
EGFR ECD	XII	S492	R
		G465	R E
		S464	L
		V441	D G



CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE

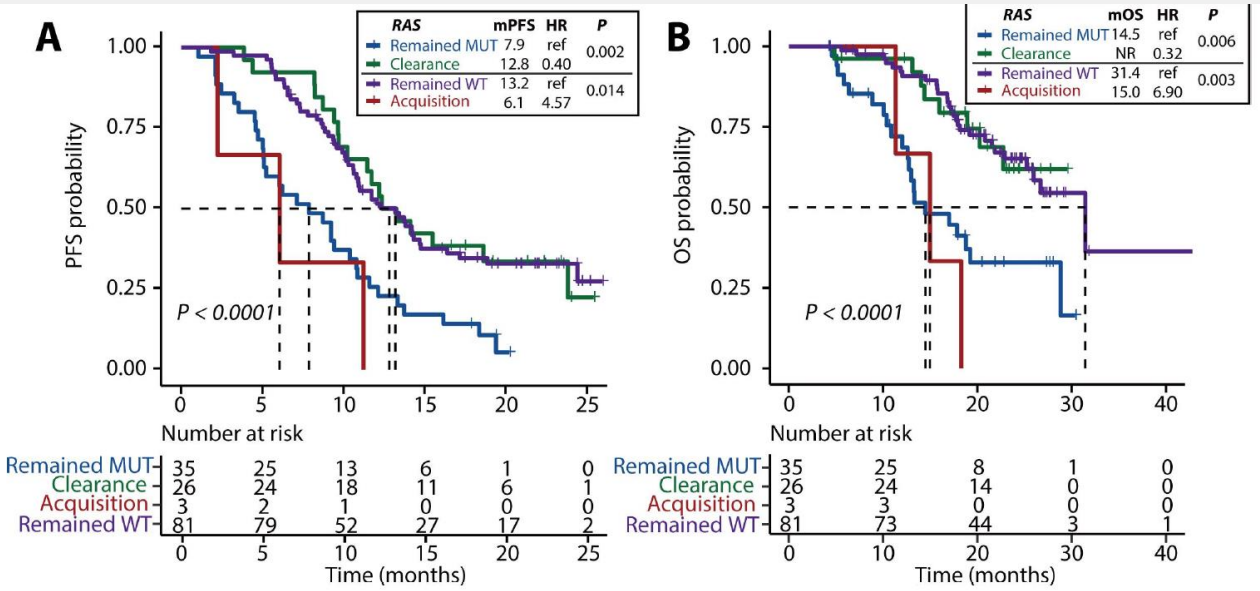


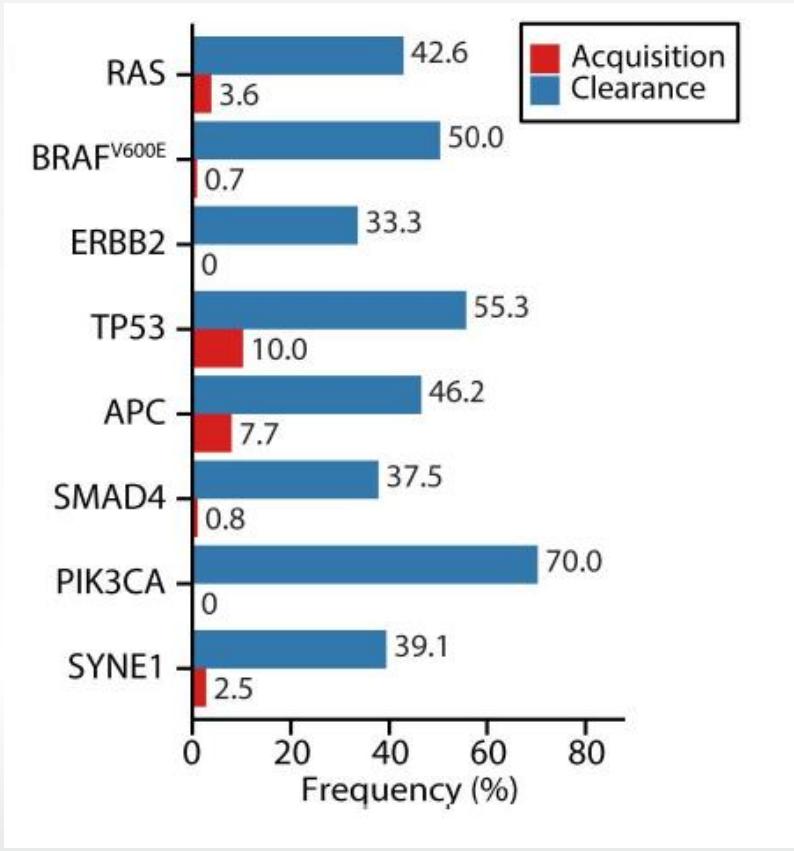
Figure 4 Kaplan-Meier estimates of progression-free survival (PFS) (A) and overall survival (OS) (B) in patients stratified according to different changes in plasma RAS status under first-line treatment Statistical significance was determined by Wald test of the multivariable Cox models. The change in the circulating tumour DNA (ctDNA) fraction of cfDNA, estimated by maximum somatic allele frequency, was included as a variable. mPFS, median progression-free survival; mOS, median overall survival; MUT, mutant; ref, reference; WT, wild-type.

Original research

Genomic temporal heterogeneity of circulating tumour DNA in unresectable metastatic colorectal cancer under first-line treatment

Feng Wang,[1,2] You-Sheng Huang,[1,2,3] Hao-Xiang Wu,[1,2] Zi-Xian Wang,[1,2] Ying Jin,[1,2] Yi-Chen Yao,[1,2] Yan-Xing Chen,[1,2,3] Qi Zhao,[1,2,3] Shifu Chen,[4] Ming-Ming He,[1,2] Hui-Yan Luo,[1,2] Miao-Zhen Qiu,[1,2] De-shen Wang,[1,2] Feng-Hua Wang,[1,2] Mingyan Xu,[4] Yu-Hong Li,[1,2] Rui-Hua Xu [1,2]

Wang F, *et al*. *Gut* 2021;**0**:1–10. doi:10.1136/gutjnl-2021-324852

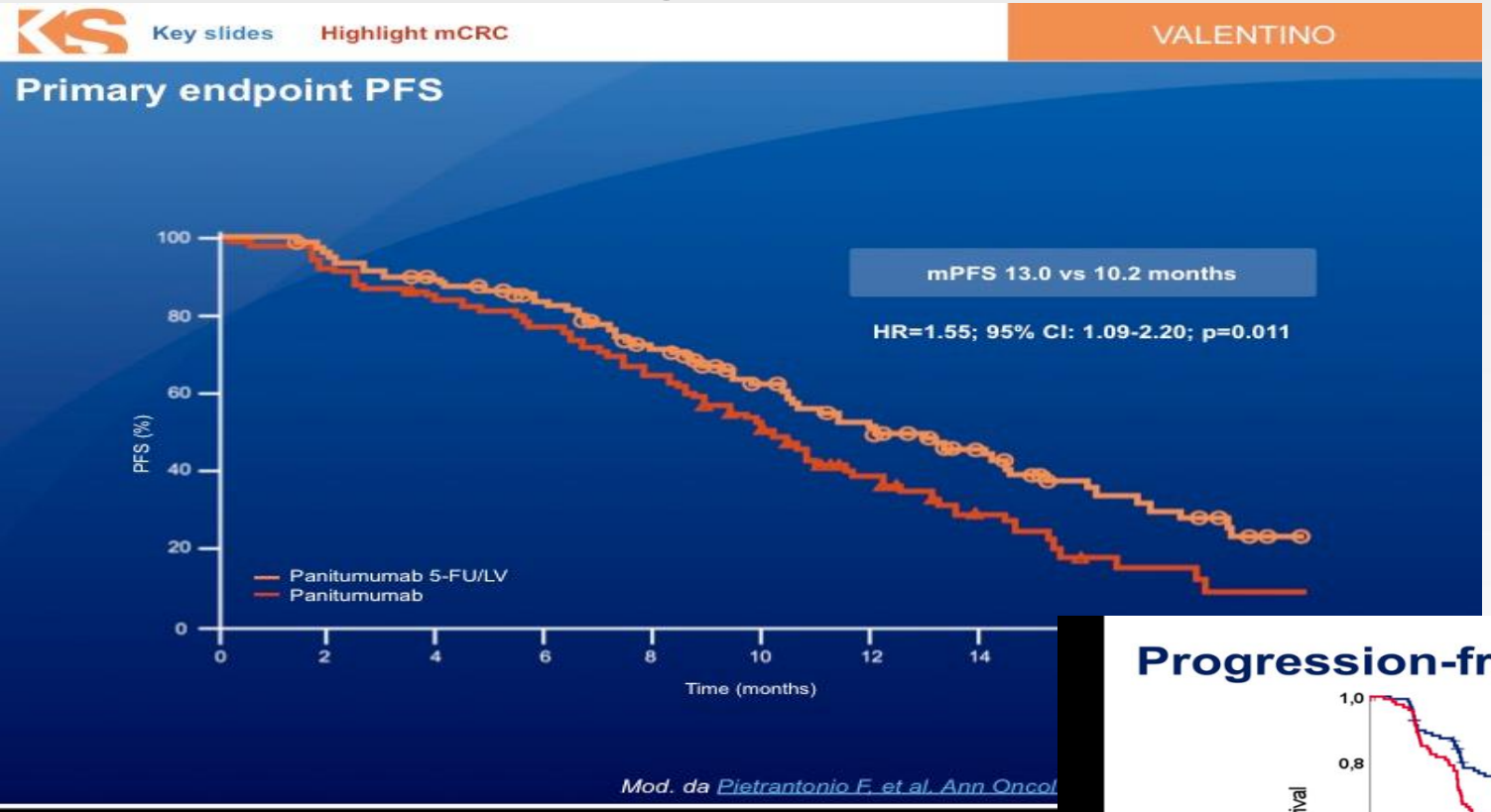


SNODO DECISIONALE N.6

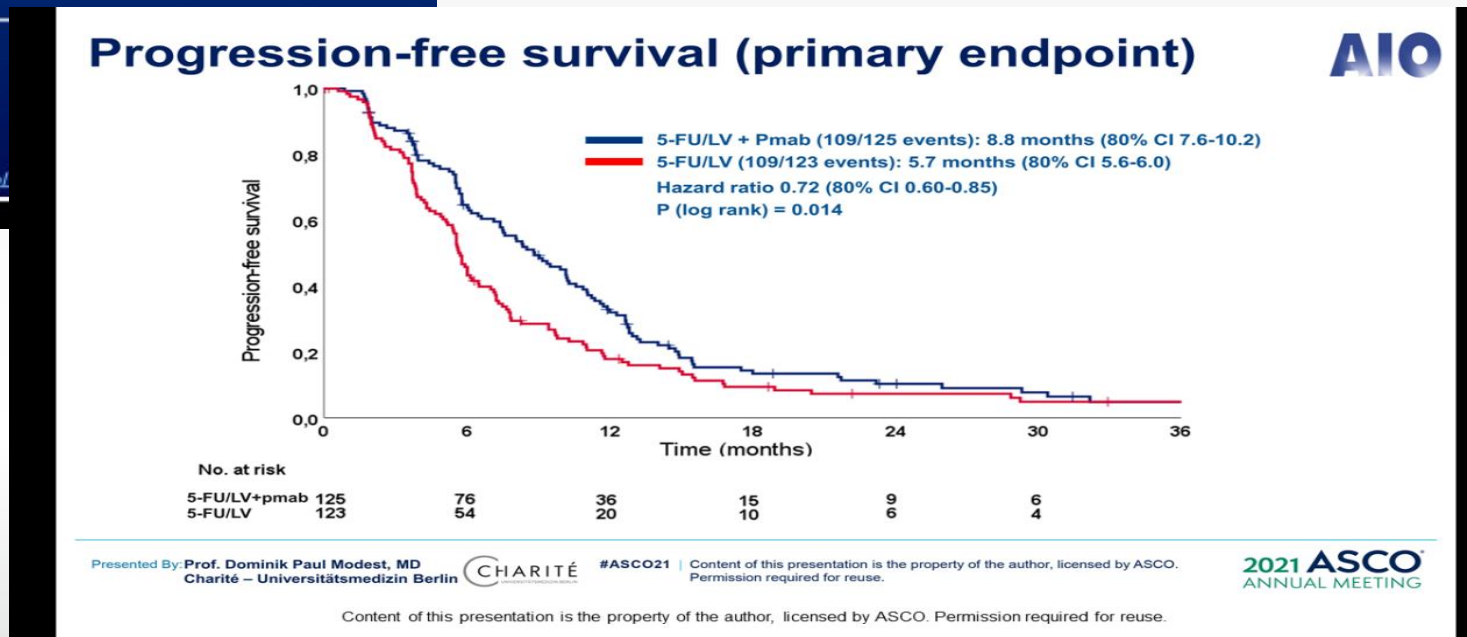
- Quale terapia?

CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE 2ª EDIZIONE

VALENTINO



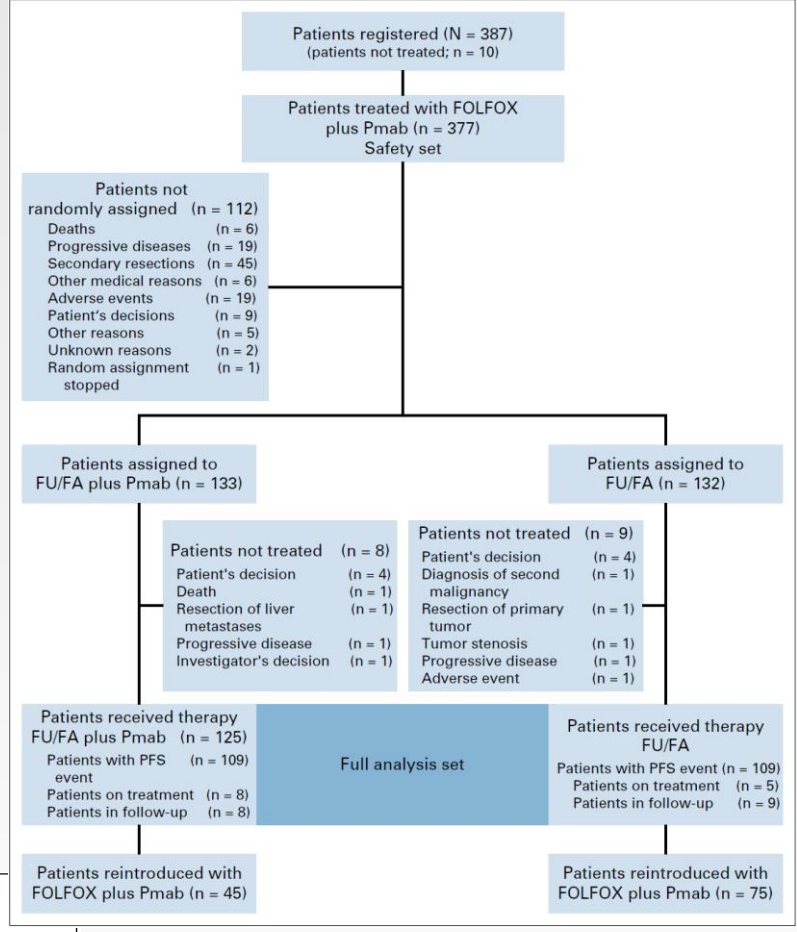
PANAMA

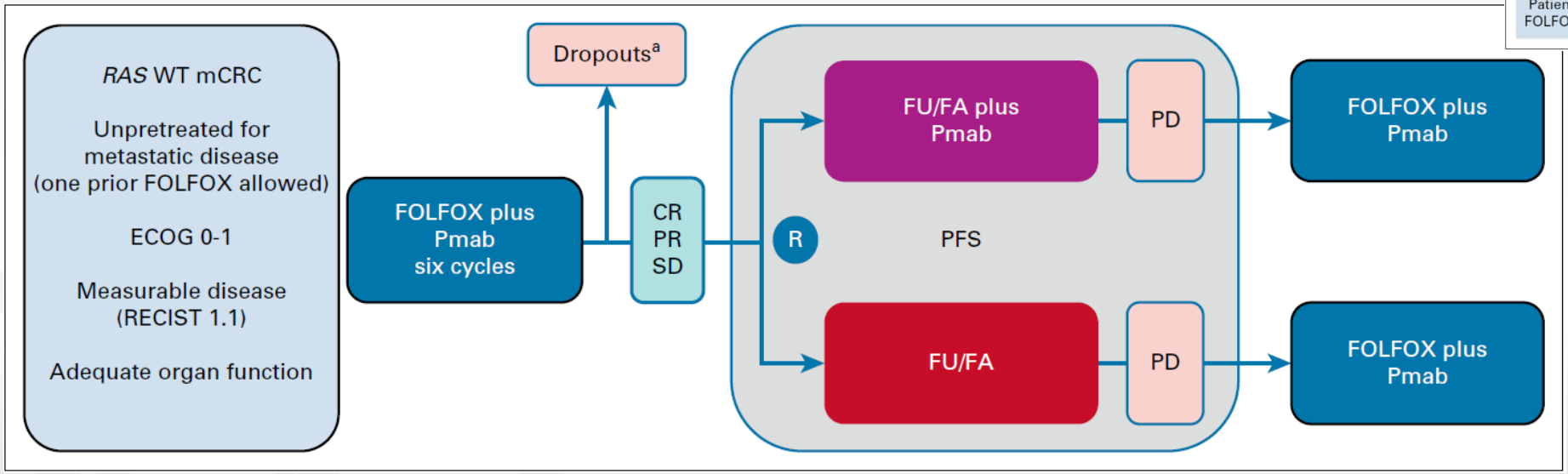


Panitumumab Plus Fluorouracil and Folinic Acid Versus Fluorouracil and Folinic Acid Alone as Maintenance Therapy in *RAS* Wild-Type Metastatic Colorectal Cancer: The Randomized PANAMA Trial (AIO KRK 0212)

J Clin Oncol 40:72-82. © 2021

Dominik Paul Modest, MD[1,2]; Meinolf Karthaus, MD[3]; Stefan Fruehauf, MD[4]; Ullrich Graeven, MD[5]; Lothar Müller, MD[6]; Alexander Otto König, MD[7]; Ludwig Fischer von Weikersthal, MD[8]; Karel Caca[9], Albrecht Kretzschmar, MD[10]; Eray Goekkurt, MD[11,12]; Siegfried Haas, MD[13]; Annika Kurreck, MD[1]; Arndt Stahler, MD[1]; Swantje Held, MSc[15]; Armin Jarosch, MD[15]; David Horst, MD[2,15]; Anke Reinacher-Schick, MD[16]; Stefan Kasper, MD[2,17]; Volker Heinemann, MD[2,18]; Sebastian Stintzing, MD[1,2]; and Tanja Trarbach, MD[19]





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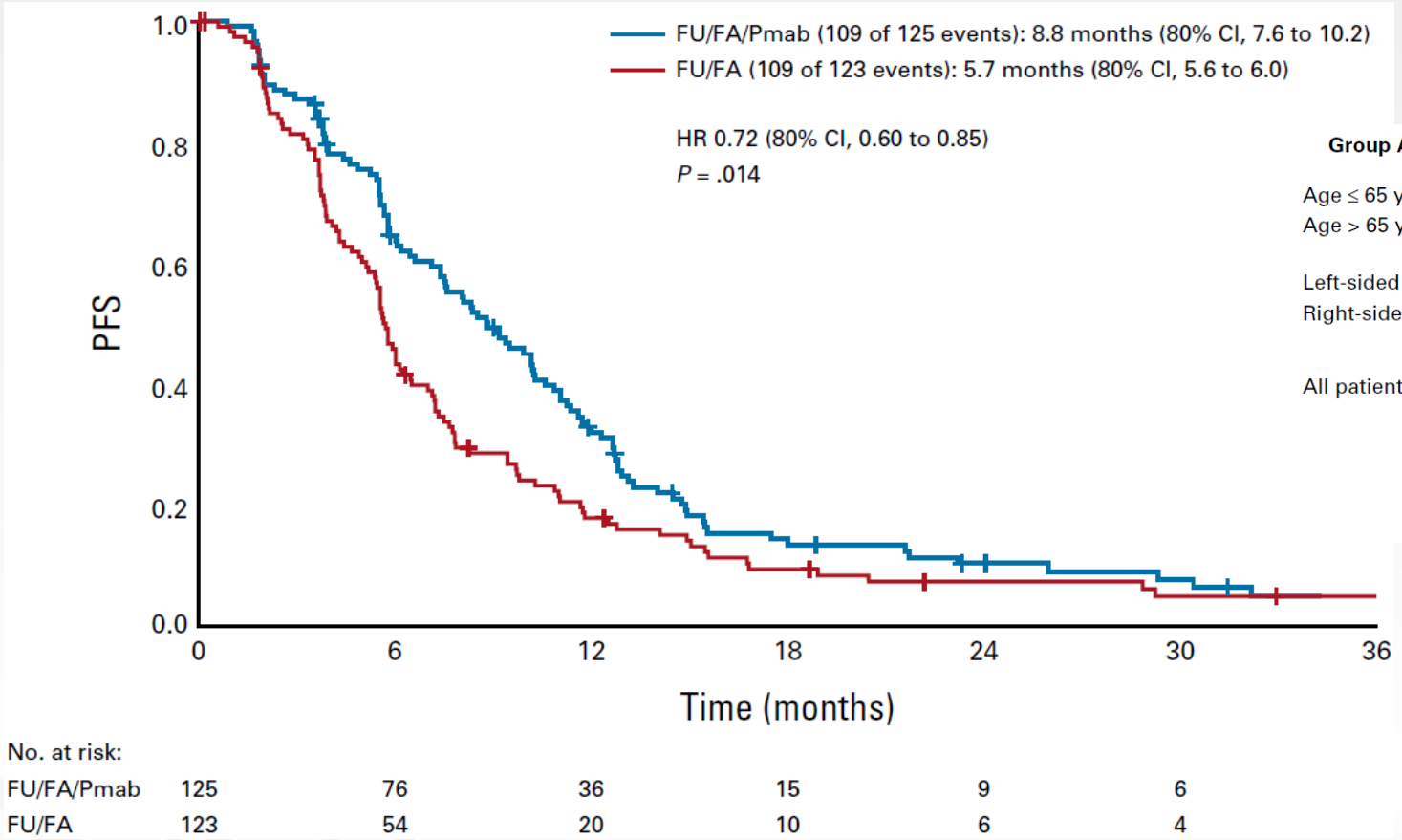
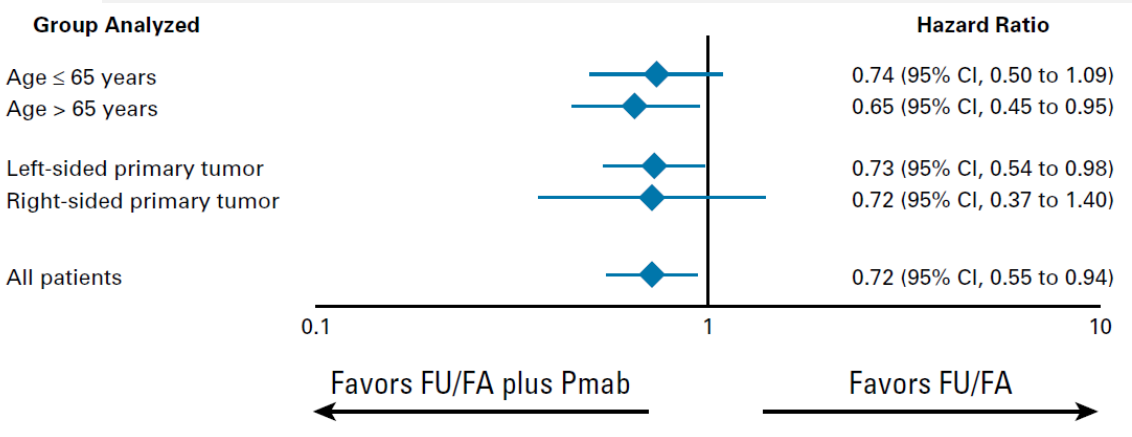
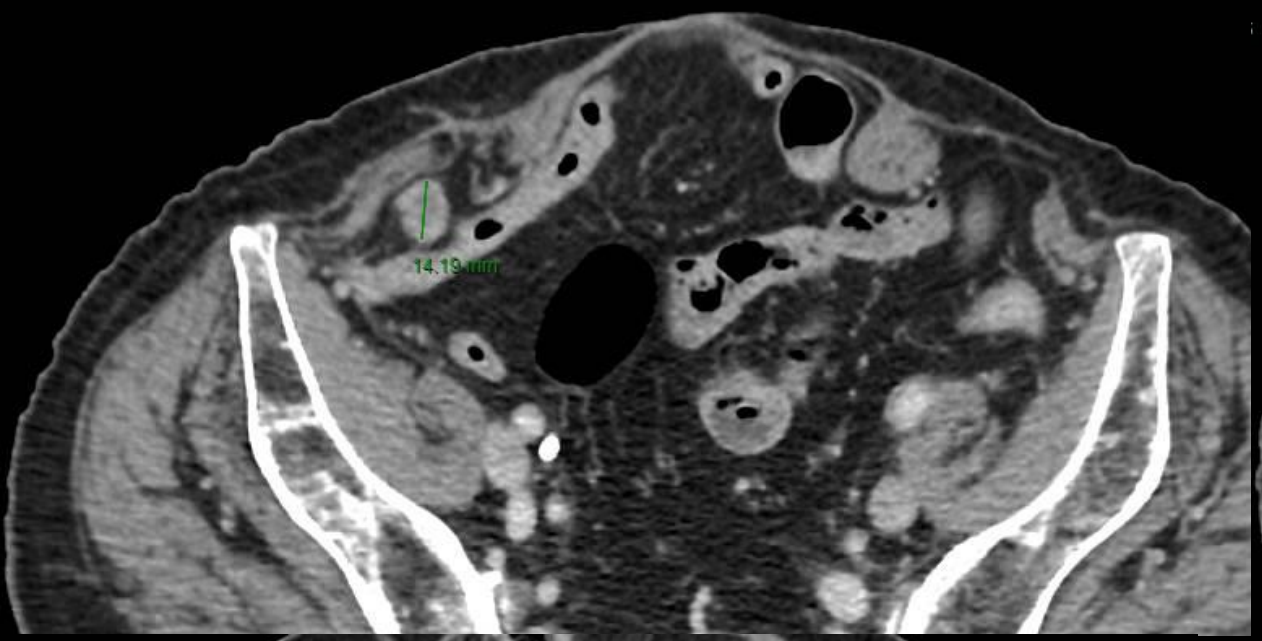




Storia Oncologica

- Avvia degramont/panitumumab di mantenimento
- Gen 2020 – aprile 2020: 6 cicli degramont-pani: TC: SD, prosegue mantenimento
- Mantenimento proseguito con SD fino a set 2020, quando ripete tc che mostra PD di malattia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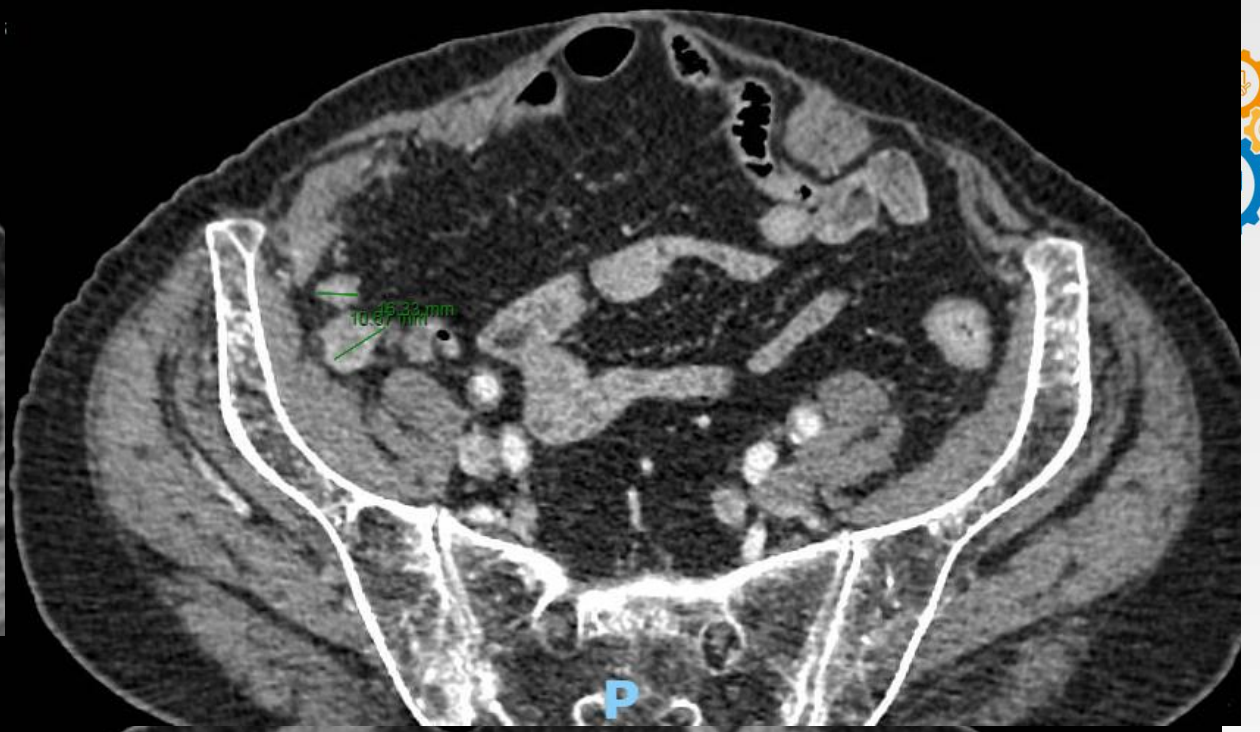
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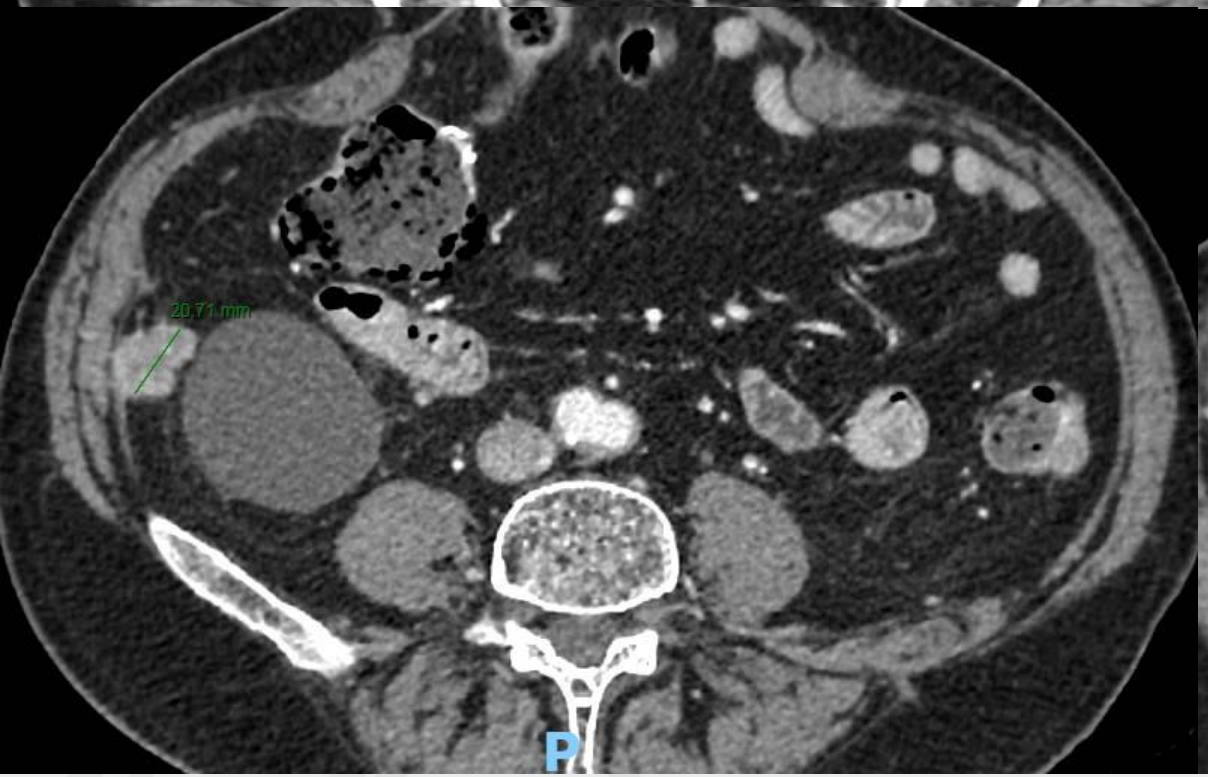
20.71 mm
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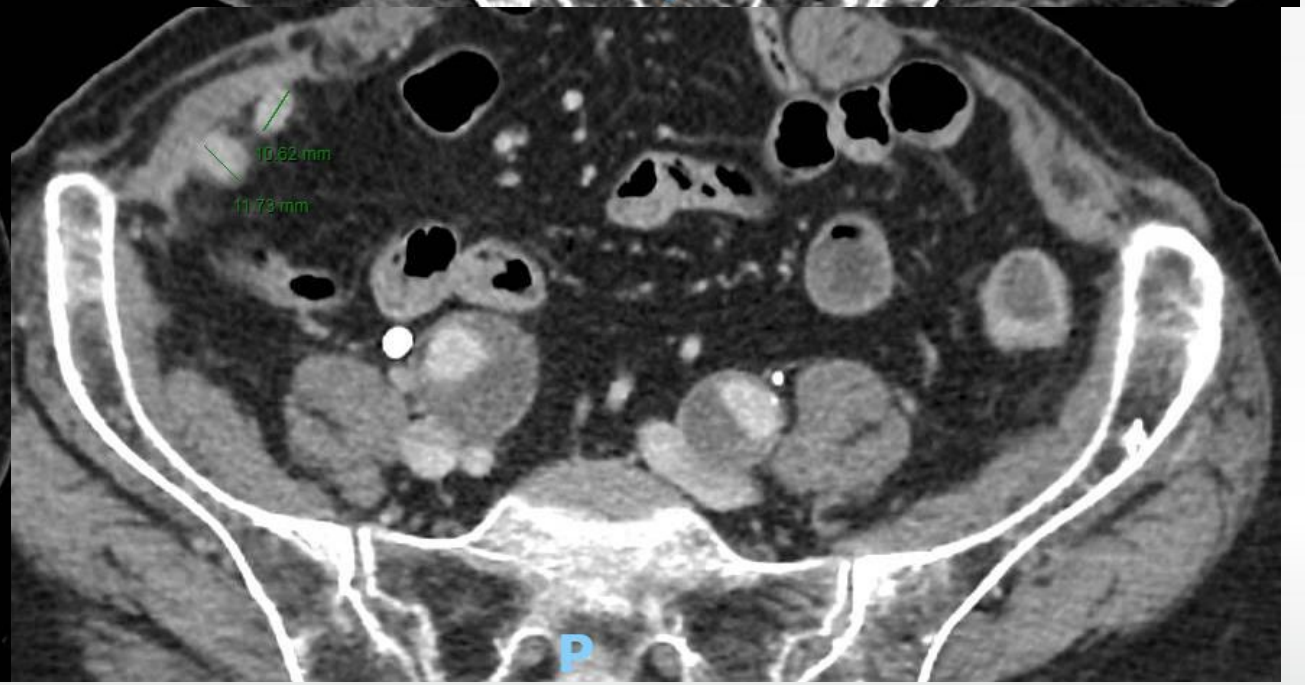

10.62 mm
11.73 mm
P

SNODO DECISIONALE N.7

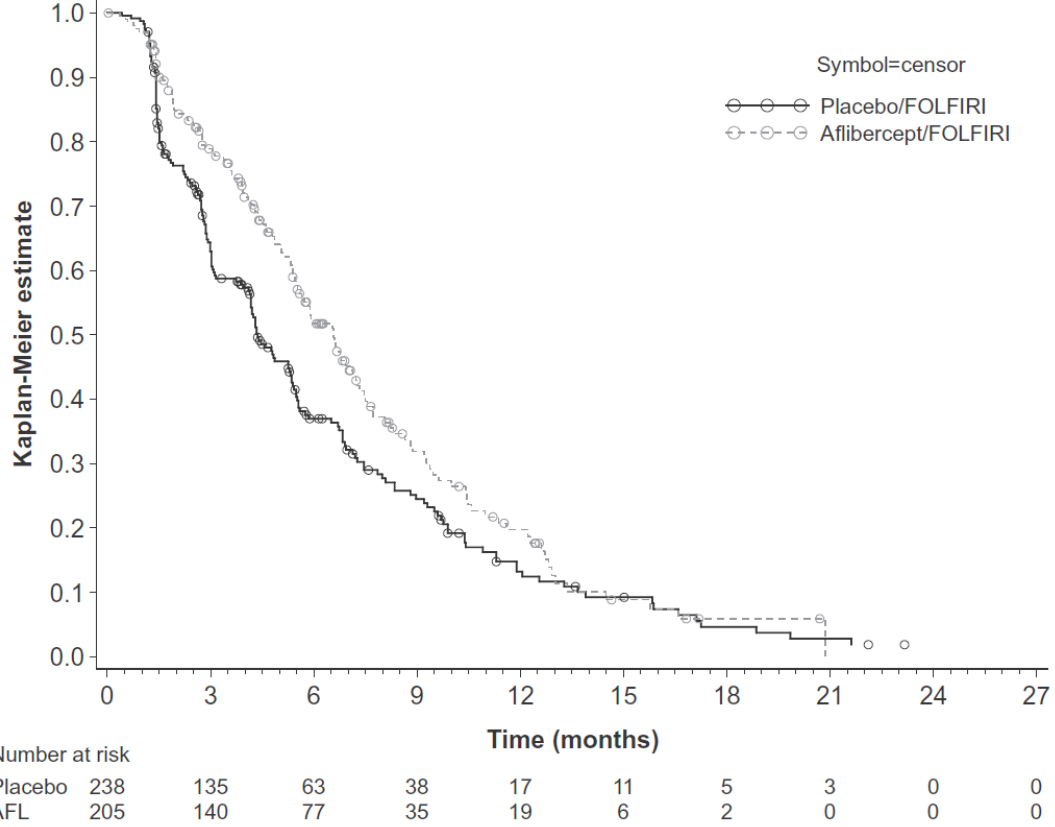
- Quale terapia?

Contents lists available at ScienceDirect

Journal of Geriatric Oncology

Observed benefit and safety of aflibercept in elderly patients with metastatic colorectal cancer: An age-based analysis from the randomized placebo-controlled phase III VELOUR trial

Paul Ruff [a,*], Eric Van Cutsem [b], Radek Lakomy [c], Jana Prausova [d], Guy A. van Hazel [e], Vladimir M. Moiseyenko [f], Karen Soussan-Lazard [g], Emmanuelle Dochy [h], Emmanuelle Magherini [g], Teresa Macarulla [i], Demetris Papamichael [j]



Efficacy in the ITT, <65 years and ≥65 years population.

Parameter	ITT[23]		<65 years		≥65 years	
	Placebo + FOLFIRI (n = 614)	Aflibercept + FOLFIRI (n = 612)	Placebo + FOLFIRI (n = 376)	Aflibercept + FOLFIRI (n = 407)	Placebo + FOLFIRI (n = 238)	Aflibercept + FOLFIRI (n = 205)
Median OS	12.06	13.50	12.50	14.50	11.3	12.6
95.34% CI	11.07–13.11	12.52–14.95	11.40–13.77	13.01–16.85	9.66–12.65	10.97–14.39
Stratified HR	0.82		0.80		0.85	
95.34% CI	0.71–0.94		0.67–0.95		0.68–1.07	
P-value for interaction			0.68			
Median PFS	4.67	6.90	4.90	6.90	4.4	6.6
99.99% CI	4.07–5.55	5.88–7.85	4.01–6.47	5.98–8.34	3.02–6.51	5.03–8.64
Stratified HR	0.76		0.77		0.75	
99.99% CI	0.58–0.99		0.55–1.08		0.48–1.17	
P-value for interaction			0.93			

CI, confidence interval; HR, hazard ratio; ITT, intention to treat; PFS, progression-free survival; OS, overall survival.

Storia Oncologica

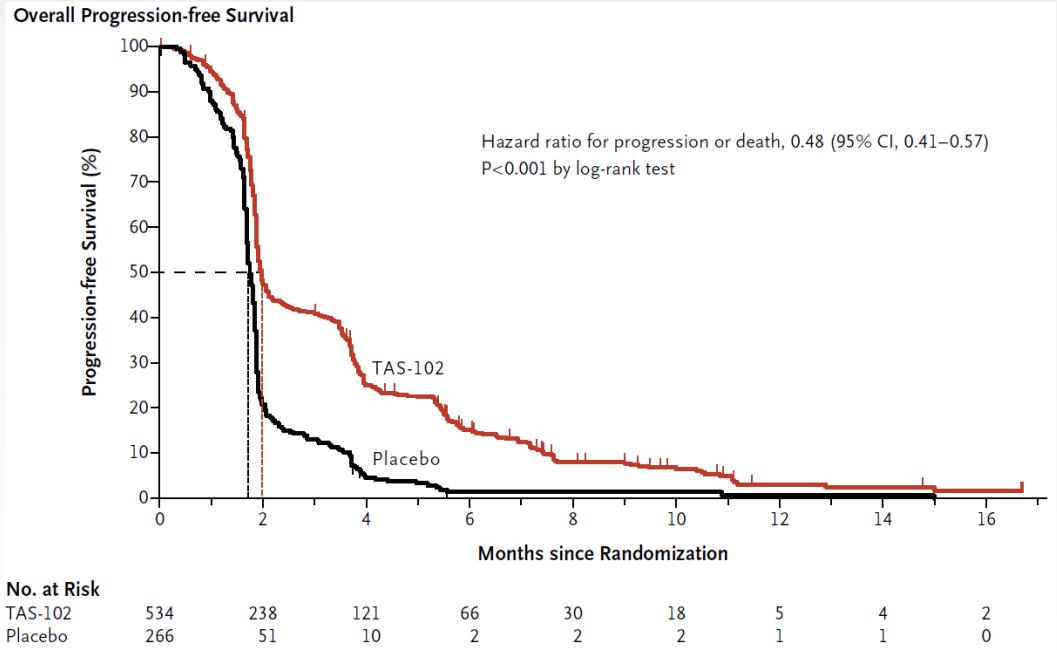
- Si decide di Avviare seconda linea FOLFIRI-aflibercept – protocollo DISTINCTIVE
- Set 2020: avvia folfiri-aflibercept 2° linea
- SD dopo 6 cicli, avvia mantenimento con degramont aflibercept
- Aprile 2021: TC di rivalutazione: pd

SNODO DECISIONALE N.8

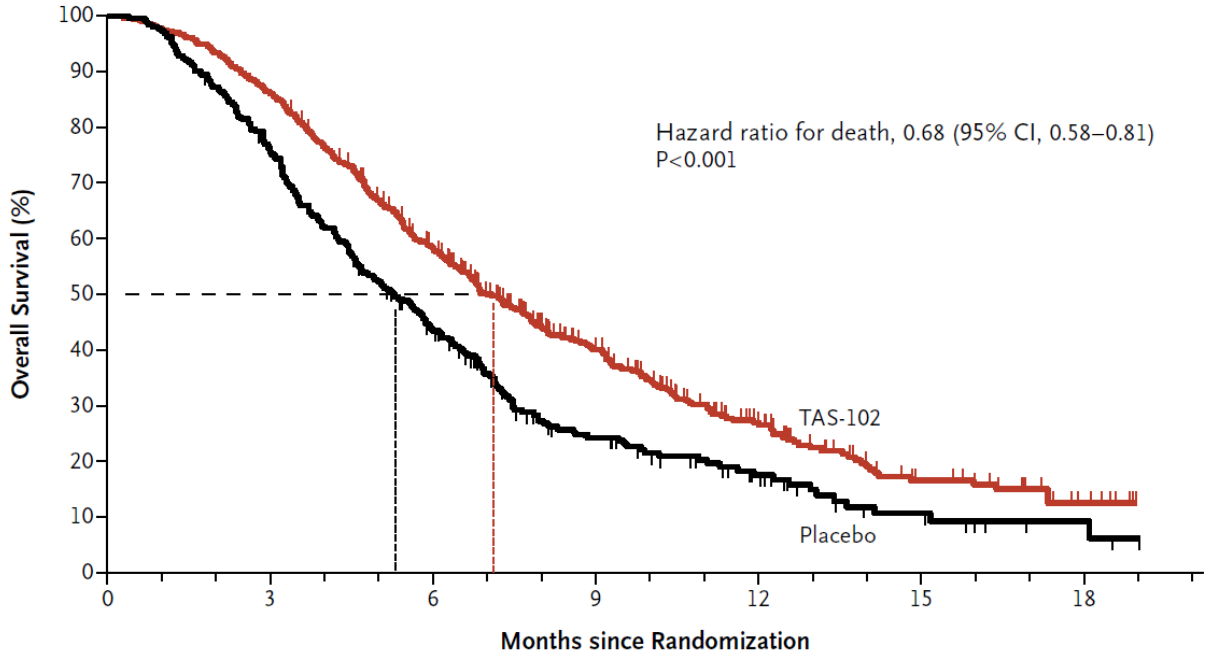
- Quale terapia?

ORIGINAL ARTICLE

Randomized Trial of TAS-102 for Refractory Metastatic Colorectal Cancer



A Overall Survival



No. at Risk

TAS-102	534	459	294	137	64	23	7
Placebo	266	198	107	47	24	9	3

B Overall Survival

Subgroup	No. of Patients	Hazard Ratio (95% CI)
All patients	800	0.68 (0.58–0.81)
KRAS status		
Wild type	393	0.58 (0.45–0.74)
Mutant	407	0.80 (0.63–1.02)
Time since diagnosis of first metastases		
<18 mo	166	0.84 (0.58–1.21)
≥18 mo	634	0.64 (0.53–0.78)
Geographic region		
Japan	266	0.75 (0.57–1.00)
United States, Europe, and Australia	534	0.64 (0.52–0.80)
Sex		
Male	491	0.69 (0.56–0.87)
Female	309	0.68 (0.51–0.90)
Age		
<65 yr	448	0.74 (0.59–0.94)
≥65 yr	352	0.62 (0.48–0.80)

Storia Oncologica

- Aprile 2021: avvia TFD/TPI 3° linea
- Aprile - Ottobre 2021 lonsurf con SD clinica e radiologica
- Ottobre 2021: pd clinica e radiologica, avvia bsc
- Feb 2022 exitus

Colon dx, carcinosi peritoneale: OS 40 mesi (avvio prima linea ott 2018 – exitus Feb 2022)

CCA - COLORECTAL CANCER ACADEMY: COSTRUIRE IL SAPERE

2ª EDIZIONE

v.formica1@gmail.com

GRAZIE DELL'ATTENZIONE