UNIVERSITY & RESEARCH
HOSPITALS

Nuove strategie terapeutiche della malattia metastatica e ruolo dei farmaci biologici

Dr Antonello Quadri

Medicina Oncologica

Policlinico San Pietro

POLICLINICO
SAN PIETRO

Contenuti

- Quale 1°linea nel k plurimetastatico Paziente fit e unfit
- Quali Linee successive alla prima
- Quale trattamento nel k metastatico localizzato solo al fegato

Tutti i Farmaci disponibili

- Chemioterapia (5 FU/Xeloda, Oxaliplatino, CPT11, Tas 102)
- Antiangiogenetici (Bevacizumab,Aflibercept,Ramucirumab)
- Anti-EGFR (Cetuximab,Panitumumab)
- Inibitori Multichinasici (Regorafenib)
- Immunoterapia (Nivolumab, Pembrolizumab)

Colorectal Cancer: 20 Years Later

meta-analysis 1992 **80405 results**

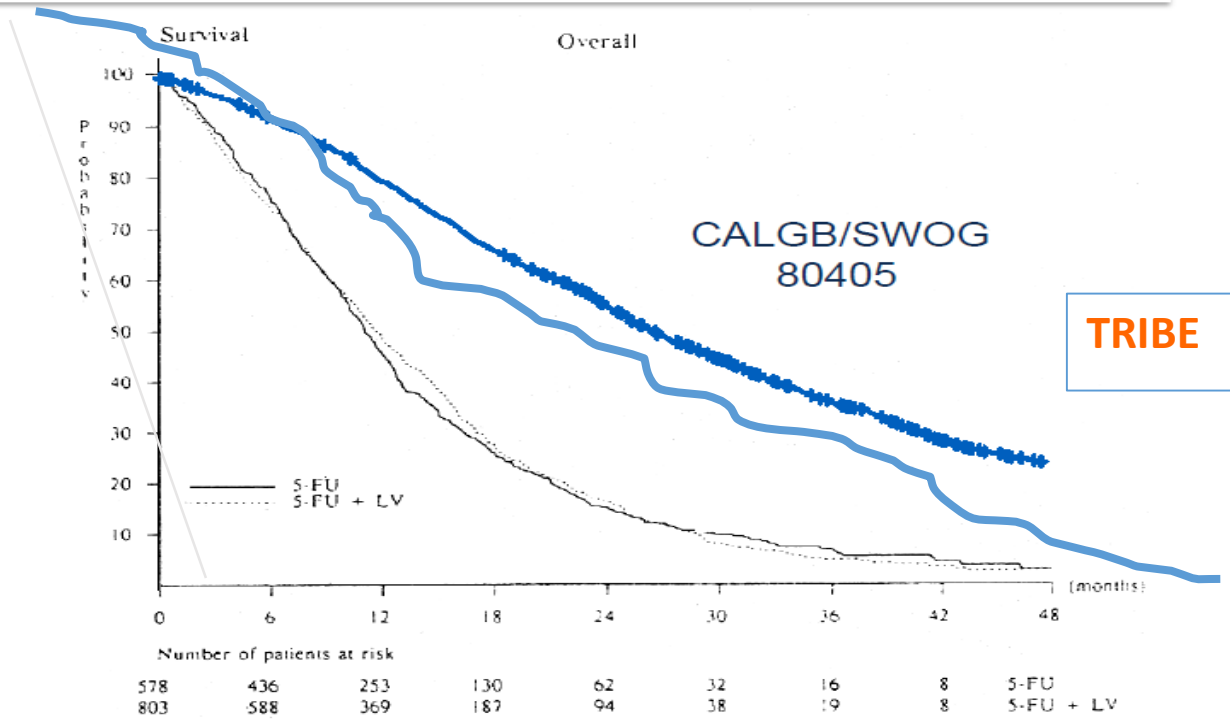
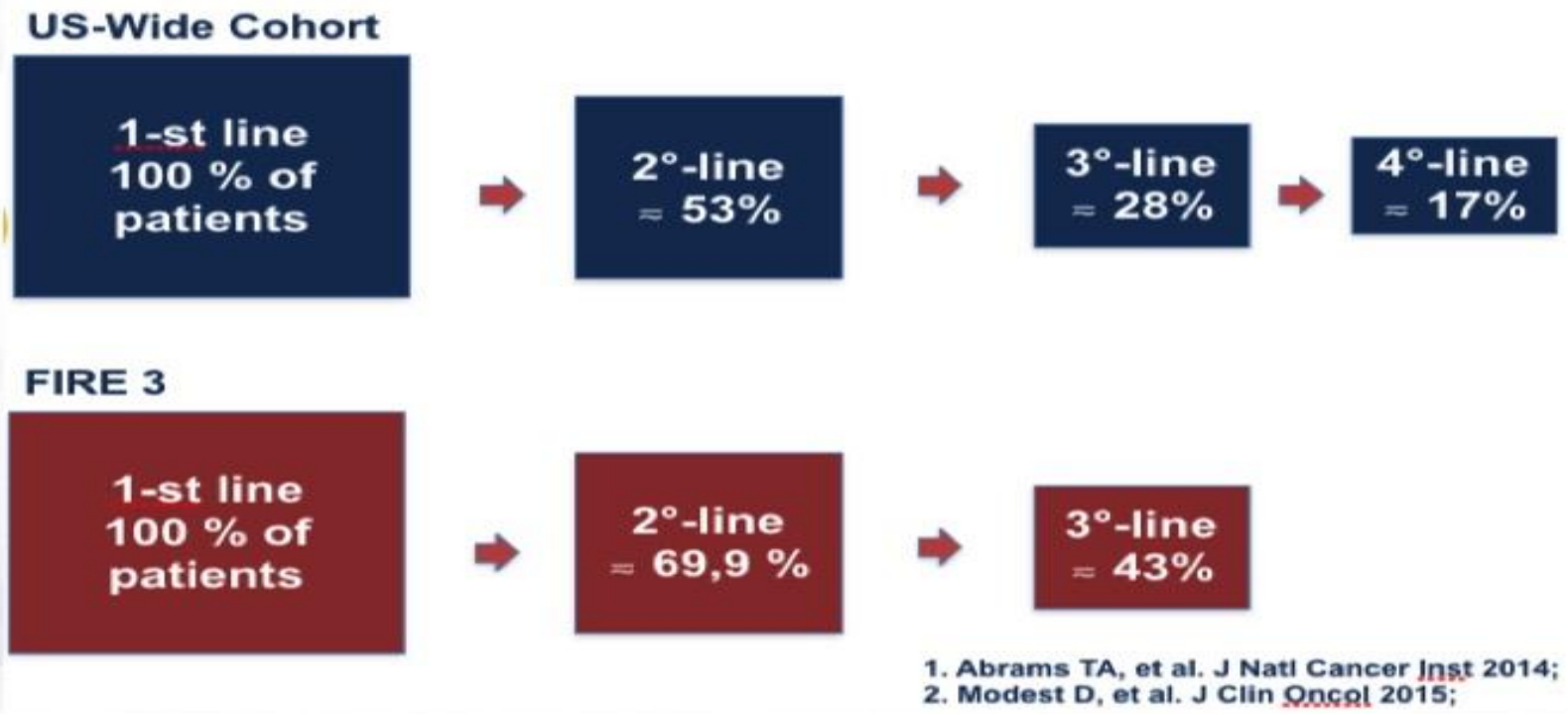


Fig 2. Overall survival. J Clin Oncol, 1992

Dal 1992 ad oggi la OS è passata dai 6 mesi con in solo 5FU ai 36 mesi con tutti i farmaci disponibili

Importanza della 1° linea e di una corretta programmazione terapeutica

How many patients receive a second- or third-line therapy?



1. Abrams TA, et al. J Natl Cancer Inst 2014;
2. Modest D, et al. J Clin Oncol 2015;

Le 4 possibili scelte iniziali

- Doppietta + Bevacizumab
- Doppietta + anti EGFR (Panitumumab, Cetuximab)
- Tripletta + Bevacizumab
- Cape/5 Fu + o - Bevacizumab

special articles

Annals of Oncology

Annals of Oncology 27: 1386–1422, 2016
doi:10.1093/annonc/mdw235
Published online 5 July 2016

ESMO consensus guidelines for the management of patients with metastatic colorectal cancer

E. Van Cutsem[1*], A. Cervantes[2], R. Adam[3], A. Sobrero[4], J. H. Van Krieken[5], D. Aderka[6], E. Aranda Aguilar[7], A. Bardelli[8], A. Benson[9], G. Bodoky[10], F. Ciardiello[11], A. D'Hoore[12], E. Diaz-Rubio[13], J.-Y. Douillard[14], M. Ducreux[15], A. Falcone[16,17], A. Grothey[18], T. Gruenberger[19], K. Haustermans[20], V. Heinemann[21], P. Hoff[22], C.-H. Köhne[23], R. Labianca[24], P. Laurent-Puig[25], B. Ma[26], T. Maughan[27], K. Muro[28], N. Normanno[29], P. Österlund[30,31], W. J. G. Oyen[32], D. Papamichael[33], G. Pentheroudakis[34], P. Pfeiffer[35], T. J. Price[36], C. Punt[37], J. Ricke[38], A. Roth[39], R. Salazar[40], W. Scheithauer[41], H. J. Schmoll[42], J. Tabernero[43], J. Taïeb[25], S. Tejpar[1], H. Wasan[44], T. Yoshino[45], A. Zaanan[25] & D. Arnold[46]

UNIVERSITY & RESEARCH HOSPITALS

Historical Groups

Table 5. Historical ESMO groups for treatment stratification of fit patients with metastatic CRC [3]

	Group 0 Resectable	Group 1 Potentially resectable	Group 2 Not resectable	Group 3 Not resectable
Clinical presentation	Clearly resectable R0 liver and/or lung dis	Unresectable liver/lung limited disease which might become ectable after response to ersion therapy	Multiple metastases/sit Tumour-related s Able to with	Asymptomatic Multiple metastases Never able to undergo resection Unsuitable for intensive therapy Frail with co-morbidities
Treatment goal	Cure (NE	rinkage		Halt/slow tumour progression Tumour shrinkage less relevant Tolerability most relevant
Treatment intensity	*Aggressive surgery* Immediate surgery with no prior chemotherapy or moderate (FOLF perioperative chen	Upfr	combination (at doublet)	*Less aggressive treatment approach* Treatment selected according to patient preference Sequential approach (start with single agent or doublet with low toxicity) FOLFOX an exception

FOLFOX, infusional 5-fluorouracil, leucov no evidence of disease

New categories

Patient's classification	'Fit' patients		'Unfit' patients
	Group 1	Group 2	
Clinical presentation	• Symptomatic patients • Impending clinical threat • Treatment biomarker driven • *RAS* wt, *RAS* mt, *BRAF* mt patient subgroups	• Asymptomatic patients • Impending clinical threat • Resection not an option • Treatment biomarker driven • *RAS* wt, *RAS* mt, *BRAF* mt patient subgroups	Best supportive care
Treatment goal	Cytoreduction, followed by: • R0 resection • NED achieved by LAAT	Disease control without symptoms of disease or from treatment	Palliative

LAAT, local and ablative therapy; mt, mutant; NED, no evidence of disease; wt, wild-type

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

Treatment of metastatic disease

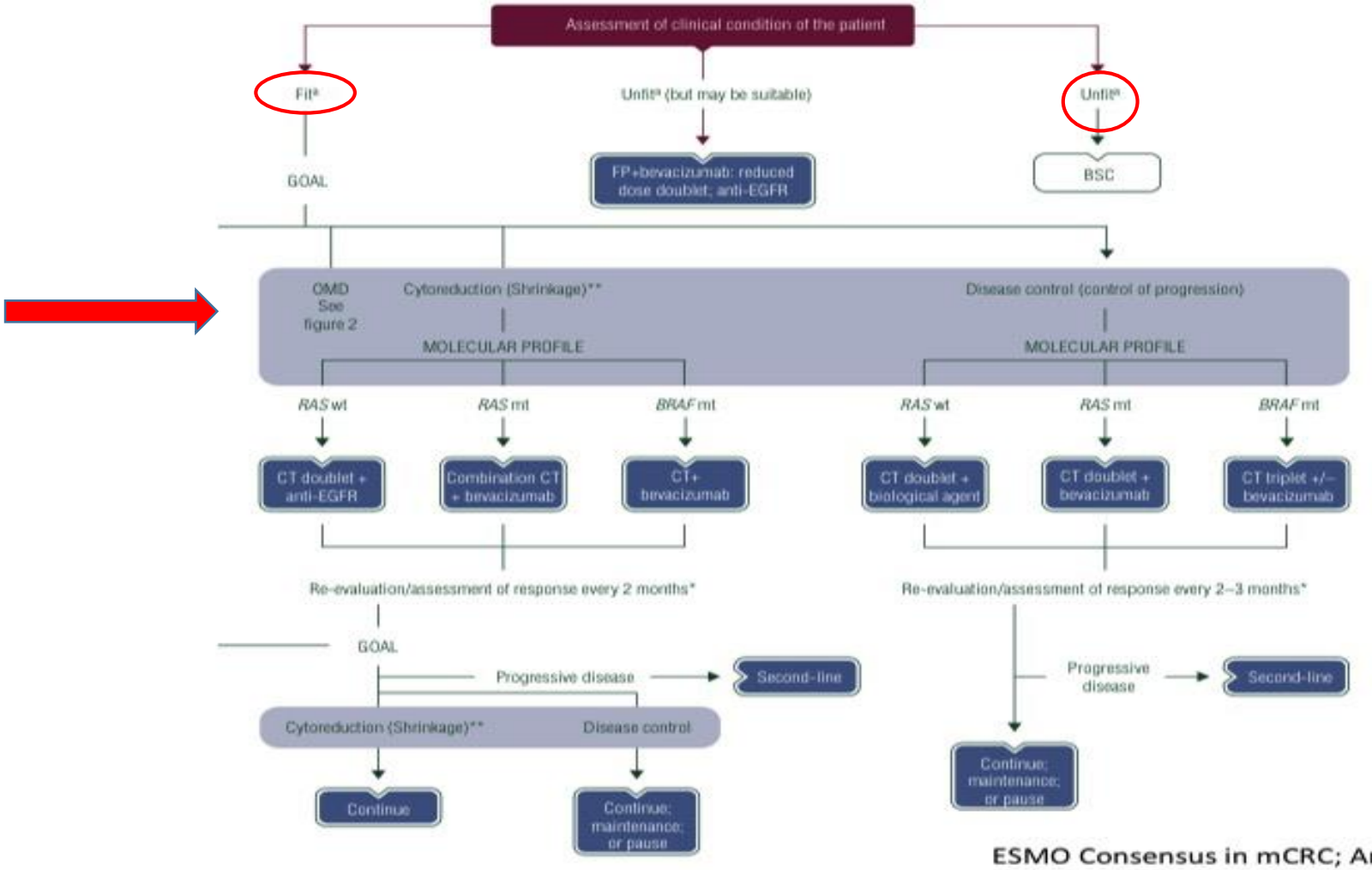
Drivers for decison making in 1st line treatment

Table 4. Treatment drivers for first-line treatment

Tumour characteristics	Patient characteristics	Treatment characteristics
Clinical presentation: Tumour burden Tumour localisation	Age	Toxicity profile
Tumour biology	Performance status	Flexibility
RAS mutation status	Organ function	Socio-economic factors
BRAF mutation status	Comorbidities	Quality of life, patient expectation and preference

UNIVERSITY & RESEARCH HOSPITALS

Quale Ct di 1° linea nel k retto metastatico?



ESMO Consensus in mCRC; Ann Oncol 2016

Nella nostra pratica clinica cosa facciamo in 1° linea?

Pz fit

Obiettivo citoriduzione

- Ras e BRAF WT: Doppietta + anti EGFR, Folfoxiri + Beva
- Ras mutati e/o Braf mutati: Fofoxiri + Beva,doppietta + Beva

Obiettivo stabilizzazione, continuum of care

- RAS e BRAF WT: Doppietta + anti EGFR, doppietta + Beva, doppietta senza biologico
- Ras e BRAF mutato: Doppietta + Beva, doppietta senza biologico

Nella nostra pratica clinica cosa facciamo in 1° linea?

Pz unfit/ Pz anziano

- Ras WT: monoCt (5 FU/Xeloda) + o – Bevacizumab o anti EGFR, doppietta con dosaggi ridotti
- Ras mutati: monoCt (5 FU/Xeloda) + o – Bevacizumab, doppietta con dosaggi ridotti

UNIVERSITY & RESEARCH HOSPITALS

...e per le linee successive alla prima?

Maintenance

BEV BEYOND PD

RAMUCIRUMAB

AFLIBERCEPT

CETUXIMAB

PANITUMUMAB

Continuous infusion

Monotherapy

Oral drugs

Triplet

Doublets

Biological agents

Which doublet?

Surgery on Mets

Locoregional Treatments

Chemo-holidays?

Therapy beyond progression?

TAS-102

REGORAFENIB

anti-EGFR Re-CHALLENGE

CHEMO Re-CHALLENGE

POLICLINICO SAN PIETRO

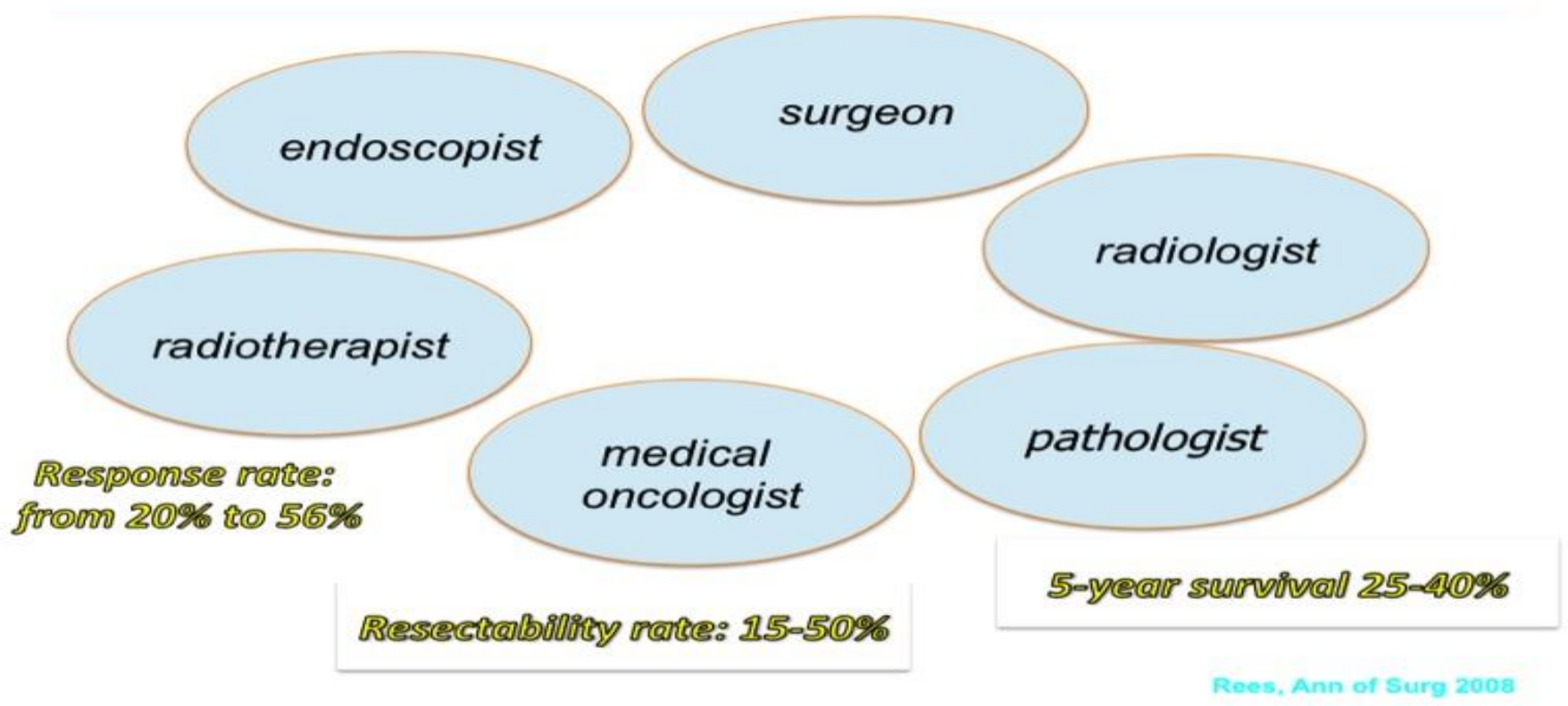
...e per le linee successive alla prima?

Da valutare in funzione:

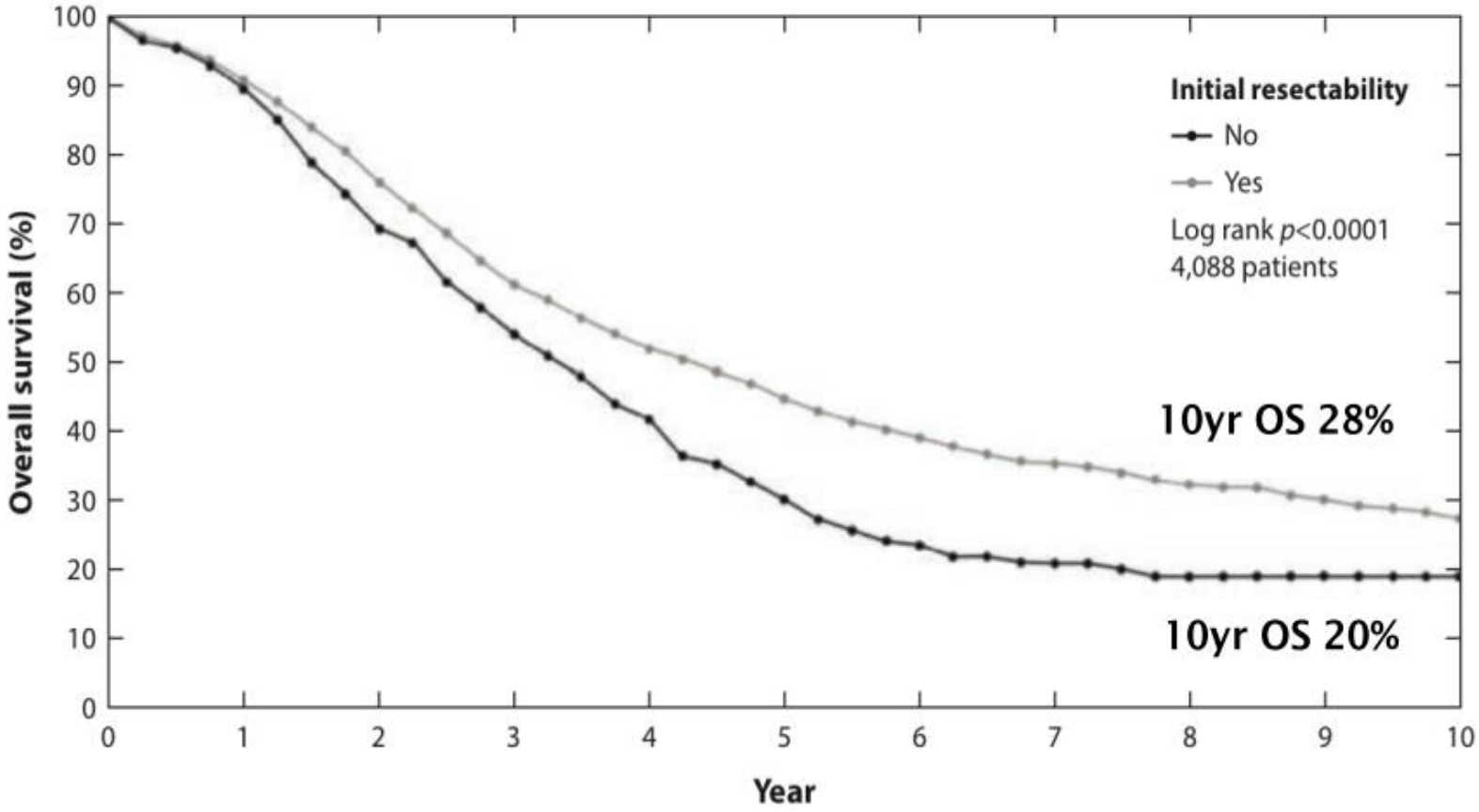
- Della 1° linea somministrata e della risposta ottenuta
- Delle condizioni generali del Paziente e della progressione della malattia

Diverse opzioni (Doppietta + antiangiogenetico, doppietta + anti EGFR, anti EGFR da solo……..
e per le linee successive Regorafenib, Lonsurf….)

Approccio Multidisciplinare nel trattamento delle metastasi epatiche di k retto



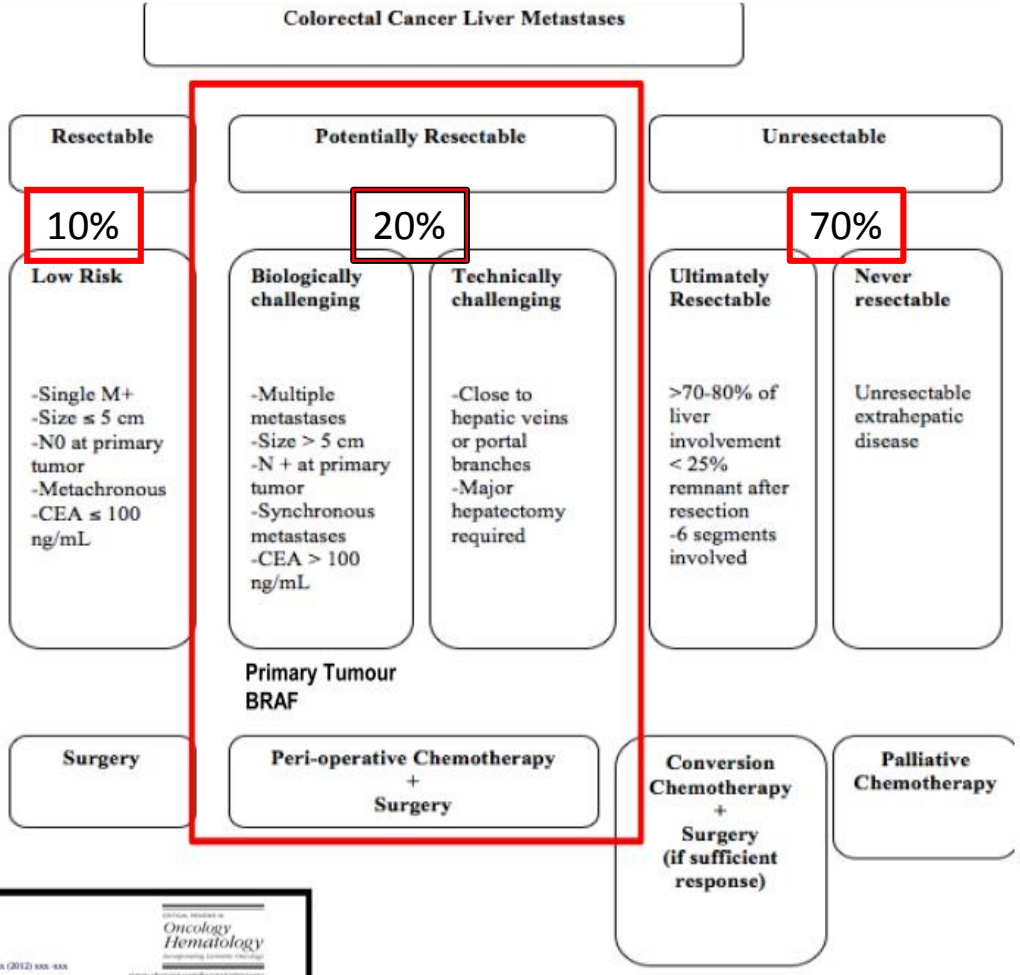
I tumori del retto metastatico sono curabili !!!!!

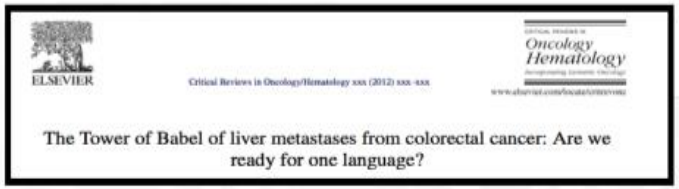


Jones and Poston, Ann Rev Med 2017


Those that could be resected
(sooner or later)
Those that will never be resected

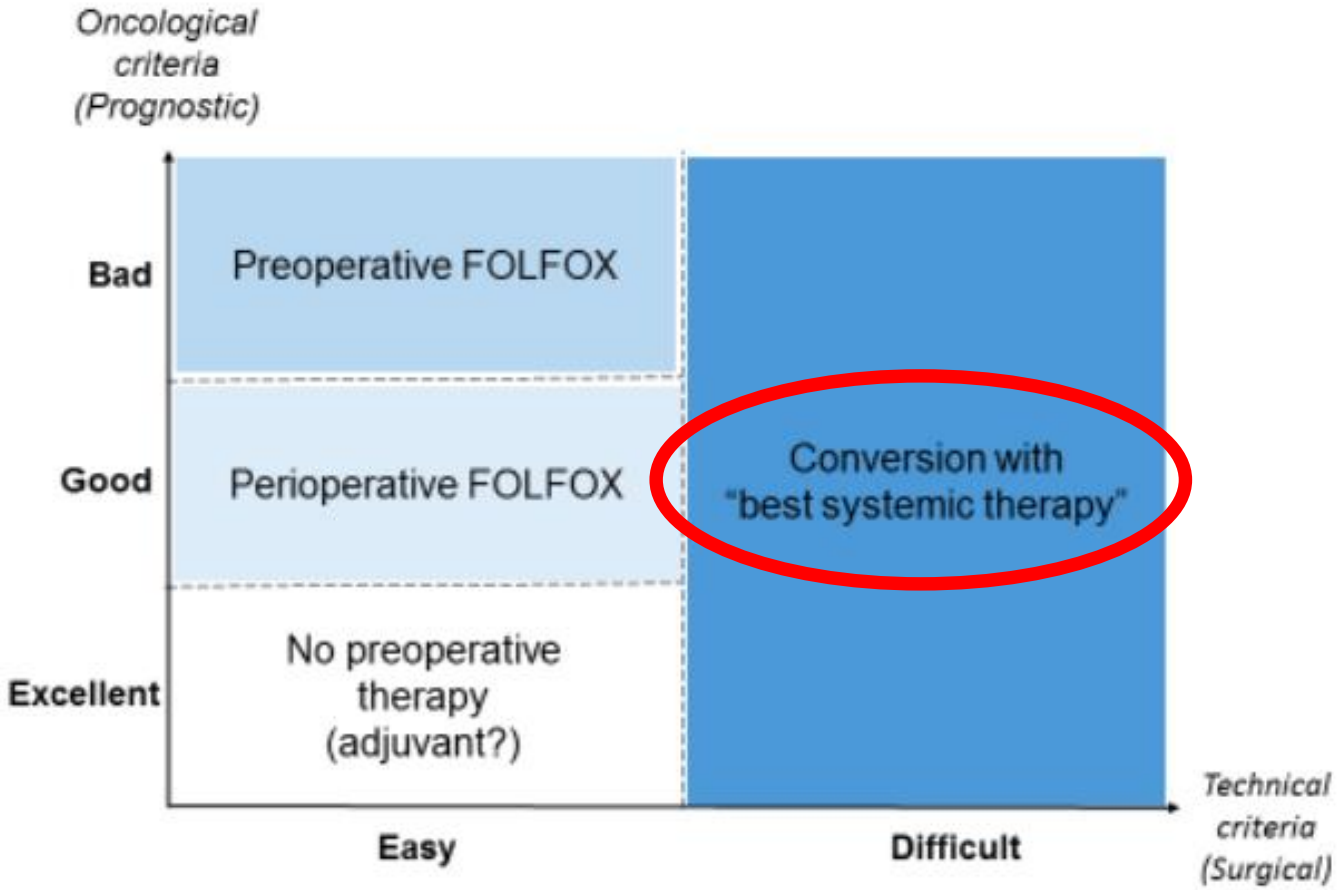
Neoplasie del retto con metastasi epatiche sincrone





Bittoni, Giampieri et al, CROH 2012

Resectable: Which Systemic Treatment?



Liver metasteses

1) Neoadiuvant chemotherapy (resectable)

Facilitate surgery

prognostic information

Folfox

2) Conversion therapy (potentially resectable)

Allow R0 resection via downsizing

Doublet + antiEGFR

Folfoxiri+ Bevacizumab

10-30% of initially unresectable liver metastases may become resectable with conversion CT

Grazie per l'attenzione……..