

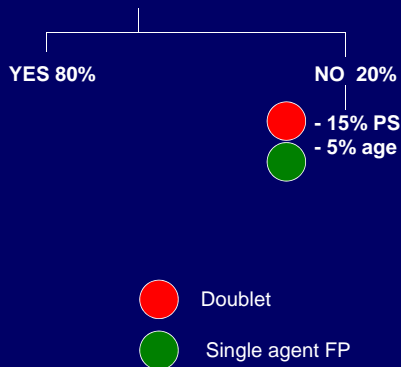
## Is there a best sequence to treat metastatic CRC?

Alberto Sobrero  
Ospedale San Martino Genova Italy

## Is there a best sequence to treat metastatic CRC?

1. Will I be able to give more than 1 line ?
2. If no what is the best choice ?
3. If yes , what is the best choice ?
  - Always start with treatment or just wait ?
  - Always doublets or single agent FP ?
  - Folfox or folfiri ?
  - Capecitabine or FU as doublet partner ?
  - Always a bio upfront or just the doublets ?
  - When anti VEGF and when anti EGFR first ?

will I be able to use more than 1 line ?



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## Treat right away or wait for symptoms ?

183 asymptomatic patients

	CT	WAIT, then CT
• MST	14	9
• Sy-free S	10	2
• PFS	8	3

Nordic JCO 92

## A meta-analysis of two randomised trials of early chemotherapy in asymptomatic metastatic colorectal cancer.

Ackland S. , Br J Cancer. 2005 Nov

*Early treatment of asymptomatic patients with metastatic colorectal cancer (N=168) did not provide a survival benefit or improved QoL compared to withholding treatment until symptoms occurred.*

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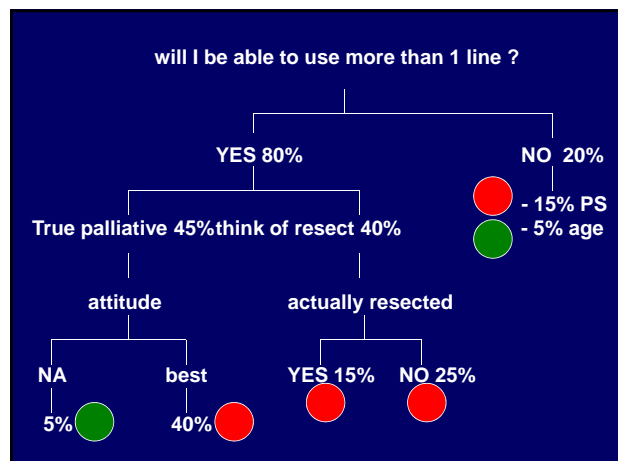
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## Efficacy of CT in advanced CRC: MST

No CT	5 mo
FU alone	12 mo
Doublets	16 mo
All 3 agents	20 mo

## Lessons from FOCUS LIFE CAIRO I

1. Sequential : valuable “defensive strategy”
2. OK for non pot. resectable, but good PS
3. Fewer pts will receive 2nd and 3rd line CT
4. Lower RR and Shorter PFS
5. Hint about folfiri better than iri as second line



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## FIRST LINE

- Colucci 2004: folfiri = folfox MST 15 mo
- Tournigand 2004: folfiri = folfox MST 20 mo
- Goldberg 2004: IFL < folfox MST 19 mo
- Grothey 2004: Capiri = Capox MST 18 mo

## Phase III Data in 2<sup>nd</sup> Line mCRC

Study	N	Treatment	Efficacy		
			ORR	PFS	OS
<b>Oxaliplatin failure</b>					
Tournigand 2004	69	FOLFIRI	4	2.5	NR
Sobrero 2008	650	IRINOTECAN	4	2.6	10.0
<b>Irinotecan failure</b>					
Rothenberg 2003	152	FOLFOX	9.9	4.6	NR
Tournigand 2004	69	FOLFOX	15	4.2	NR
	290	FOLFOX	9.2	4.8	10.8
Giantonio 2005	289	FOLFOX+B	21.8	7.2	12.9
	243	Bevacizumab	3.0	2.7	10.8

## Phase III Data in 3<sup>rd</sup> Line mCRC

1 FU	1 FU	
2 FOLFOX	2 Irinotecan	
3 Irinotecan	3 FOLFOX	
N	94	126
RR	4%	16%
PFS	2.7 months	5.0 months
OS	8.7 months	10.0 months

Rowland K, ASCO 05, 3519

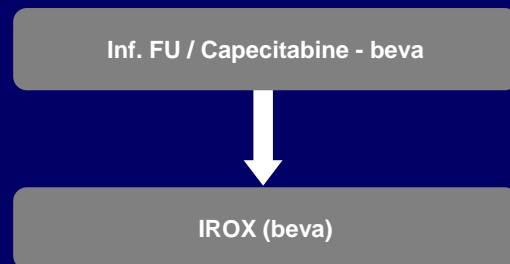
## IROX compared to standard treatment in second-line mCRC (EFC4585)

	IROX	Irinotecan
RR (%)	23.1	7.3
TTP (months)	5.3	2.8
OS (months)	13.4	11.1

TTP = time to progression

Haller et al. JCO 08

## Non aggressive first line approach

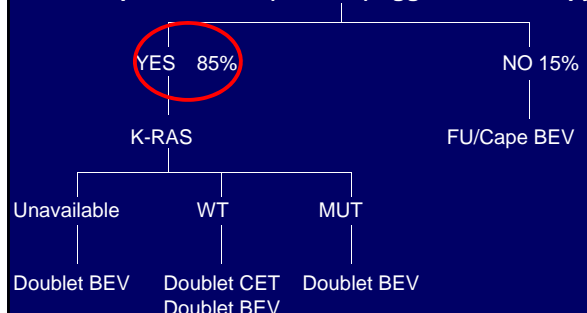


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## State of the art first line strategy

Does the patient need (and like) aggressive therapy?



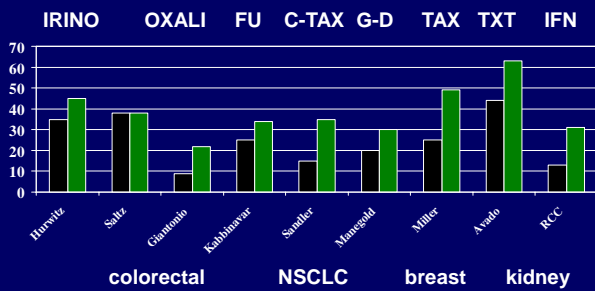
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## BEVACIZUMAB vs CET (PANI)

	P delaying	T shrinking
BEVA	+++	+
BEVA K-RAS wt	( +++++ )	( +++) )
BEVA K-RAS mut	( +++ )	( + )
CET	+	++
CET in K-RAS wt	++	+++
CET in K-RAS mut	-	-

## Beva: effects on tumor shrinkage



## When doublets plus cet (pani) instead of doublets plus bevacizumab as 1st line

1. K ras wt
2. Shrinkage will lead to resection
3. Few (large) lesions
4. Dominant tumor associated symptoms

AGE	PS	SITES	BULK	SX	DECISION
60	0	Li lu n	No	No	

AGE	PS	SITES	BULK	SX	DECISION
60	0	Li lu n	No	No	wait, sequential or doublet
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60	0	Li lu n	Yes	No	doublet or sequential
60	0	Li lu n	No	Yes	doublet
60	0	Periton.	No	No	

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60	0	Periton.	No	No	doublet
60	2 T	Li lu n	Yes	Yes	

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60	2 T	Li lu n	Yes	Yes	doublet
60	2 G	Li lu n	No	No	

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60	0	Periton.	No	No	doublet
60	2 T	Li lu n	Yes	Yes	doublet
60	2 G	Li lu n	No	No	wait or single agent
40	0	Li lu n	No	No	

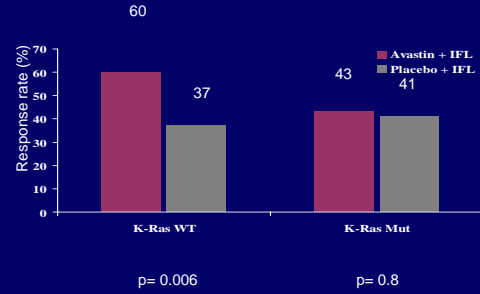
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## CET and K ras wt

	P delaying	T shrinkage
• First line :	modest mPFS + 1.9 HR PFS= 0.68	substantial RR + 16%
• Third line	outstanding mOS + 5.1 HR OS= 0.57	modest RR + 13%

Data from Crystal and C-07 studies, 2008

## AVF2107: response according to K-Ras status



Hurwitz et al, WCGC 2008