

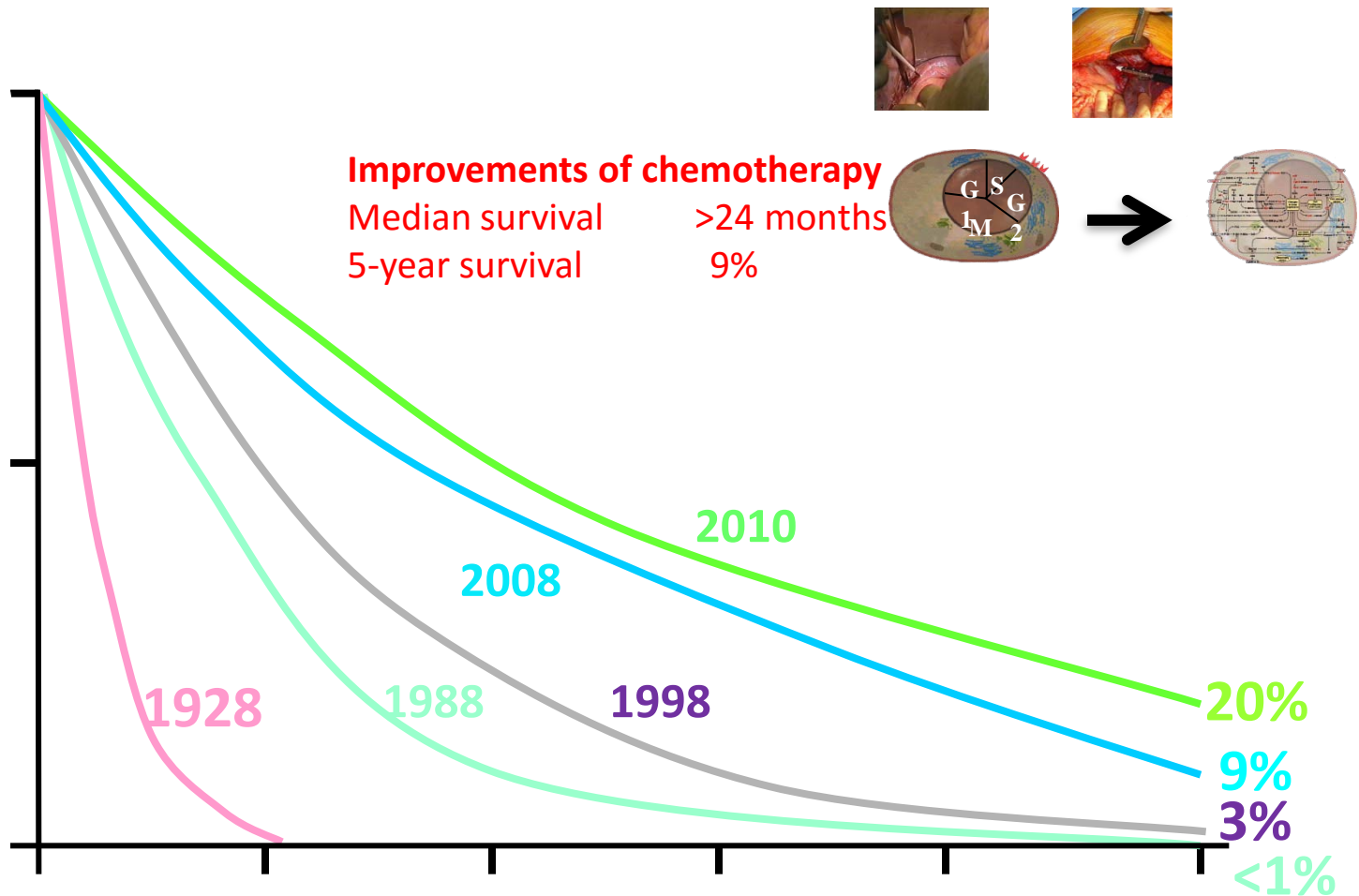
**Royal- Continental Napoli 22 Giugno 2017**

**La valutazione Multidisciplinare Strategie di Follow up e  
Terapia Adjuvante**

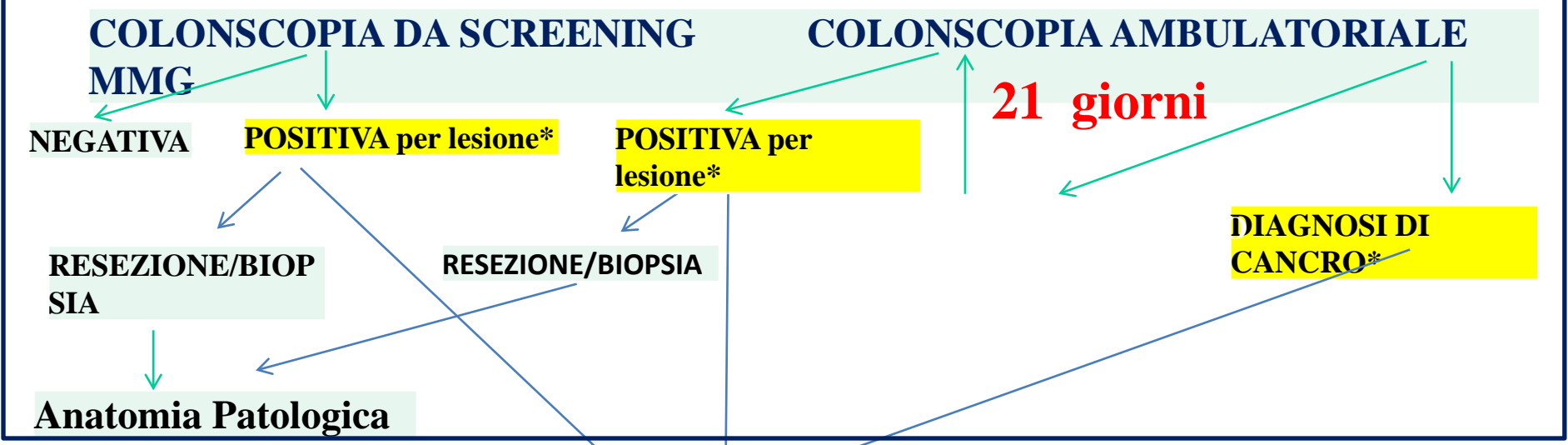
**Antonio Avallone  
National Cancer Institute of Naples,  
Fondazione G. Pascale**



# OS in Advanced CRC in 2008: The Impact of Multidisciplinary Management



**FASE DIAGNOSTICA T**



**CASE**

\* Contatto Case Manager e prenotazione per prima visita in tempo reale

**15 giorni**

**3 giorni**

**GOM**

**4 settimane**

**chirurgia ( Pascale)**

**Chemioterapia ( ASL Na3 /Pas**

**Radioterapia ( Pascale)**

**Terapia del dolore ( ASL Na3)**

Anatomia Patologica

15  
giorni

CASE

\* Contatto Case Manager e prenotazione per prima visita in tempo reale

3 giorni

Core GOM Pascale

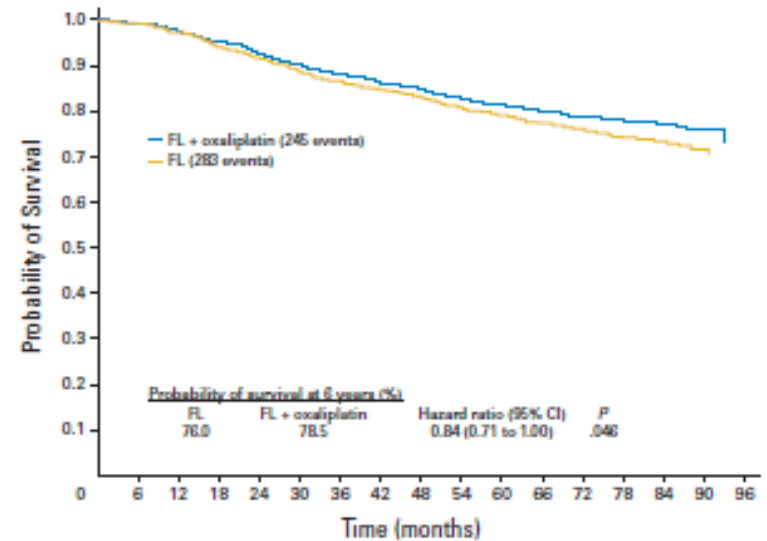
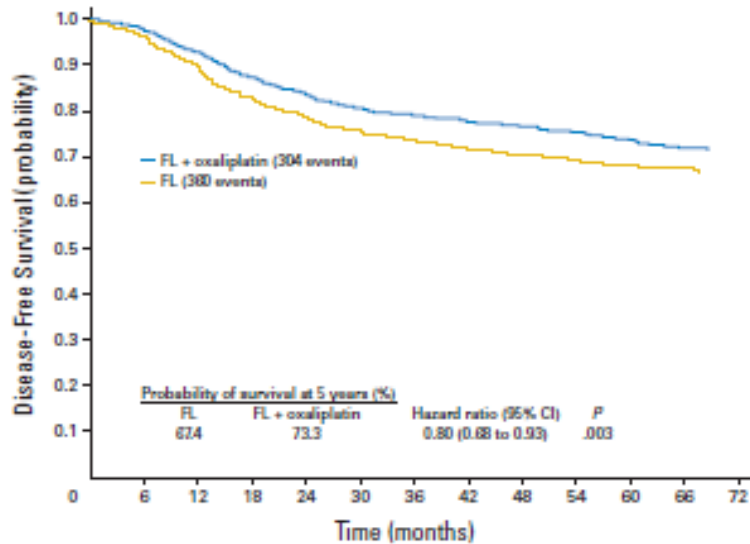
4 settimane

↓

GOM Interaziendale  
ASL-Na-3/Pascale



# Adjuvant Treatment in Stage II/III Colon Cancer: MOSAIC TRIAL



Terapia adiuvante: **FOLFOX6/CAPOX per 6 mesi**

Indicazione: stadio III (N+)

Terapia adiuvante: **FOLFOX6/CAPOX per 6 mesi**

Indicazione: stadio II alto rischio (T4, intervento in urgenza, N valutati <12)

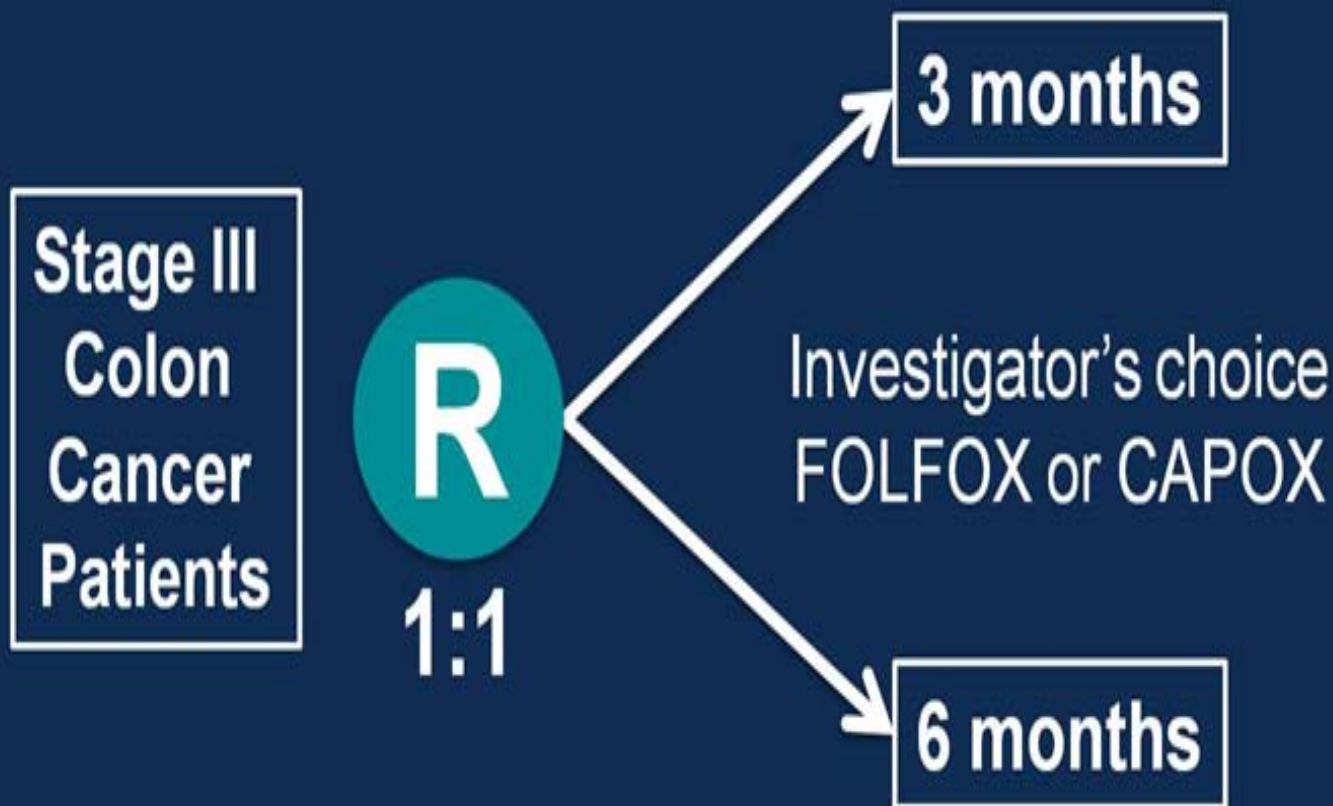
Terapia adiuvante: **Capecitabina per 6 mesi**

Indicazione: casi selezionati di stadio III o II ad alto rischio

# Study Schema



Total planned accrual  $\geq 10,500$



FOLFOX: 5FU/LV + Oxaliplatin

CAPOX: Capecitabine + Oxaliplatin

# IDEA Trials Summary

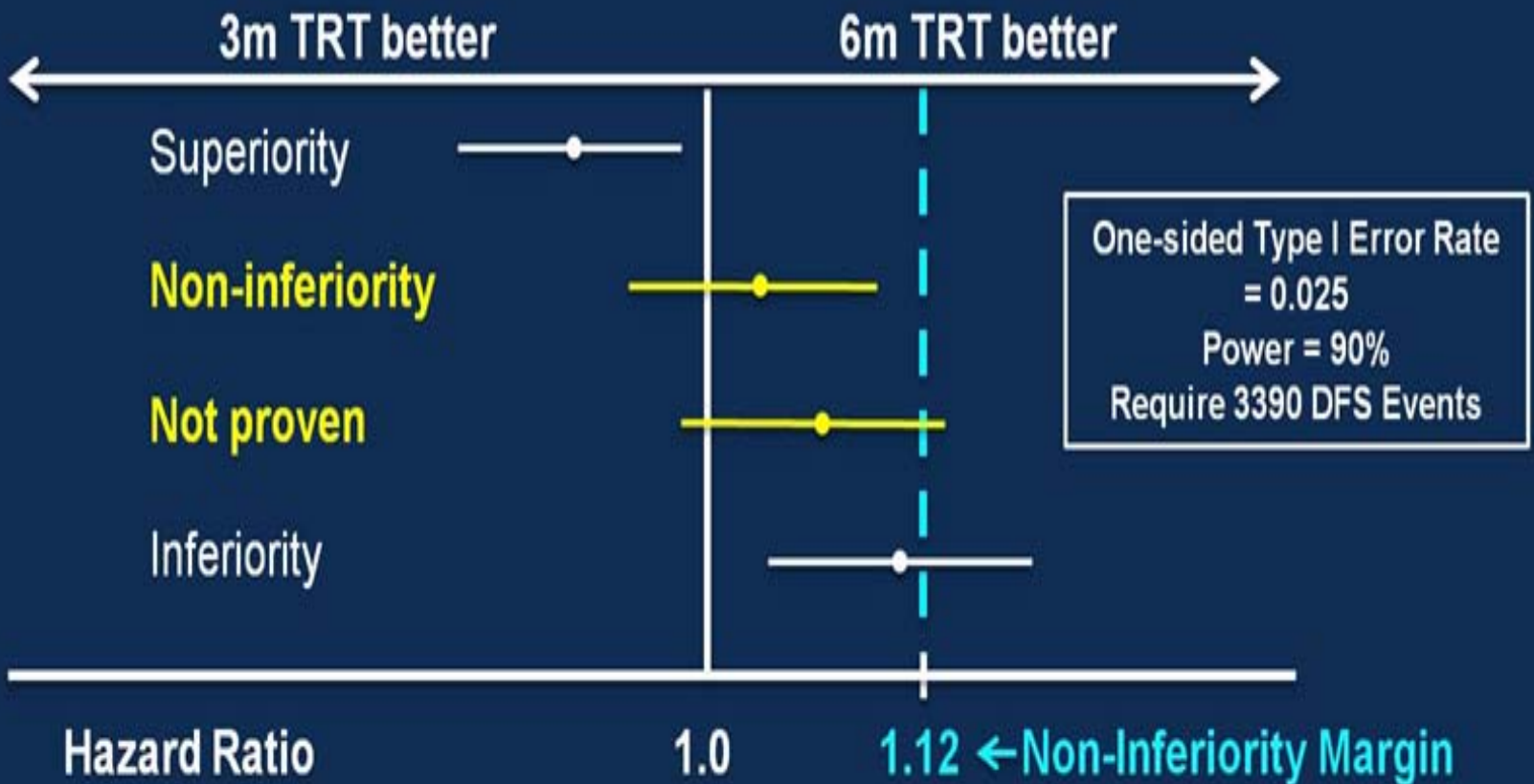
Trial	Regimen(s)	Stage III Colon Cancer Patients*	Enrolling Country
TOSCA	CAPOX or FOLFOX4	2402	Italy
SCOT	CAPOX or mFOLFOX6	3983	UK, Denmark, Spain, Australia, Sweden, New Zealand
IDEA France	CAPOX or mFOLFOX6	2010	France
C80702	mFOLFOX6	2440	US, Canada
HORG	CAPOX or FOLFOX4	708	Greece
ACHIEVE	CAPOX or mFOLFOX6	1291	Japan

\*Only stage III colon cancer patients were included in the pooled primary analysis

# Non-inferiority Hypothesis Testing



## Statistical Conclusions Under Different Scenarios

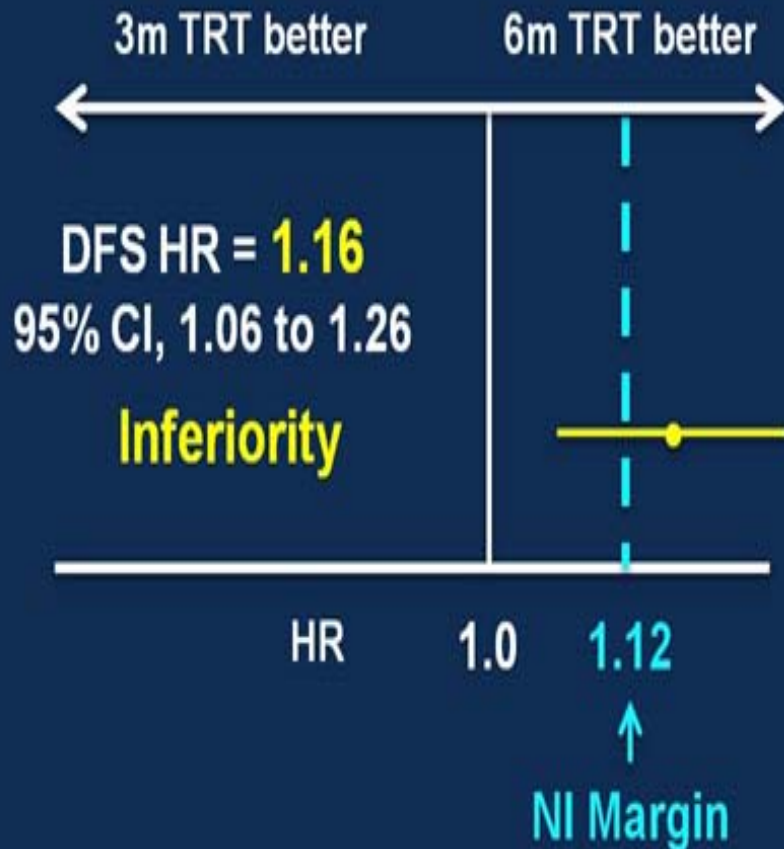




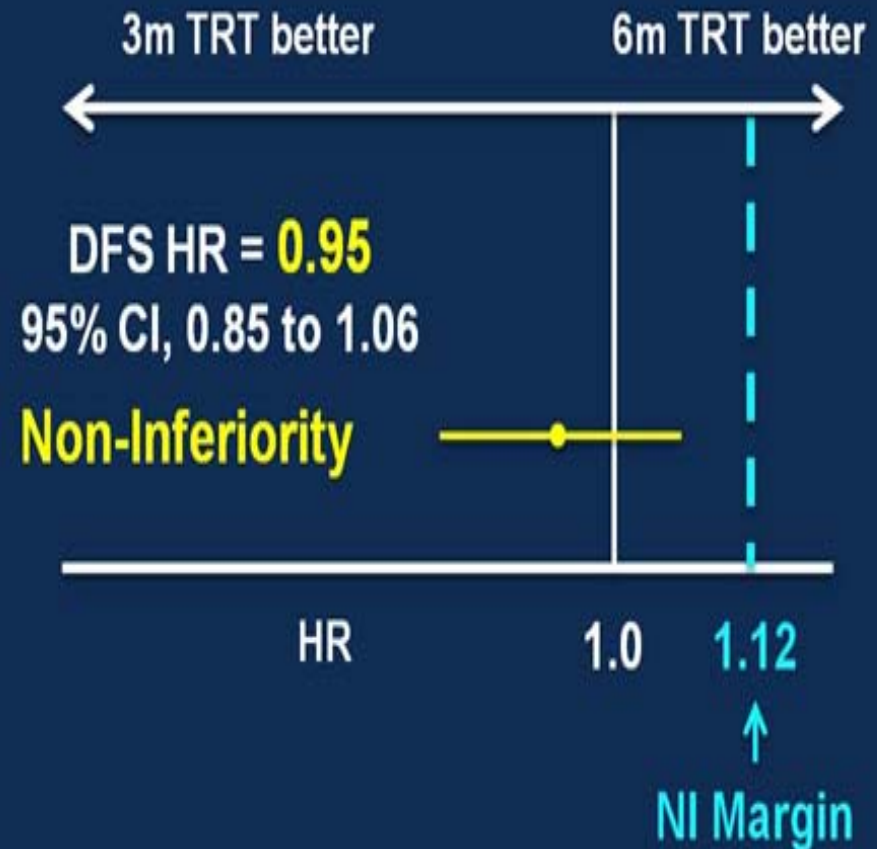
# DFS Comparison by Regimen, cont.



## FOLFOX



## CAPOX



Interaction p-value = 0.0051

# DFS Comparison by Regimen, cont.



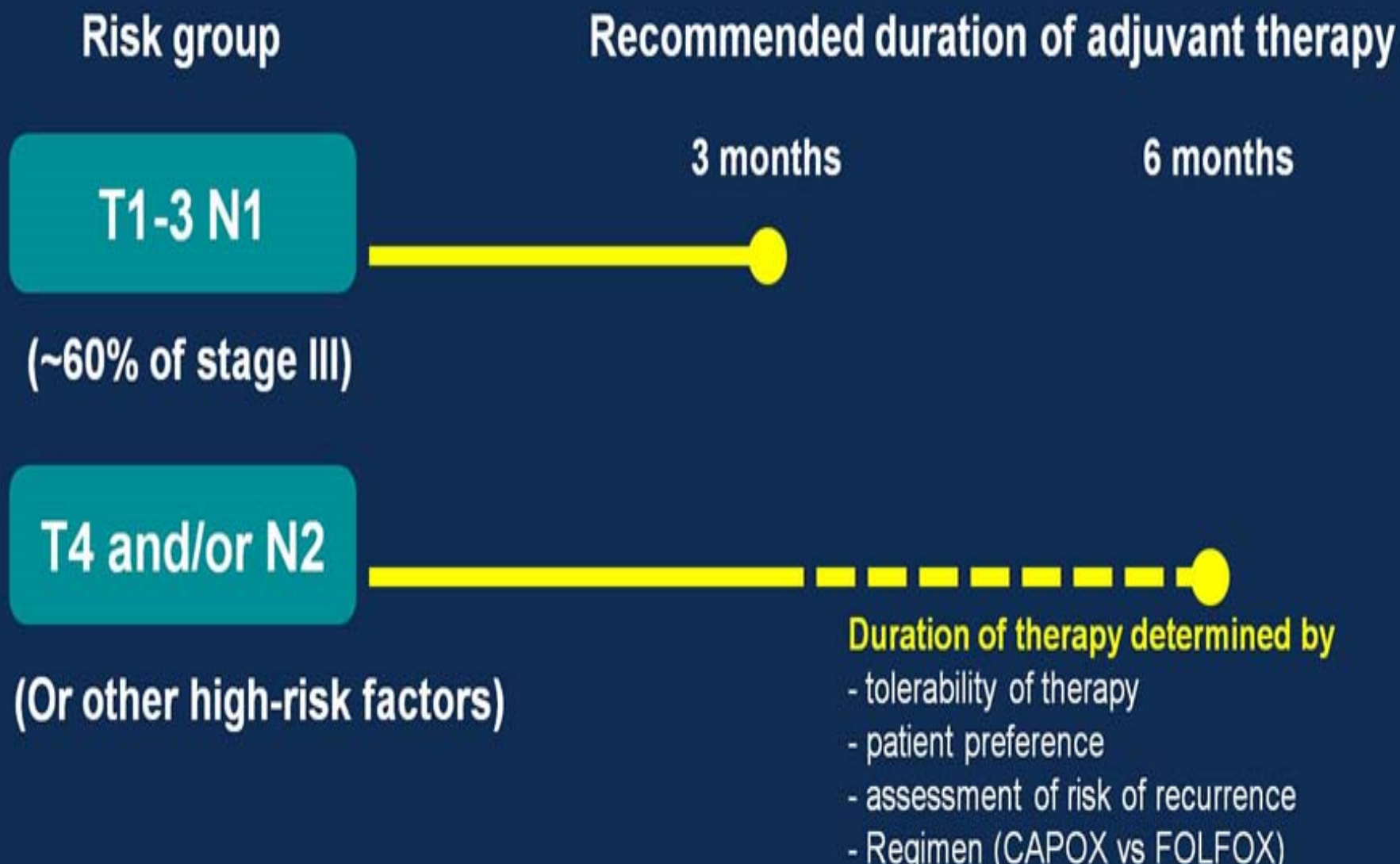
## FOLFOX



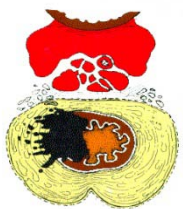
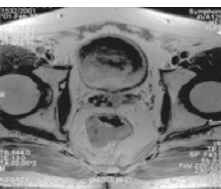
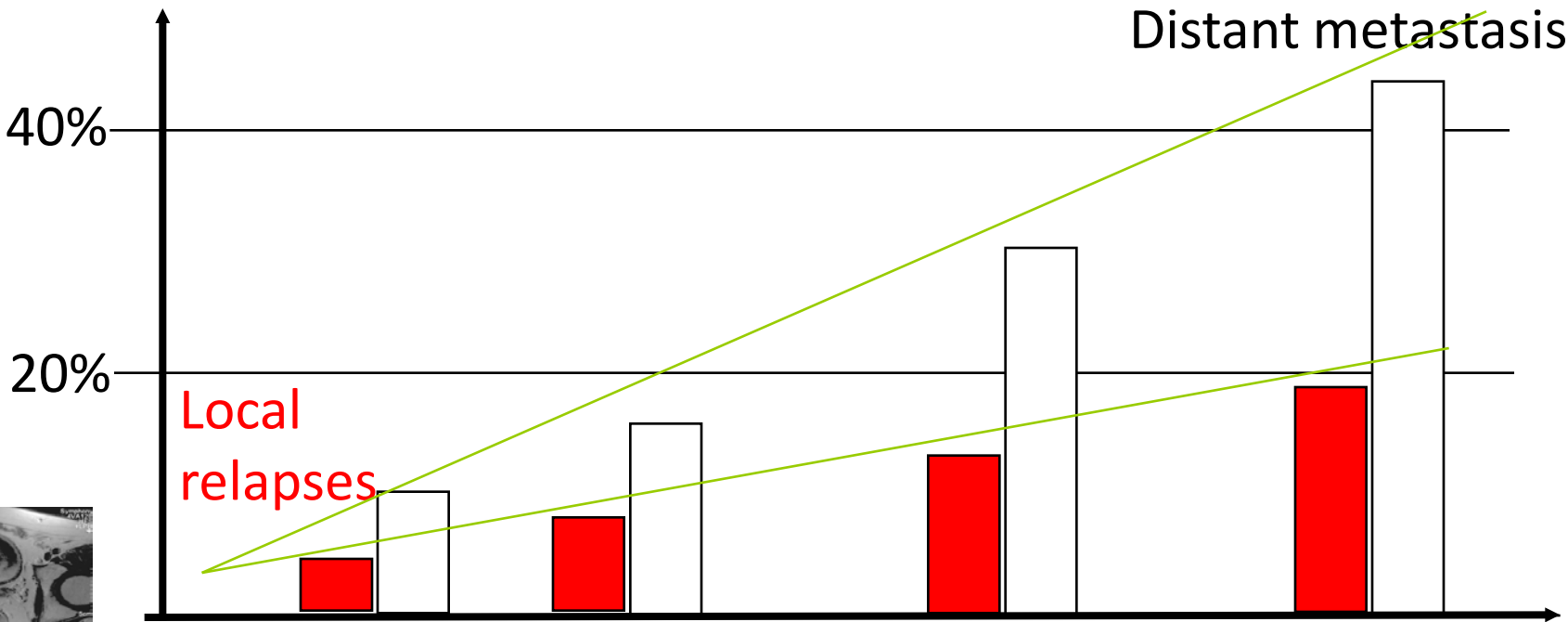
## CAPOX



# IDEA Clinical Consensus: Risk-based approach to adjuvant chemotherapy in stage III colon cancer



# The Tumor Heterogeneity of Rectal Cancer

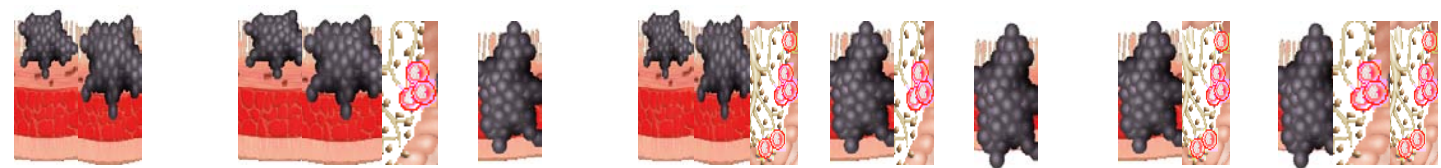


**Low Risk**  
 T1-2/N0

**Intermediate Risk**  
 T1-2/N1; T3/N0

**Moderately High Risk**  
 T1-2/N2; T3/N1; T4/N0

**High Risk**  
 T3/N2; T4/N1-2





# Rectal Cancer Treatment Paradigm

Stage II (T3/T4 N-) and Stage III (T3/T4 N+)

**Chemo-  
Radiotherapy**

**Rectal  
Surgery**

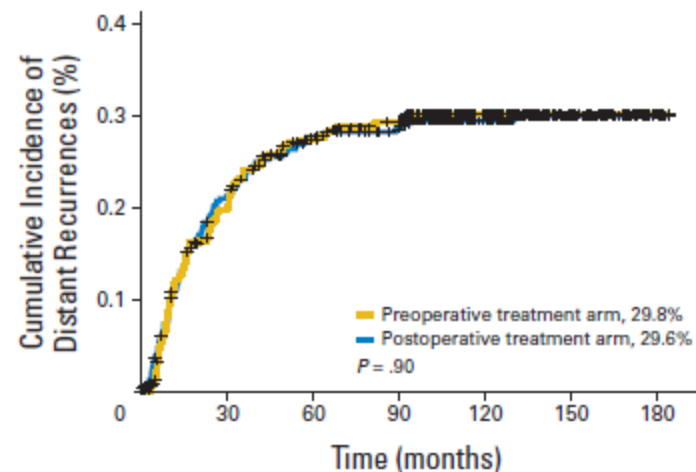
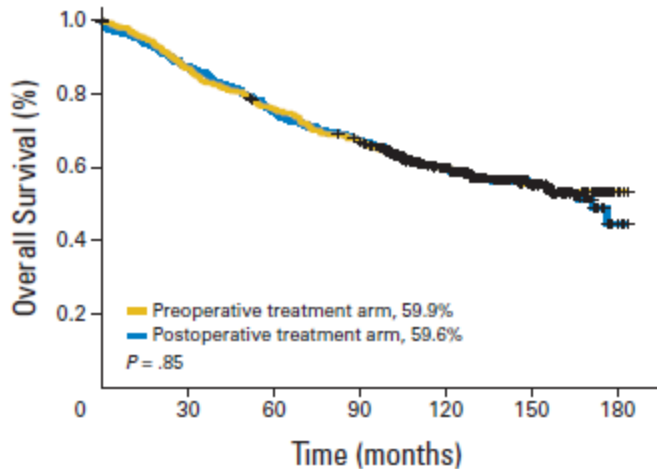
**Adjuvant  
Chemotherapy**

↓  
**5FU**

↓ **Local recurrence rate**

↓ **Short and long-term toxicity**

↑ **Sphincter preservation**



# Total Neoadjuvant Treatment Paradigm

Short-RT



TME



Adjuvant  
Chemotherapy

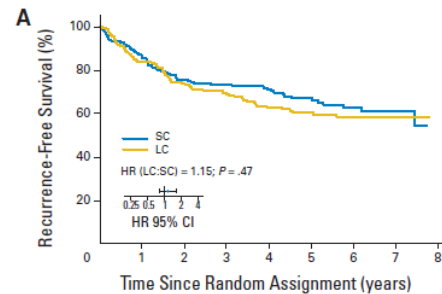
VOLUME 30 • NUMBER 31 • NOVEMBER 1 2012

JOURNAL OF CLINICAL ONCOLOGY

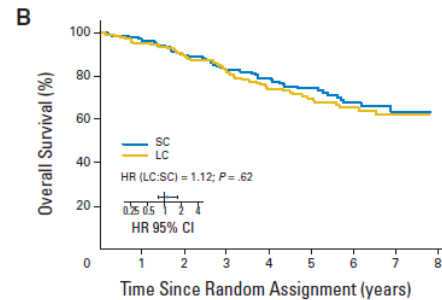
ORIGINAL REPORT

## Randomized Trial of Short-Course Radiotherapy Versus Long-Course Chemoradiation Comparing Rates of Local Recurrence in Patients With T3 Rectal Cancer: Trans-Tasman Radiation Oncology Group Trial 01.04

Samuel Y. Ngan, Bryan Burmeister, Richard J. Fisher, Michael Solomon, David Goldstein, David Joseph, Stephen P. Ackland, David Schache, Bev McClure, Sue-Anne McLachlan, Joseph McKendrick, Trevor Leong, Cris Hartoapeanu, John Zalberg, and John Mackay



No. at risk	0	1	2	3	4	5	6	7	8
SC	162	138	121	115	99	69	43	22	0
LC	161	134	118	109	87	64	46	20	0



No. at risk	0	1	2	3	4	5	6	7	8
SC	162	155	143	129	104	78	46	22	0
LC	161	152	143	130	100	71	50	21	0

**Table 4.** Late RT Toxicities by Worst Grade

Late RT Toxicity Type	SC (n = 155)		LC (n = 158)	
	Grade 3	Grade 4	Grade 3	Grade 4
Skin, pelvic	0	1	0	1
Subcutaneous tissue	0	1	0	1
Small or large intestine	2	3	6	2
Bladder	3	0	2	0
Other*	2	1	3	0
Any toxicity	6	3	10	3

# Adjuvant Chemotherapy in Rectal cancer

- **Muddy waters**



Adiuvante: ypN+; ypCRM; ypT4?

**Trial Registration:**

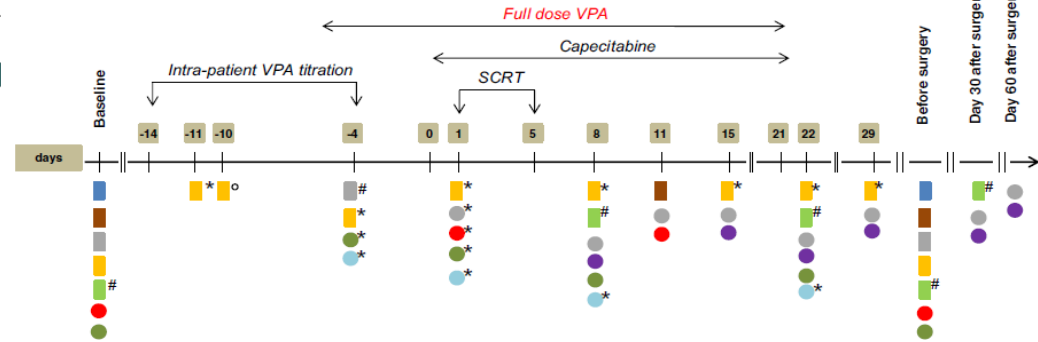
NCT01898104

**STUDY PROTOCOL**

**Open Access**

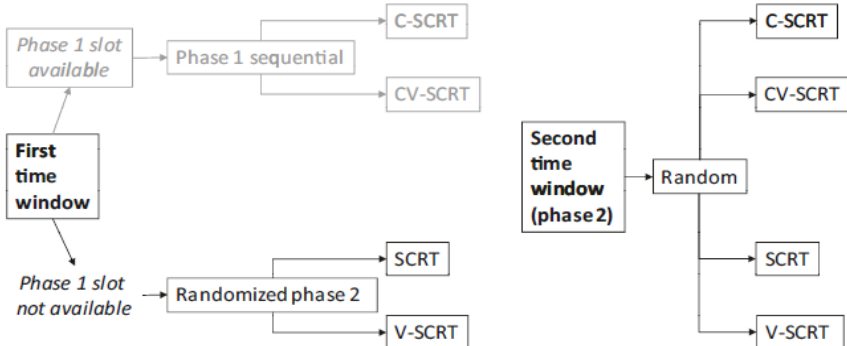
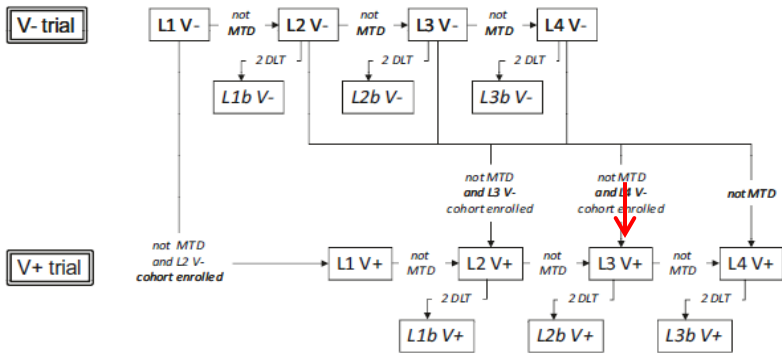
**Phase 1/2 study of valproic acid and short-course radiotherapy plus capecitabine as preoperative treatment in low-moderate risk rectal cancer-V-shoRT-R3 (Valproic acid - short RadioTherapy - rectum 3rd trial)**

Antonio Avallone<sup>1</sup>, Maria Carmela Piccirillo<sup>2</sup>, Paolo Delrio<sup>3</sup>, Biagio Pecori<sup>4</sup>, Elena Di Gennaro<sup>5</sup>, Luigi Aloj<sup>6</sup>, Fabiana Tatangelo<sup>7</sup>, Valentina D'Angelo<sup>8</sup>, Cinzia Granata<sup>9</sup>, Ernesta Cavalcanti<sup>10</sup>, Nicola Maurea<sup>11</sup>, Piera Maiolino<sup>12</sup>, Franco Bianco<sup>13</sup>, Massimo Montano<sup>1</sup>, Lucrezia Silvestro<sup>1</sup>, Manuela Terranova Barberio<sup>5</sup>, Maria Serena Roca<sup>5</sup>, Massimo Di Maio<sup>2</sup>, Pietro Marone<sup>8</sup>, Gerardo Botti<sup>7</sup>, Antonella Petrillo<sup>9</sup>, Gennaro Daniele<sup>2</sup>, Secondo Lastoria<sup>6</sup>, Vincenzo R Iaffaioli<sup>1</sup>, Giovanni Romano<sup>13</sup>, Corradina Caraco<sup>6</sup>, Paolo Muto<sup>4</sup>, Ciro Gallo<sup>14</sup>, Francesco Perrone<sup>2\*</sup> and Alfredo Budillon<sup>5</sup>



- Usual work-up (History and Physical Examination, Blood count, Biochemistry, Toracic/Abdomen CT scan, Pelvic MRI or CT scan, Echocardiography, Endosonography, CEA, Ca 19.9.
- ECG (\*patient treated with VPA only, \* only in patients with QT prolongation seen at ECG on day -11)
- 18FDG-PET
- Rectal biopsies
- Quality of Life
- Blood for PBMC
- Valproate test
- Blood count
- Blood for CEC and CEP count and Biomarkers
- Biochemistry

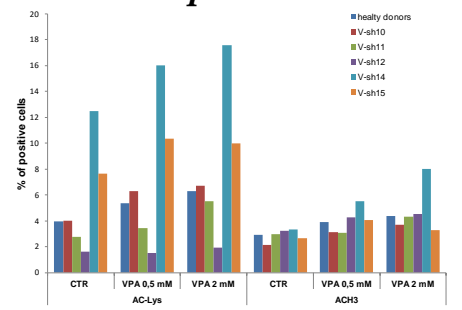
\*patient treated with VPA only,  
 ° only in patients with QT prolongation  
 # patients enrolled in the four-arm phase 2 only



**21 patients enrolled**

Patients Characteristics	Number of patients n = 20 (%)
<b>Gender</b>	
Male/ Female	16 / 5
<b>Age Median (range)</b>	61 (46-69)
<b>ECOG Performance status</b>	
0	21 (100%)
<b>Clinical Stage</b>	
T2N0	2 (7.5)
T2N1	1 (2.5%)
T3N0	9 (45%)
T3N1	9 (45%)

**Acetyl-Lys and AC-H3-histone in patient's PBMC**

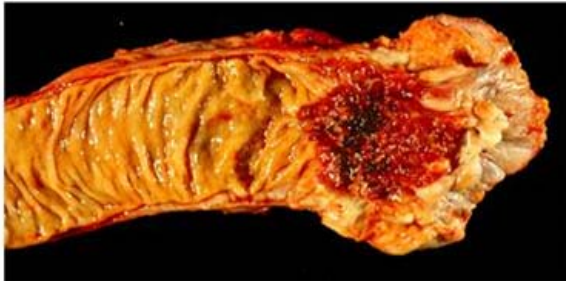



 Ministero della Salute  
 Direzione Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli Enti  
**BANDO 2011-2012 Progetti Ordinari RF**  
 Project Code: RF-2011-02346914

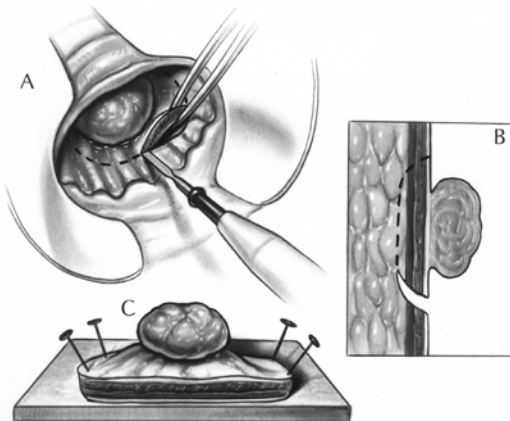
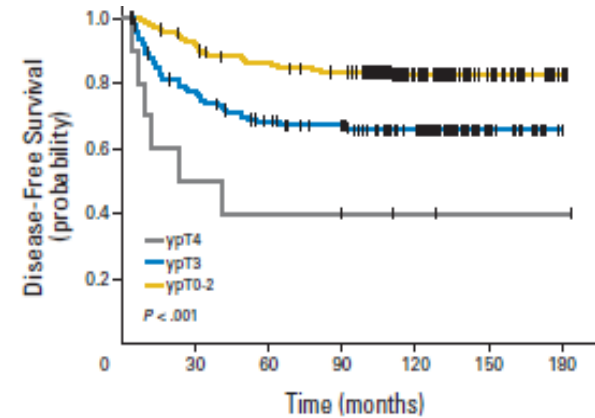
# Selective Use of Surgery



Minimal Response



Complete Response

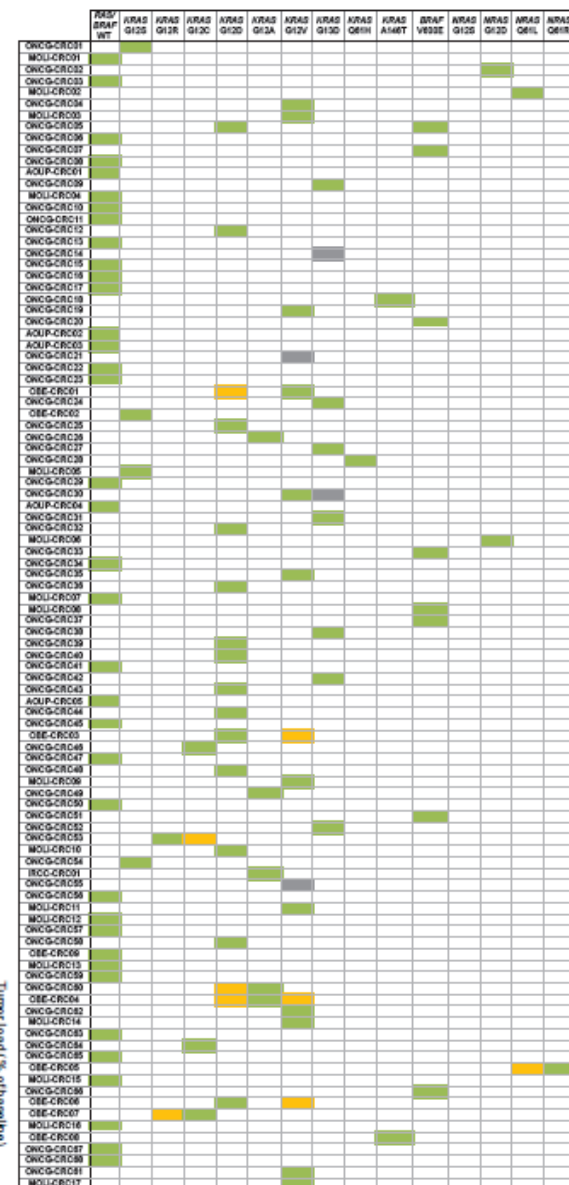
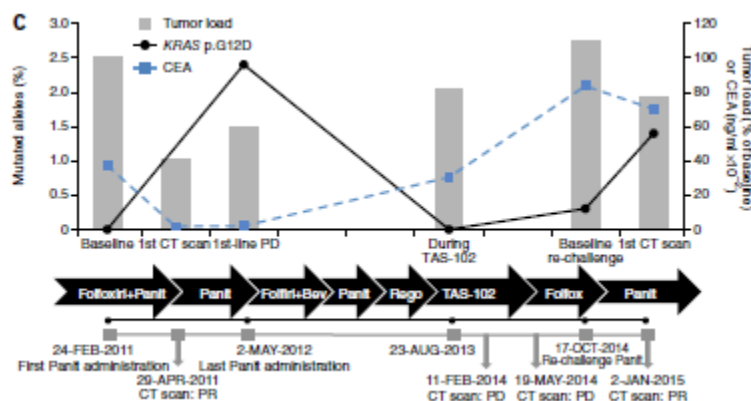
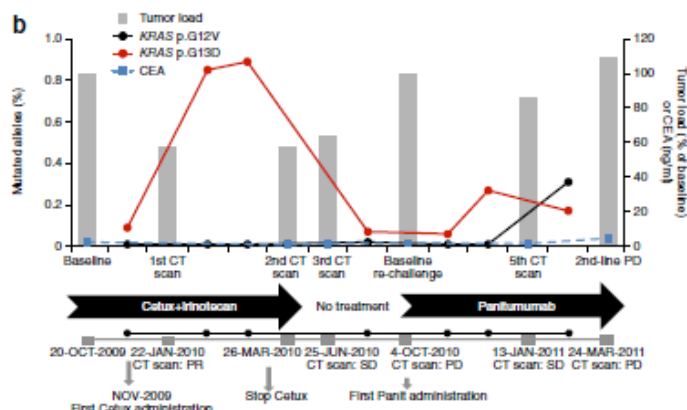


Fokas E. *J Clin Oncol* 2014, 20:1554-62

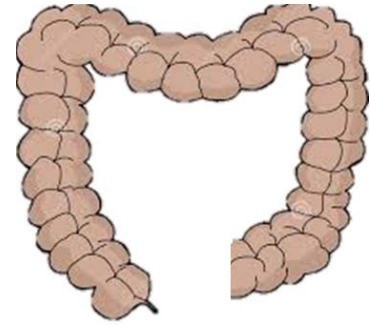
# Clonal evolution and resistance to EGFR blockade in the blood of colorectal cancer patients

Giulia Siravegna<sup>1-3</sup>, Benedetta Mussolin<sup>2</sup>, Michela Buscarino<sup>2</sup>, Giorgio Corti<sup>2</sup>, Andrea Cassingena<sup>4</sup>, Giovanni Crisafulli<sup>2</sup>, Agostino Ponzetti<sup>5</sup>, Chiara Cremonini<sup>6</sup>, Alessio Amatu<sup>4</sup>, Calogero Lauricella<sup>4</sup>, Simona Lamba<sup>2</sup>, Sebastijan Hobor<sup>2,10</sup>, Antonio Avallone<sup>7</sup>, Emanuele Valtorta<sup>4</sup>, Giuseppe Rospo<sup>2</sup>, Enzo Medico<sup>1-2</sup>, Valentina Motta<sup>4</sup>, Carlotta Antoniotti<sup>6</sup>, Fabiana Tatangelo<sup>7</sup>, Beatriz Bellosillo<sup>8</sup>, Silvio Veronese<sup>4</sup>, Alfredo Budillon<sup>7</sup>, Clara Montagut<sup>8</sup>, Patrizia Racca<sup>5</sup>, Silvia Marsoni<sup>2</sup>, Alfredo Falcone<sup>6</sup>, Ryan B Corcoran<sup>9</sup>, Federica Di Nicolantonio<sup>1-2</sup>, Fotios Loupakis<sup>6</sup>, Salvatore Siena<sup>4</sup>, Andrea Sartore-Bianchi<sup>4</sup> & Alberto Bardelli<sup>1-2</sup>

published online 1 June 2015;



# Follow up nel Tumore del Colon e del Retto Stadi II e III



**COLON**

Colonscopia

(q 3-5 anni)

TAC t.b. con mdc

(q 6 mesi x 5 anni)

**RETTO**



Retto-Colonscopia

(q 3-5 anni)

TAC t.b. con mdc

(q 6 mesi x 5 anni)

RMN pelvi

(q 6 mesi x 5 anni)



**“Some things require a revolution, rather than an evolution, in thinking. The problem is we can be locked into an orthodoxy of thinking that prevents us from thinking in novel ways”.**

**Gates Foundation**

**Thank You  
for your attention**

