

Opportunities and Challenges for Neoadjuvant Trials in GI Cancers

Alan Venook, MD
UC San Francisco

What is a biomarker?

- “Any measurable diagnostic indicator that is used to assess the risk or presence of disease”

Gutman and Kessler. *Nat Rev Cancer*. 2006;6(7).

- AKA “*in vitro* diagnostic”

www.fda.gov

- Includes tests for:
 - Future risk
 - Screening
 - Diagnosis
 - Prognosis
 - Staging
 - Monitoring response
 - Optimizing treatment outcomes

GI “Neoadjuvant” Trials

Accruing

- N1048
 - Selective XRT in rectal cancer
- C80303
 - PET-directed combined modality in esophageal

Completed / successor planned

- A021101
 - Borderline resectable pancreas pilot

GI “Neoadjuvant” Trials

Completed

- C80405
 - Chemo /biologic metastatic CRC

Pending

- A021302
 - PET-directed chemotherapy in gastric cancer

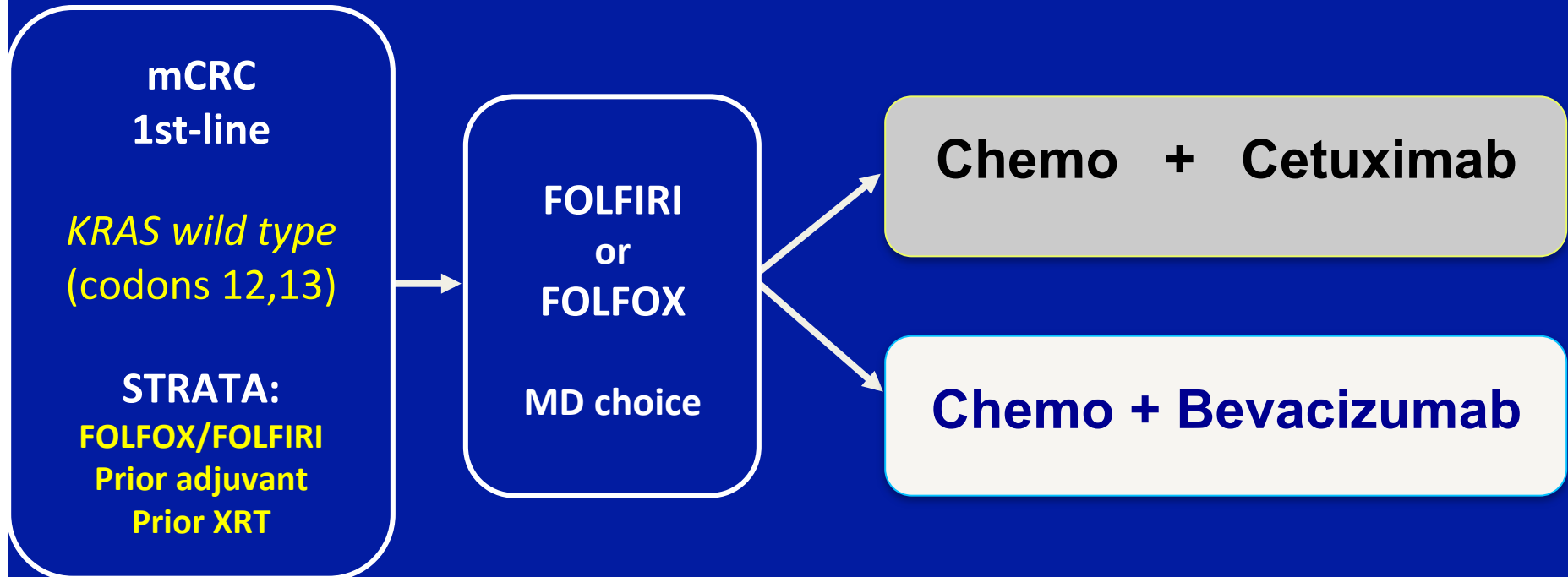
Opportunities: GI Neoadjuvant Setting

- Standard approach
 - Esophageal
 - Gastric
 - Rectal
- Large volume disease
- Access to tissue
 - Liver commonest site of metastases

Opportunities: CRC Neoadjuvant Setting

- CRC Liver metastases amenable to curative approach
- 30% of patients with synchronous disease
- Ready access to tissue

CALGB/SWOG 80405: FINAL DESIGN



N = 1140

1° Endpoint: Overall Survival



CALGB/SWOG 80405:

Patient Characteristics

	ARM A CHEMO + BEV N=559 (%)	ARM B CHEMO + CETUX N=578 (%)	TOTAL N=1137 (%)
Age median (range)	59 (21-85)	59 (20-89)	59 (20-89)
Male	348 (62.3)	349 (60.4)	697 (61.3)
Primary in place	157 (28)	154 (27)	311 (28)
Palliative Intent	465 (86.4)	458 (82.5)	923 (84.4)
FOLFOX / FOLFIRI (%)	73 / 27	74 / 26	73 / 27

CALGB/SWOG 80405: Baseline Characteristics Resected Patients

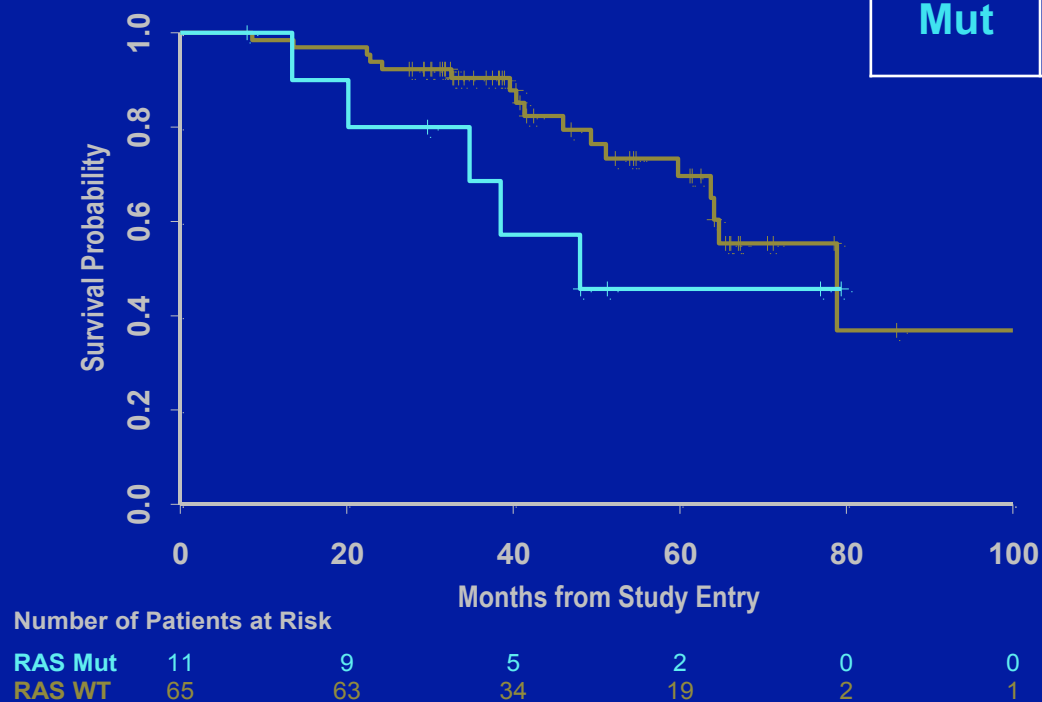
Characteristic	Kras WT codons 12/13 n=1137		Resected Pts n=180	
	Chemo + Bev n=559	Chemo + Cetux n=578	Chemo + Bev n=75	Chemo + Cetux n=105
Age, years				
Median (range)	59 (21–85)	59 (20–89)	55 (24–82)	55 (21–79)
Male, %	62.3	60.4	64.0	60.0
Non-Caucasian, %			9.3	20.0
FOLFOX, %*			77	81
Prior Radiation, %*			8.0	6.7
Prior Adjuvant Chemotherapy, %*			6.7	9.5
Palliative intent, %	86.4	82.5	62.7	60.0
Primary in place, %	28	27	30	20
Liver metastases only, %	29.3	39.8	53.3	50.0

**Achieve NED:
132 /180**

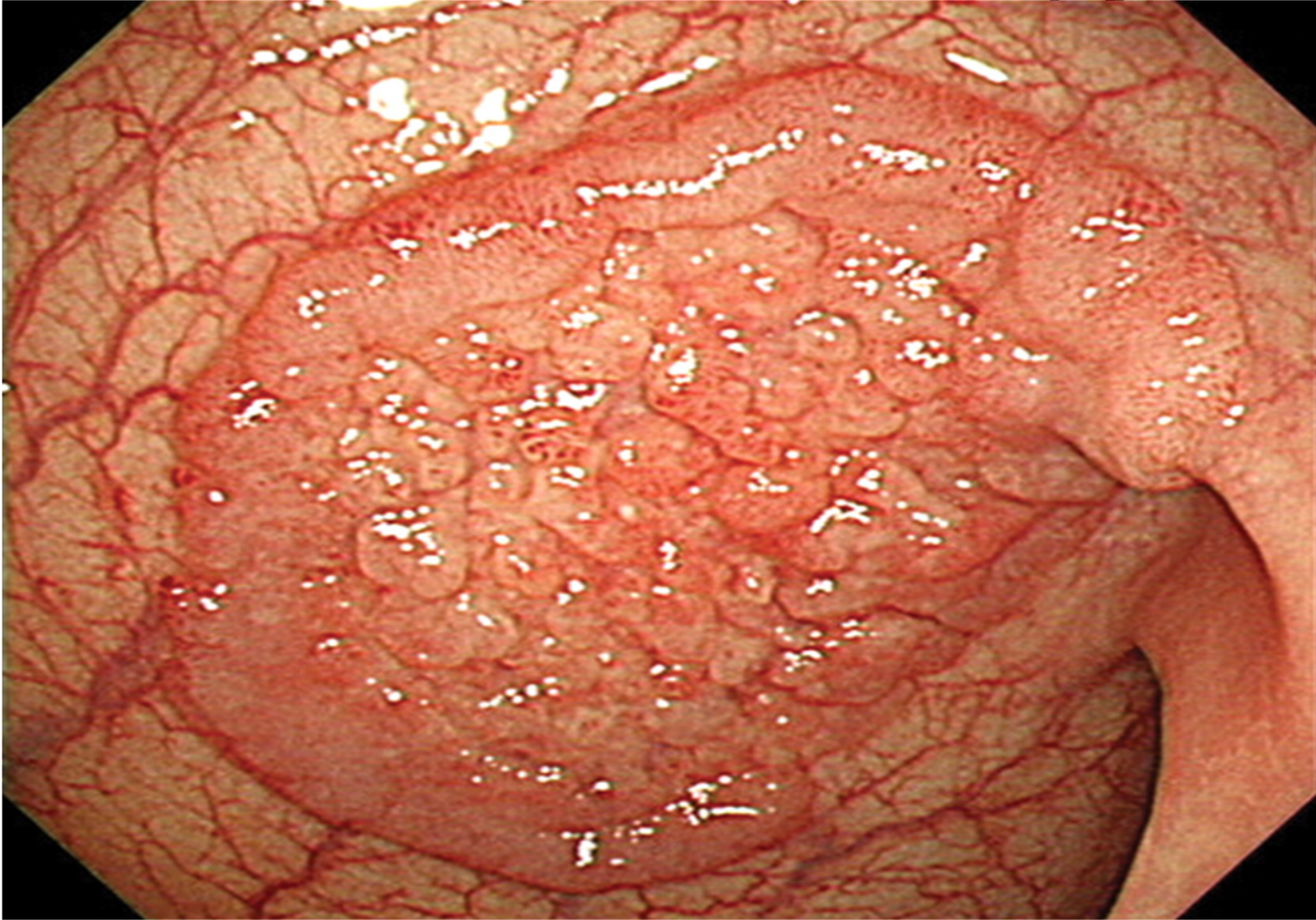
*Stratification Factor

CALGB/SWOG 80405: OS from Randomization (*NED Post-Surgery*)

RAS	N (Events)	Median (95% CI)	HR (95% CI)	p
WT	65 (17)	78.8 (63 – NR)	0.52 (0.2-1.4)	0.2
Mut	11 (5)	47.9 (13.4 - NR)		



Endoscopy



Challenges: GI Neoadjuvant Setting

- Coordination
- Cost
- Invasive
- Heterogeneity of tumor
- Delay treatment

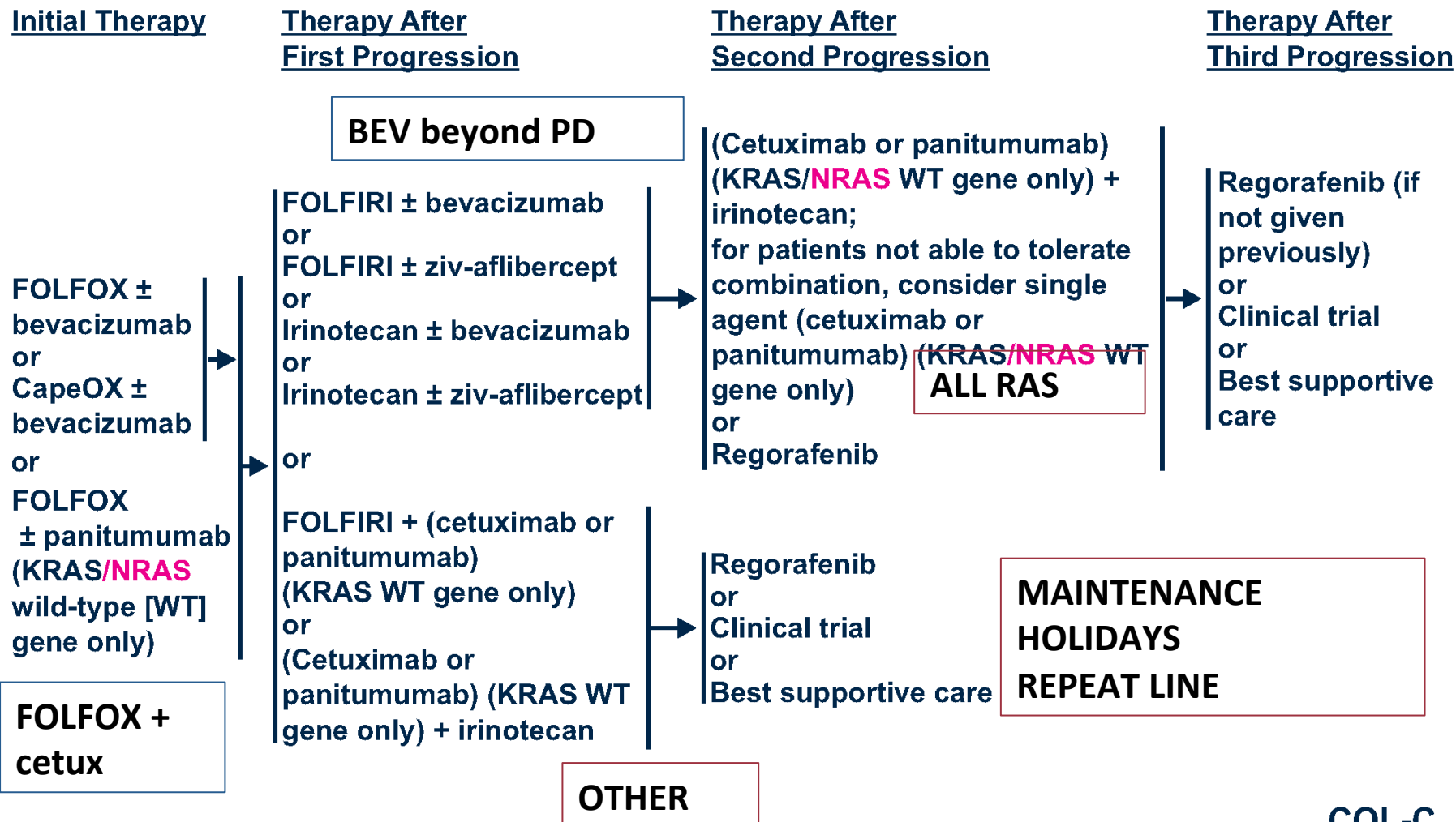


National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 3.2014 Colon Cancer

CONTINUUM OF CARE - CHEMOTHERAPY FOR ADVANCED OR METASTATIC DISEASE

PATIENT APPROPRIATE FOR INTENSIVE THERAPY



Challenges: GI Neoadjuvant Setting

- Coordination
- Cost
- Invasive
- Heterogeneity of tumor
- Delay treatment
- Risk

General Schema: *Matched Patient PDX-Directed Clinical Trial*

