

# *Biologic and Clinical Factors in the Selection and Sequencing of Systemic Therapy for Patients with Metastatic CRC (mCRC)*

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*The Ruesch Center for the Cure of Gastrointestinal Cancers*

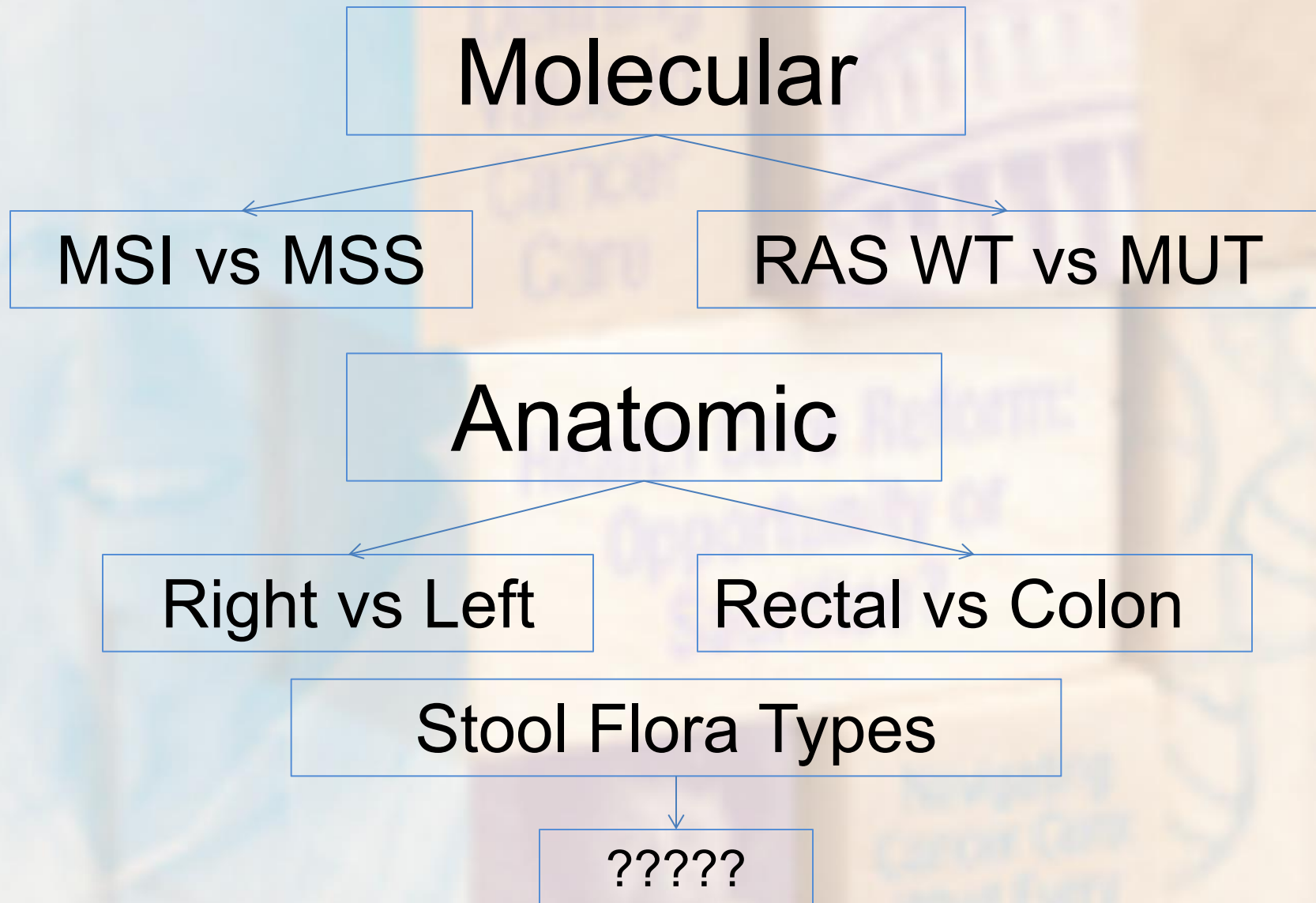


AT GEORGETOWN LOMBARDI COMPREHENSIVE CANCER CENTER

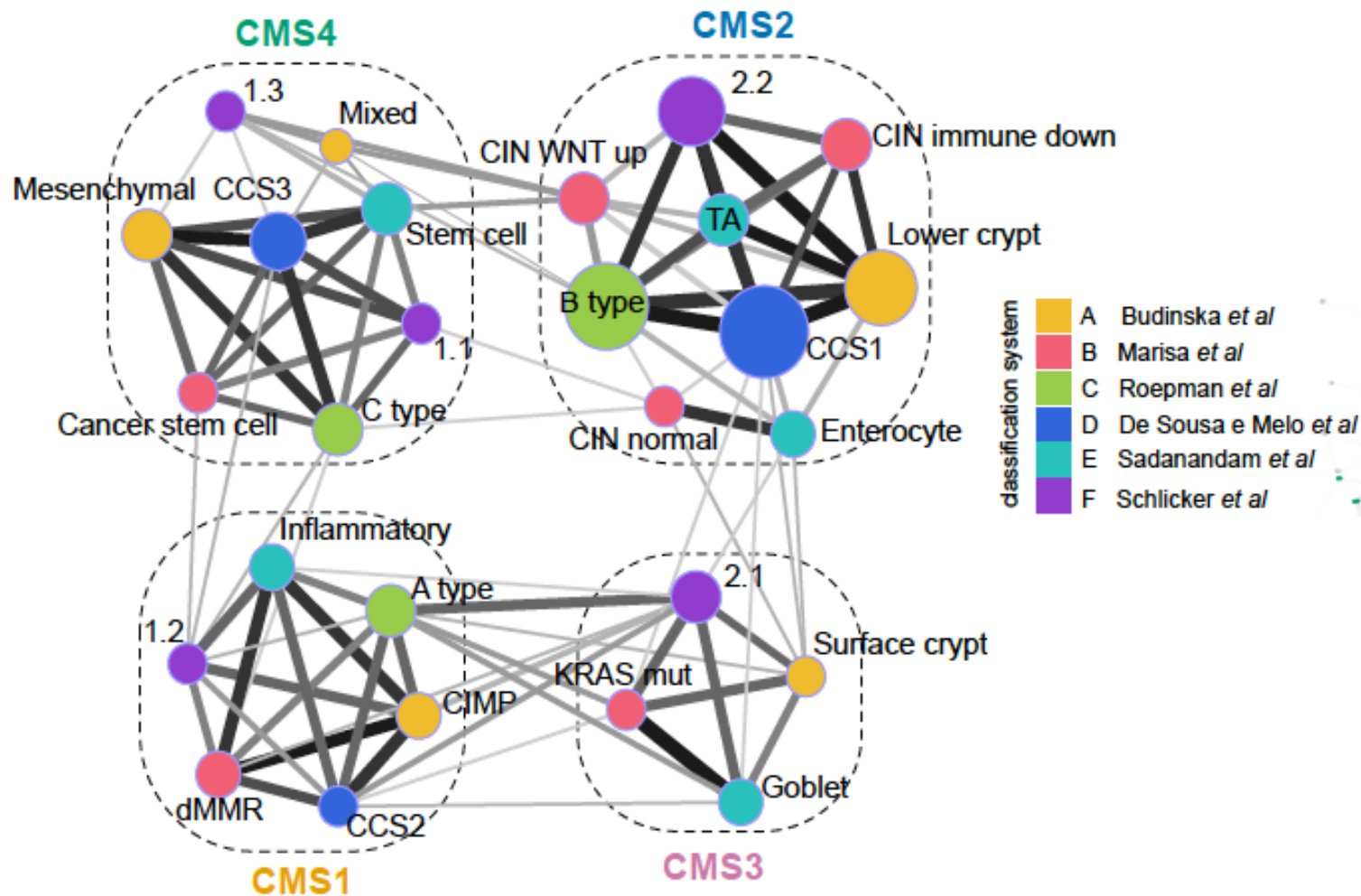
# Disclosures

<b>Advisory Committee, Consulting Agreements and Speakers Bureau</b>	Amgen Inc, Bayer HealthCare Pharmaceuticals, Celgene Corporation, Genentech BioOncology
<b>Contracted Research</b>	Amgen Inc, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, EMD Serono Inc, Genentech BioOncology, Lilly

# Colon Cancer: More than One Disease

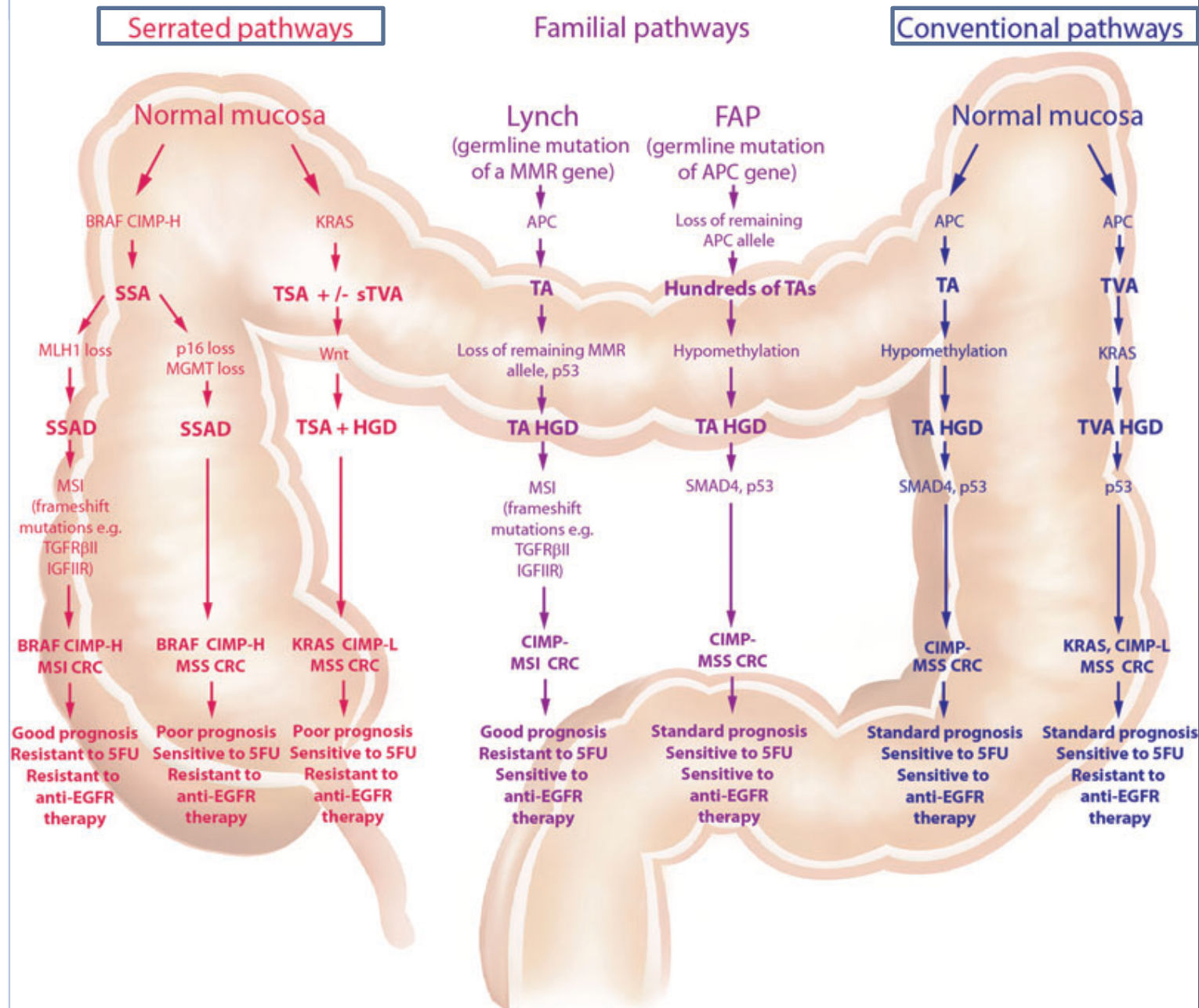


# The Colorectal Cancer Consortium Consensus for Molecular Subtypes (n >4500)





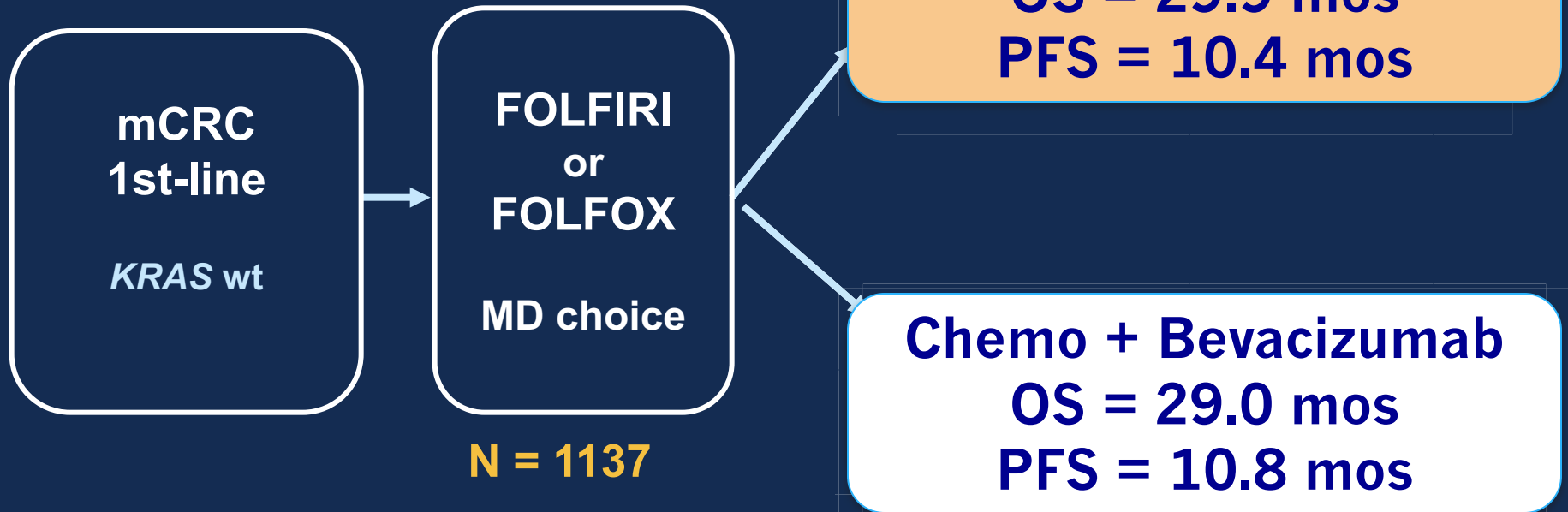
## PUTATIVE MOLECULAR PATHWAYS TO COLORECTAL CARCINOMA



# CALGB/SWOG 80405

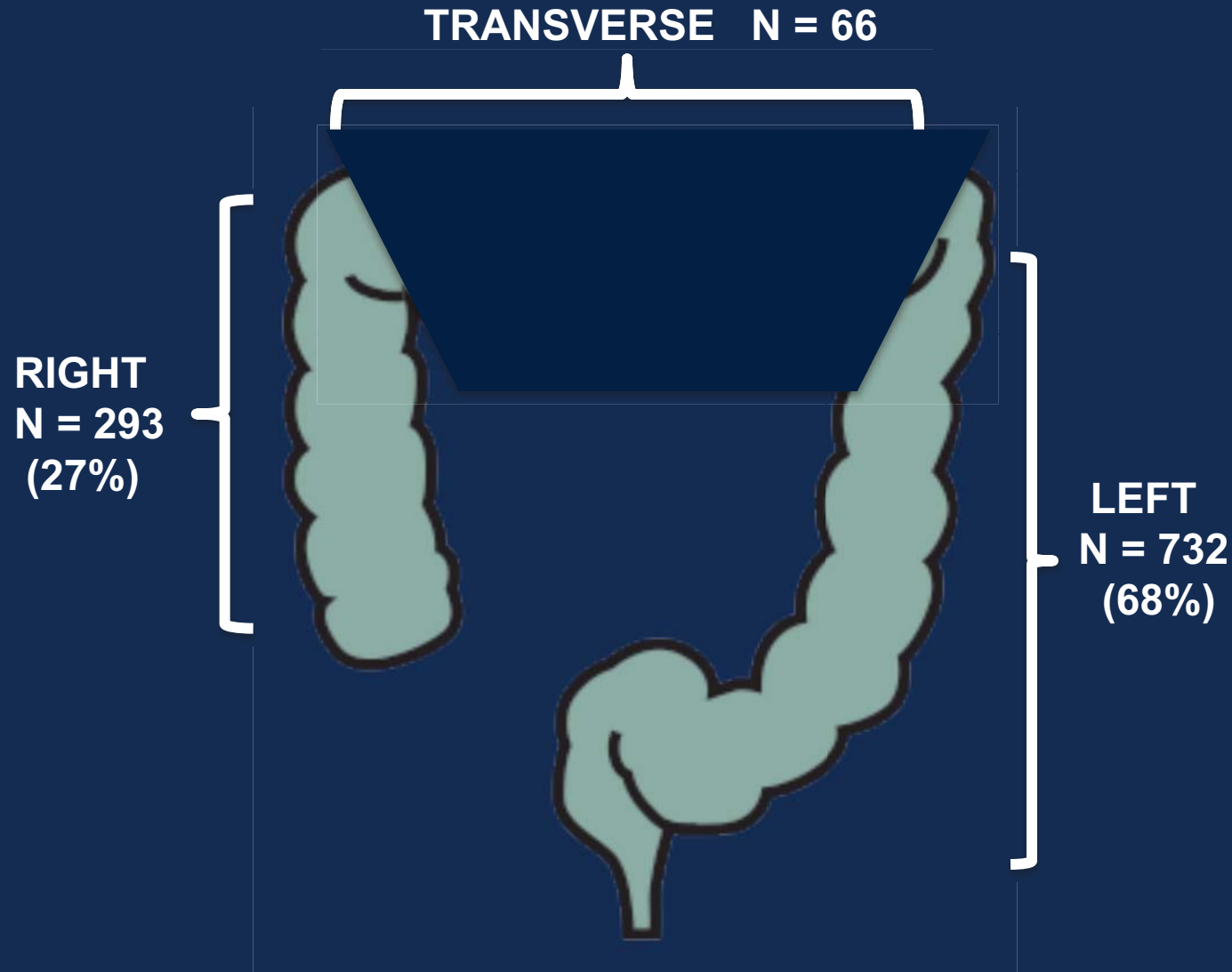
Amended June, 2008

Reported June, 2014

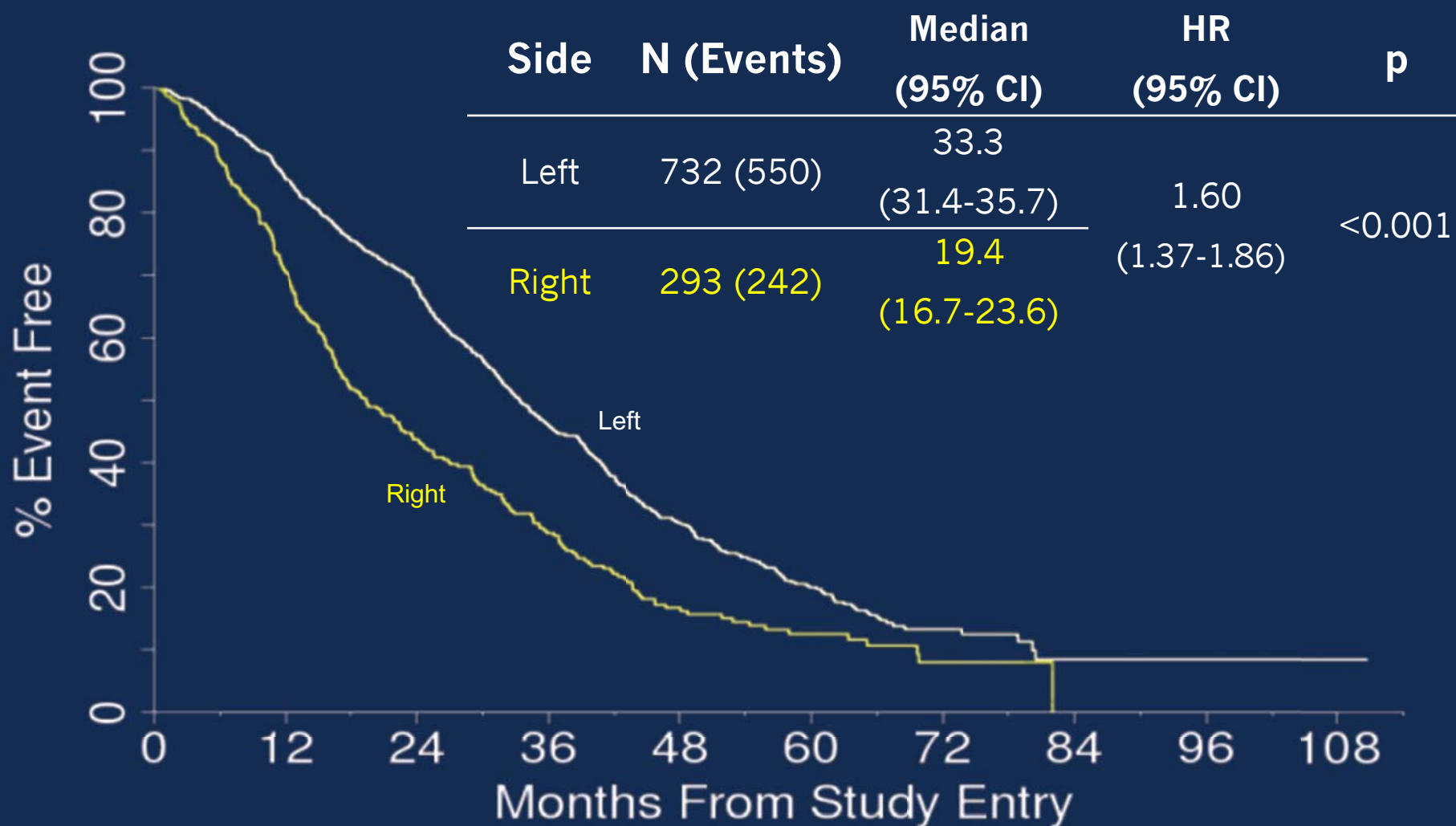


**Conclusion: No difference in 1st line**

# 80405: Side of Primary Tumors

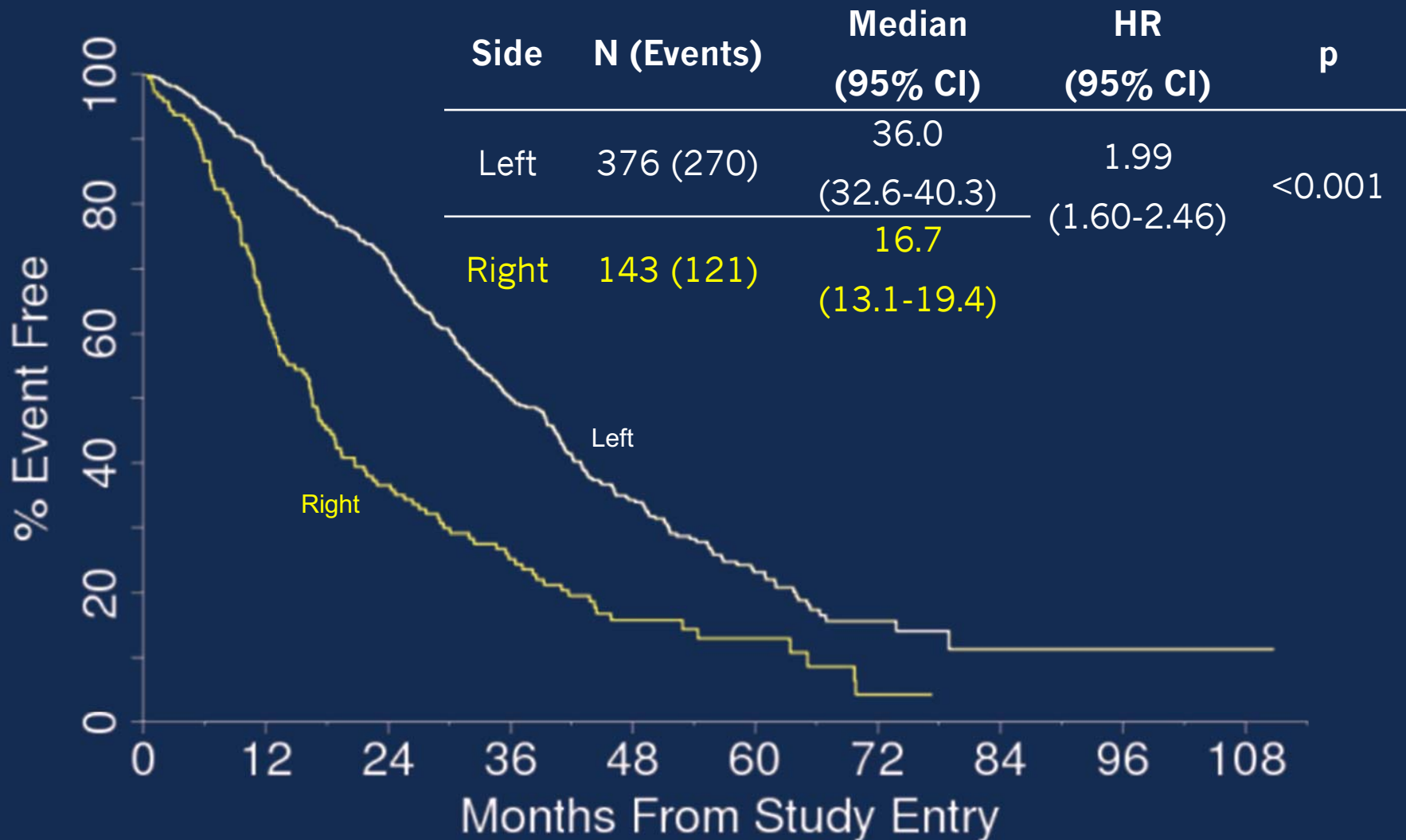


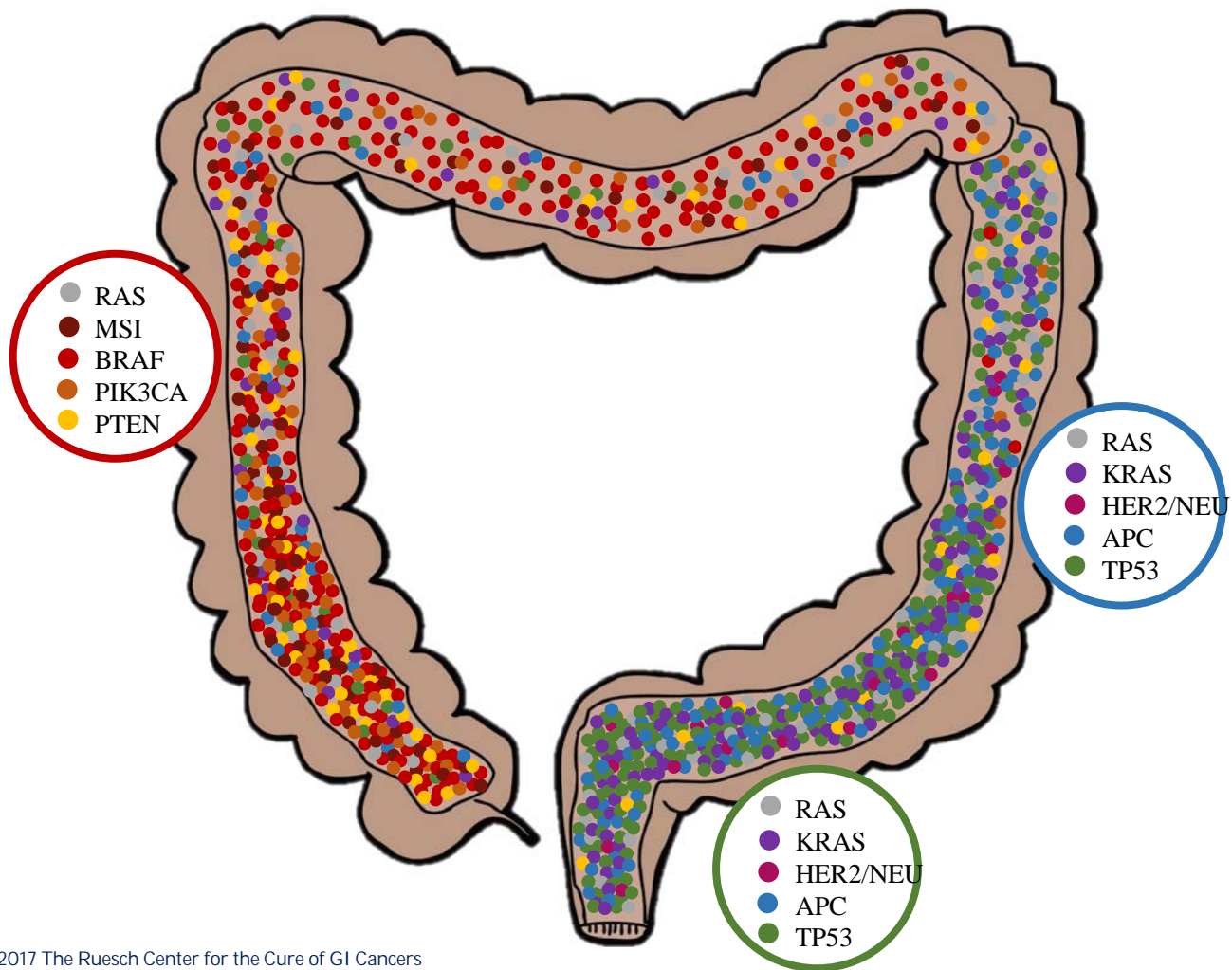
# 80405: Overall Survival by Sidedness





# 80405: OS by Sidedness (Cetuximab)

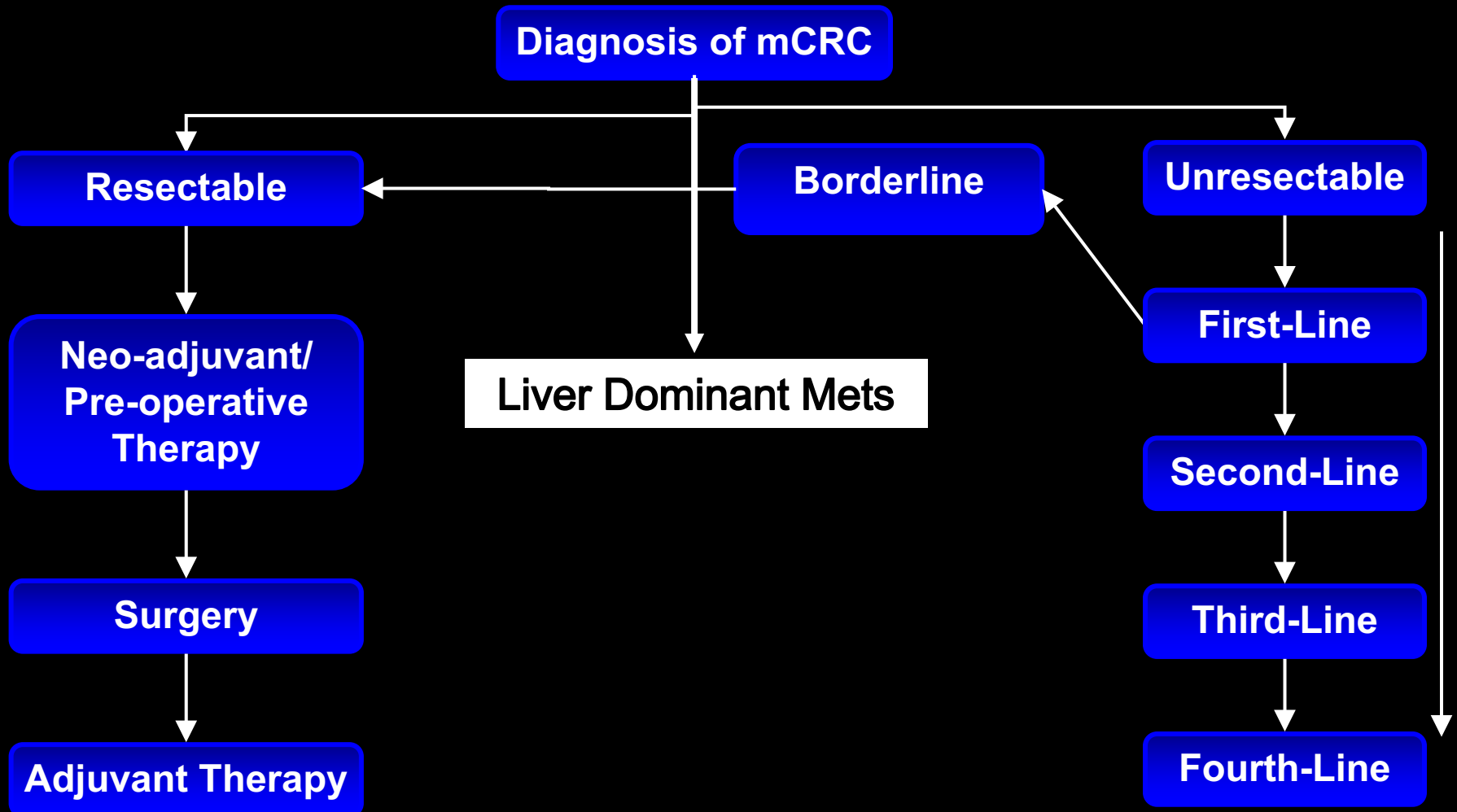




# NCCN Nov 2016

- “There is a preponderance of data to suggest lack of activity of cetuximab and panitumumab in initial therapy of patients whose primary tumors originated on the right side of the colon”

# Management of mCRC: An Evolving Treatment Algorithm



# Basic Principles

	Adjuvant	Metastatic
Strategy	Curative	Palliative
Target	Mesenchymal Cells	Epithelial Cells
Drugs	5FU/Capecitabine Oxaliplatin	5FU/Capecitabine Oxaliplatin Irinotecan VEGF EGFR TAS-102 Regorafenib
Duration	No more than 6 months	Treat to progression Maintenance therapy

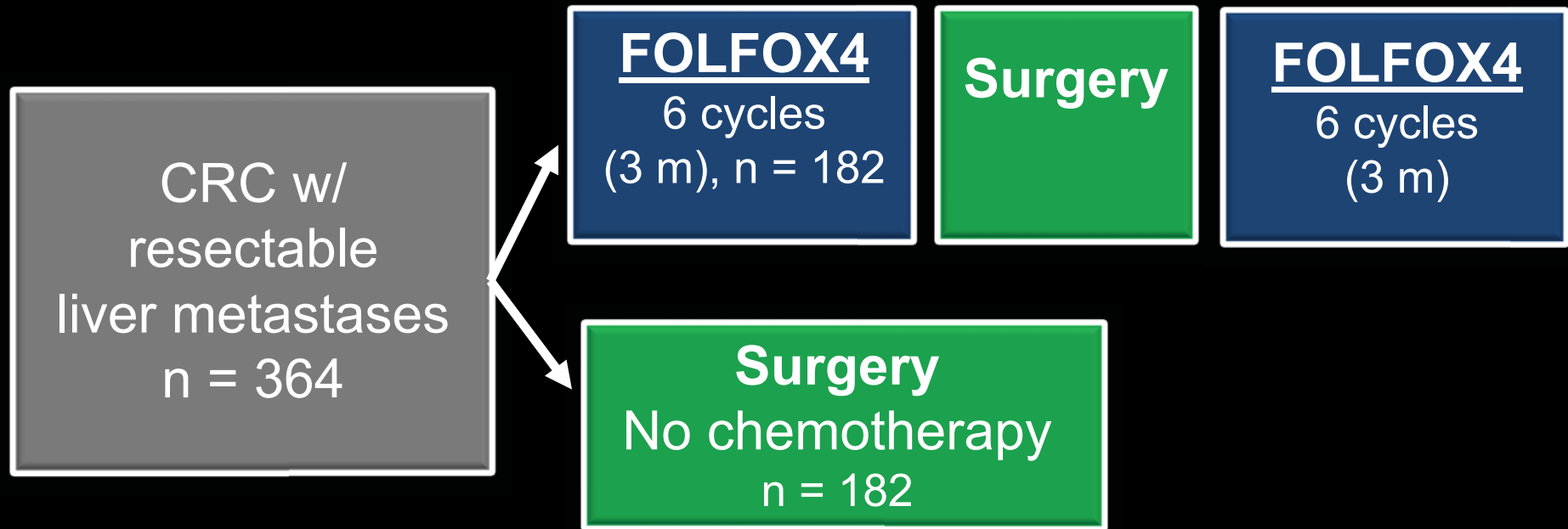


# Rationale for Neoadjuvant Therapy

- Assess biology / chemo-responsiveness of disease
  - Treat micro-metastatic disease (which chemotherapy can cure) as soon as possible
  - *Potentially decrease surgical complications by making surgery more feasible*
- **Potential downsides:** hepatotoxicity; complications; complete response can hide metastatic sites; fear of “lost opportunity” if progression; etc

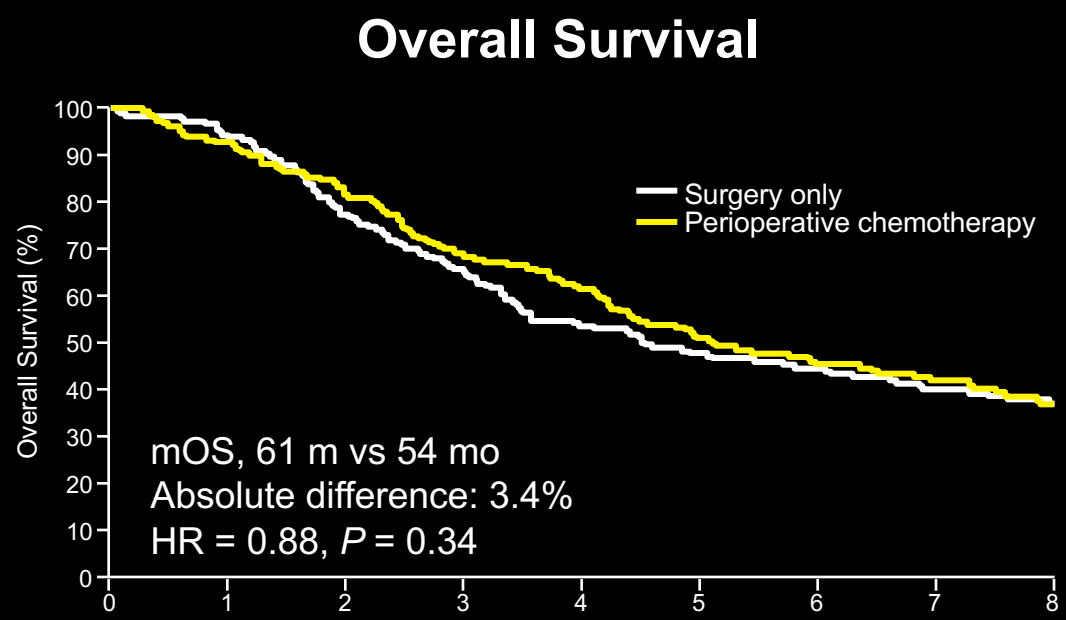
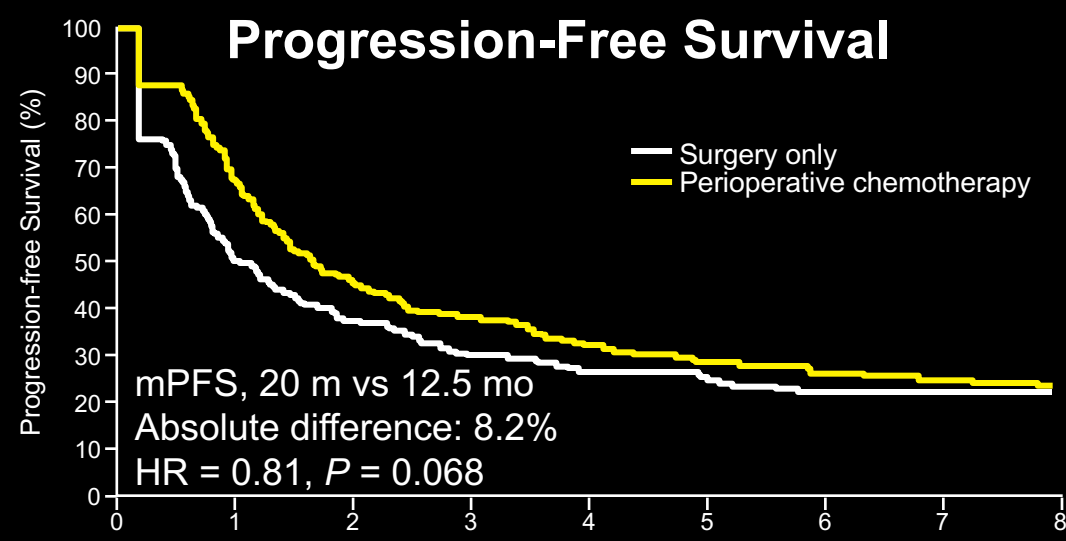
# EORTC-40983, Peri-Operative FOLFOX for Hepatic Metastases

(For patients with initially resectable disease)



**Important toxicity data:** only small increase in peri-operative complications with chemo, although only 63% in chemo group received it post-operatively

# EORTC-40983: Peri-Op FOLFOX for Liver Mets



Nordlinger B. *Lancet Oncology*. 2013;14:1208-1215.

# New EPOC Study: Chemotherapy $\pm$ Cetuximab Before and After Liver Resection in *KRAS* WT CRC

Operable (including  
borderline operable)  
colorectal liver  
metastases

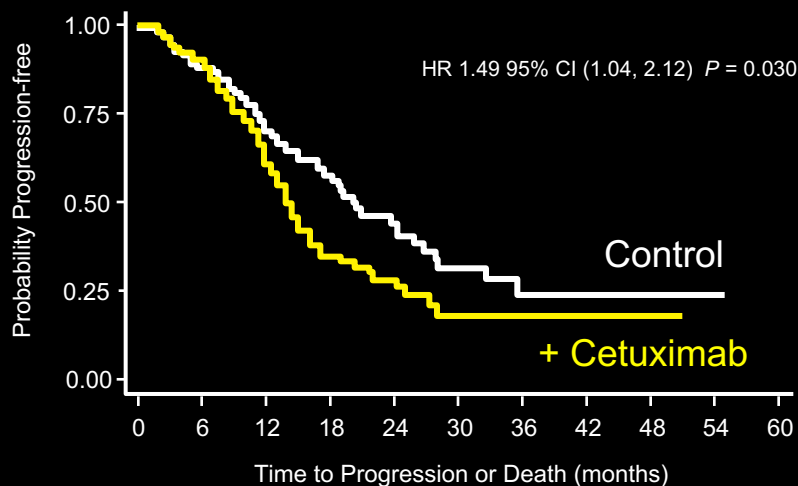
R

CT  $\rightarrow$  Liver Resection  $\rightarrow$  Chemotherapy

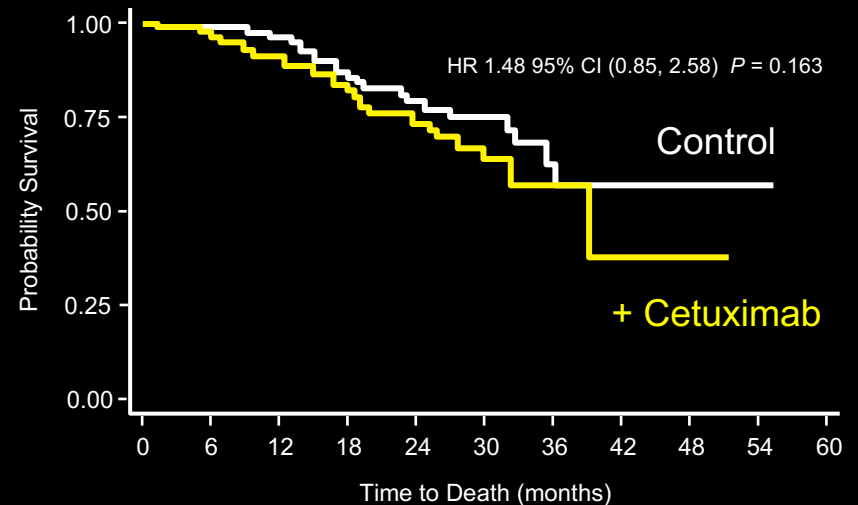
CT + Cetuximab  $\rightarrow$  Liver Resection  $\rightarrow$   
CT + Cetuximab

- Cetuximab + CT  $\uparrow$  the pre-operative RR

Progression-Free Survival



Overall Survival



# “Facts” and Observations

- FOLFOX did not have an “adjuvant” effect
- FOLFIRINOX + Bevacizumab has the highest RR
- EGFR combo has high response and resection rates but a negative trial
  - Have to know RAS/BRAF



# Unknowns

- Role of biologics
- Duration of treatment pre- and post-op
- Impact of systemic treatment in general

