Colorectal Cancer: What's New?

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Objectives

- Describe the current landscape of colorectal cancer in Puerto Rico
- Describe recent updates in treatment paradigms for metastatic colorectal cancer
- Describe the *next generation* molecular landscape of colorectal cancer and future directions

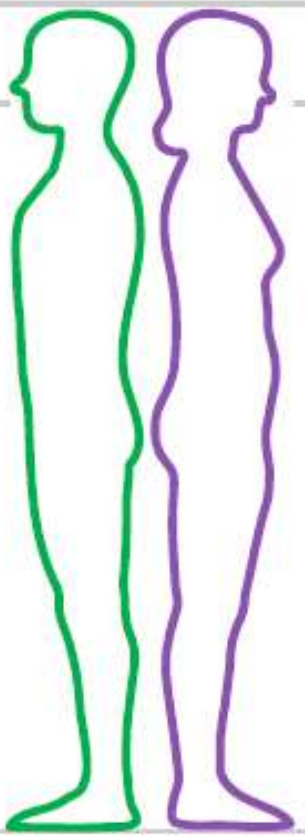
Disclosures

- Research funding from NIH/NCI Community Oncology Research Program (NCORP)
- Immuno-Oncology advisory board member and speaker with Bristol-Myers Squibb, 3401 Princeton Pike, Lawrenceville, NJ 08648
- Pfizer Speaker Program, 235 East 42nd Street NY, NY 10017

FIGURA 3: PRIMEROS DIEZ SITIOS DE CÁNCER: INCIDENCIA: PUERTO RICO, 2010-2014

FIGURE 3: TOP TEN CANCER SITES: INCIDENCE: PUERTO RICO, 2010-2014

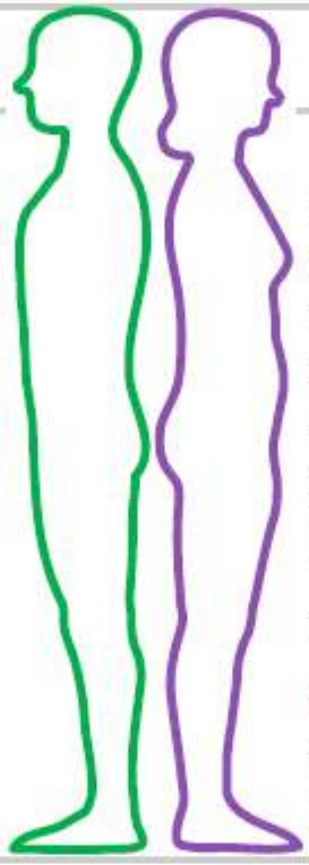
Hombres / Males (N = 40,725)	%	Mujeres / Females (N = 36,331)	%
Próstata/Prostate	37.7	Mama/Breast	29.0
Colon y recto/Colon and rectum	12.7	Colon y recto/Colon and rectum	11.6
Pulmón y bronquios/Lung and bronchus	6.0	Tiroides/Thyroid	10.8
Cavidad oral y faringe/Oral cavity and pharynx	4.0	Cuerpo del útero, NOS/Corpus and uterus, NOS	7.9
Vejiga urinaria/Urinary bladder	3.9	Pulmón y bronquios/Lung and bronchus	4.2
Linfoma no-Hodgkin/Non-Hodgkin Lymphoma	3.8	Linfoma no-Hodgkin/Non-Hodgkin Lymphoma	4.0
Hígado y ducto biliar/Liver and bile duct	3.2	Cérvix uterino/Cervix uteri	3.5
Leucemia/Leukemia	2.7	Ovario/Ovary	2.6
Riñón y pelvis renal/Kidney and renal pelvis	2.7	Leucemia/Leukemia	2.6
Estómago/Stomach	2.6	Páncreas/Pancreas	2.2
Otros sitios primarios/Other sites	20.8	Otros sitios primarios/Other sites	21.7



Estadísticas fueron generadas para cáncer maligno solamente; incluye cáncer de la vejiga urinaria *in-situ*.
Statistics were generated for malignant tumors only; includes urinary bladder cancer in situ.
Fuente de Datos: Archivo de Casos de Incidencia del Registro Central de Cáncer de Puerto Rico, 2 de noviembre de 2017.
Data Source: Incidence Case File from the Puerto Rico Central Cancer Registry, November 2, 2017.

FIGURA 8: PRIMEROS DIEZ TIPOS DE CÁNCER: MORTALIDAD: PUERTO RICO, 2010-2014
FIGURE 8: TOP TEN CANCER SITES: MORTALITY: PUERTO RICO, 2010-2014

Hombres / Males (N = 14,848)	%	Mujeres / Females (N =11,694)	%
Próstata/Prostate	16.9	Mama/Breast	18.4
Pulmón y bronquios/Lung and bronchus	13.5	Colon y recto/Colon and rectum	13.4
Colon y recto/Colon and rectum	13.0	Pulmón y bronquios/Lung and bronchus	9.6
Hígado y ducto biliar/Liver and bile duct	6.7	Páncreas/Pancreas	6.0
Páncreas/Pancreas	5.0	Hígado y ducto biliar/Liver and bile duct	4.6
Estómago/Stomach	4.3	Cuerpo del útero, NOS/Corpus and uterus, NOS	4.4
Leucemia/Leukemia	3.3	Ovario/Ovary	4.4
Cavidad oral y faringe/Oral cavity and pharynx	3.2	Estómago/Stomach	3.8
Linfoma no-Hodgkin/Non-Hodgkin Lymphoma	3.1	Leucemia/Leukemia	3.3
Esófago/Esophagus	3.1	Linfoma no-Hodgkin/Non-Hodgkin Lymphoma	2.8
Otros sitios primarios/Other sites	27.9	Otros sitios primarios/Other sites	29.5



Fuente de Datos: Archivo de Mortalidad provisto por el Registro Demográfico de Puerto Rico, octubre de 2016.
(Data Source: Mortality Case File provided by the Demographic Registry of Puerto Rico, October, 2016.)

Key Points

In the period 2010-2014:

- Colorectal cancer accounted for 12.7% of all cancer cases in men and 11.6% of all cancers in women.
- It also represented 13.0% of all cancer deaths in men and 13.3% of cancer deaths in women .
- On average, 1,035 men and 842 women were diagnosed annually with colorectal cancer.
- On average, 387 men and 312 women died from colorectal cancer each year .
- The risk of developing colorectal cancer was 1.5 times higher in men than women (95% CI: 1.4, 1.6).
- The risk of dying from colorectal cancer was 1.6 times higher in men than women (95% CI: 1.5, 1.7).

Registro Central de Cáncer de Puerto Rico
Centro Comprensivo de Cáncer
Universidad de Puerto Rico

Puerto Rico Central Cancer Registry
Comprehensive Cancer Center
University of Puerto Rico

Cáncer en Puerto Rico: 2010-2014

Cancer in Puerto Rico: 2010-2014

Incidencia, Mortalidad y Sobrevivencia

Incidence, Mortality and Survival

REGISTRO CENTRAL DE CANCER DE PUERTO RICO

CENTRO COMPRENSIVO DE CÁNCER

ESTADO LIBRE ASOCIADO DE PUERTO RICO
Departamento de Salud

FIGURA 26: TASAS DE INCIDENCIA AJUSTADAS POR EDAD (POBLACIÓN ESTÁNDAR DE ESTADOS UNIDOS - 2000) - CÁNCER DE COLON Y RECTO POR SEXO: PUERTO RICO, 1987-2014

FIGURE 26: AGE-ADJUSTED (2000 US STD. POP.) INCIDENCE RATES - COLON AND RECTUM CANCER BY SEX: PUERTO RICO, 1987-2014

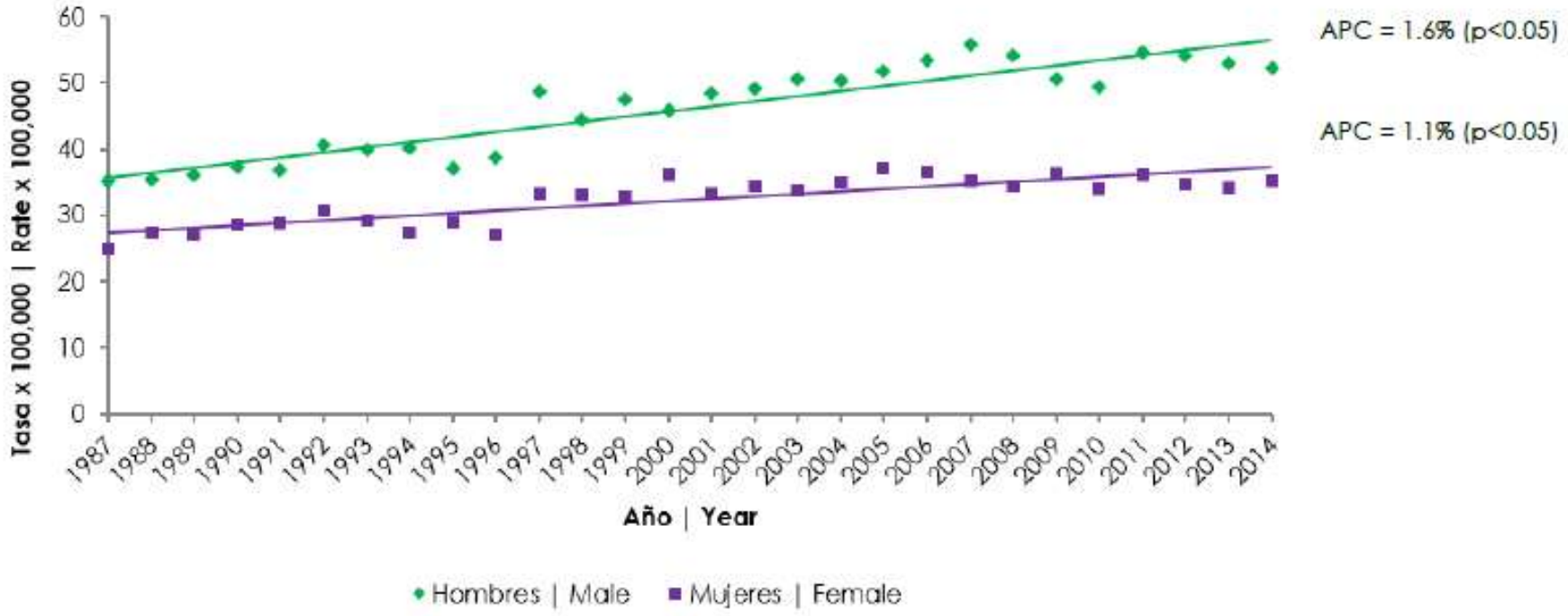
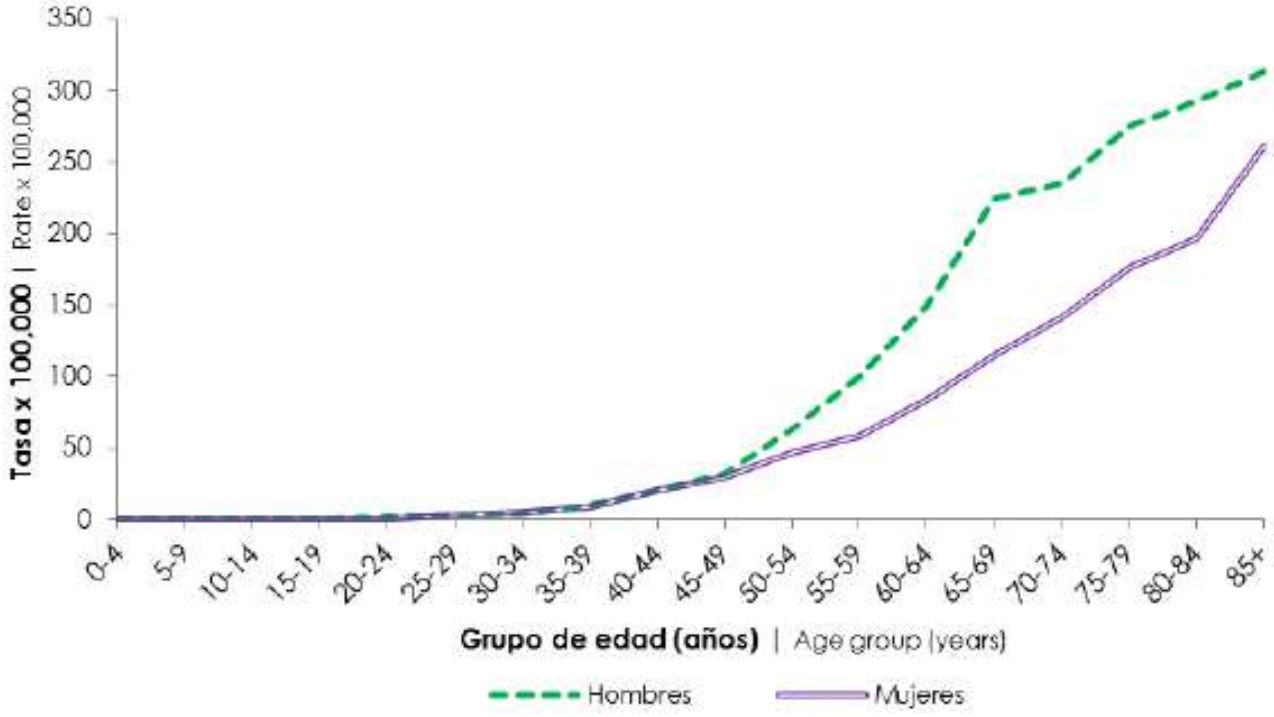
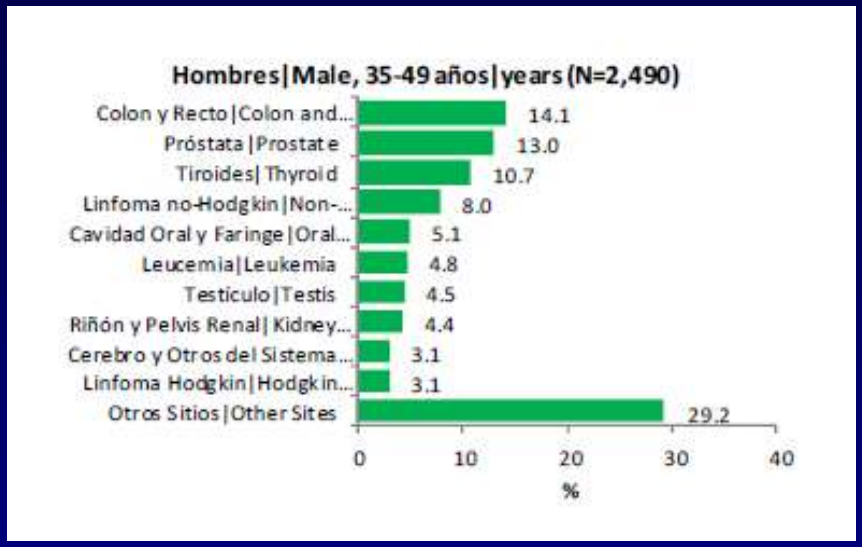


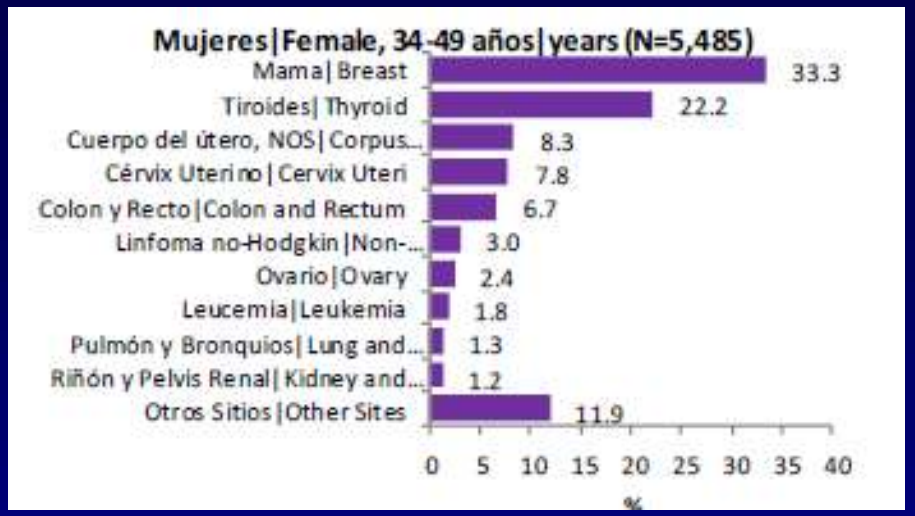
FIGURA 28: TASAS DE INCIDENCIA ESPECÍFICAS POR EDAD – CÁNCER DE COLON Y RECTO POR SEXO: PUERTO RICO, 2010-2014

FIGURE 28: AGE-SPECIFIC INCIDENCE RATES – COLON AND RECTUM CANCER BY SEX: PUERTO RICO, 2010-2014

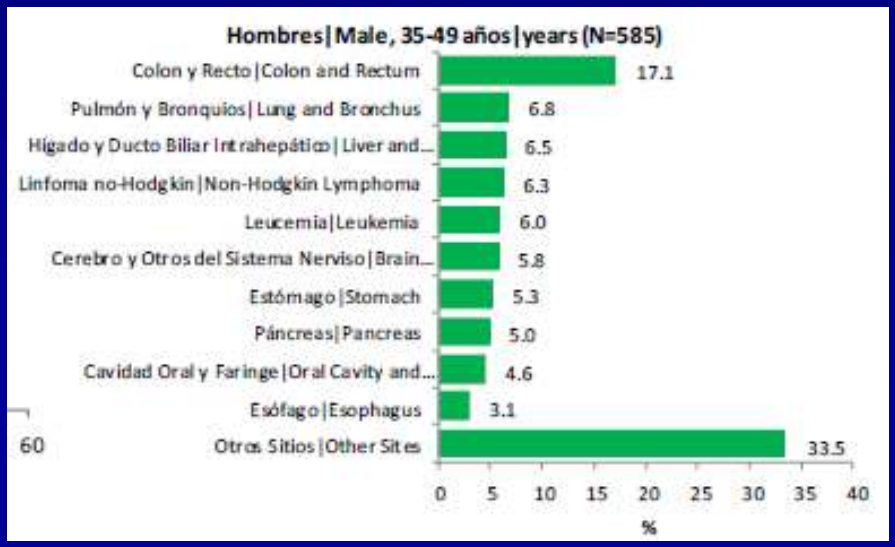


INCIDENCIA / INCIDENCE





MUERTES / DEATHS



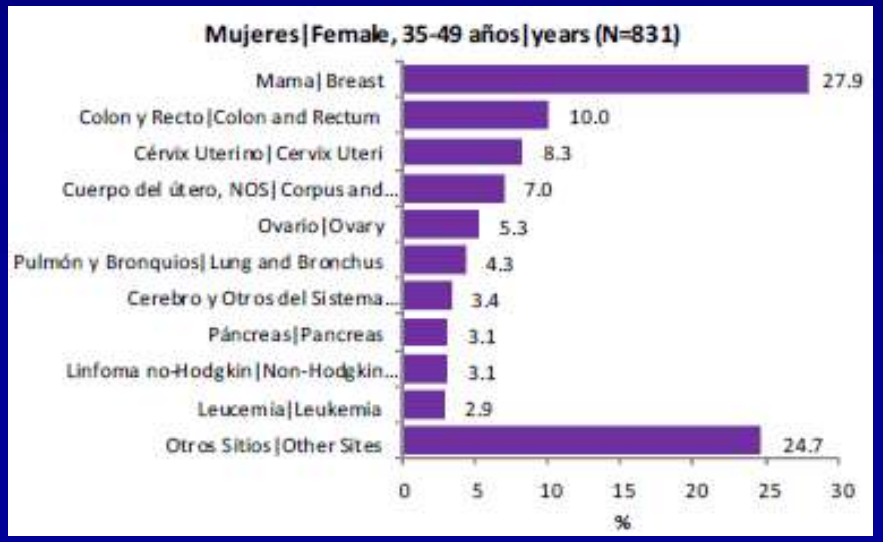
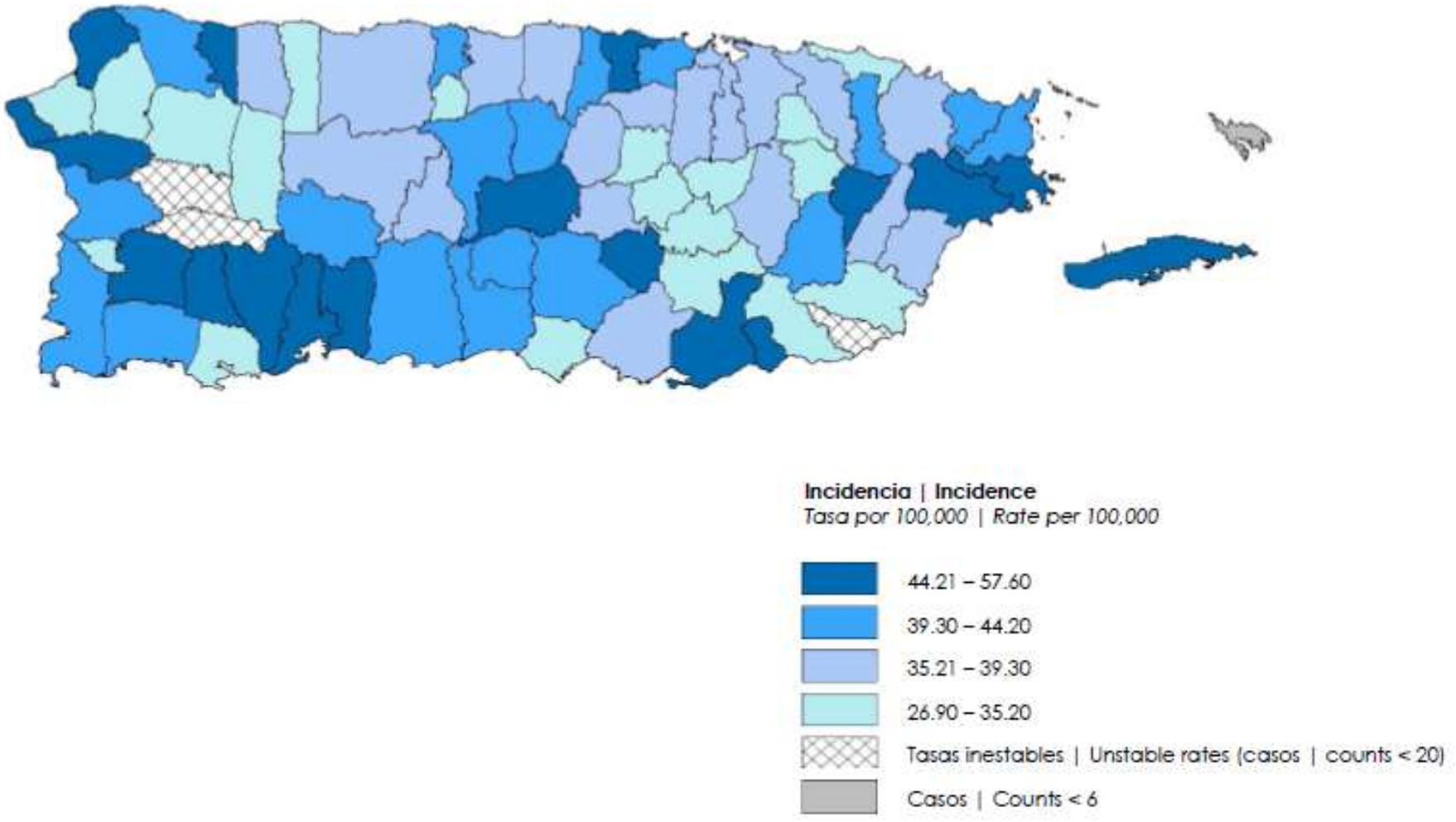


FIGURE 30: TASAS DE INCIDENCIA AJUSTADAS POR EDAD (POBLACIÓN ESTÁNDAR DE PUERTO RICO - 2000) - CÁNCER DE COLON Y RECTO POR MUNICIPIO EN PUERTO RICO, 2010-2014

FIGURE 30: AGE-ADJUSTED (2000 PR STD. POP.) INCIDENCE RATES - COLON AND RECTUM CANCER BY MUNICIPALITY IN PUERTO RICO, 2010-2014



General Principles

Colorectal Cancer Screening Guidelines

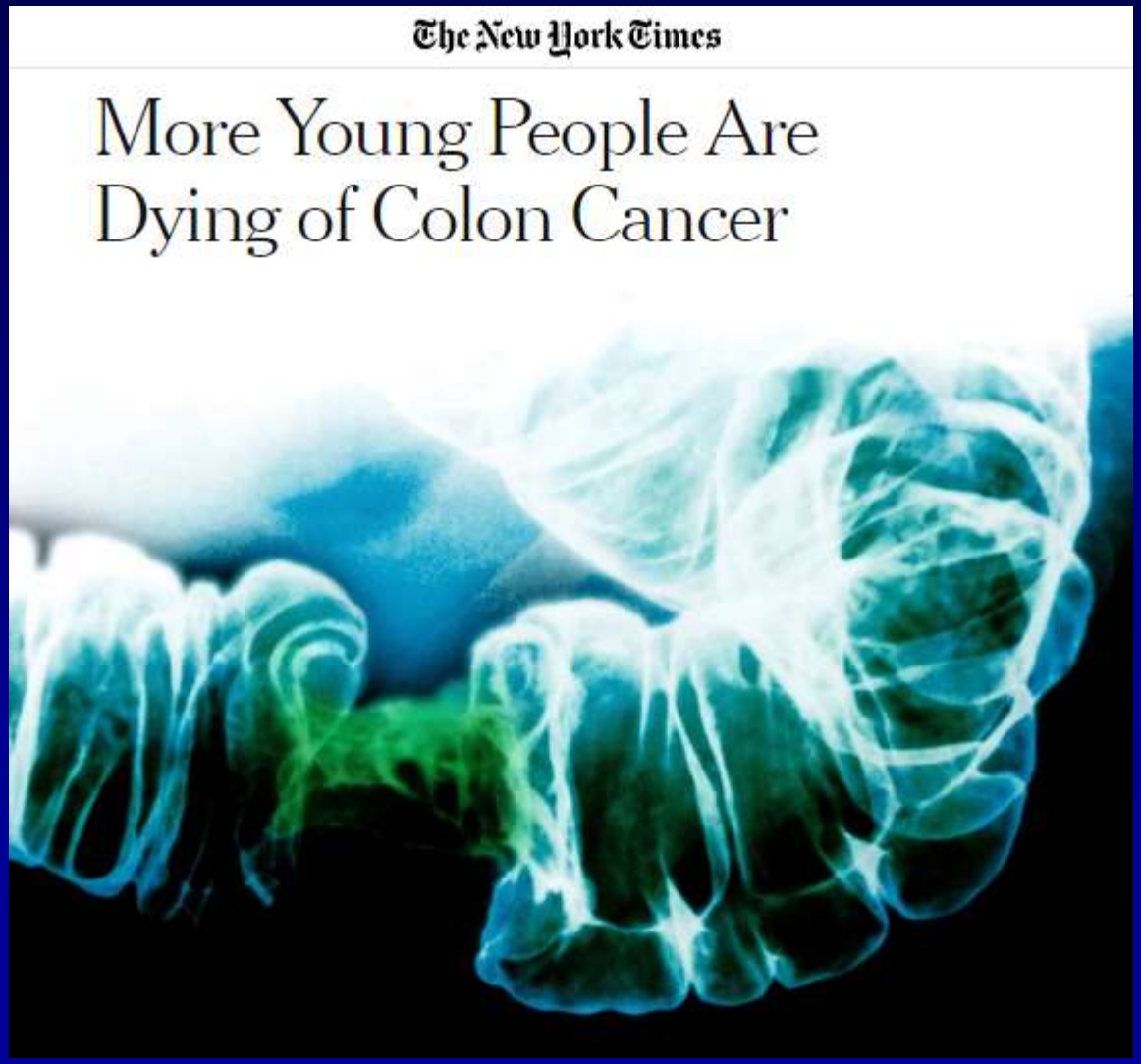
Metastatic Setting

- General Approach
- Right versus Left Sided Cancers
- Intensifying Front-Line Therapy
  - Side matters
  - Conversion Therapy
- BRAF Mutated
- Peritoneal Metastases

Future Directions

- Precision Medicine
  - HER2 & Others
- Tissue vs Liquid Biopsies

Colorectal Cancer (CRC)



CA: A Cancer Journal for Clinicians

Article | Free Access

Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society

Andrew M.D. Wolf MD, Elizabeth T.H. Fontham MPH, DrPH, Timothy R. Church PhD, Christopher R. Flowers MD, MS, Carmen E. Guerra MD, Samuel J. LaMonte MD, Ruth Etzioni PhD, Matthew T. McKenna MD, Kevin C. Oeffinger MD, Ya-Chen Tina Shih PhD, Louise C. Walter MD, Kimberly S. Andrews BA, Otis W. Brawley MD, Durado Brooks MD, MPH, Stacey A. Fedewa PhD, MPH, Deana Manassaram-Baptiste PhD, MPH, Rebecca L. Siegel MPH, Richard C. Wender MD, Robert A. Smith PhD
... See fewer authors

First published: 30 May 2018 | https://doi.org/10.3322/caac.21457

- **Begin screening age 45**
- **Screen through age 75**
- **Individualized screening ages 75 – 85**
- **Discouraged screening beyond age 85**

Options for CRC screening

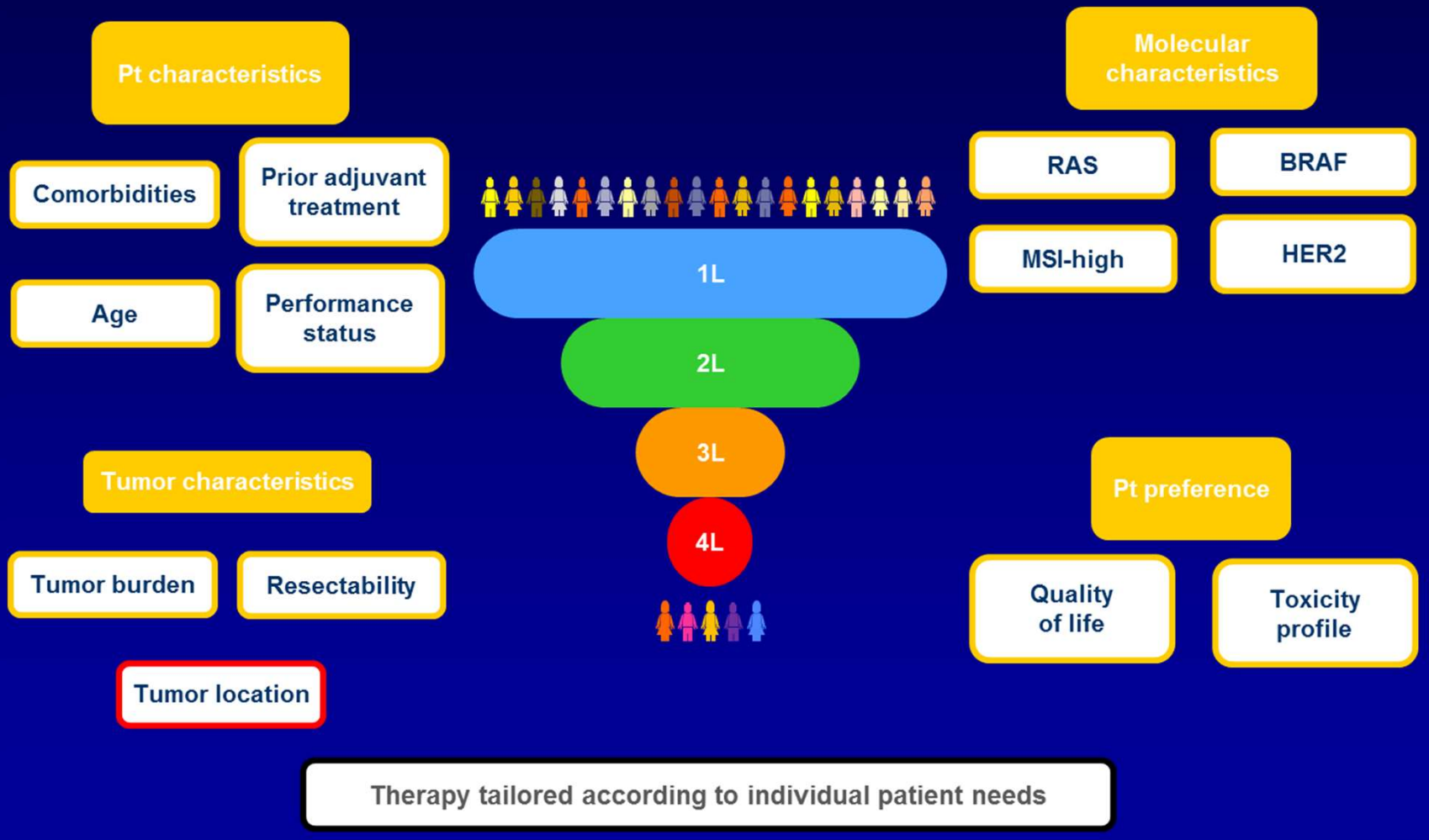
Stool-based tests

- Fecal immunochemical test every y
- High-sensitivity, guaiac-based fecal occult blood test every y
- Multitarget stool DNA test every 3 y

Structural examinations

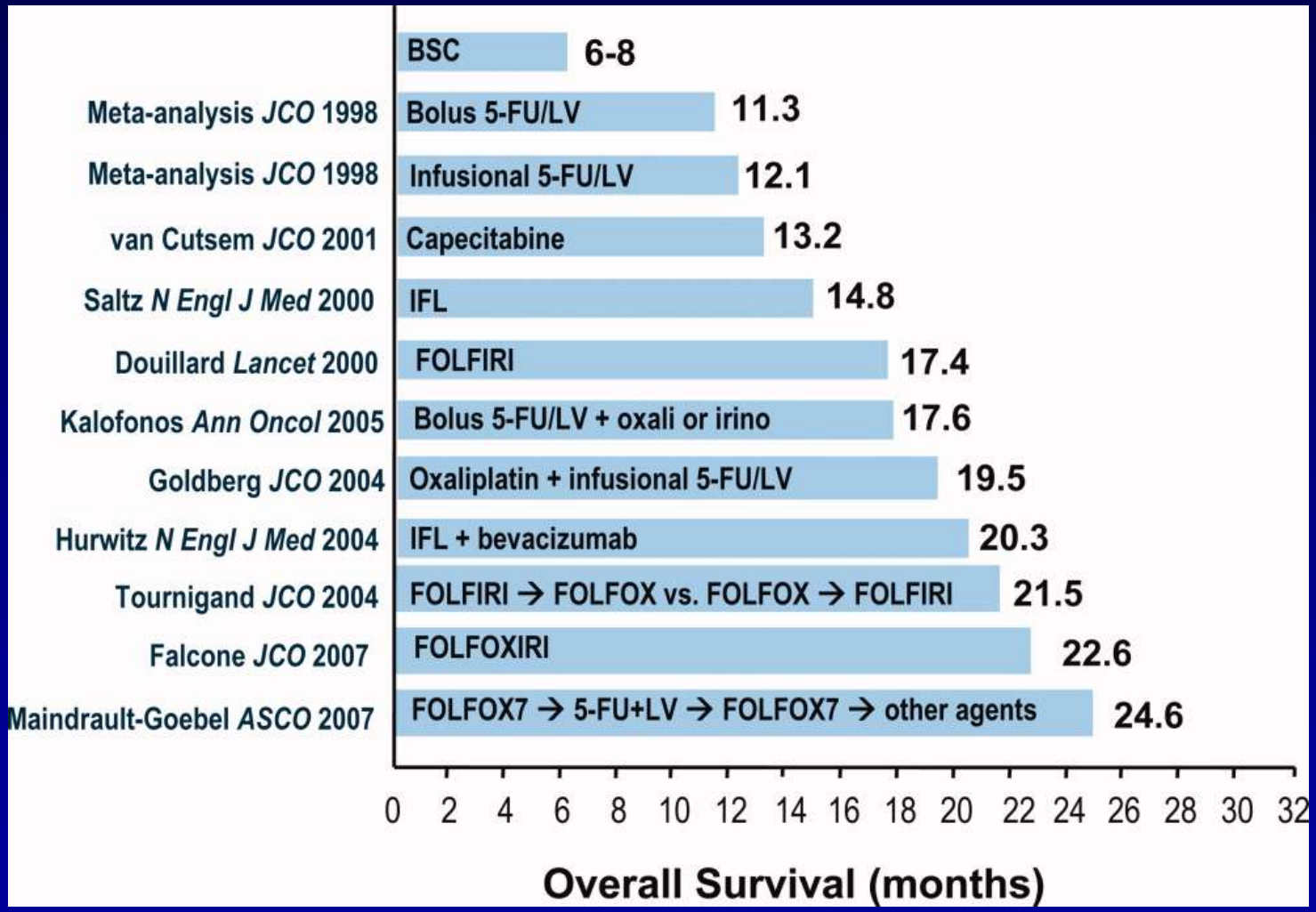
- Colonoscopy every 10 y
- CT colonography every 5 y
- Flexible sigmoidoscopy every 5 y

General Approach to Advanced CRC



Slide credit: clinicaloptions.com

Advances in Metastatic Colorectal Cancer



Zuckerman DS. Cancer. 2008;112:1879-1891.

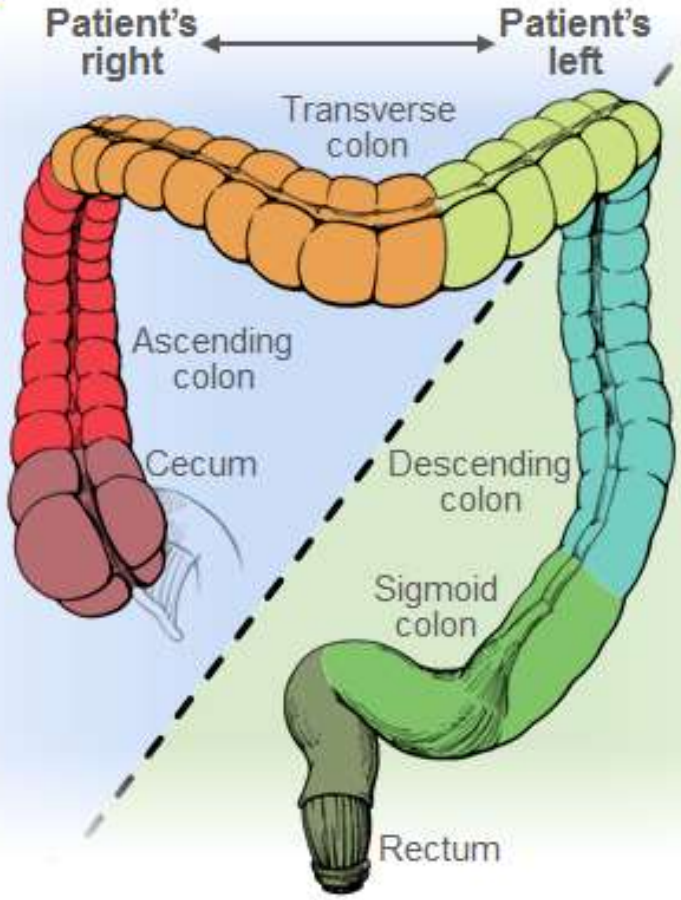
Colorectal Cancer (CRC)

MIDGUT DERIVATIVE

- ↑ females
- ↑ sessile serrated lesions
- ↑ mucinous tumors

Overall WORSE prognosis

- ↑ CIMP-high
- ↑ BRAF
- ↑ MSI-high
- ↑ CMS-1-MSI immune tumors
- ↑ CMS-3-metabolic tumors
  (↑ KRAS)



HINDGUT DERIVATIVE

- ↑ males

Overall BETTER prognosis

- ↑ CMS-4-MSI mesenchymal
- ↑ CMS-2-canonical distally
- ↑ TP53
- ↑ APC

CALGB/SWOG 80405

ESMO, SEP, 2014

1ST LINE
MET / ADVANCED
COLORECTAL

All *RAS* wt

FOLFIRI
or
FOLFOX

MD choice

N = 526

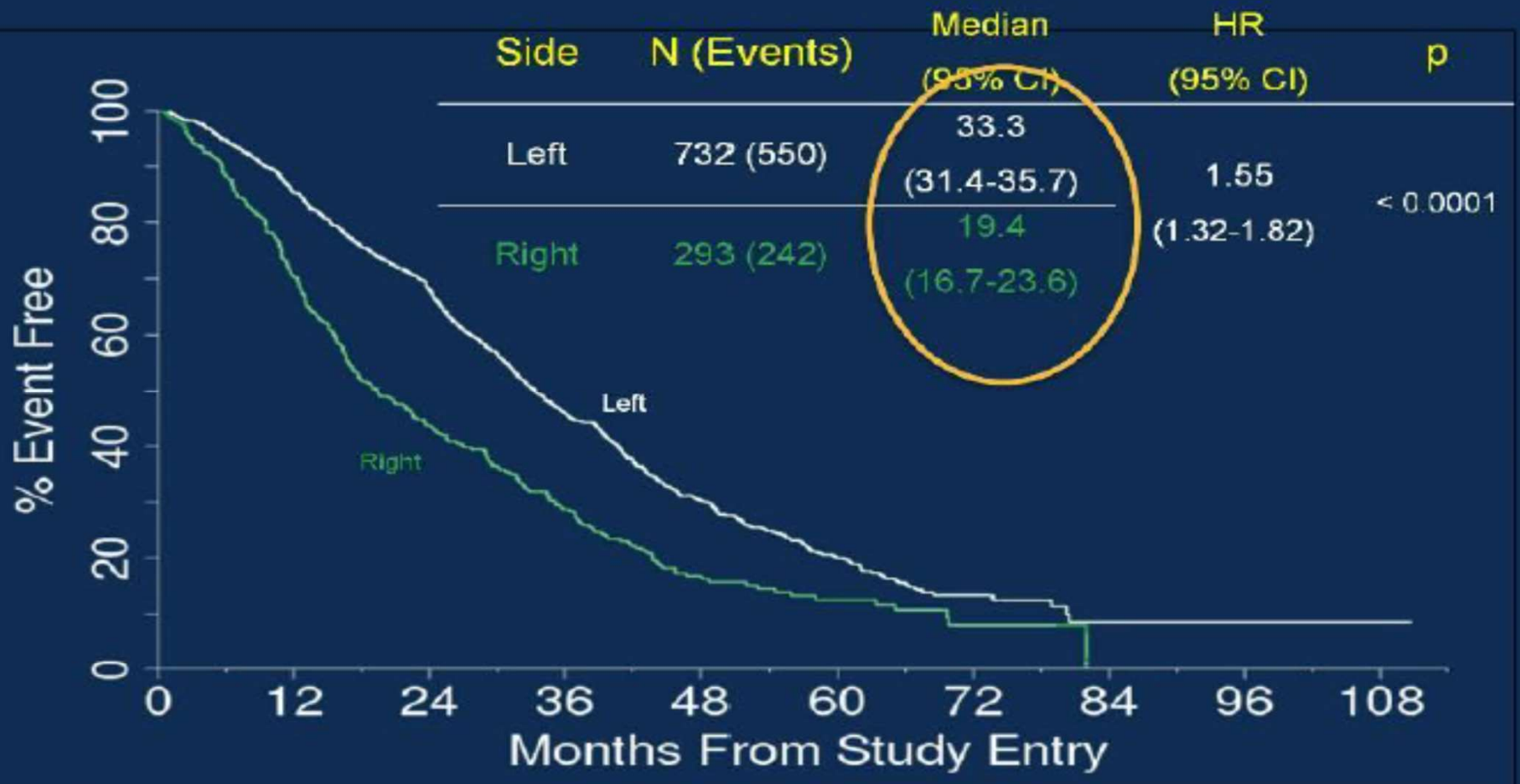
Chemo + Cetuximab
OS = 32.0 mos
PFS =11.4 mos

CONCLUSION: NO DIFFERENCE

Chemo + Bevacizumab
OS = 31.2 mos
PFS = 11.3 mos

OS better than anticipated in both arms:
Treatment effect and/or Patient selection

80405: Overall Survival by Sidedness



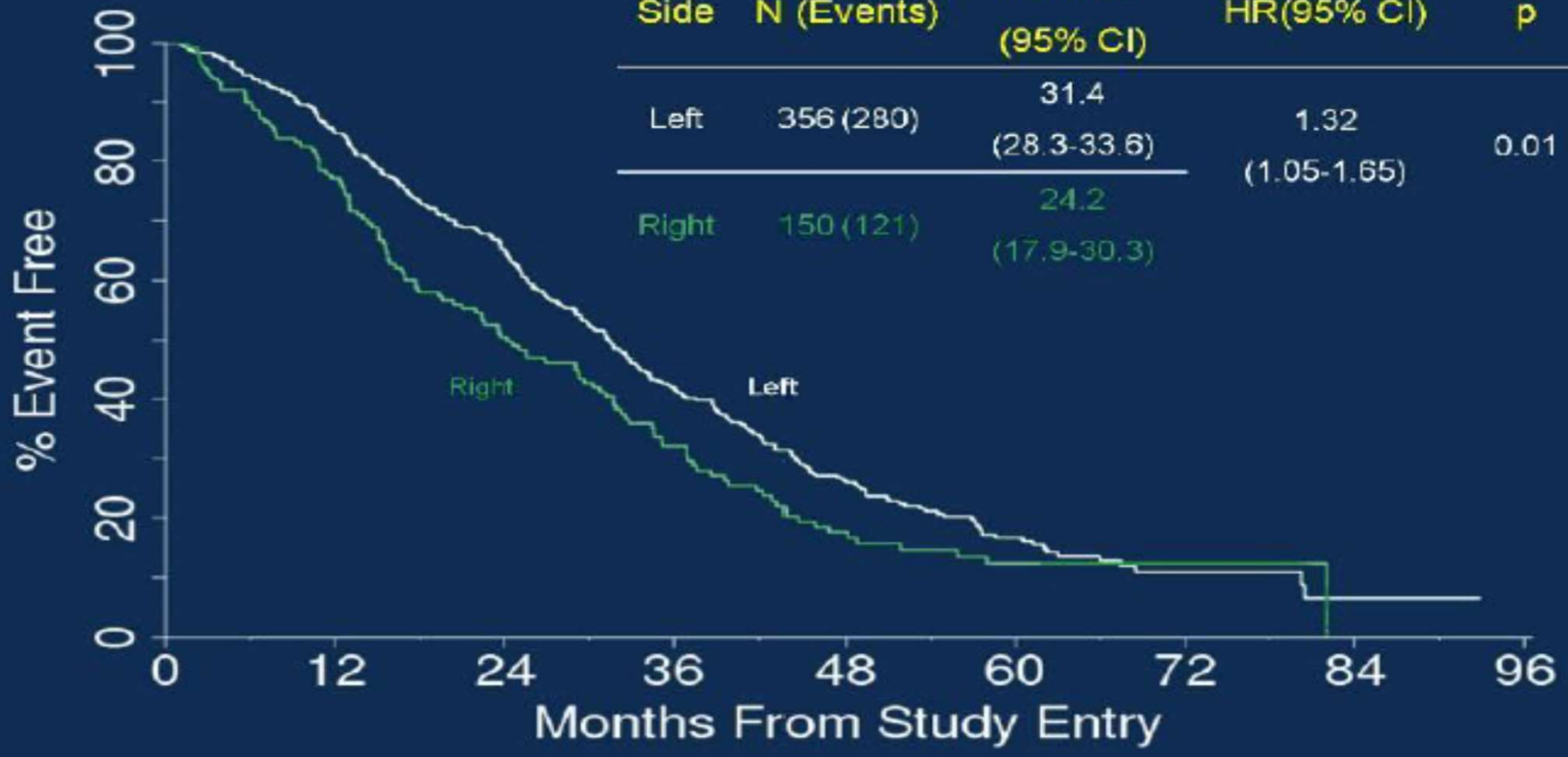
PRESENTED AT: ASCO ANNUAL MEETING '16

Presented by:

Presented By Alan Venook at 2016 ASCO Annual Meeting

80405: OS by Sidedness (Bevacizumab)

Side	N (Events)	Median (95% CI)	HR(95% CI)	p
Left	356 (280)	31.4 (28.3-33.6)	1.32 (1.05-1.65)	0.01
Right	150 (121)	24.2 (17.9-30.3)		



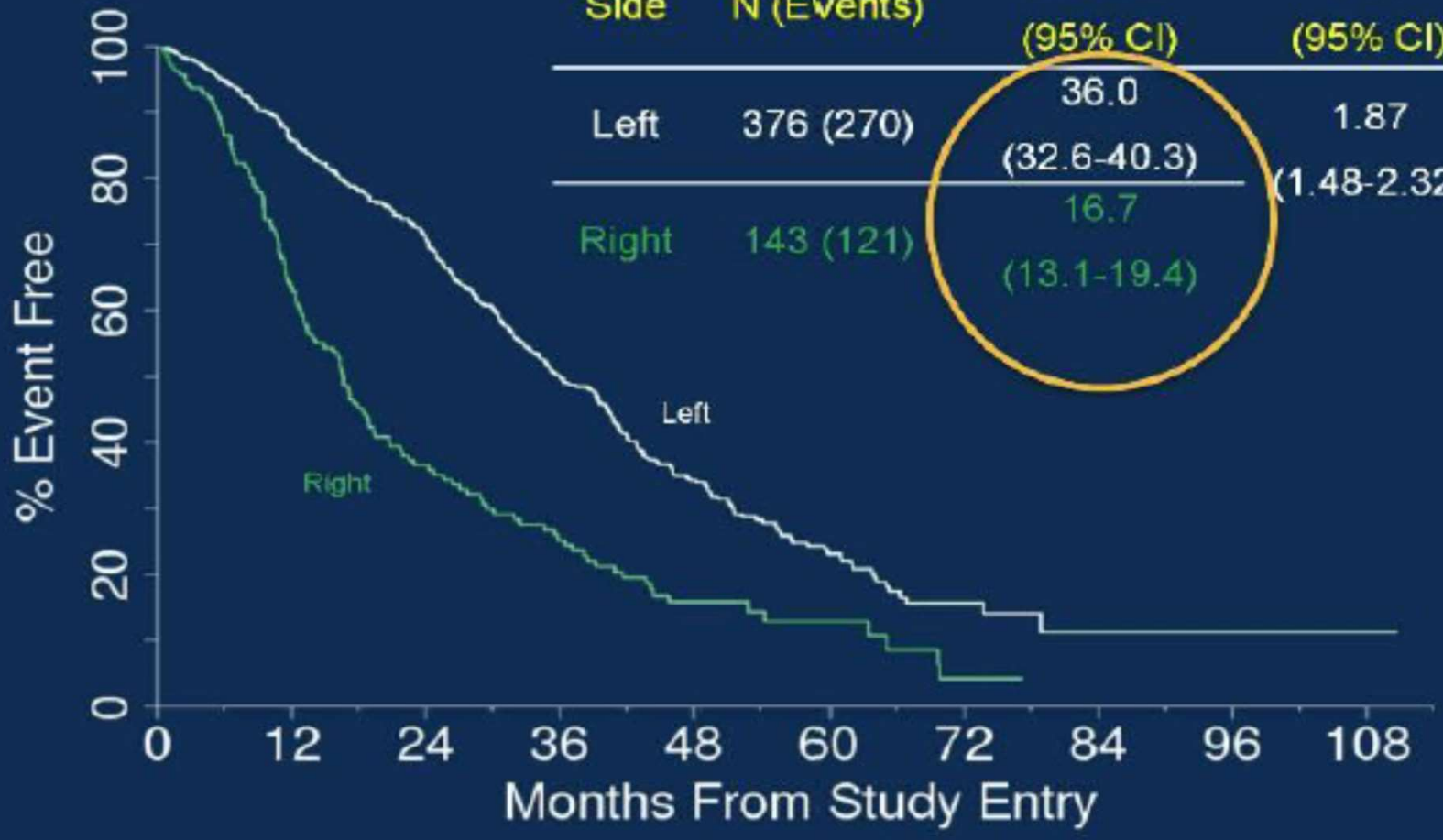
PRESENTED AT: ASCO ANNUAL MEETING '16

Presented by:

Presented By Alan Venook at 2016 ASCO Annual Meeting

80405: OS by Sidedness (Cetuximab)

Side	N (Events)	Median (95% CI)	HR (95% CI)	p
Left	376 (270)	36.0 (32.6-40.3)	1.87 (1.48-2.32)	<0.0001
Right	143 (121)	16.7 (13.1-19.4)		



PRESENTED AT: ASCO ANNUAL MEETING '16

Presented by:

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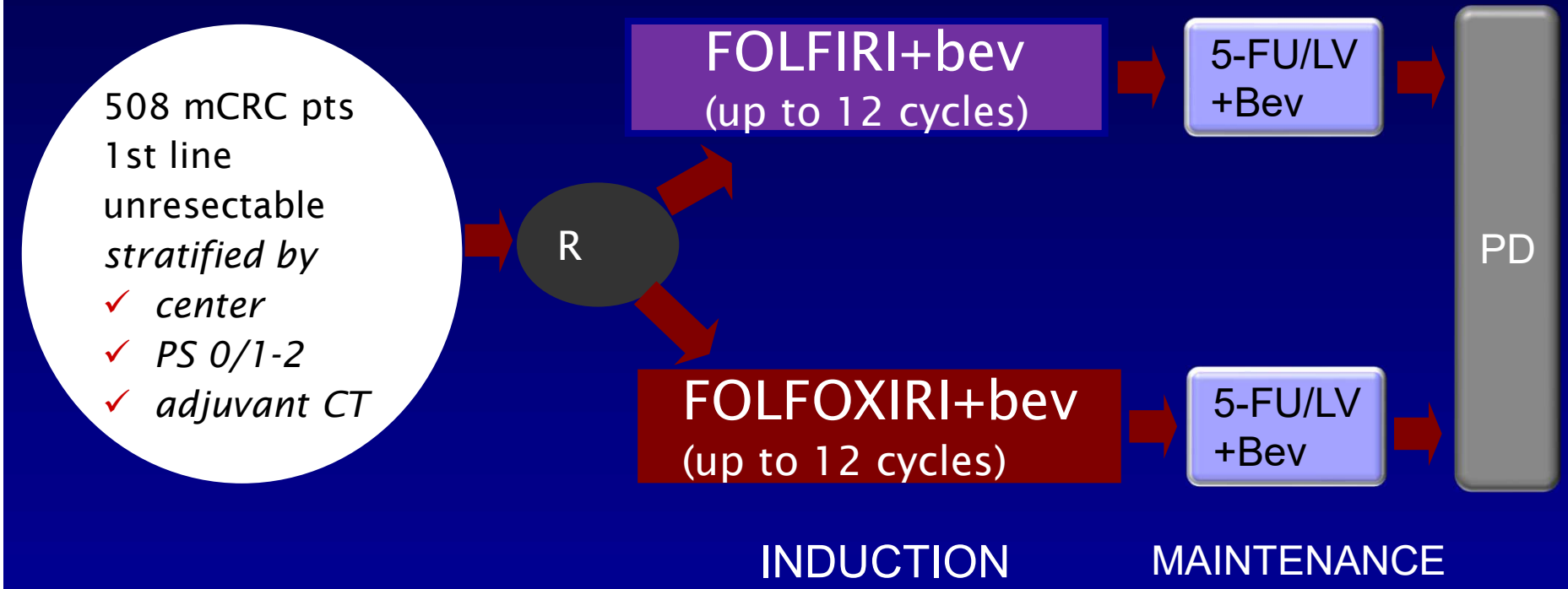
EGFR inhibitors for Right Sided Tumors

- Patients with mCRC and right-sided primary tumors have inferior survival compared to patients with left-sided tumors
- Patients with right-sided primaries LACK benefit from EGFRi in the first-line setting

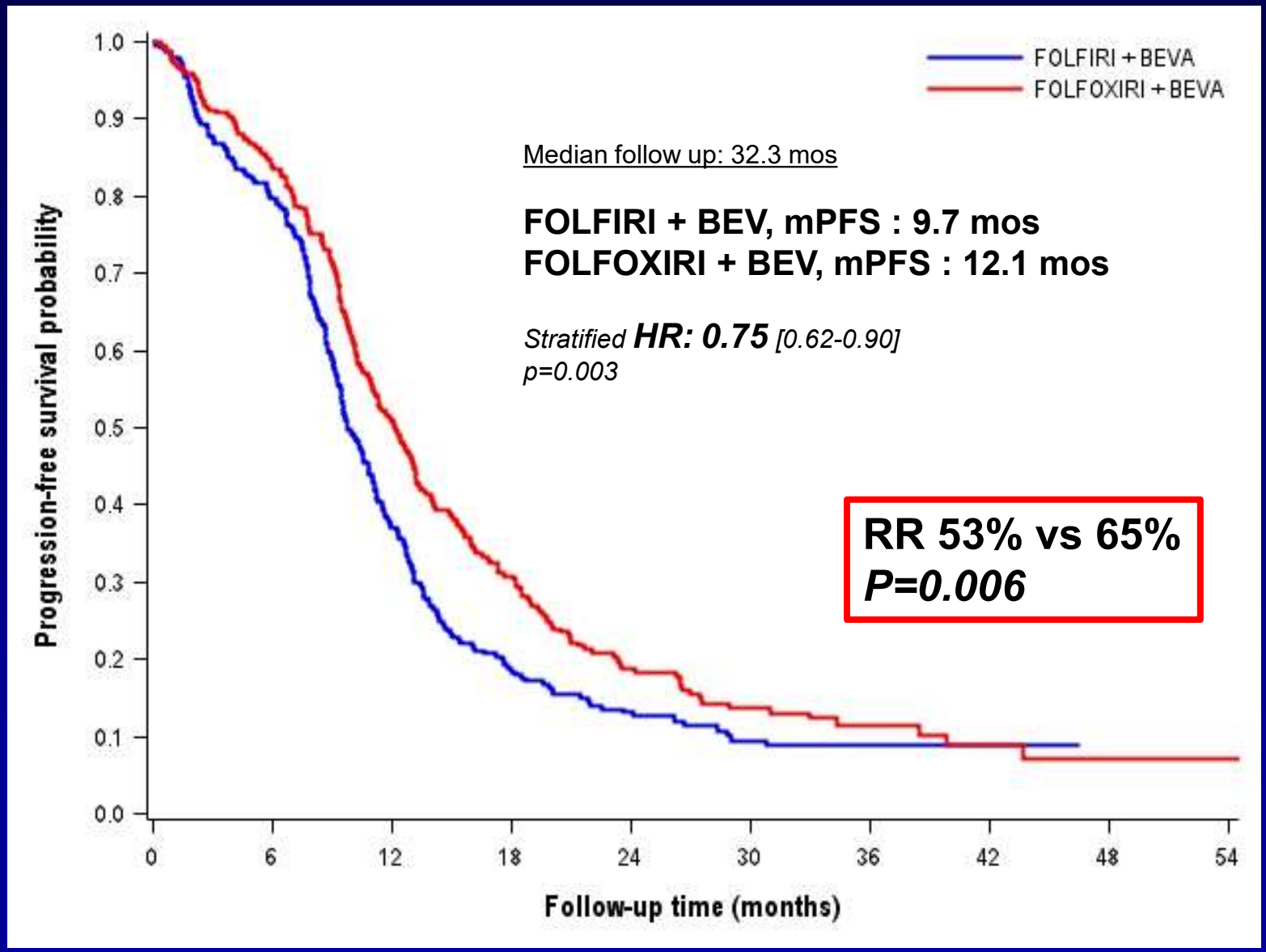
Intensifying Front-line Therapy

TRIBE Study Design



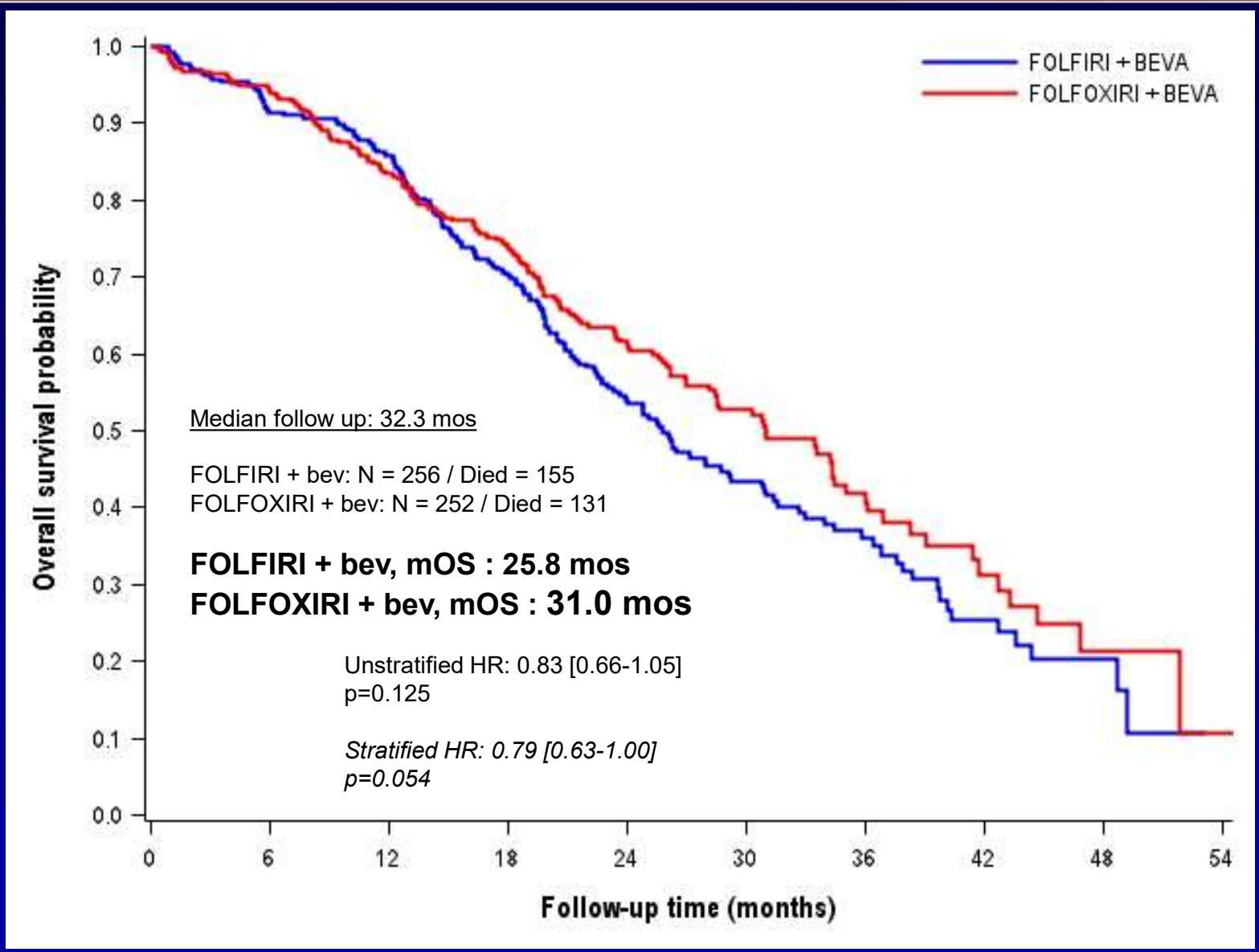
Loupakis et al., NEJM 2014

TRIBE study primary endpoint: PFS



Loupakis et al., NEJM 2014

TRIBE study secondary endpoint: OS



Loupakis et al., NEJM 2014

2019 ASCO Annual Meeting

Chicago, 31st May – 4th June 2019

Updated results of TRIBE2, a phase III, randomized strategy study by GONO in the 1st- and 2nd-line treatment of unresectable mCRC

C. Cremolini, C. Antoniotti, S. Lonardi, D. Rossini, F. Pietrantonio, S.S. Cordio, F. Bergamo, F. Marmorino, E. Maiello, A. Passardi, G. Masi, E. Tamburini, D. Santini, R. Grande, A. Zaniboni, C. Granetto, S. Murgioni, G. Aprile, L. Boni, A. Falcone

on behalf of the GONO Investigators

Background

Main concerns about the use of the triplet plus bevacizumab:

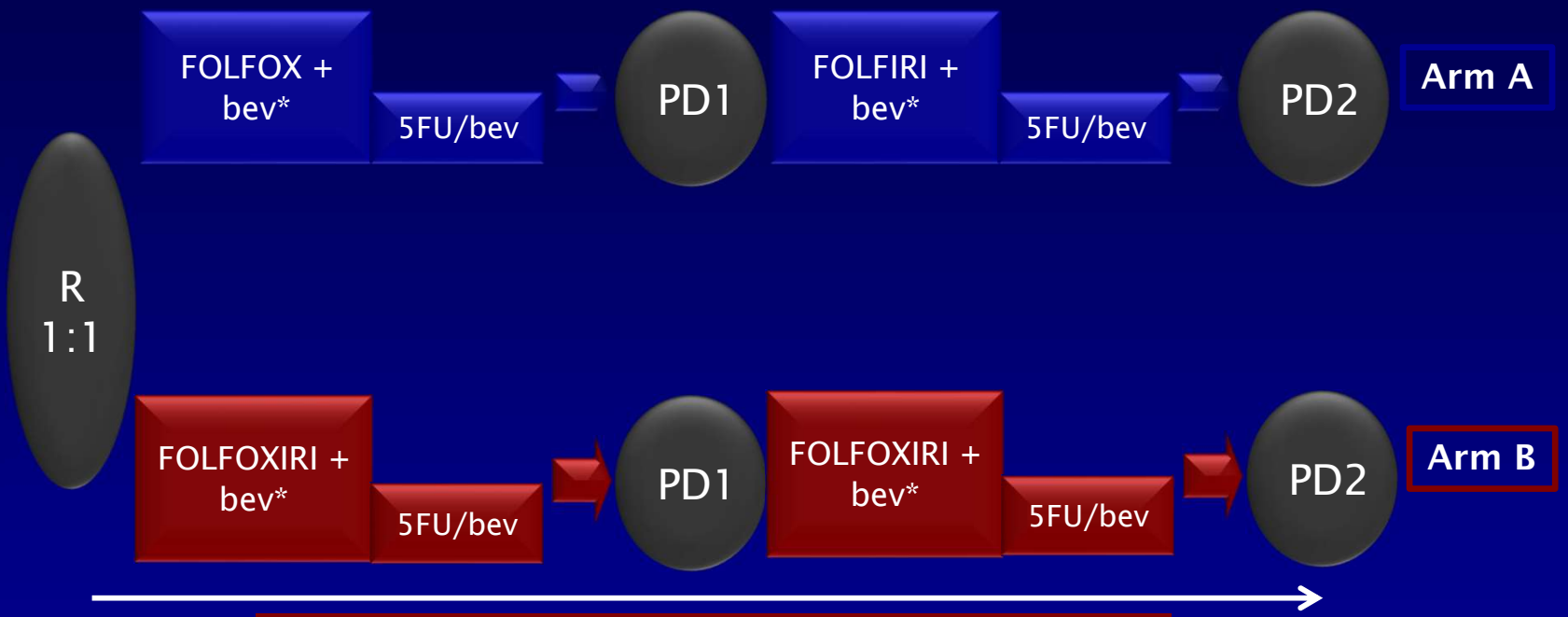
→ feasibility and efficacy of treatments after progression

→ actual advantage versus a pre-planned sequential exposure to all cytotoxics

To verify whether the upfront exposure to all the three active chemotherapy agents (triplet FOLFOXIRI) is beneficial when compared to a pre-planned sequential strategy of exposure to the same agents in two subsequent lines of therapy (FOLFOX – FOLFIRI), in combination with a sustained antiangiogenic treatment

Cremolini C et al., ASCO 2019

TRIBE2: Study design



PRIMARY ENDPOINT: Progression Free Survival 2

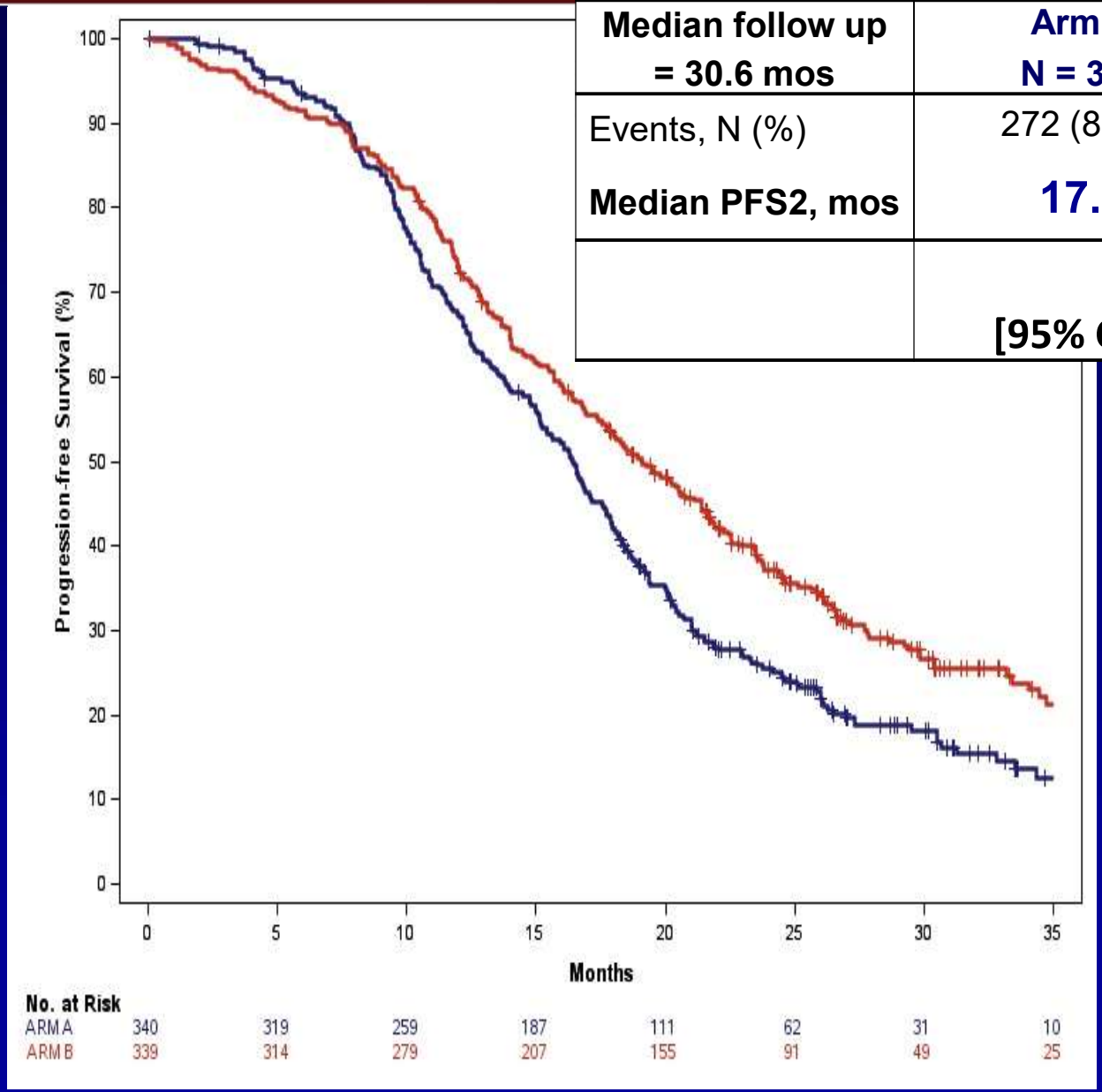
- Previously untreated, unresectable mCRC

*** Up to 8 cycles**

- ECOG PS ≤ 2

Cremolini C et al., ASCO 2019

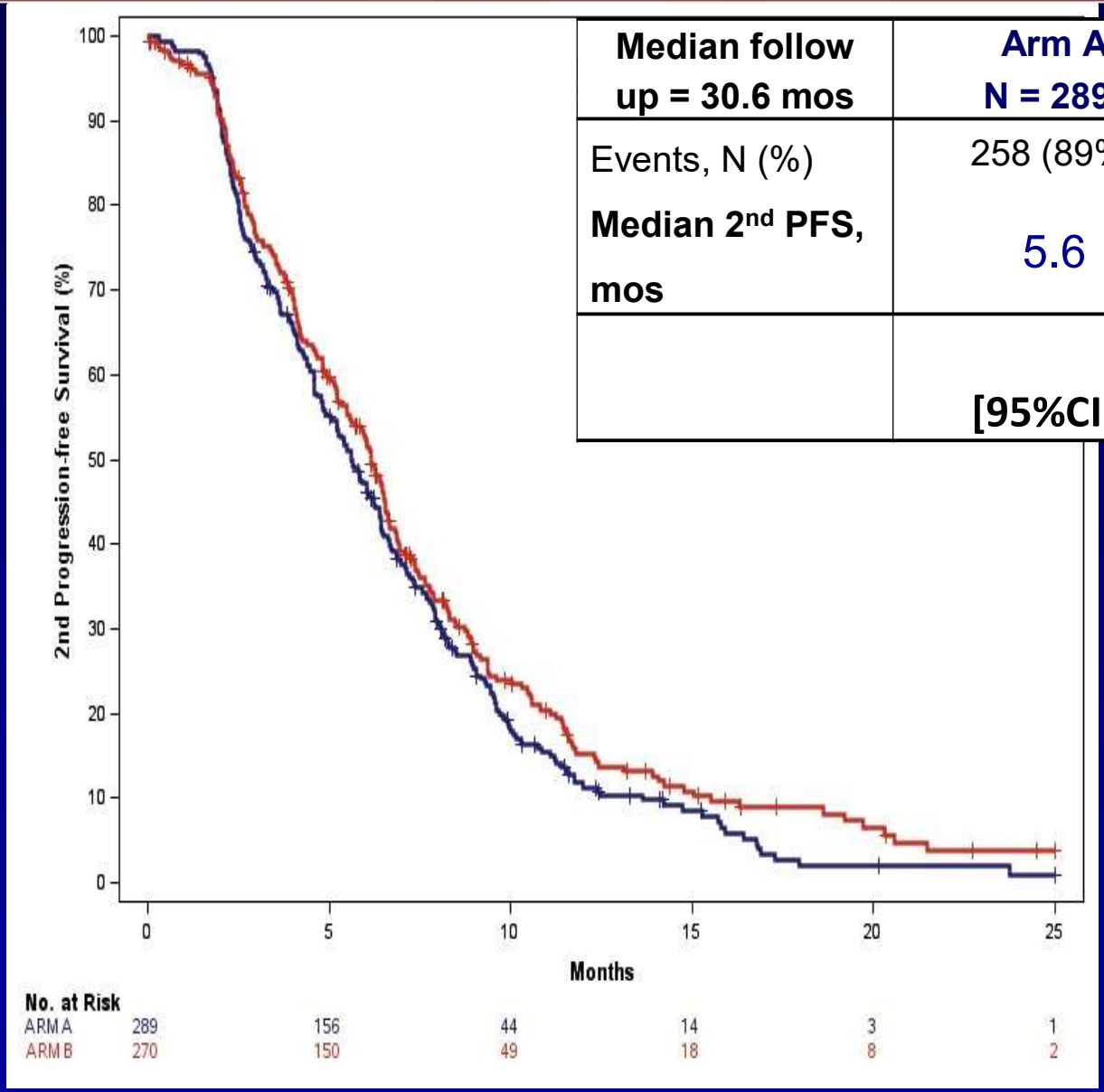
Primary endpoint: Progression Free Survival 2



Median follow up = 30.6 mos	Arm A N = 340	Arm B N = 339
Events, N (%)	272 (80%)	242 (71%)
Median PFS2, mos	**17.5**	**19.1**
	HR = 0.74 [95% CI: 0.62-0.88] p<0.001	

Cremolini C et al., ASCO 2019

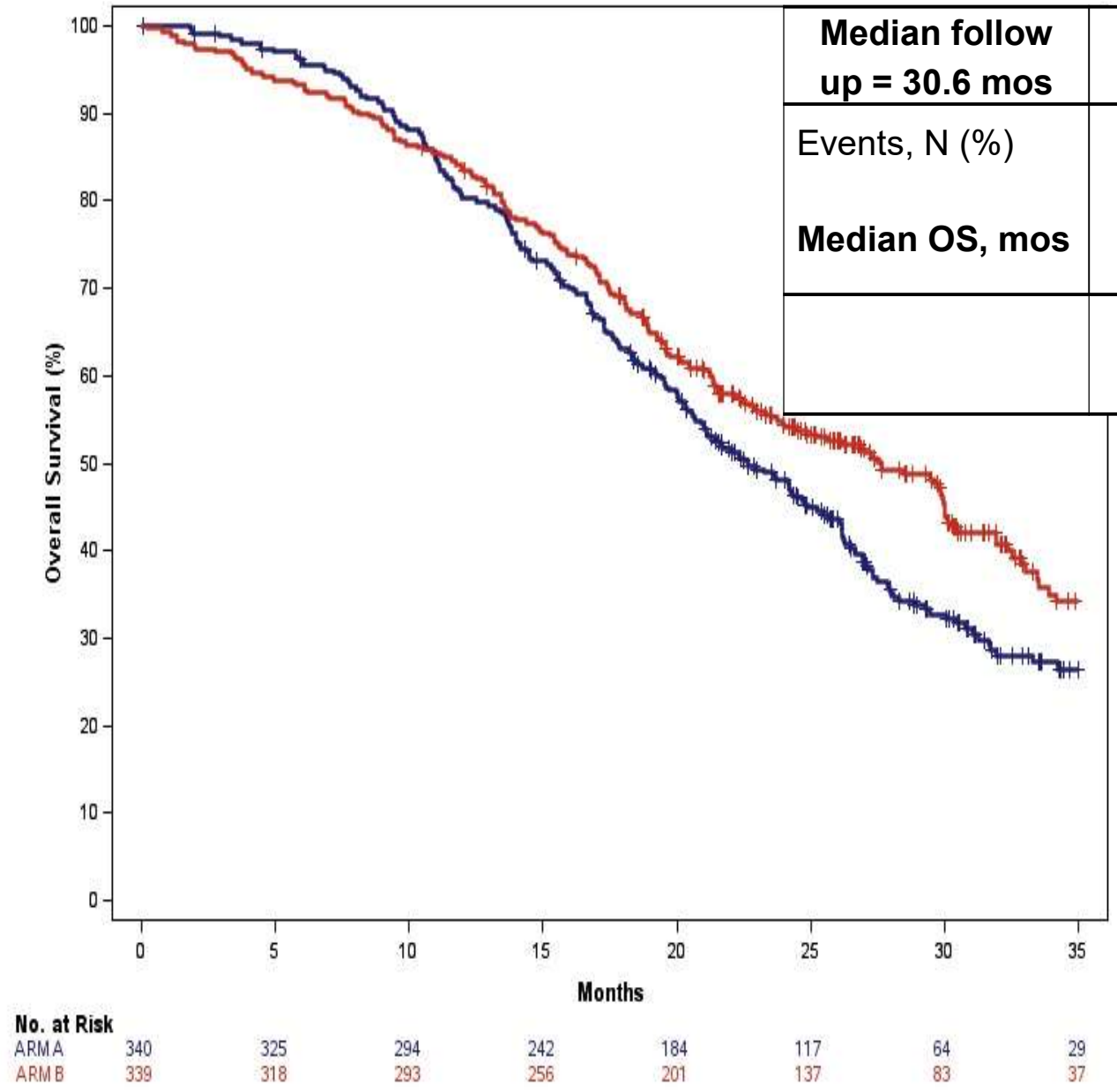
2nd line - Progression Free Survival (Patients alive at the time of PD1)



Median follow up = 30.6 mos	Arm A N = 289*	Arm B N = 270*
Events, N (%)	258 (89%)	221 (82%)
Median 2nd PFS, mos	5.6	6.2
	HR = 0.87 [95%CI: 0.73-1.04] p=0.122	

Cremolini C et al., ASCO 2019

Overall Survival – preliminary results



Median follow up = 30.6 mos	Arm A N = 340	Arm B N = 339
Events, N (%)	217 (64%)	191 (56%)
Median OS, mos	22.6	27.6
	HR = 0.81 [95%CI: 0.67-0.98] p=0.033	

Cremolini C et al., ASCO 2019

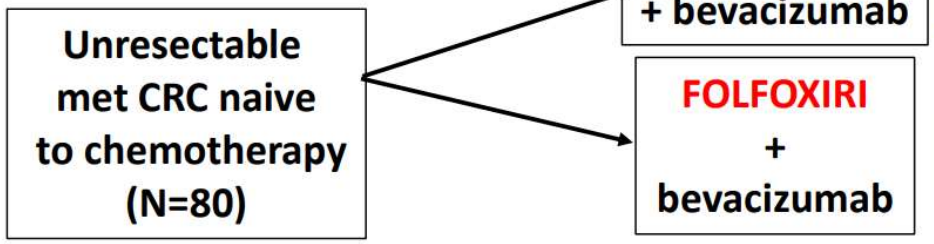
Side: does it matter for intensifying therapy?

- Data present for evaluation of impact on sidedness of primary tumor for patients enrolled on TRIBE phase III trial
- As expected, worse OS was seen in patients with right-sided tumors, despite a higher percentage receiving FOLFOXIRI in this analyzed population than for left-sided primary tumors (62% vs 47%)
- Improvements in survival outcomes WAS seen for patients with right-sided tumors receiving FOLFOXIRI/avastin BUT NOT observed for left-sided tumors

	Study population			
	Right-sided (*N* = 116)		Left-sided (*N* = 242)	
PFS				
Median (mos)	10.2		11.5	
HR [95% CI]	1.24 [0.98–1.56]			
P	0.083			
OS				
Median (mos)	23.7		31.0	
HR [95% CI]	1.42 [1.09–1.84]			
P	0.010			
ORR				
Rate, %	60.3		60.3	
OR [95% CI]	0.98 [0.61–1.57]			
P	0.937			
	FOLFOXIRI +bev *N*=72	**FOLFIRI +bev *N*=44**	**FOLFOXIRI +bev *N*=113**	**FOLFIRI +bev *N*=129**
PFS				
Median (mos)	11.2	9.4	10.7	11.0
HR [95% CI]	0.59 [0.40–0.88]		0.89 [0.68–1.16]	
P	0.099[a]			
OS				
Median (mos)	26.0	20.2	28.6	31.6
HR [95% CI]	0.56 [0.37–0.85]		0.99 [0.73–1.35]	
P	0.030[a]			
ORR				
Rate, %	63.9	54.6	64.6	56.6
OR [95% CI]	1.48 [0.68–3.26]		1.43 [0.84–2.44]	
P	0.942[a]			

Conversion therapy: does it matter for intensifying therapy?

OLIVIA trial



	Resection rate (%)	R0 resection rate (%)
FOLFOX/bev	49	23
FOLFOXIRI/bev	61	49
P-value	.003	.03

Median PFS, OS, TTP, and RR were significantly longer in the FOLFOXIRI/bev arm.

Reasonable to consider FOLFOXIRI/avastin as treatment choice for untreated patients being considered for possible resection of colorectal liver metastases.

Gruenberger T et al. Annals of Oncology 2015

Intensifying First Line Therapy in mCRC

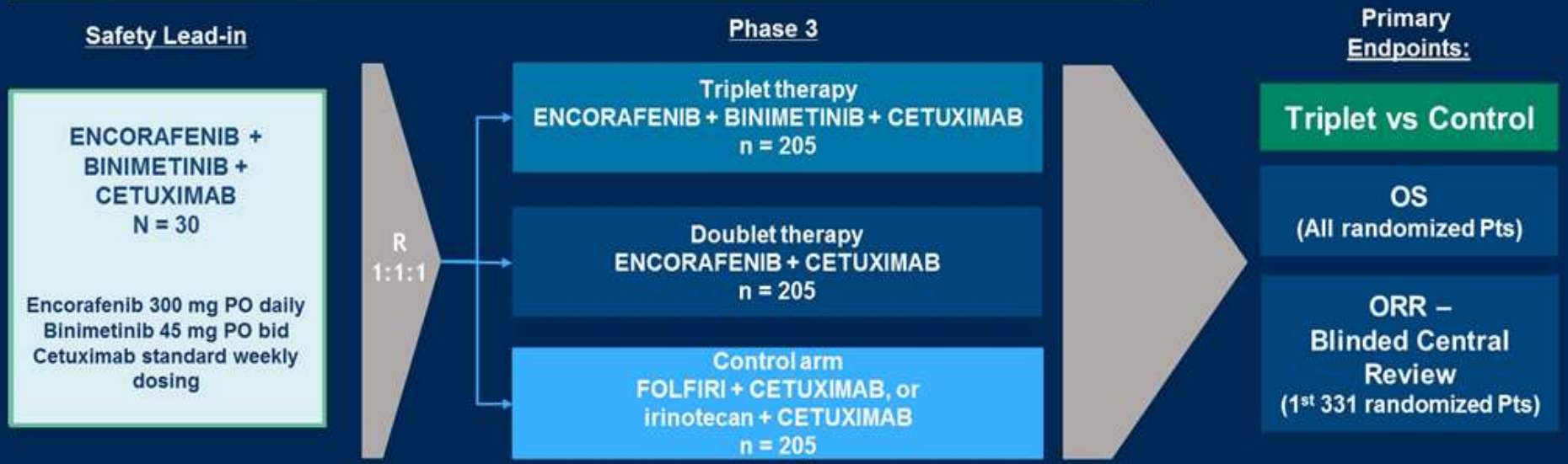
- TRIBE2 confirms survival advantage for more intensive treatment regimen upfront
  - 4 month OS improvement TRIBE
  - Prelim 5 month OS improvement TRIBE2
- **For good PS patients w/ RIGHT-sided tumors +/- RAS MUT, FOLFOXIRI + bev should be considered for 1st-line tx**
- Especially for patients where a response is needed
    - Higher RR 12% in both studies
    - Higher R0 resection rates
  - BRAF mutant cases
- FOLFOXIRI + bev upfront doesn't impair 2nd line treatment
- **FOLFOXIRI + EGFRi is reasonable for good PS, LEFT-sided, RAS/BRAF^{WT} advanced CRC (MACBETH & VOLFI)**

BRAF Mutant Colorectal Cancer

BEACON Trial

Study Design

Patients with *BRAF*^{V600E} mCRC with disease progression after 1 or 2 prior regimens; ECOG PS of 0 or 1; and no prior treatment with any RAF inhibitor, MEK inhibitor, or EGFR inhibitor



Randomization was stratified by ECOG PS (0 vs. 1), prior use of irinotecan (yes vs. no), and cetuximab source (US-licensed vs. EU-approved)

Secondary Endpoints: Doublet vs Control and Triplet vs Doublet - OS & ORR, PFS, Safety, QOL

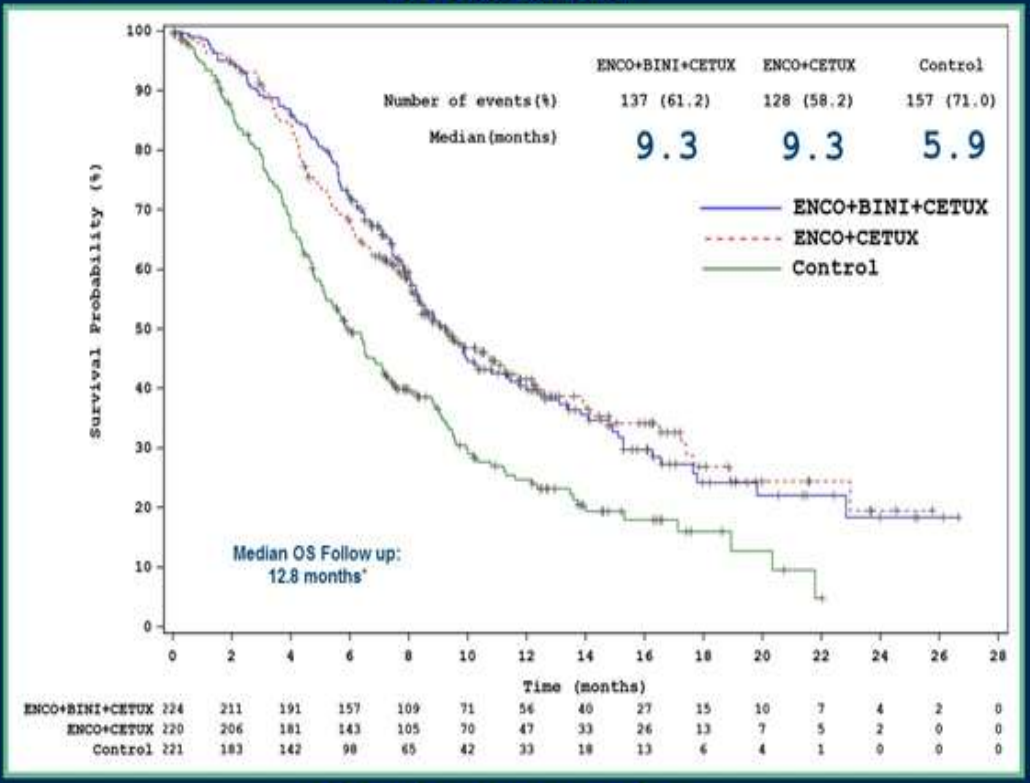
QOL Assessments: EORTC QOL Questionnaire (QLQ C30), Functional Assessment of Cancer Therapy Colon Cancer, EuroQol 5D5L, and Patient Global Impression of Change.

BEACON CRC: Updated Analysis

- In this updated analysis of BEACON CRC (which includes ORR for all randomized patients (additional 364 patients) and 6 months additional follow-up):
  - The triplet and doublet demonstrated improved OS and ORR in patients with BRAF V600E-mutant mCRC when compared with current standard of care chemotherapy

The full updated BEACON results with subgroup analysis will be submitted to a future congress

Overall Survival

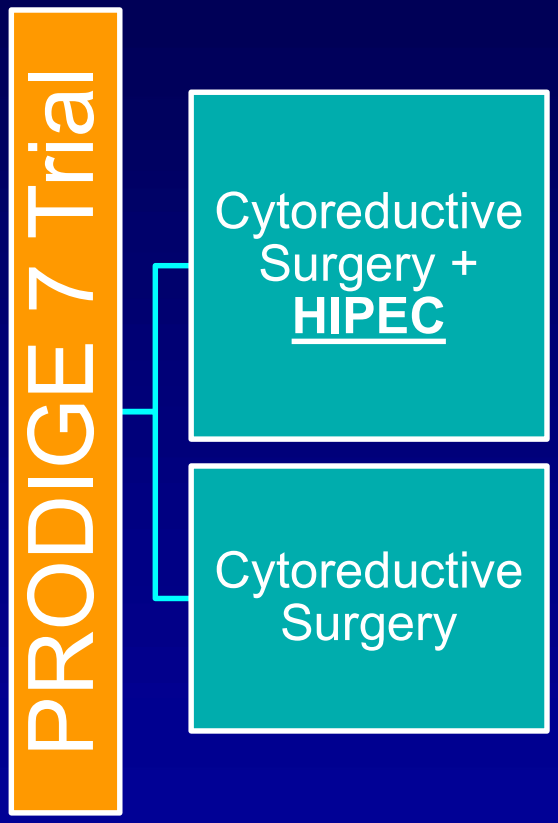


Objective Response Rate

Confirmed Response by blinded central review	Triplet N=224	Doublet N=220	Control N=221
Objective Response Rate	**27%**	**20%**	**2%**
95% (CI)	(21%, 33%)	(15%, 25%)	(<1%, 5%)
p-value vs. Control	<0.0001	<0.0001	

CRC Peritoneal Metastases - HIPEC

CRC Peritoneal Metastases - HIPEC



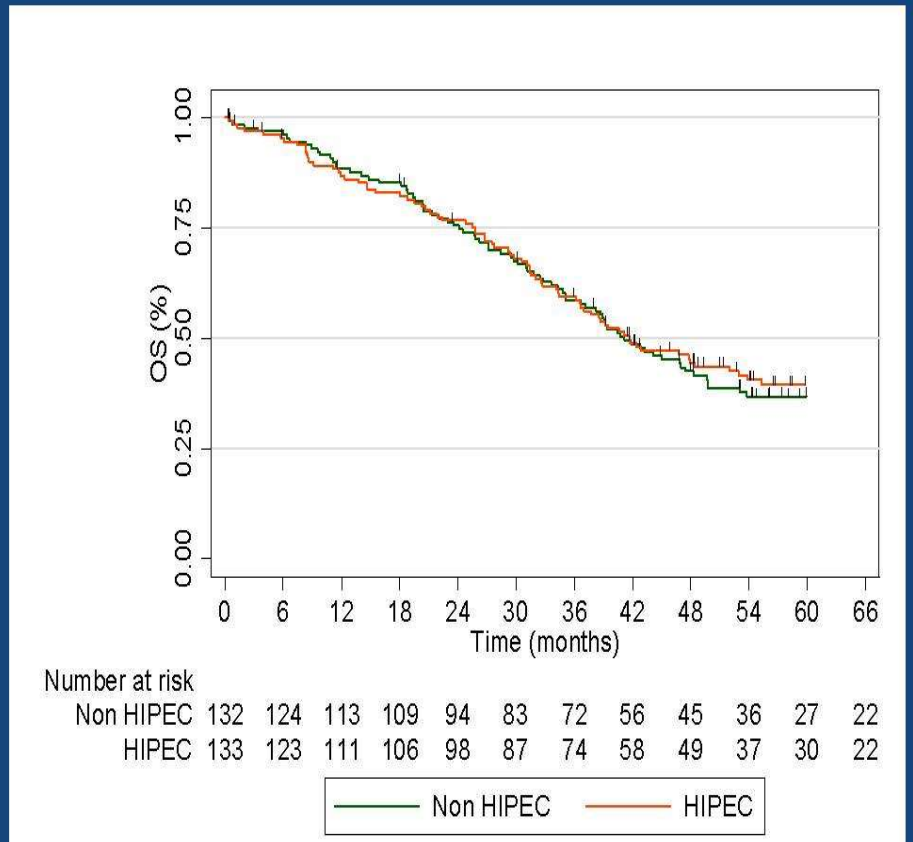
N = 265 patients with colorectal peritoneal carcinomatosis

Received standard chemotherapy before and/or after cytoreductive surgery

HIPEC w/ oxaliplatin

ASCO 2018 LBA 3503.

Overall survival (ITT)



Median Follow Up: 64 months [95% CI:58.9-69.8]

	HIPEC	Non-HIPEC	P-value
Median Survival (months) [95% CI]	41.7 [36.2-52.8]	41.2 [35.1-49.7]	0.995
1-year Survival	86.9%	88.3%	
5-year Survival	39.4%	36.7%	

HR=1.00: 95%CI [0.73 - 1.37] p=0.995

Future Directions

Precision Medicine Platforms

- Platforms with access for Puerto Rico patients:
  - Caris
  - Foundation One
  - Tempus
  - Guardant360

MI PROFILE®

CARIS® LIFE SCIENCES

FINAL REPORT

PATIENT

Name
Date of Birth: 14-Jul-1988
Sex: Male
Case Number:
Diagnosis: Adenocarcinoma, metastatic, NOS

SPECIMEN INFORMATION

Primary Tumor Site: Ascending colon
Specimen Site: Connective tissue, NOS
Specimen ID:
Specimen Collected: 18-Dec-2018
Completion of Testing: 07-Feb-2019

ORDERED BY

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BIOMARKER HIGHLIGHTS (SEE PAGE 2 AND APPENDIX FOR MORE DETAILS)

Biomarker	Method	Result
Lineage Relevant Biomarkers		
MSI	NGS	Stable
Mismatch Repair Status*		Proficient
MLH1	IHC	Positive | 1+, 30%
MSH2	IHC	Positive | 1+, 90%
MSH6	IHC	Positive | 1+, 70%
PMS2	IHC	Positive | 1+, 40%
Tumor Mutational Burden		Intermediate | 7 Mutations/Mb
KRAS	NGS	Mutation Not Detected
NRAS	NGS	Mutation Not Detected
BRAF	NGS	Mutation Not Detected

Biomarker	Method	Result
Lineage Relevant Biomarkers (cont)		
PIK3CA	NGS	Mutation Not Detected
ERBB2 (Her2/Neu)	NGS	Amplified
	CISH	Amplified
	IHC	Positive | 3+, 100%
PTEN	IHC	Positive | 1+, 100%
Other Notable Biomarker Results		
PD-L1	SP142 IHC	Negative | 0
TP53	NGS	Mutated, Pathogenic
		Exon 4 | p.L93fs

HER2+ Colorectal Cancer (CRC)

- 5-8% of colorectal cancer may be HER2+
  - Established therapeutic target in other tumor types
  - Role as a CRC prognosis biomarker remains unclear
    - Emerging data suggest worse outcome in RAS/BRAF/PI3K WT due to poor response to EGFR therapy
      - *Martin et al. Br J Cancer 2013*
  - >90% association with concurrent TP53 mutation, which itself carries a poor prognosis
      - *Sienna et al. Annal Oncol 2018.*
- Trastuzumab + Lapatinib: n=27, ORR 30%, PR 26%, CR 4%(n=1); SD 44% (phase II, open, multi)
      - *Sartore-Bianchi et al. Lancet Oncology 2016. (HERACLES)*
- Trastuzumab + Irinotecan: n=9, PR 71%, with responses >=6weeks (phase II, single center)
    - *Ramanthan et al. Cancer Invest 2004.*

HER2+ CRC Trials

Trial	N = pts	Treatment	ORR	PFS mo.	OS mo.
TRIUMPH	19	Trastuzumab/ Pertuzumab	35%	4	NR
MOUNTAINEER	26	Tucatinib/ Trastuzumab	52%	8.1	18.7
MyPathway	57	Trastuzumab/ Pertuzumab	32%	2.9	NR
HERACLES-A	27	Trastuzumab/ Lapatinib	30%	4.9	11.5
HERACLES-B	30	TDM1/ Pertuzumab	10%	4.7	NR

Liquid Biopsies

- Recent data presented at ESMO showed a concordance rate of 96% between tissue and ctDNA assay.
  - Concordance of $BRAF^{V600E}$ mutation was 98.9%
- Advantages of liquid biopsy:
  - Turn around time (approx. 7 days)
  - Assessment of tumor heterogeneity
  - Dynamic test
  - Detection of resistance mechanisms (ie development of RAS clone)

Kasi, et al. Abstract 622P, ESMO 2019.

The Oncologist®

Gastrointestinal Cancer

Guardant360 Circulating Tumor DNA Assay Is Concordant with FoundationOne Next-Generation Sequencing in Detecting Actionable Driver Mutations in Anti-EGFR Naive Metastatic Colorectal Cancer

Rohan Gupta,[a] Tamer Othman,[c] Chen Chen,[b] Jaideep Sandhu,[a] Ching Ouyang,[b,d] Marwan Fakih[a]

[a]Department of Medical Oncology & Therapeutics Research and [b]Center for Informatics, City of Hope National Medical Center, Duarte, California, USA; [c]Department of Internal Medicine, Harbor-UCLA Medical Center, Torrance, California, USA; [d]Department of Computational and Quantitative Medicine, Beckman Research Institute of the City of Hope National Medical Center, Duarte, California, USA

- 75 patients who had Guardant360 and Foundation One
- 91% concordance between Guardant360 and Foundation One
- ctDNA had higher specificity (94.1%) and diagnostic accuracy (91.3%) than Foundation One for: *KRAS*, *NRAS*, *BRAF*, *HER2*
- Conclusion was that Guardant360 may be used as an alternative to Foundation One for the purpose of identifying appropriate patients for anti-EGFR or BRAF inhibitors

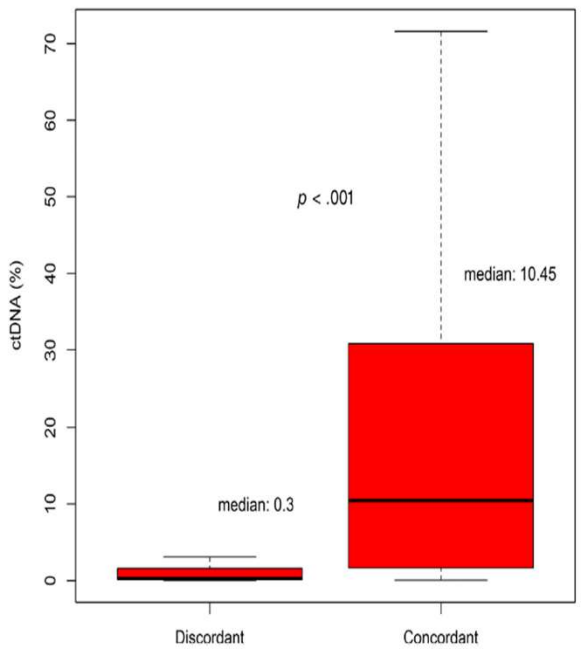


Figure 4. Comparing percentage of circulating tumor DNA (ctDNA) between concordant and discordant somatic mutations seen on G360.

Guardant was more likely to pick up a small allele fraction (< 1%) than Foundation One.
This highlights tumor heterogeneity

COLOMATE

COlorectal and Liquid biOpsy Molecularly Assigned ThErapy

- Metastatic CRC
- Prior treatment with a fluoropyrimidine, oxaliplatin, irinotecan, anti-VEGF monoclonal antibody (bevacizumab, ramucirumab, or ziv-aflibercept), and anti-EGFR if RAS WT

→ **ctDNA/ tissue screening* (n~ 500-1000)**

- **Absence of acquired KRAS, NRAS, BRAF, EGFR mutation or ERRB2/MET amplification**** → **EGFR rechallenge 120 (25%)**
- **HER2 amplified** → **Anti-HER2 N=25 (5%)**
- ***MET* amplified** → **Anti-MET N= 75 (10%)**
- **FGFR** → **Anti-FGFR *N= 30 (5%)***
- **PIK3CA + CDK** → **Anti-PI3K/CDK N= 75 (15%)**
- **NTRK/ROS/ALK** → **Anti-NTRK/ALK (1%)**
- **No actionable change** → **SOC**

Minimal Residual Disease (MRD)

Circulating tumor DNA analysis detects minimal residual disease and predicts recurrence in patients with stage II colon cancer

Jeanne Tie,[1,2,3,4*†] Yuxuan Wang,[5†] Cristian Tomasetti,[6,7] Lu Li,[6] Simeon Springer,[5] Isaac Kinde,[8]

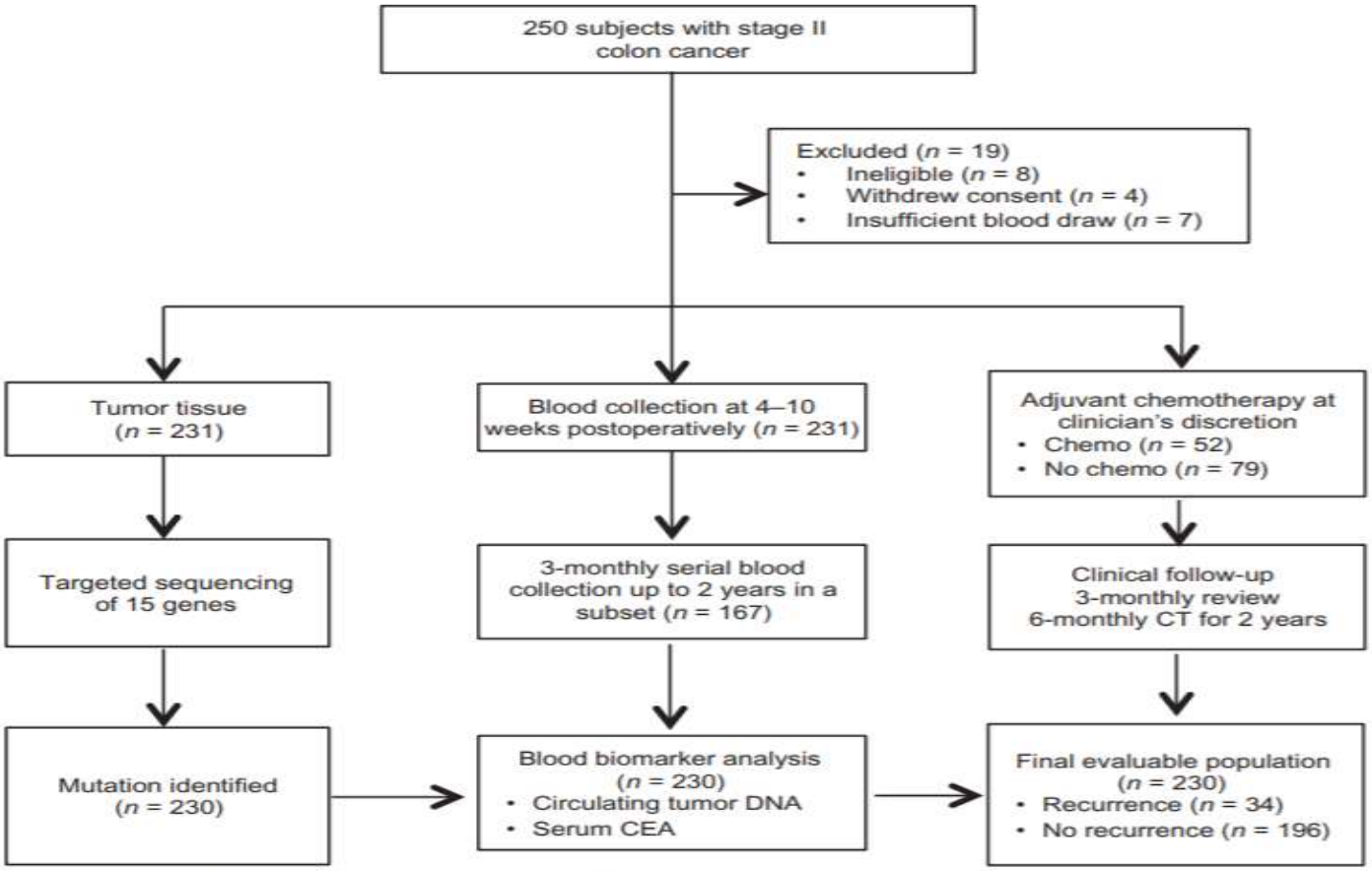


Fig. 1. Patient enrolment and sample collection.

Minimal Residual Disease (MRD)

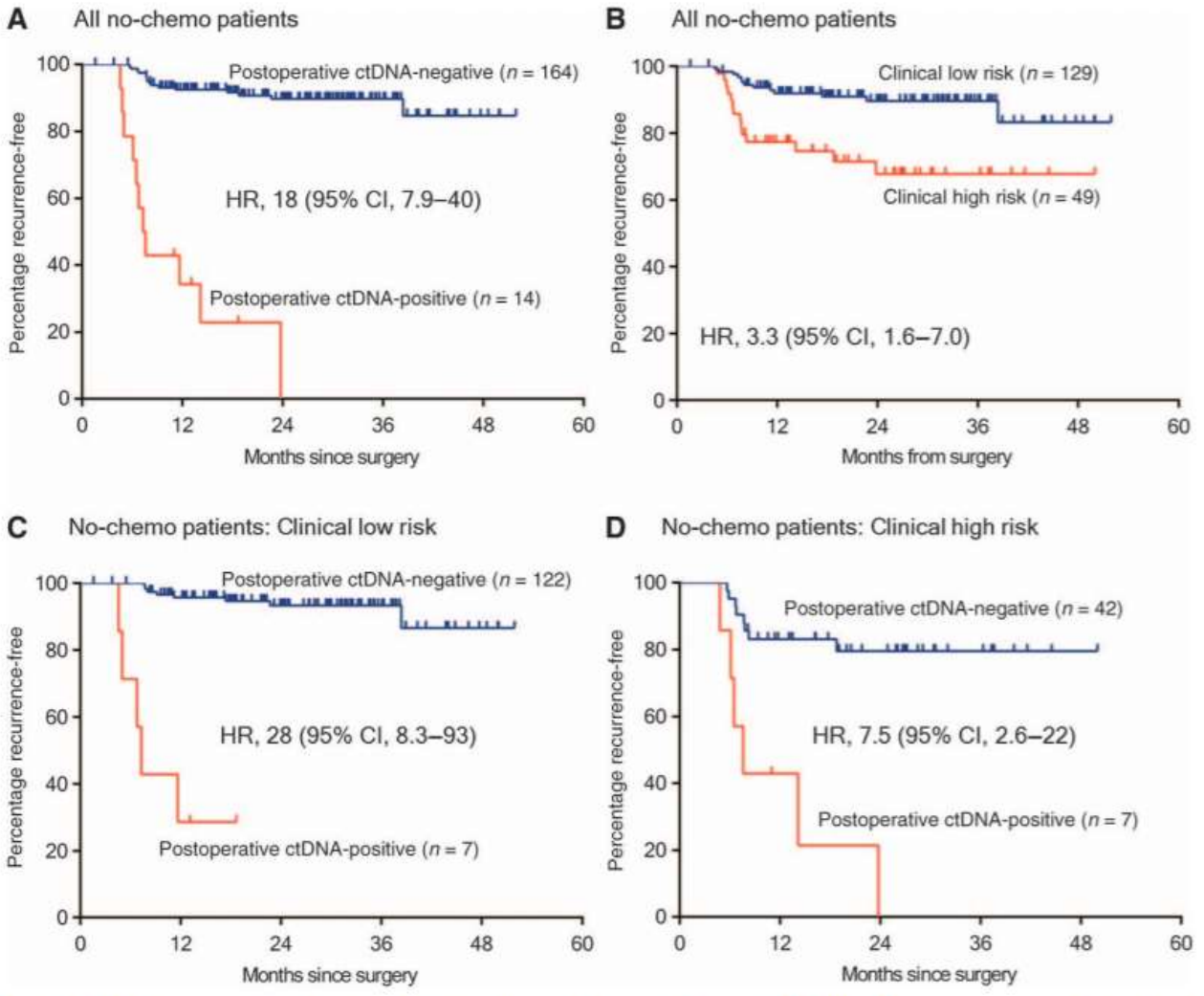


Fig. 2. RFS in patients not treated with adjuvant chemotherapy. (**A**) Kaplan-Meier estimates of RFS for all

Minimal Residual Disease (MRD)

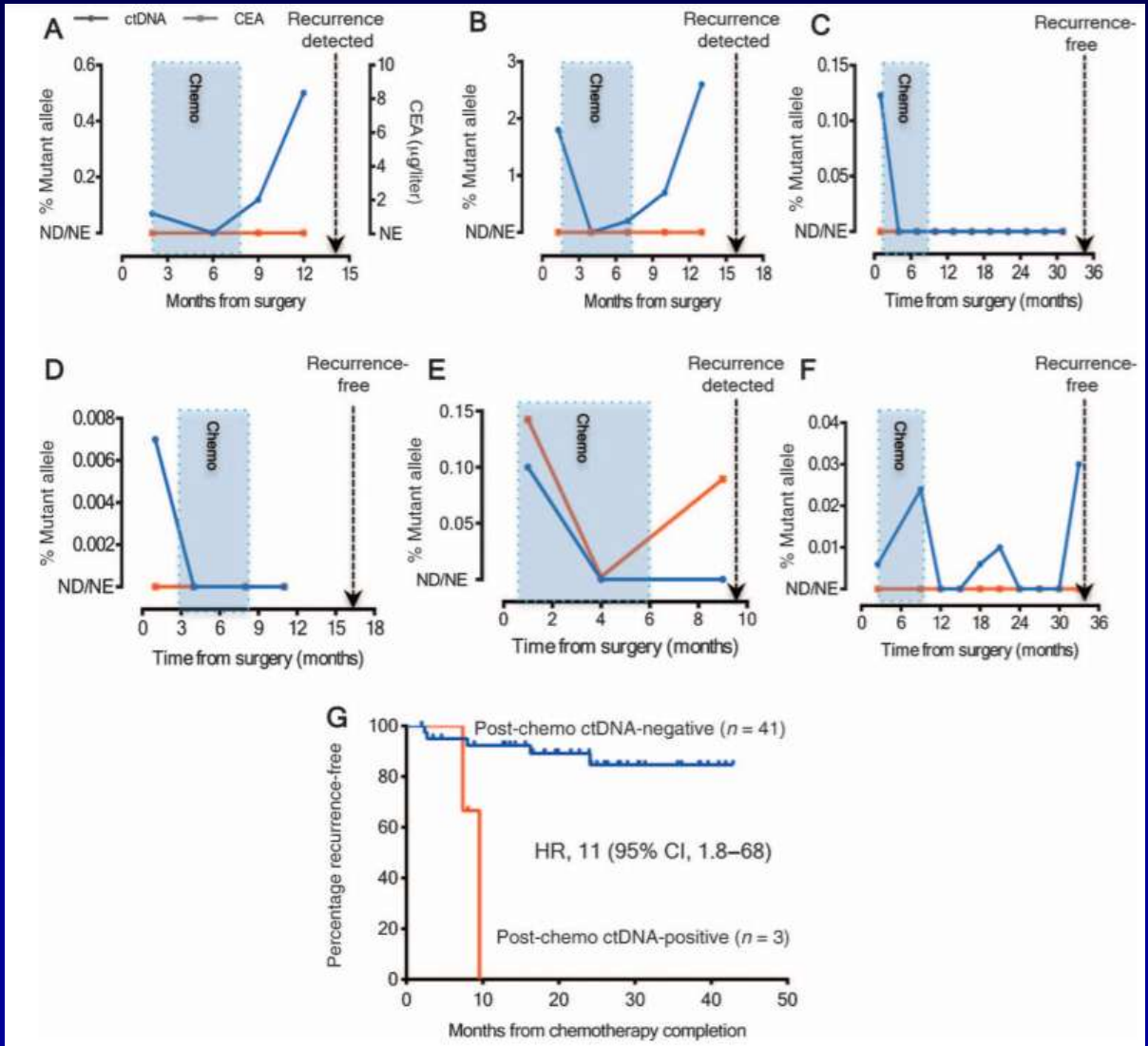


Fig. 3. ctDNA status before, during, and after adjuvant chemotherapy. (**A** to **F**) ctDNA concen-

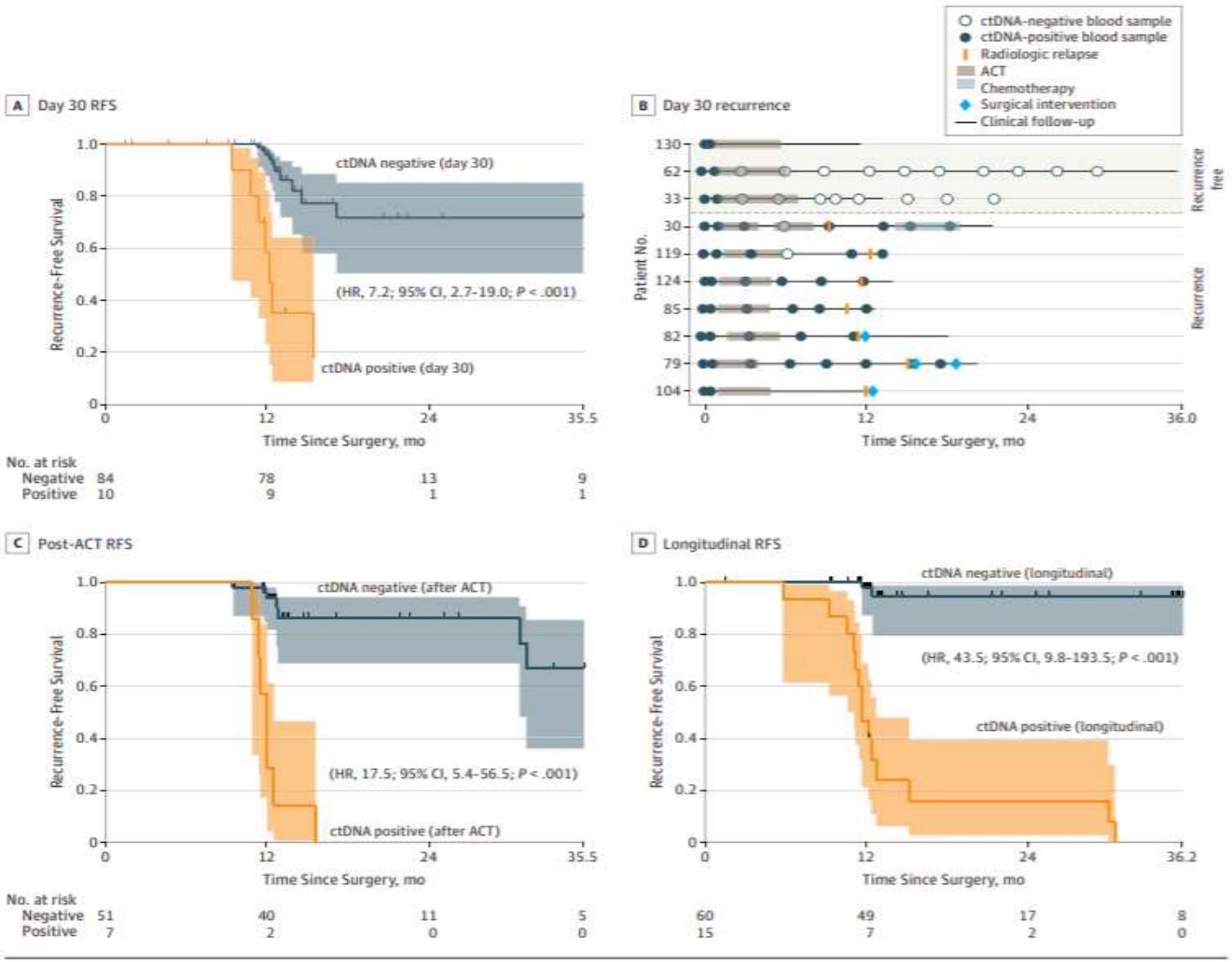
JAMA Oncology | Original Investigation

Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer

Thomas Reinert, PhD; Tenna Vesterman Henriksen, MSc; Emil Christensen, PhD; Shruti Sharma, PhD; Raheleh Salari, PhD; Himanshu Sethi, MPH;

- ctDNA sensitivity to detect recurrence 87.5%
- ctDNA specificity to detect recurrence 100%
- 3 out of 10 +ctDNA became negative with adj. chemo

Figure 2. Preoperative and Postoperative Circulating Tumor DNA (ctDNA) Monitoring in Patients With Colorectal Cancer (CRC)



“Let’s Review”

“Let’s Review”

- Avoid use of EGFRi for first line use in right-sided mCRC, regardless of RAS status
- FOLFOXIRI and biologic (bevacizumab or EGFRi) is a reasonable, if not preferred, option for first line treatment of mCRC
- ctDNA is a reasonable and accurate way to detect actionable mutations in mCRC
- ctDNA represents the future for detecting MRD in CRC

THANK YOU!

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