OVERVIEW OF COLORECTAL AND GASTRIC CANCERS

Winter Cancer Symposium
March 2021

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AdventHealth Cancer Institute

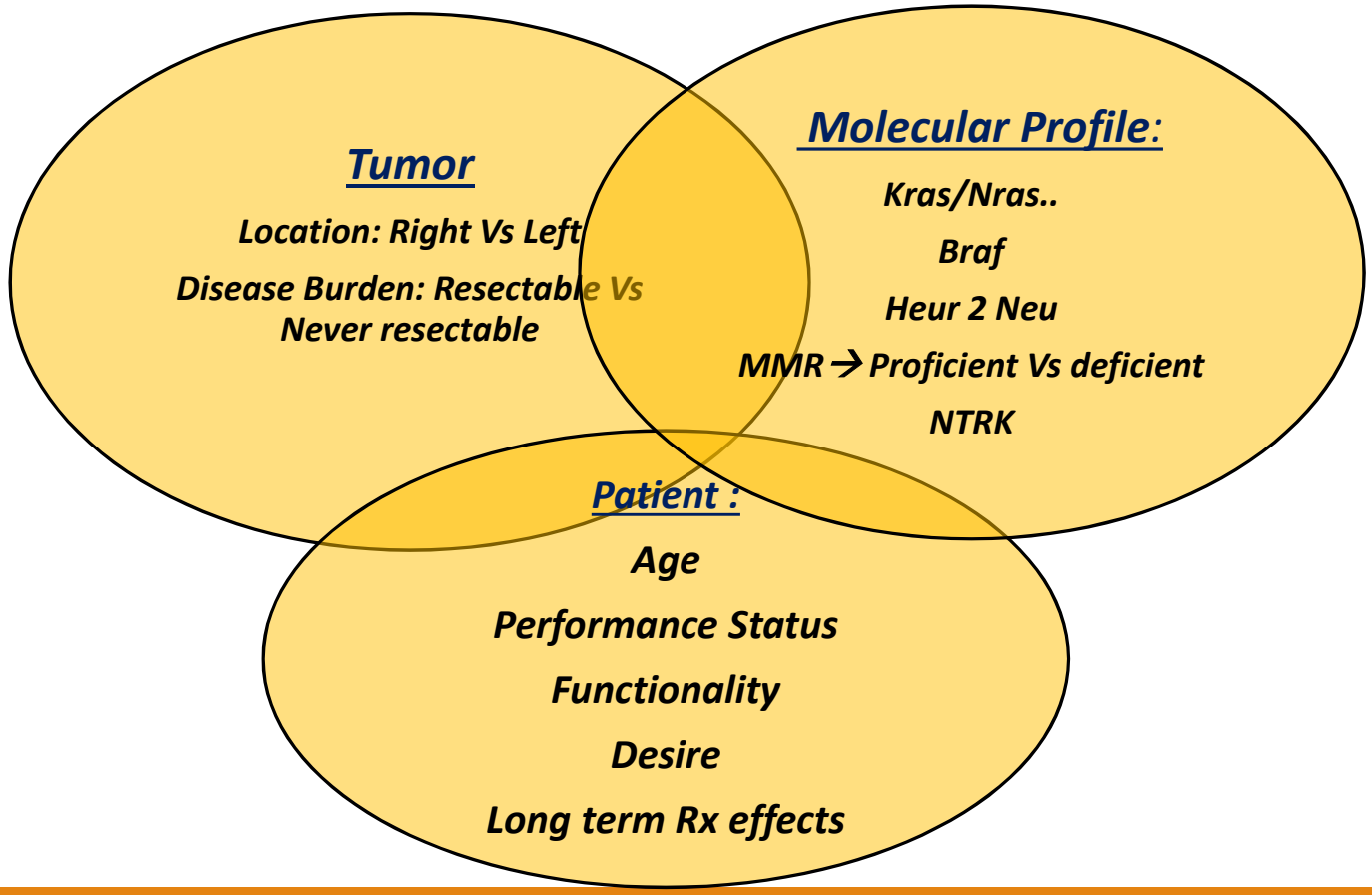
DISCLOSURES

BAYER : Speaker Program, Consulting

AMGEN : Speaker Program

LILLY : Speaker Program


10th Annual
WCS
WINTER CANCER SYMPOSIUM
March 5-7, 2021
La Concha Renaissance Hotel San Juan
San Juan, Puerto Rico
Conference Directors


Tumor
Location: Right Vs Left
Disease Burden: Resectable Vs Never resectable
Molecular Profile:
Kras/Nras..
Braf
Heur 2 Neu
MMR → Proficient Vs deficient
NTRK
Patient :
Age
Performance Status
Functionality
Desire
Long term Rx effects

1. Discuss Early stage Colorectal cancer

2. Where are in Rectal Cancer:
   - TNT, Decision making while Playing with Dynamite
   - Is Triplet Therapy ready for Primetime in Rectal cancer

3. TOSCA Trial : Impact of Age choosing 3 months Vs 6 months of adjuvant Therapy

Lessons from the Past:

1. Poor Compliance with adjuvant chemoRx after Surgery: 32-40%

2.Unclear the Benefit of chemoRx for selected Patients

3.Relapse rate:

- Local: 6-9%
- Distant: 30% 5 yrs

4. Longterm Toxicity: reported 30%

Lessons for the Future:

1. Improved Tolerability

2. Better Compliance for all treatments

3. Tumor Biology

4. Improved Local & Systemic Control

4. Possibility of watch& wait Vs Surgery

5. Less time to Ileostomy reversal

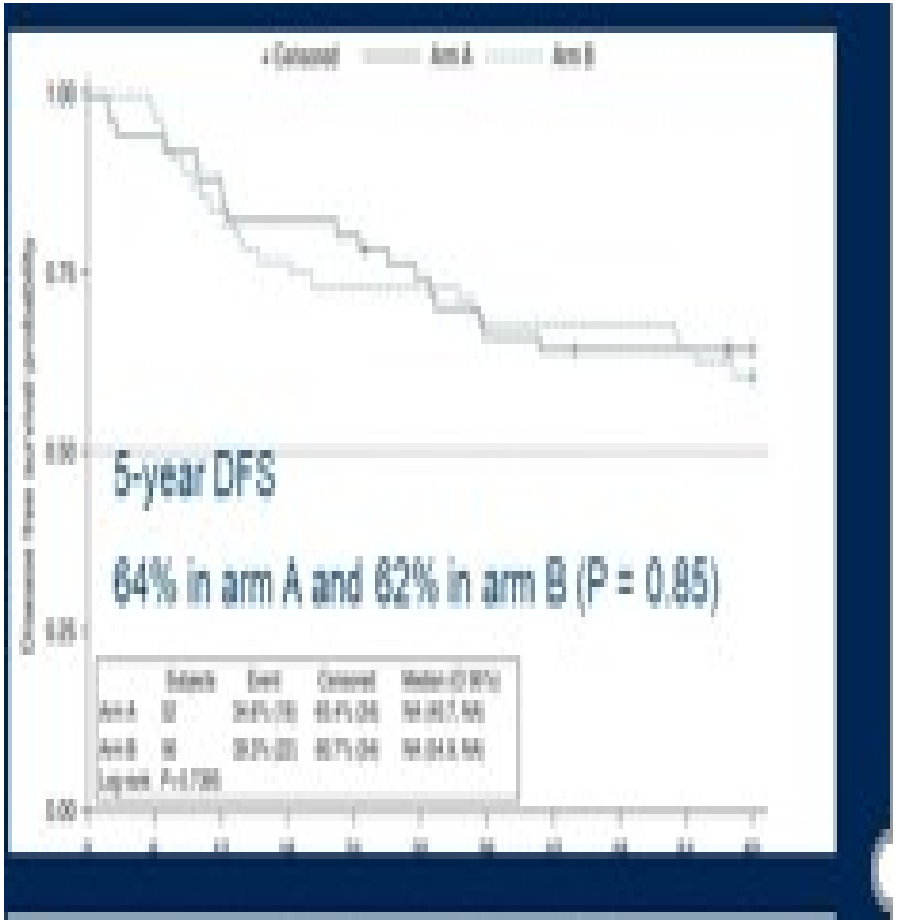
GCR-3: Standard vs. TNT (induction CT)

Fernandez-Martos et al. J Clin Oncol 2010
Fernandez-Martos et al. Annals Oncol 2015

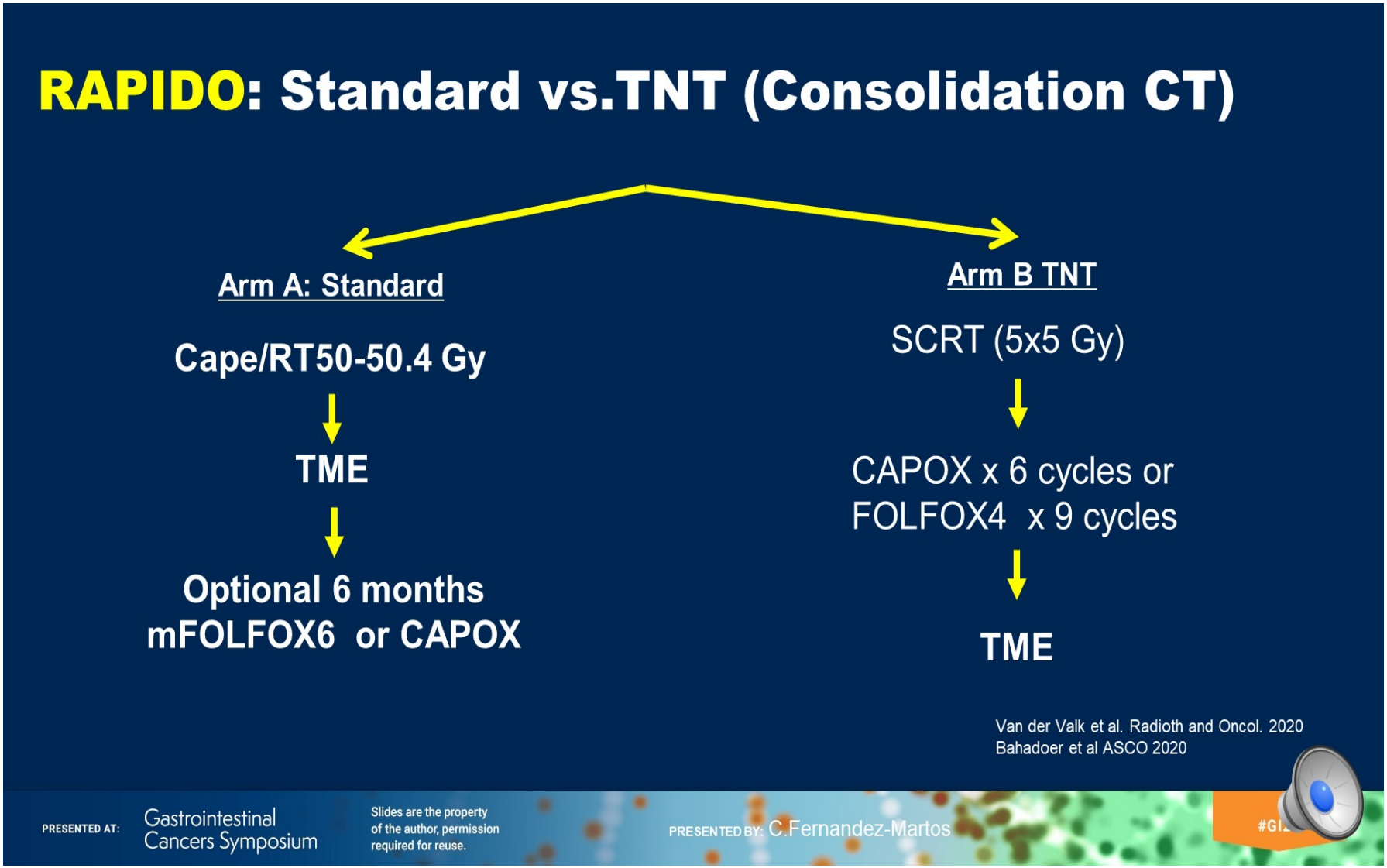
Phase	IIR pick-the-winner; F/U 69 m		
Number patients	108		
1º endpoint	pCR		
MRI risk criteria	mrT3(low, N+ ,CRM+); mrT4		
Tumor location	Middle and low third		
Interval CRT to surgery	5-6 weeks		
Results			
	Standard	TNT	p
CT G3-4 toxicity	54%	19%	.0004
Compliance CT (CAPOX x 4)	54%	91%	<.001
Compliance to RT	80%	85%	n.s
pCR	13%	14%	.94
5-y Local failiure	2%	5%	.61

PRESENTED AT: Gastrointestinal Cancers Symposium

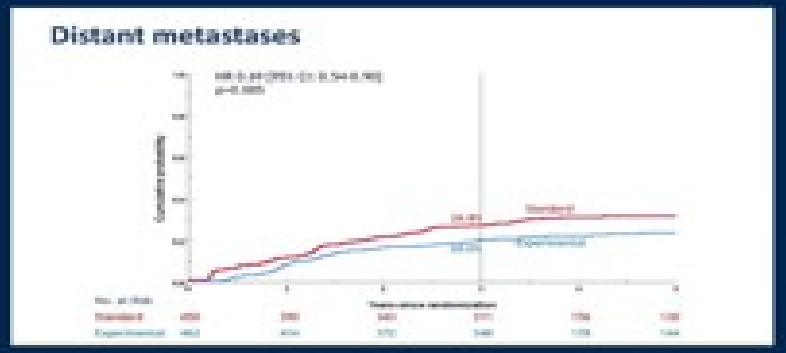
PRESENTED BY: C.Fernandez-Martos

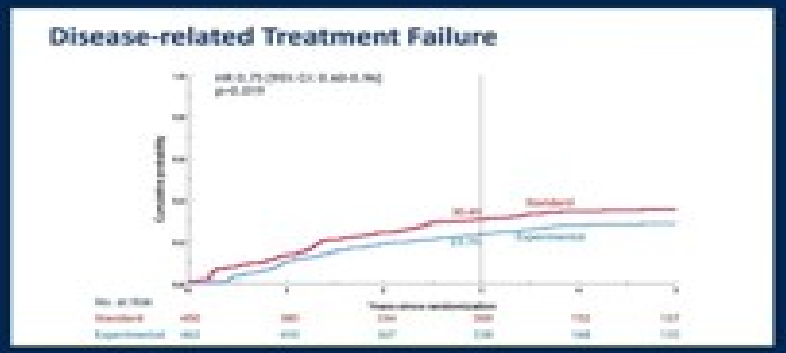


RAPIDO: Standard vs.TNT (Consolidation CT)

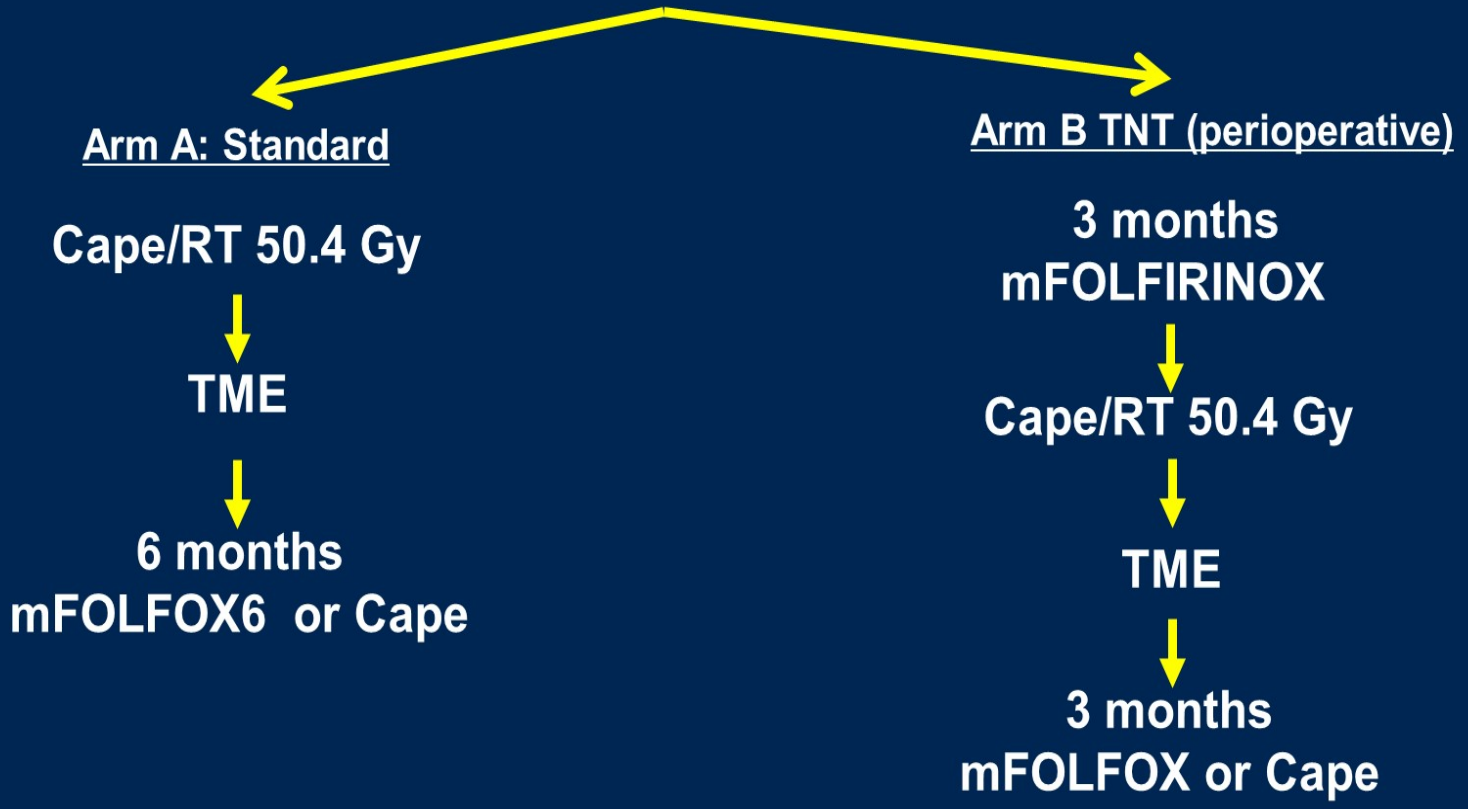


Phase	III (1:1); F/U: 54 m		
Number patients	920		
1º endpoint	3-y DrTF		
MRI risk criteria	mrT4, mrN2, mrEMVI+, mrMRF+		
Tumor location	High, middle and low third		
Interval CRT to surgery	Standard: 8+/- 2 w; TNT 22-24 w		
Results			
	Standard	TNT	p
Toxicity ≥ G3 during preop	25%	48%	nr
Compliance CRT/SCRT	93%	100%	nr
Compliance 75% adj/consolidationCT	58%	84%	nr
Completed planned cycles	47%	67%	nr
pCR	14%	28%	<.001
Locoregional failiure	8.7%	6%	.09



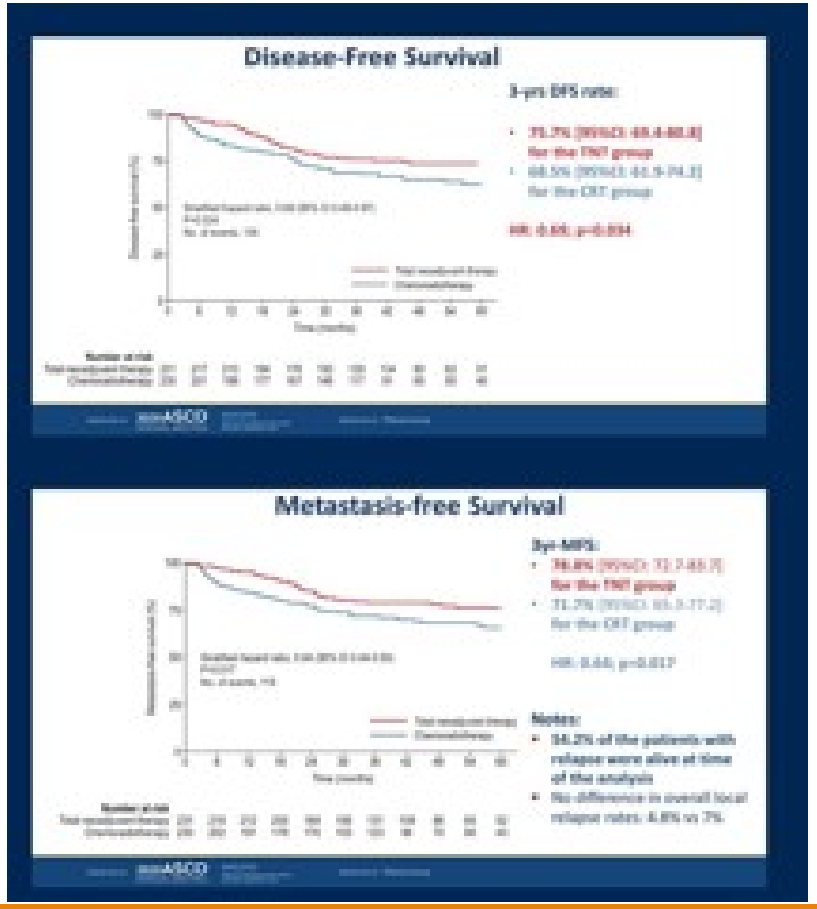


PRODIGE 23: Standard vs TNT (induction+adj CT)



Conroy et al. AS 020

Phase	III ; F/U 46 m		
Number patients	461		
1º endpoint	3-y DFS		
MRI risk criteria	mrT3,mrT4		
Tumor location	High, middle and low third		
Interval CRT to surgery	7 weeks		
Results			
	Standard	TNT	p
Compliance (mFOLFIRINOX x 6)	-	92%	-
G3+ AEs adjuvant CT	74%	44%	<.001
All cycles completed adjuvant CT	75	80	ns
Compliance RT	98%	98%	ns
pCR	12%	27%	<.001



FONDAZIONE GISCAD

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI · IRCCS

OXALIPLATIN PLUS FLUOROPYRIMIDINES AS ADJUVANT THERAPY FOR COLON CANCER IN ELDERLY PATIENTS: A SUBGROUP ANALYSIS FROM TOSCA TRIAL

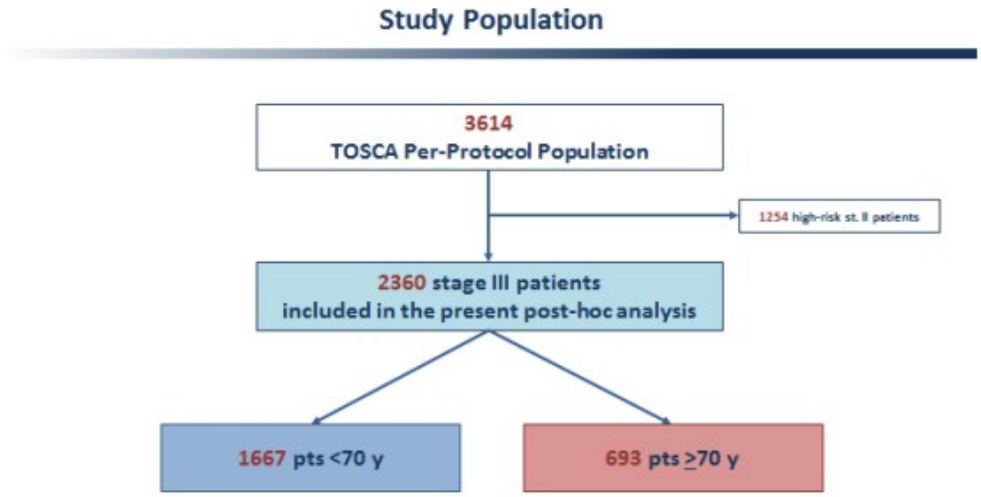
G. ROSATI, FA. GALLI, S. LONARDI, K.F. DOTTI, M. RONZONI, M.G. ZAMPINO, M. BANZI, V. PUSCEDDU, F. PASINI, S. BOZZARELLI, N. PELLA, C. CODECÀ, V. MONTESARCHIO, A. MAMBRINI, A. DE STEFANO, L. CIUFFREDA, S.E. REBUZZI, FR. GALLI, D. BILANCIA, R. LABIANCA

ON BEHALF OF ALL TOSCA (THREE OR SIX COLON ADJUVANT) INVESTIGATORS

TOSCA TRIAL subgroup Analysis

(ESMO 2020)

TOSCA age study population



Post-hoc analysis of stage III

Stage III = 65% of total population available

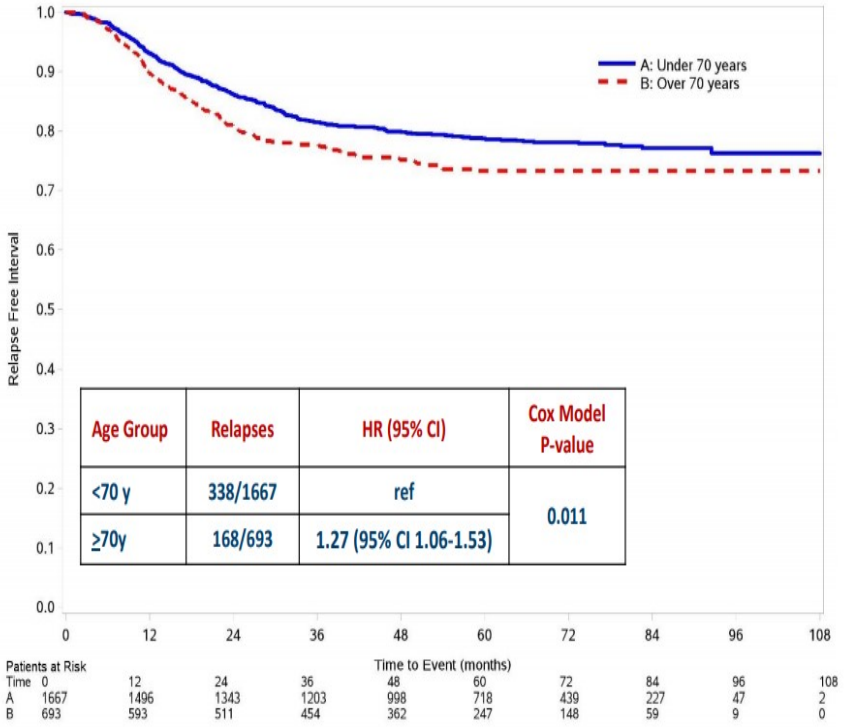
30% of included group >70 yo

TOSCA TRIAL subgroup Analysis
(ESMO 2020)

Events

	< 70 y. n = 1667	≥ 70 y. n = 693	Chi-square p-value
Follow-up (months)			-
Median	62.5	60.6	
Inter-quartile Range (1°-3°)	48.1-78.8	46.8-75.8	
Relapse – n (%)	338 (20.3)	168 (24.2)	**0.033**
Relapse site – n (%)			
Local	25 (7.5)	13 (7.7)	
Distant	293 (87.5)	142 (84.5)	
Both	17 (5.1)	13 (7.7)	
Missing	3	0	

Primary End-Point: Relapse-Free Interval



Age Group	Relapses	HR (95% CI)	Cox Model P-value
<70 y	338/1667	ref	0.011
≥70y	168/693	1.27 (95% CI 1.06-1.53)	

TOSCA TRIAL subgroup Analysis

(ESMO 2020)

- Patients 70 years or older :
- More PS 1
- More right sided cancers
- More T3-4
- Regimens equally distributed

- Patients 70 years or older :
- Statistically lower mean treatment duration, treatment completed, and greater rate of dose reduction
- Higher Relapse Rate %;

  24.2 % v 20.3 % (p=0.033)
- Relapse Free interval HR 1.27

  LR p=0.011
- In multivariate analysis impact of age was not significant

  (HR 1.19 (95% CI 0.98-1.44) LR

  p=0.82

TOSCA TRIAL subgroup Analysis
(ESMO 2020)

- ✓ TOSCA[1] is a phase III non-inferiority trial randomizing 3759 patients within the IDEA[2] collaboration investigating adjuvant treatment duration in colon cancer.
- ✓ The study failed to show noninferiority of 3 vs 6 months of treatment to the predefined margin of 20% relative increase.
- ✓ However, a qualitative, non statistically significant interaction between regimen and treatment duration was observed: for CAPOX, 3 months were as good as 6 months; for FOLFOX, 6 months added extra benefit.
- ✓ The results of TOSCA Trial were consistent with those of the pooled analysis IDEA on more than 12.800 patients enrolled in 6 studies.

[1] Sobrero A et al, J Clin Oncol 2018
[2] Grothey A et al, N Engl J Med 2018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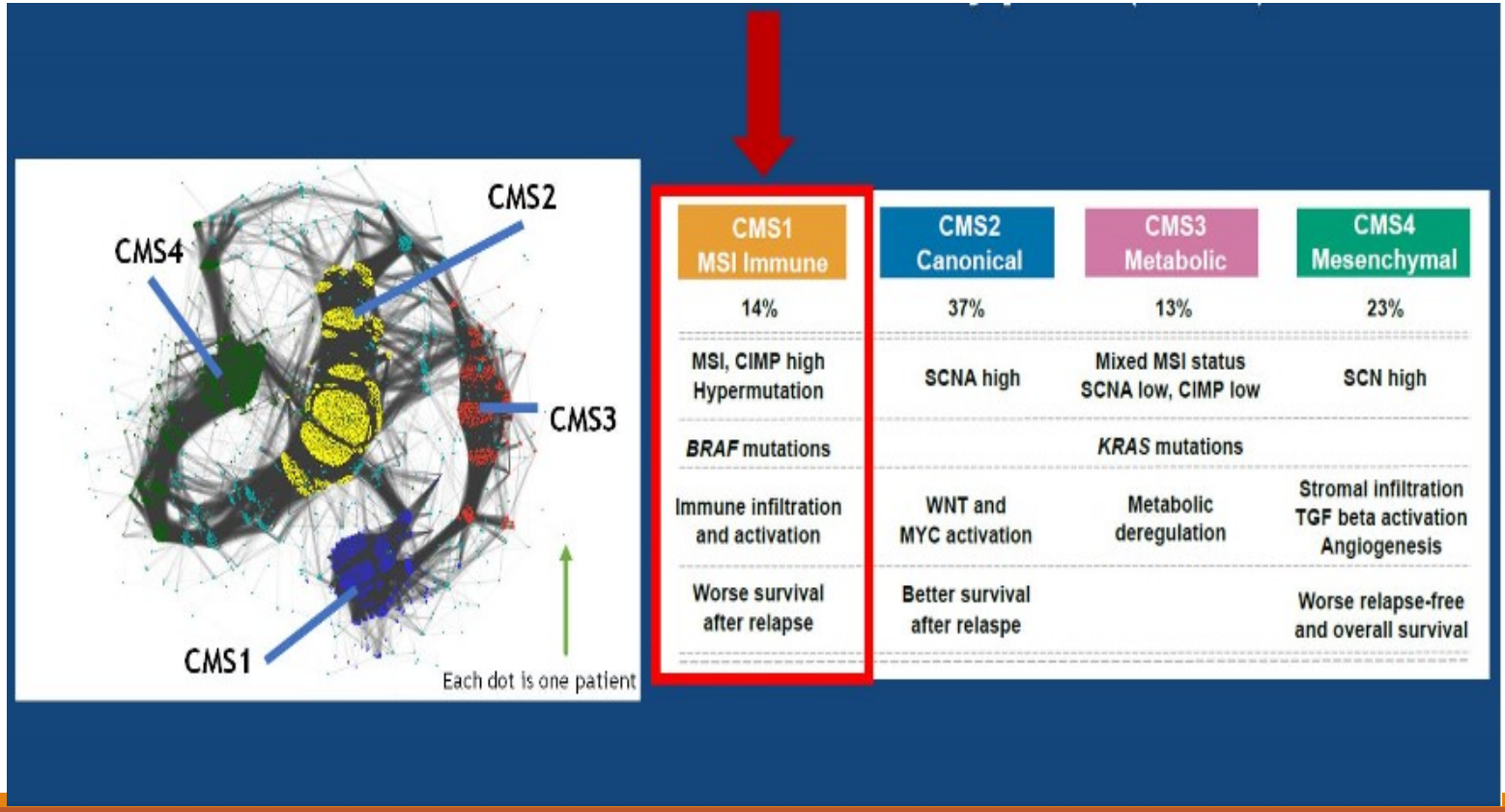
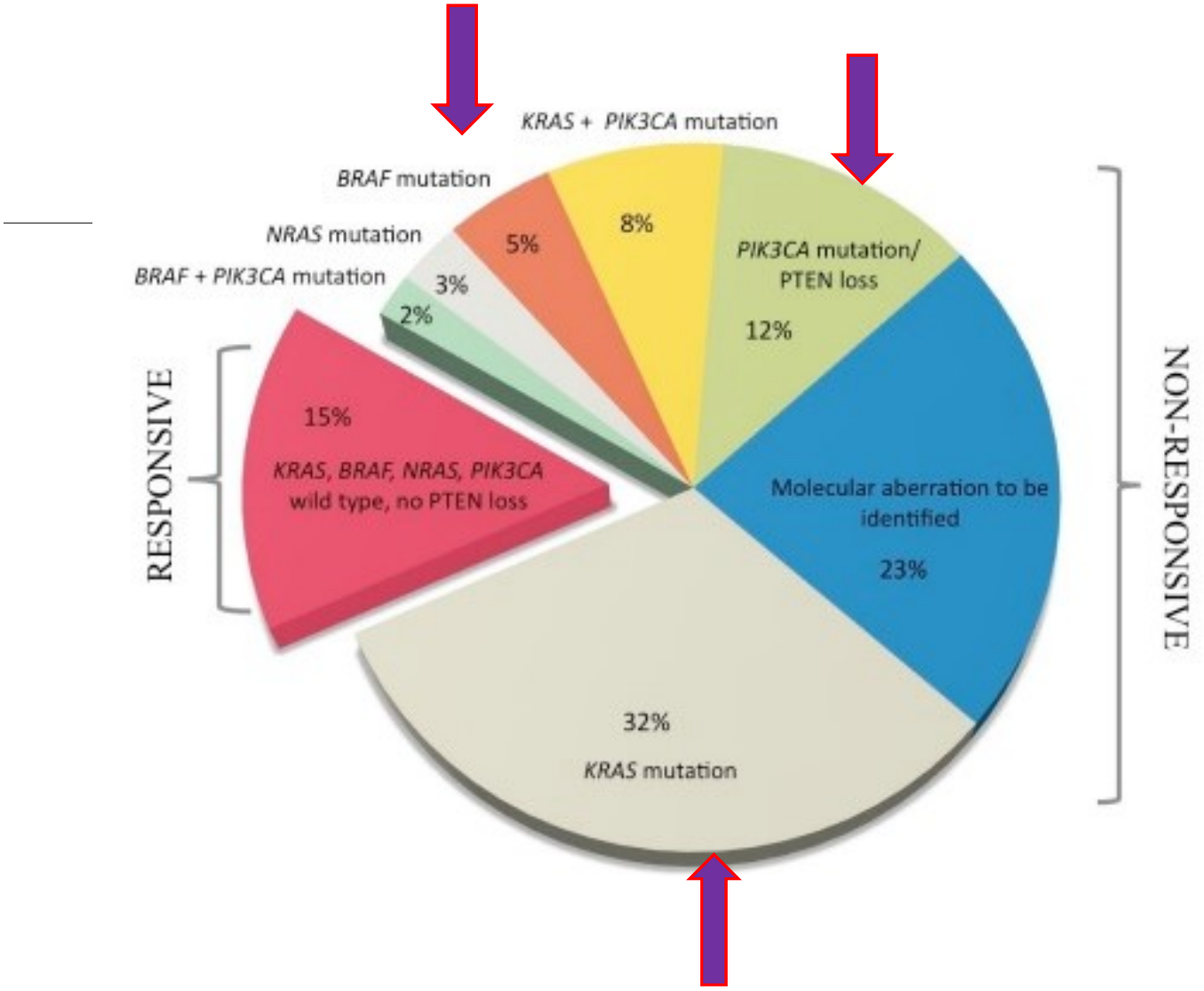

CMS2
CMS4
CMS3
CMS1
Each dot is one patient
CMS1 MSI Immune
CMS2 Canonical
CMS3 Metabolic
CMS4 Mesenchymal
14%
37%
13%
23%
MSI, CIMP high Hypermutation
SCNA high
Mixed MSI status SCNA low, CIMP low
SCN high
BRAF mutations
KRAS mutations
Immune infiltration and activation
WNT and MYC activation
Metabolic deregulation
Stromal infiltration TGF beta activation Angiogenesis
Worse survival after relapse
Better survival after relaspe
Worse relapse-free and overall survival


KRAS + PIK3CA mutation
8%
BRAF mutation
5%
NRAS mutation
3%
BRAF + PIK3CA mutation
2%
PIK3CA mutation/
PTEN loss
12%
RESPONSIVE
15%
KRAS, BRAF, NRAS, PIK3CA
wild type, no PTEN loss
Molecular aberration to be
identified
23%
NON-RESPONSIVE
32%
KRAS mutation

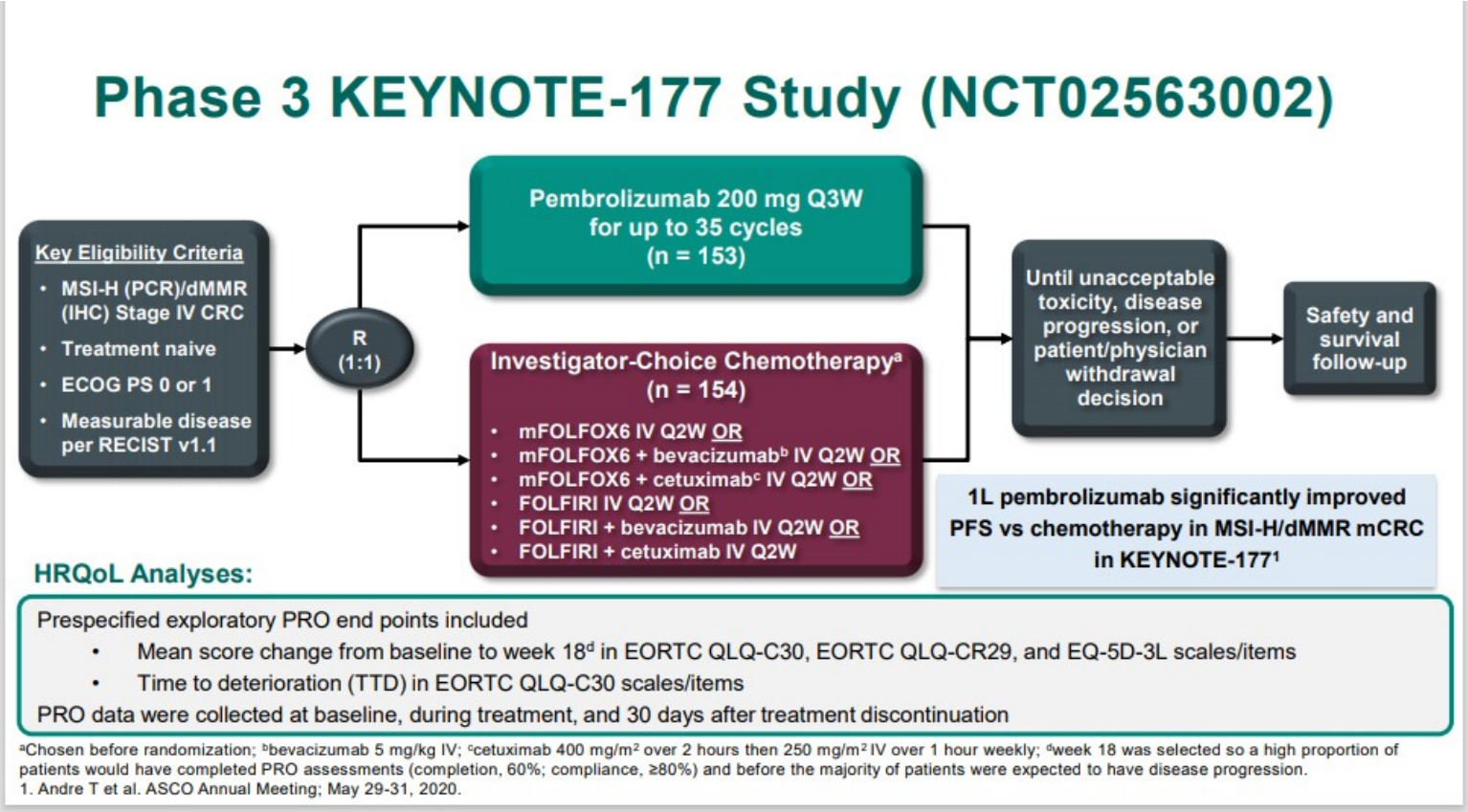
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 3, 2020 VOL. 383 NO. 23

Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer

T. André, K.-K. Shiu, T.W. Kim, B.V. Jensen, L.H. Jensen, C. Punt, D. Smith, R. Garcia-Carbonero, M. Benavides, P. Gibbs, C. de la Fouchardiere, F. Rivera, E. Elez, J. Bendell, D.T. Le, T. Yoshino, E. Van Cutsem, P. Yang, M.Z.H. Farooqui, P. Marinello, and L.A. Diaz, Jr., for the KEYNOTE-177 Investigators*

KEYNOTE 177


Phase 3 KEYNOTE-177 Study (NCT02563002)
Key Eligibility Criteria
• MSI-H (PCR)/dMMR (IHC) Stage IV CRC
• Treatment naive
• ECOG PS 0 or 1
• Measurable disease per RECIST v1.1
R (1:1)
Pembrolizumab 200 mg Q3W for up to 35 cycles (n = 153)
Investigator-Choice Chemotherapy[a] (n = 154)
• mFOLFOX6 IV Q2W OR
• mFOLFOX6 + bevacizumab[b] IV Q2W OR
• mFOLFOX6 + cetuximab[c] IV Q2W OR
• FOLFIRI IV Q2W OR
• FOLFIRI + bevacizumab IV Q2W OR
• FOLFIRI + cetuximab IV Q2W
Until unacceptable toxicity, disease progression, or patient/physician withdrawal decision
Safety and survival follow-up
1L pembrolizumab significantly improved PFS vs chemotherapy in MSI-H/dMMR mCRC in KEYNOTE-177[1]
HRQoL Analyses:
Prespecified exploratory PRO end points included
• Mean score change from baseline to week 18[d] in EORTC QLQ-C30, EORTC QLQ-CR29, and EQ-5D-3L scales/items
• Time to deterioration (TTD) in EORTC QLQ-C30 scales/items
PRO data were collected at baseline, during treatment, and 30 days after treatment discontinuation
[a]Chosen before randomization; [b]bevacizumab 5 mg/kg IV; [c]cetuximab 400 mg/m² over 2 hours then 250 mg/m² IV over 1 hour weekly; [d]week 18 was selected so a high proportion of patients would have completed PRO assessments (completion, 60%; compliance, ≥80%) and before the majority of patients were expected to have disease progression.
1. Andre T et al. ASCO Annual Meeting; May 29-31, 2020.

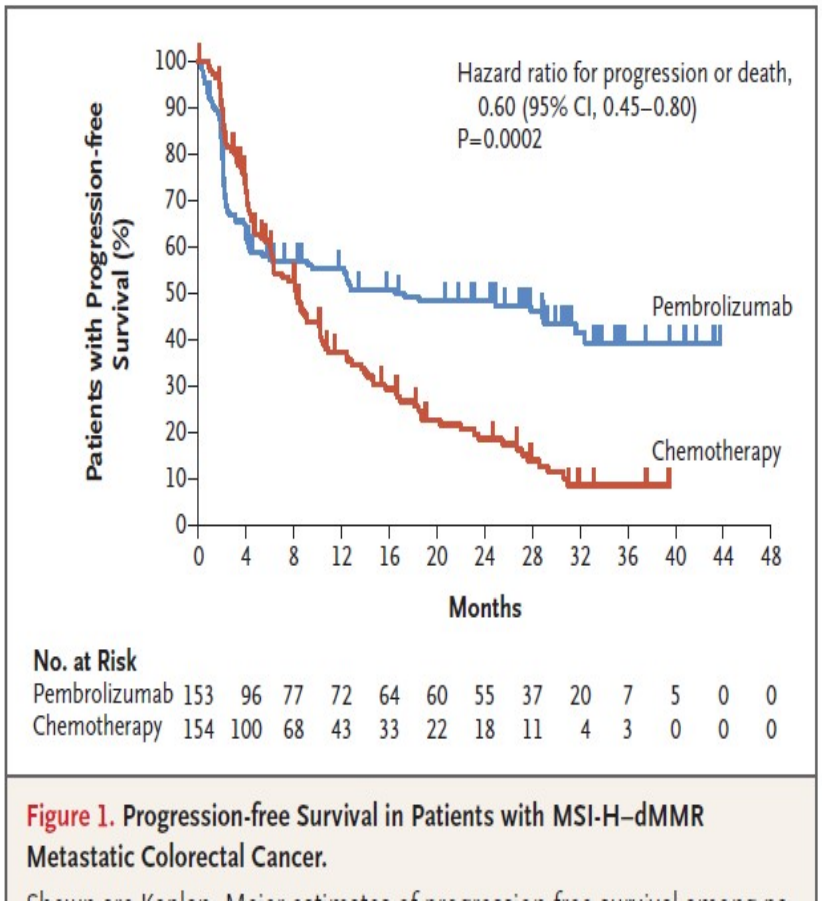
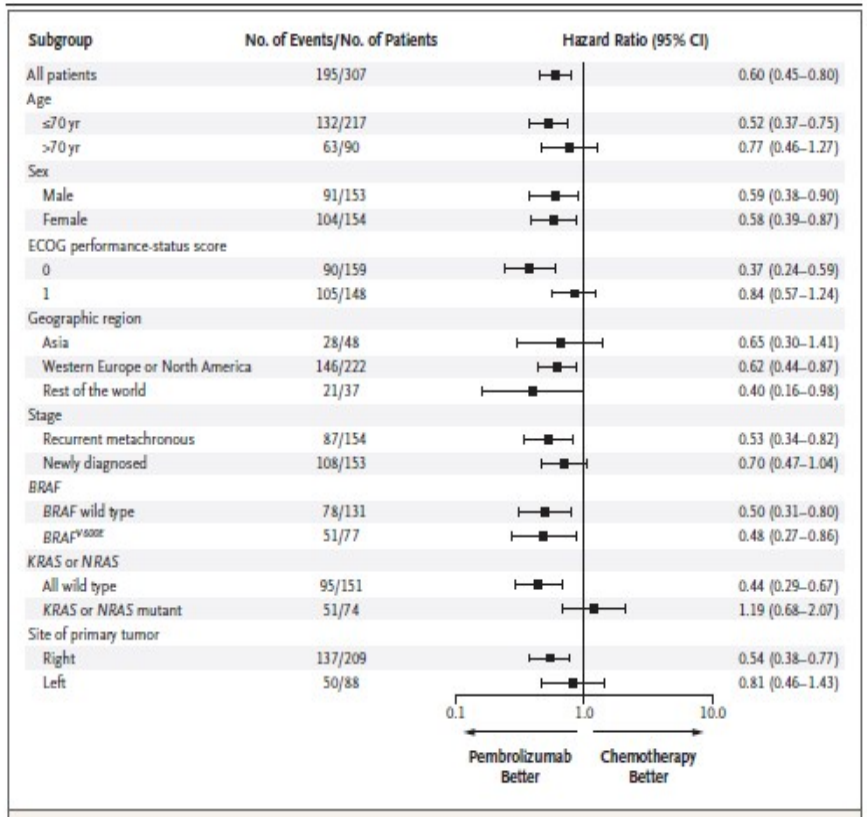


Figure 1. Progression-free Survival in Patients with MSI-H–dMMR Metastatic Colorectal Cancer.

Shown are Kaplan–Meier estimates of progression-free survival among pa



National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2021
Colon Cancer

NCCN Guidelines Index
Table of Contents
Discussion

CONTINUUM OF CARE - SYSTEMIC THERAPY FOR ADVANCED OR METASTATIC DISEASE[a,b]

Patient appropriate for intensive therapy

INITIAL THERAPY[c]

- FOLFOX ± bevacizumab[d] → Progression → See COL-D (2 of 13)
- or CAPEOX ± bevacizumab[d] → Progression → See COL-D (2 of 13)
- or FOLFOX + (cetuximab or panitumumab)[e,f] (*KRAS/NRAS/BRAF* WT and left-sided tumors only) → Progression → See COL-D (2 of 13)
- or FOLFIRI[g] ± bevacizumab[d] → Progression → See COL-D (3 of 13)
- or FOLFIRI[g] + (cetuximab or panitumumab)[e,f] (*KRAS/NRAS/BRAF* WT and left-sided tumors only) → Progression → See COL-D (3 of 13)
- or FOLFOXIRI[g,h] ± bevacizumab[d] → Progression → See COL-D (4 of 13)
- or ([Nivolumab ± ipilimumab] or pembrolizumab [preferred]*)[i,j,k,l] (dMMR/MSI-H only)[e] → Progression → See COL-D (5 of 13)

Patient not appropriate for intensive therapy

- 5-FU ± leucovorin ± bevacizumab[d]
- or Capecitabine ± bevacizumab[d]
- or (Cetuximab or panitumumab)[e,f] (category 2B) (*KRAS/NRAS/BRAF* WT and left-sided tumors only)
- or (Nivolumab or pembrolizumab [preferred])[i,j,k,l] (dMMR/MSI-H only)[e]
- or Nivolumab + ipilimumab[i,j,k,l] (dMMR/MSI-H only)[e] (category 2B)
- or (Trastuzumab[m] + [pertuzumab or lapatinib])[n] or fam-trastuzumab deruxtecan-nxki[o] (HER2-amplified and *RAS and* BRAF WT)[e]

→ Progression

- Improvement in functional status → Consider initial therapy as above[p] or If previous fluoropyrimidine, see COL-D (5 of 13)
- No improvement in functional status → Best supportive care See NCCN Guidelines for Palliative Care

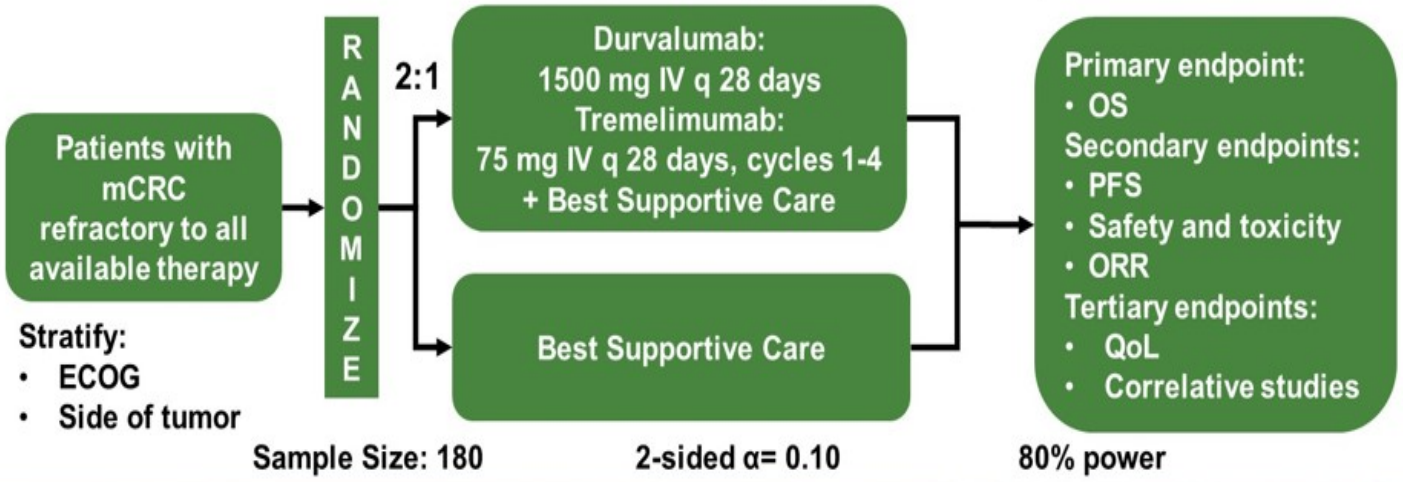
* Patients should be followed closely for 10 weeks to assess for response.

See footnotes on COL-D (7 of 13)

Canadian Cancer Trials Group
A national program of the Canadian Cancer Society

Tissue and plasma tumor mutation burden (TMB) as predictive biomarkers in the CCTG CO.26 trial of durvalumab + tremelimumab versus best supportive care in metastatic colorectal cancer

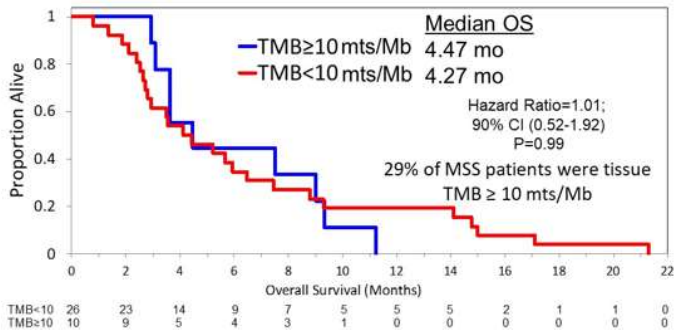
- We compared tissue and plasma TMB as predictive biomarkers for immunotherapy benefit in patients with MSS mCRC from the CO.26 trial
  - Tissue TMB: derived from exomes (SureSelect All Exon v6) of archival samples and followed TMB Harmonization Project Guidelines with a 32.1 Mb TMB denominator
  - Plasma TMB: utilized the GuardantOMNI™ 500 gene, 2.1 Mb ctDNA panel



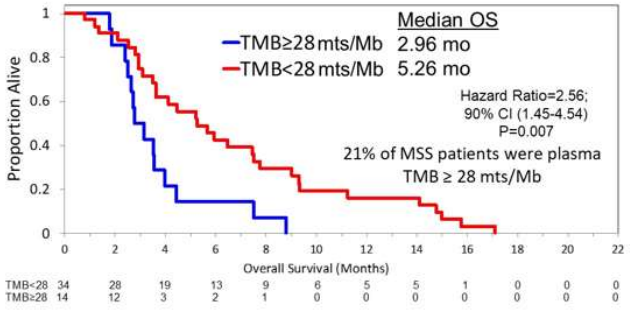
OS : WITH BSC

OS : DURVA/TREME

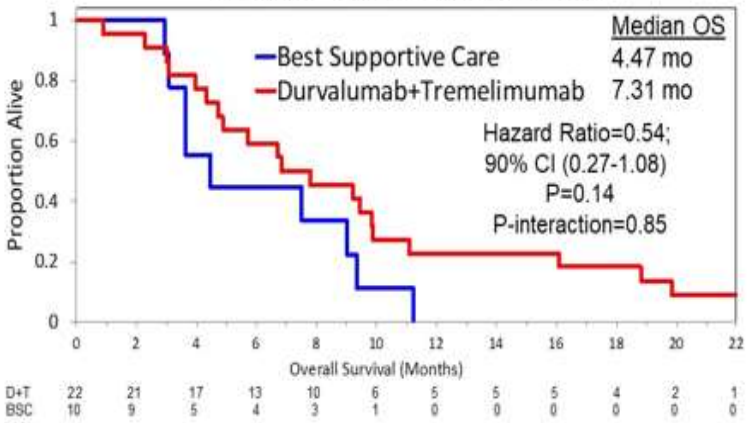
Overall Survival in Patients Receiving Best Supportive Care Stratified by Tissue TMB



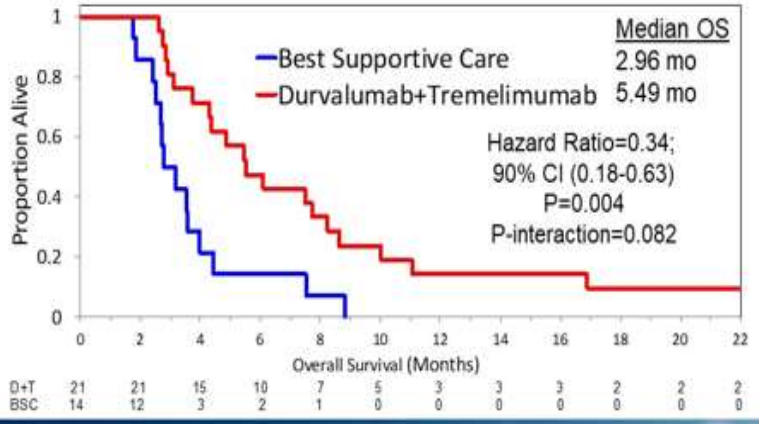
Overall Survival in Patients Receiving Best Supportive Care Stratified by Plasma TMB



Tissue TMB ≥10 mts/Mb



Plasma TMB ≥28 mts/Mb



TARGETING BRAF IN CRC

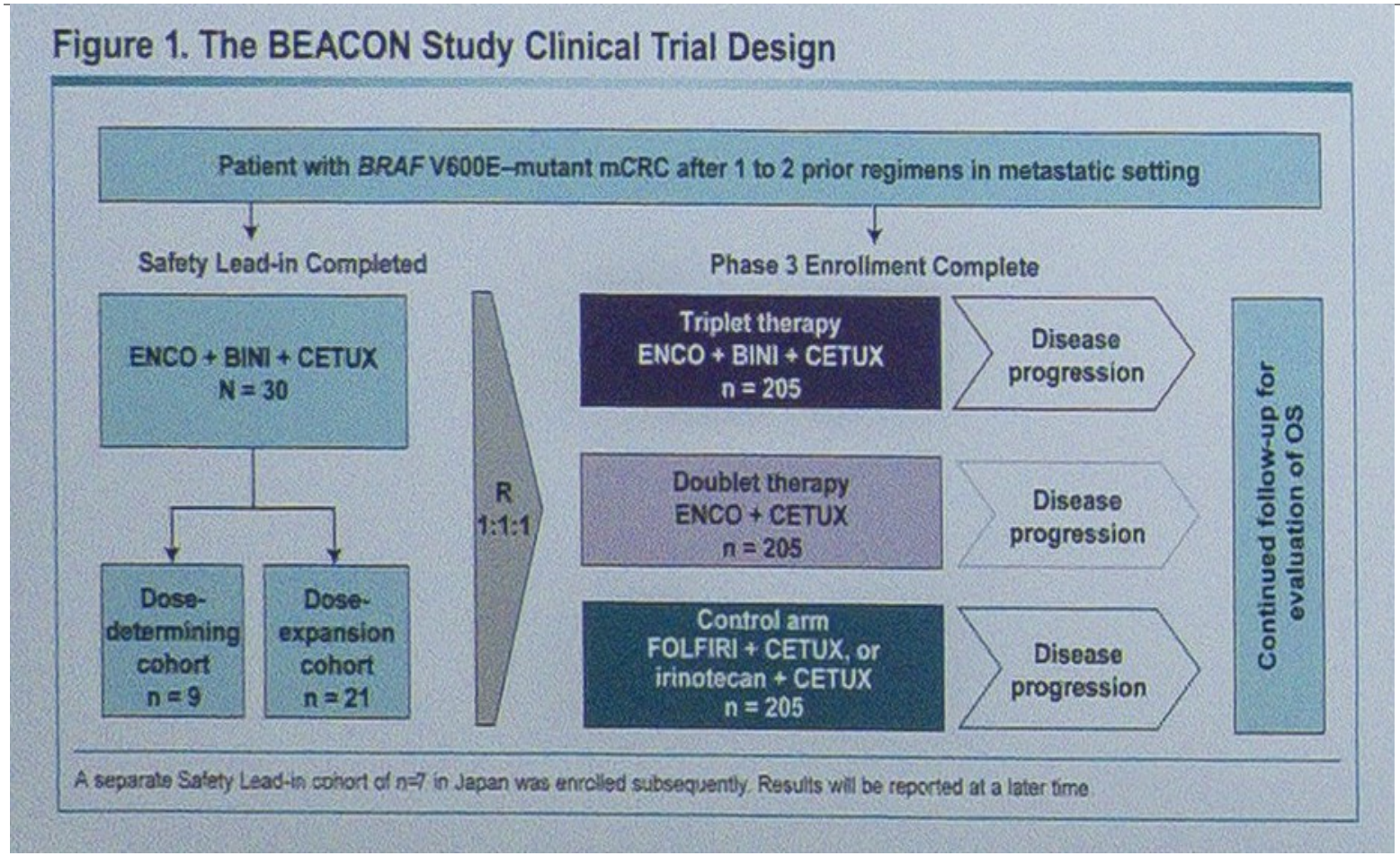
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

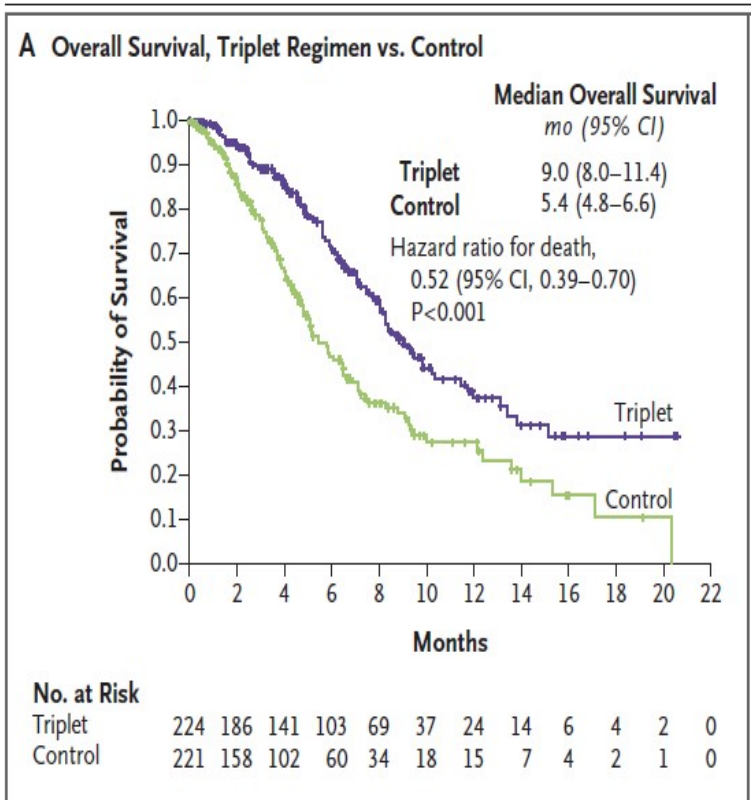
Encorafenib, Binimetinib, and Cetuximab in *BRAF* V600E–Mutated Colorectal Cancer

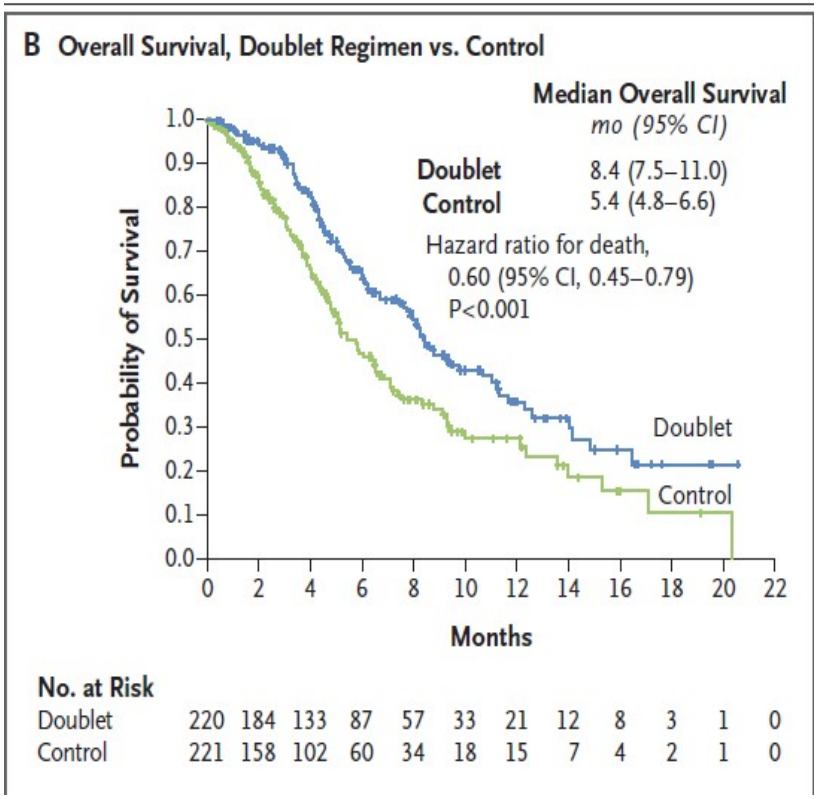
S. Kopetz, A. Grothey, R. Yaeger, E. Van Cutsem, J. Desai, T. Yoshino, H. Wasan, F. Ciardiello, F. Loupakis, Y.S. Hong, N. Steeghs, T.K. Guren, H.-T. Arkenau, P. Garcia-Alfonso, P. Pfeiffer, S. Orlov, S. Lonardi, E. Elez, T.-W. Kim, J.H.M. Schellens, C. Guo, A. Krishnan, J. Dekervel, V. Morris, A. Calvo Ferrandiz, L.S. Tarpgaard, M. Braun, A. Gollerkeri, C. Keir, K. Maharry, M. Pickard, J. Christy-Bittel, L. Anderson, V. Sandor, and J. Tabernero

TARGETING BRAF IN CRC
(BEACON Trial)

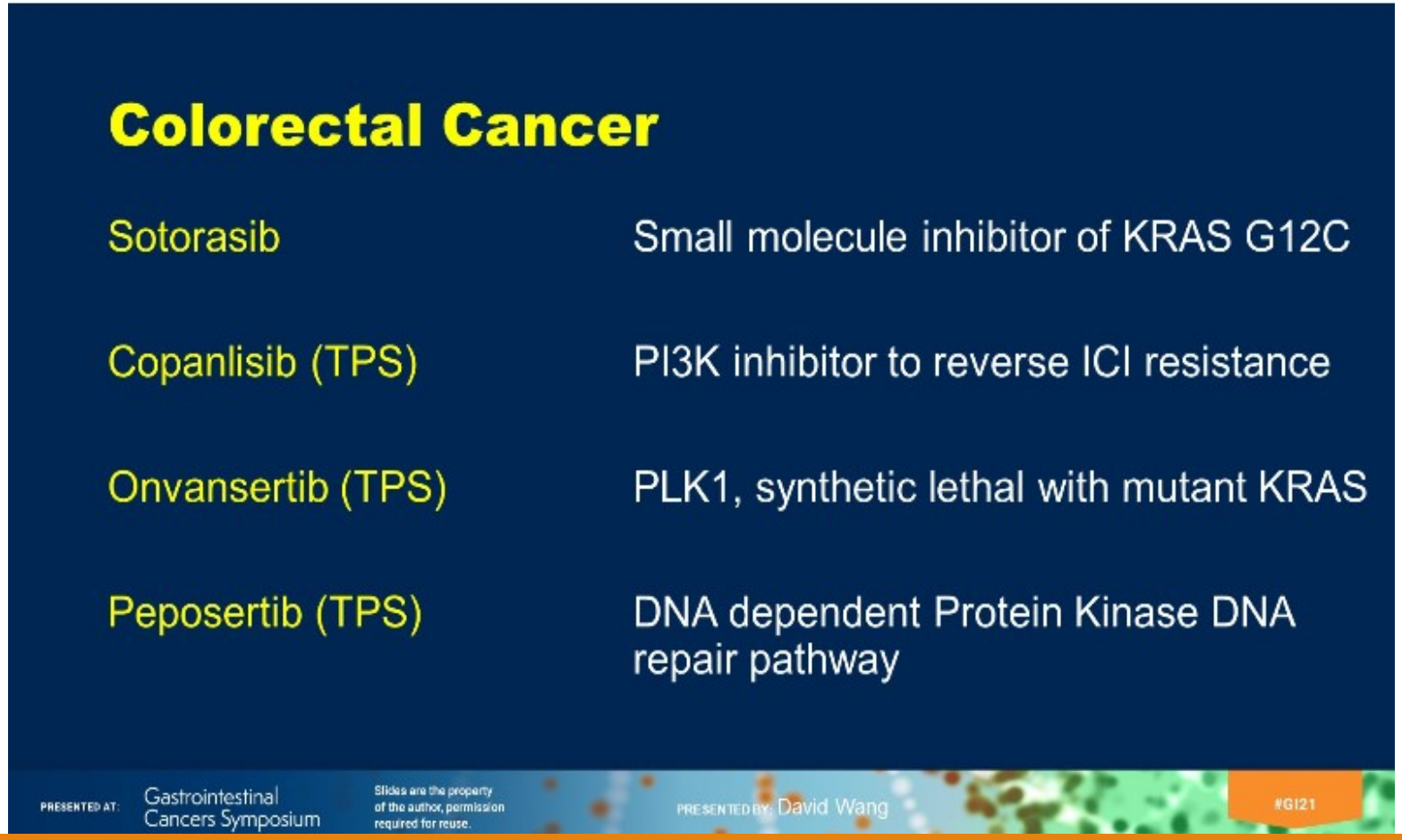


TARGETING BRAF IN CRC
(BEACON Trial)

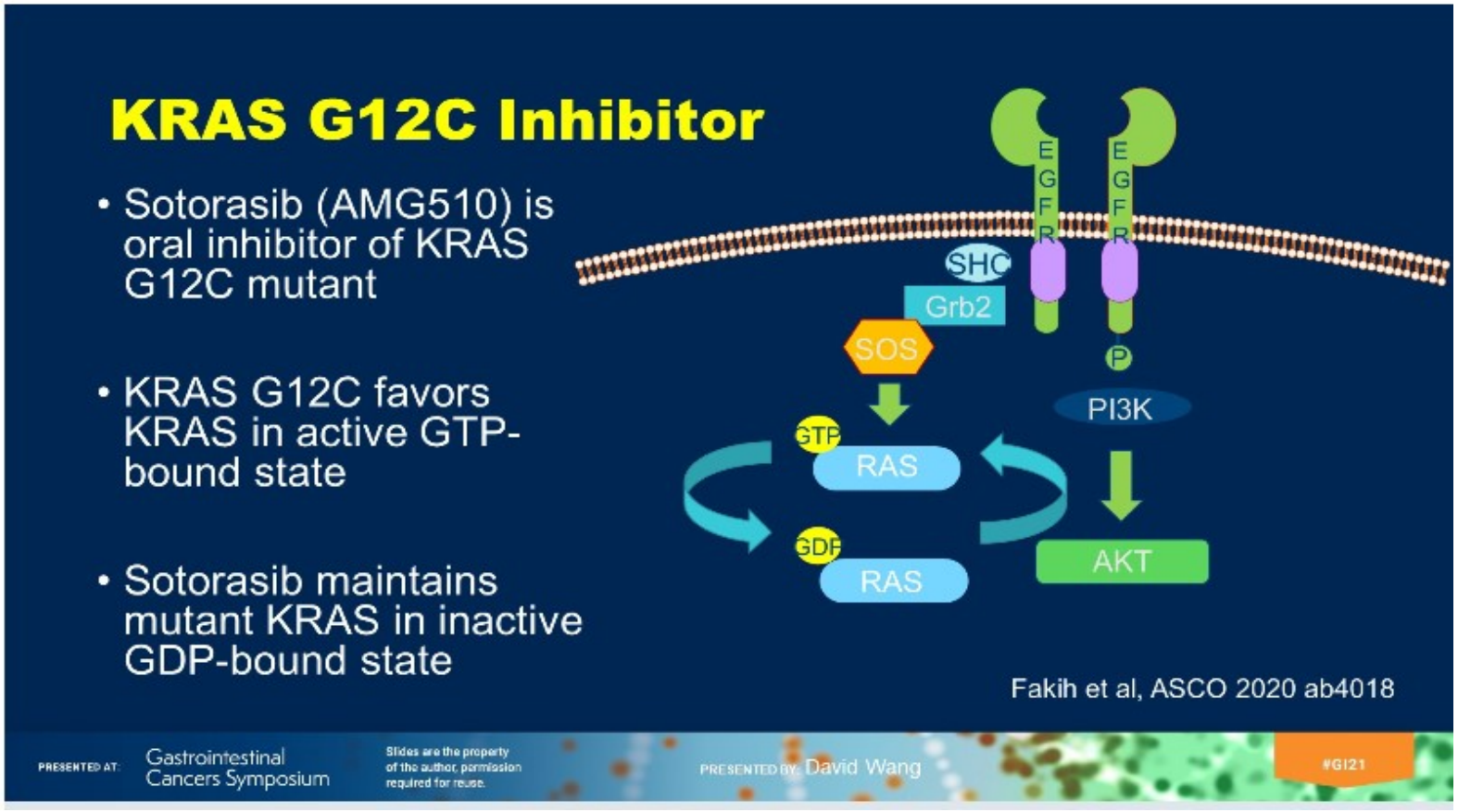




Novel targeted Therapy for CRC



TARGETING KRAS



CONCLUSIONS:

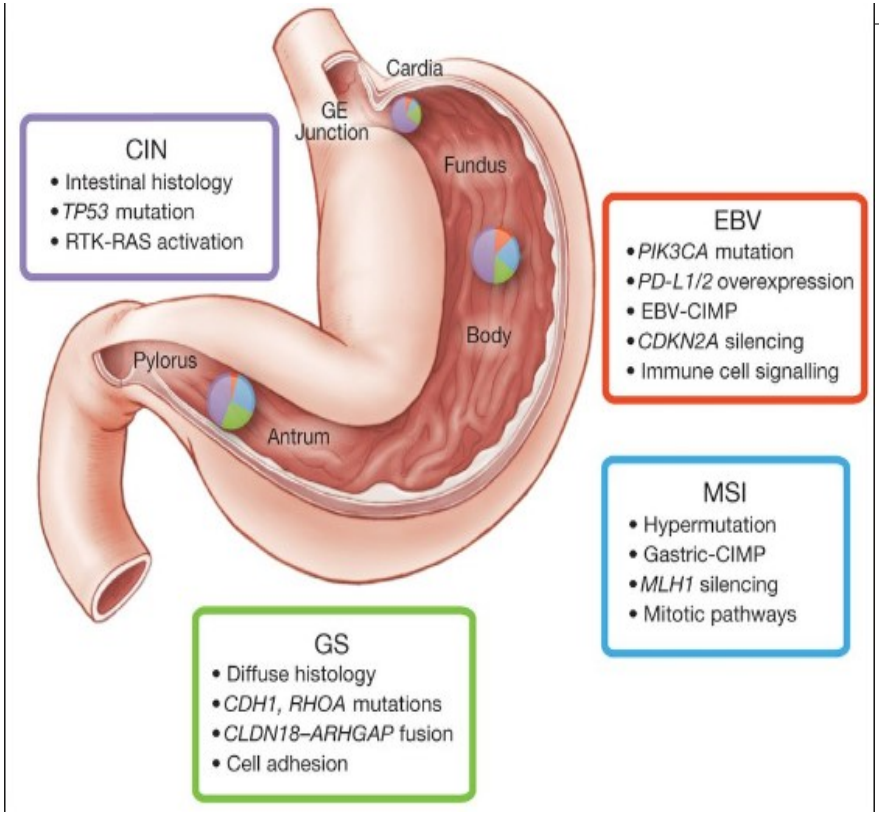
1. First-line therapy for MSI-H Metastatic colorectal cancer immunotherapy→ A new standard of care.
   - Keynote 177: Med. PFS 16.5 Vs 8.2 m (P= 0.002) Pembro Vs Chemo Rx with Biologics

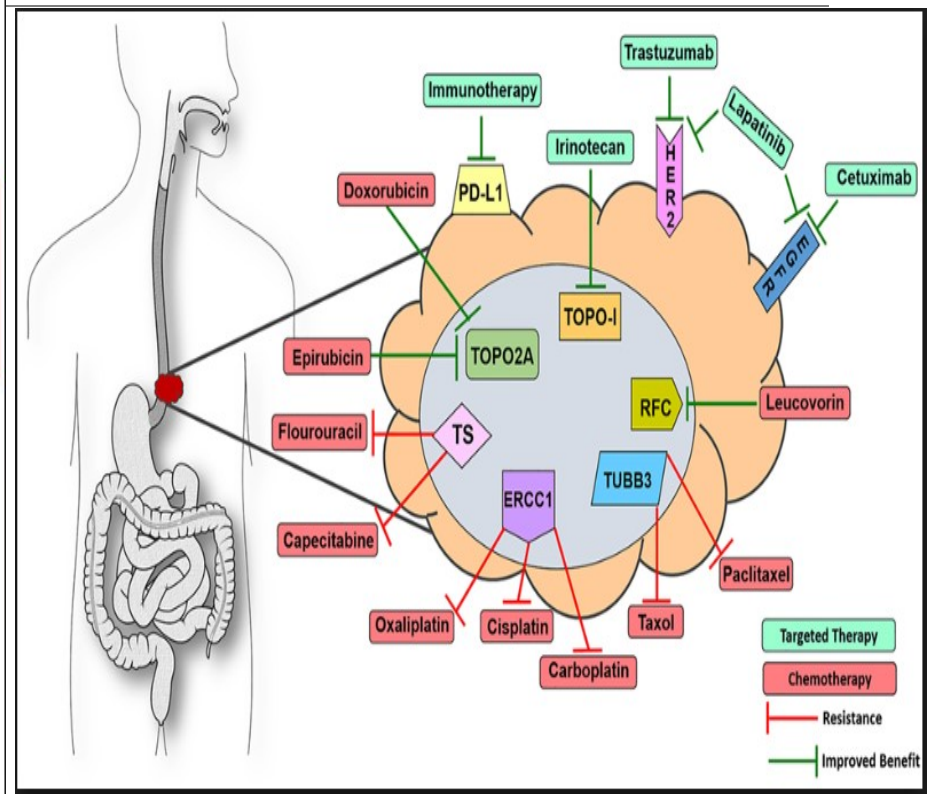
2. TOSCA trial subgroup analysis patients > 70:
   - Adjuvant Therapy Should be recommended to ALL Pts (including > 70)
   - 3 m Vs 6 m based stratification T4 Vs T and N2 Vs N : FOLFOX Vs XELOX

3. Targeting Braf mutant CRC in Kras WT opened new treatment options
4. Need for new targeted therapy against Kras mutant CRC

Gastric & Gastroesophageal Cancers

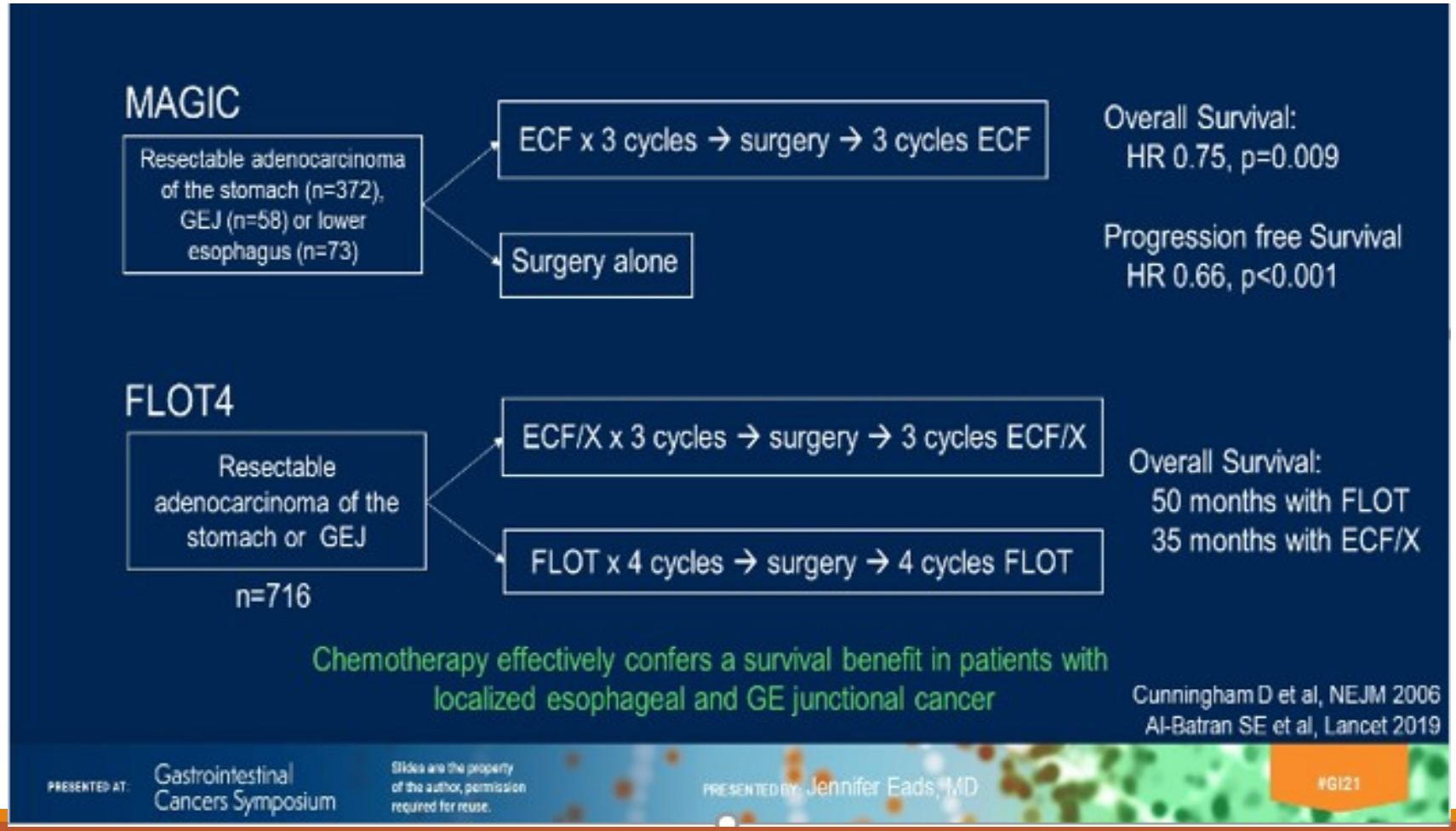
Gastroesophageal Cancers





Gastric & Gastroesophageal Cancers

(Standard Treatment Options) *WCS 2021*



Gastric & Gastroesophageal Cancers

WCS 2021

CALGB 80803 (Alliance)—Survival Analysis

- PET directed combined modality treatment for esophageal cancer
  - FOLFOX → PET → FOLFOX/RT (R), Carbo/Taxol/RT (NR)
  - Carbo/Taxol → PET → Carbo/Taxol/RT (R), FOLFOX/RT (NR)
- Positive improvement in pCR rate in non-responders (1° endpoint)

Suggestion that switch therapy may improve outcomes in an appropriately selected population

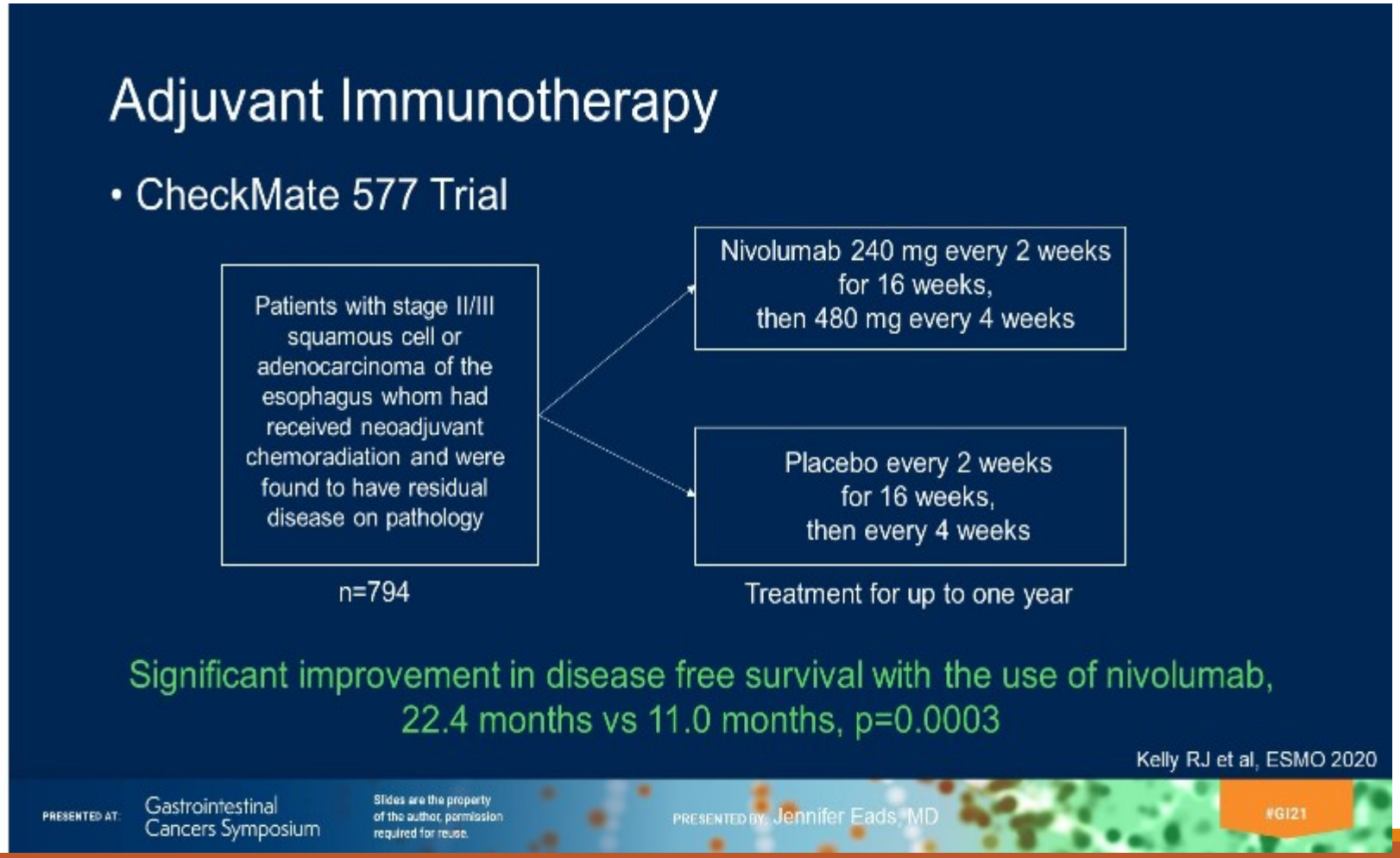
Regimen	Median Overall Survival	4-year Survival Rate
Carbo/Taxol → FOLFOX (NR)	27.6 months	41.9%
FOLFOX → Carbo/Taxol (NR)	30.9 months	37.6%
Carbo/Taxol → Carbo/Taxol (R)	39.6 months	44.7%
FOLFOX → FOLFOX (R)	50.3 months	52.7%

Suggestion that induction chemotherapy may contribute in an appropriately selected population

Goodman KA et al, ASCO 2018

Gastric & Gastroesophageal Cancers

WCS 2021



GASTRIC CANCER WCS 2021

(JACCRO-GC 07 Adjuvant Therapy)

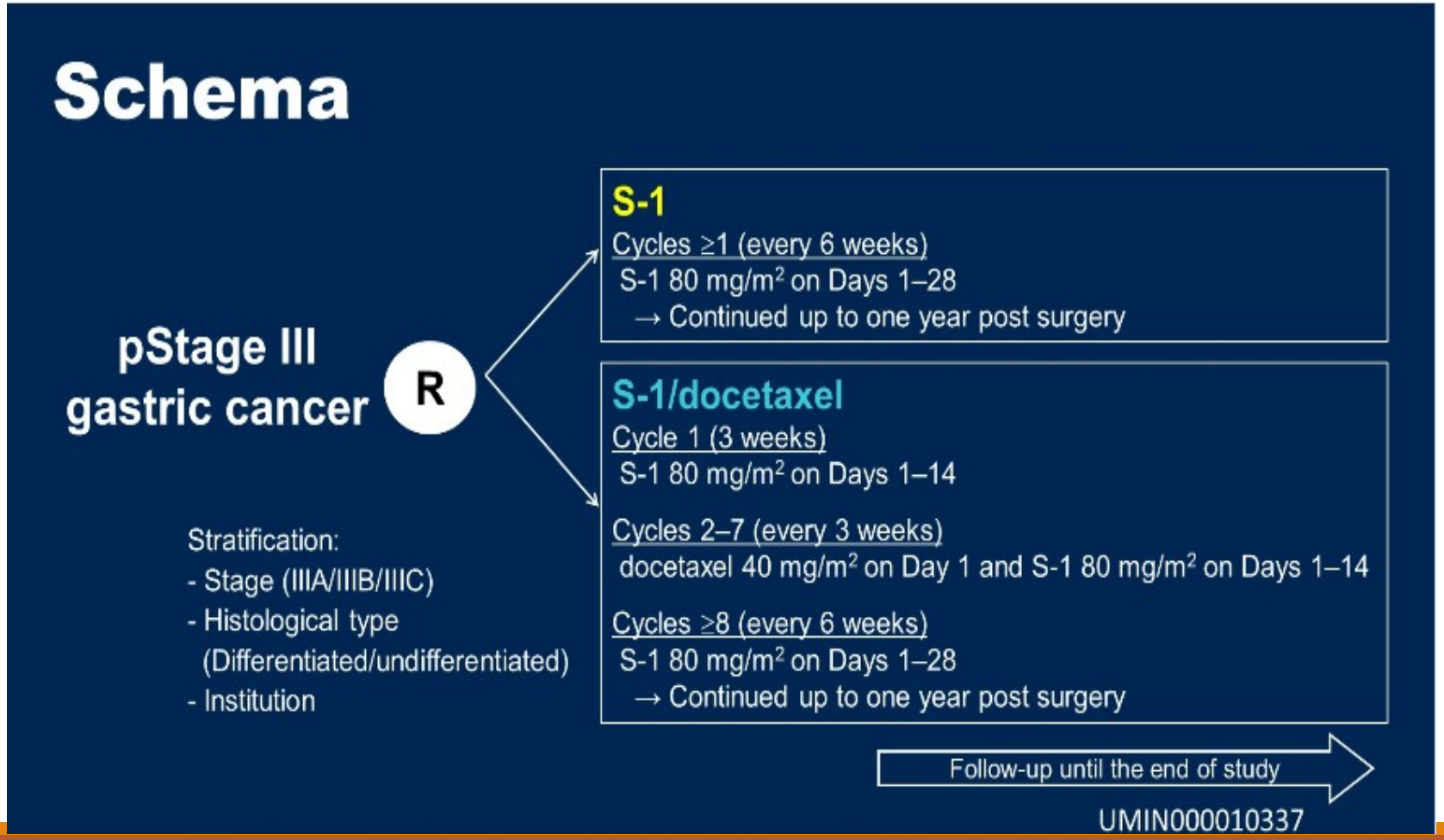
Gastrointestinal Cancers Symposium

Subgroup analyses of patients with microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer treated with nivolumab plus low-dose ipilimumab as first-line therapy: 2-year clinical update

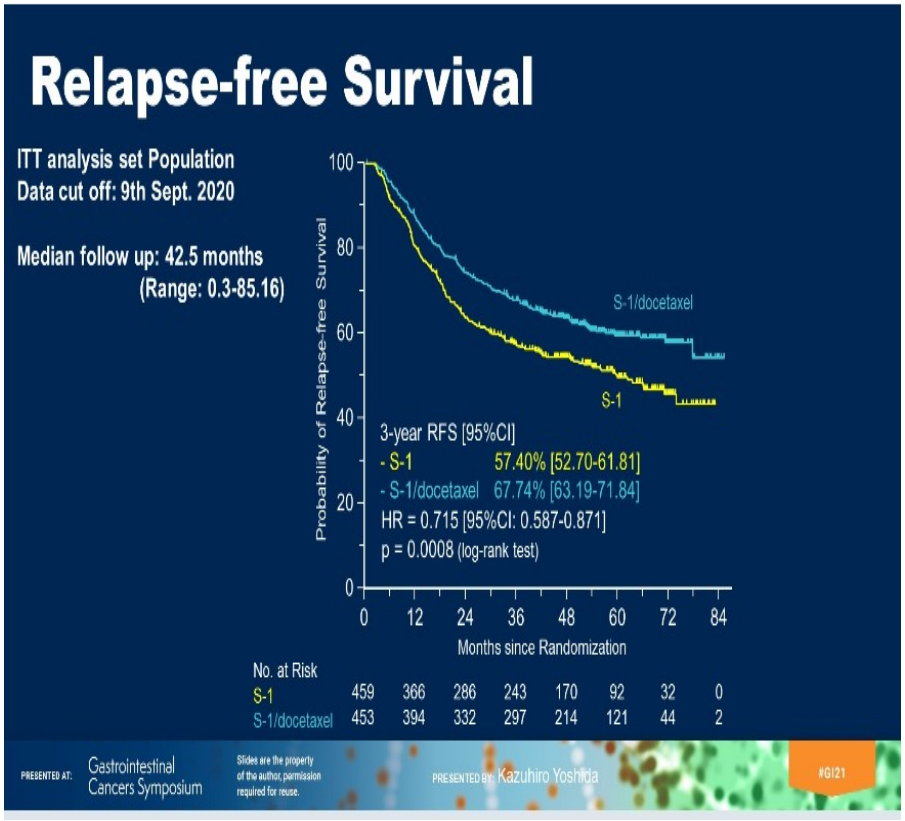
Heinz-Josef Lenz,[1] Sara Lonardi,[2] Vittorina Zagonel,[2] Eric Van Cutsem,[3] Maria Luisa Limon,[4] Ka Yeung Mark Wong,[5] Alain Hendlisz,[6] Massimo Aglietta,[7] Pilar García-Alfonso,[8] Bart Neyns,[9] Gabriele Luppi,[10] Dana B. Cardin,[11] Tomislav Dragovich,[12] Usman Shah,[13] Sandzhar Abdullaev,[14] Arteid Memaj,[14] Michael James Overman[15]

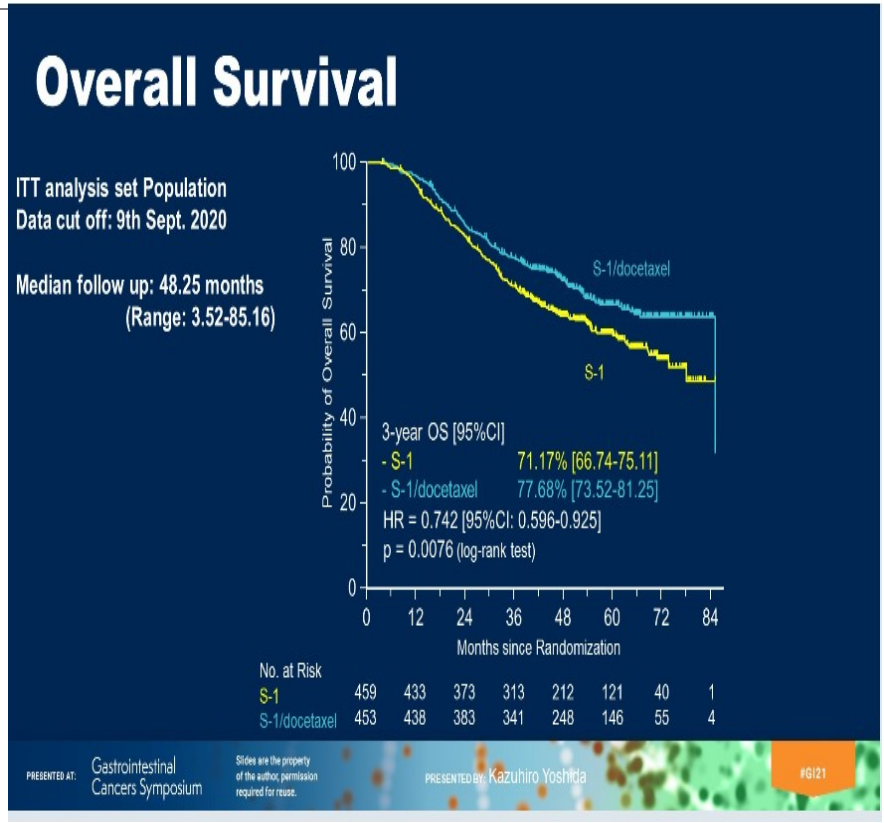
GASTRIC CANCER WCS 2021

(**JACCRO-GC 07** Adjuvant Therapy)

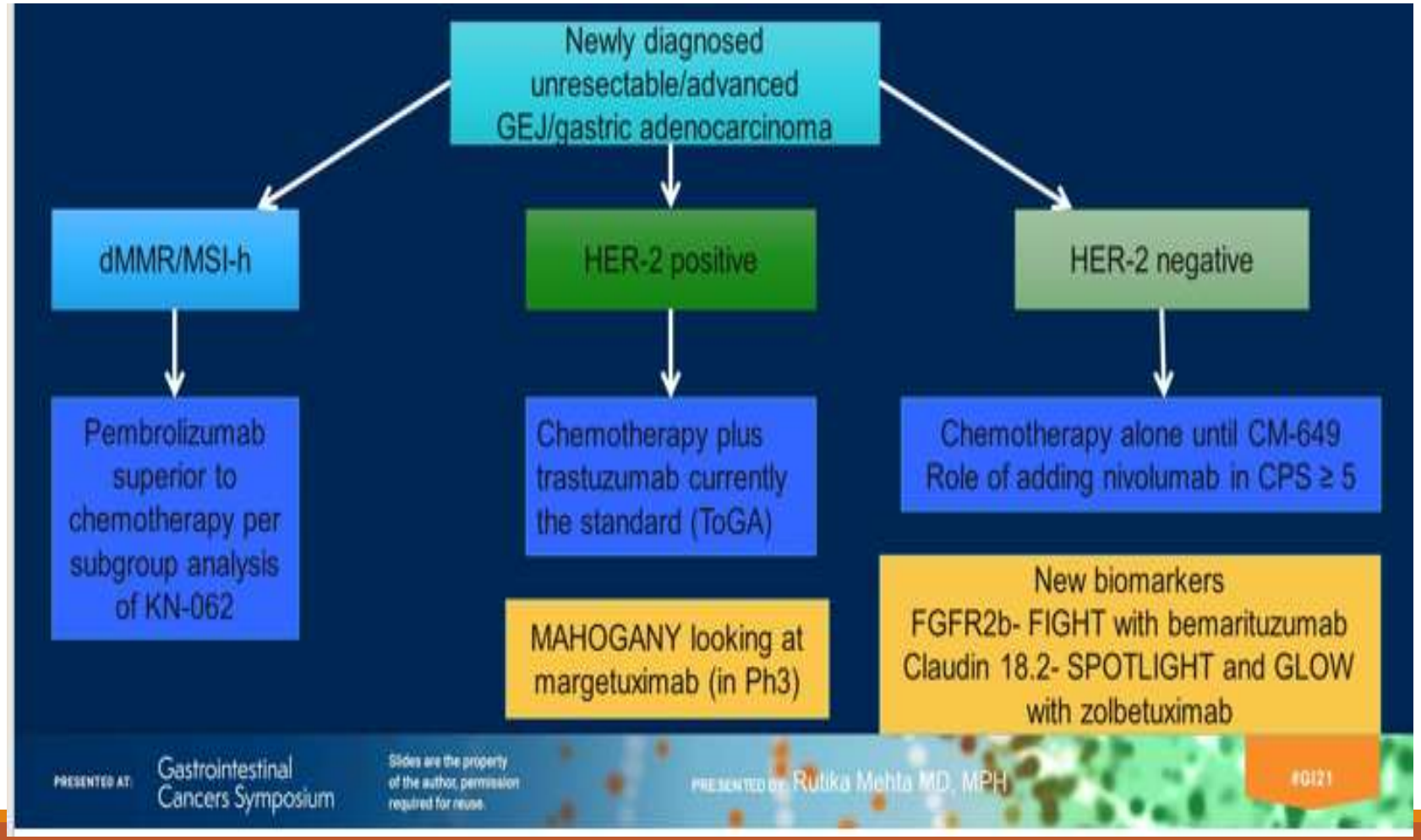


GASTRIC CANCER WCS 2021
JACCRO-GC 07



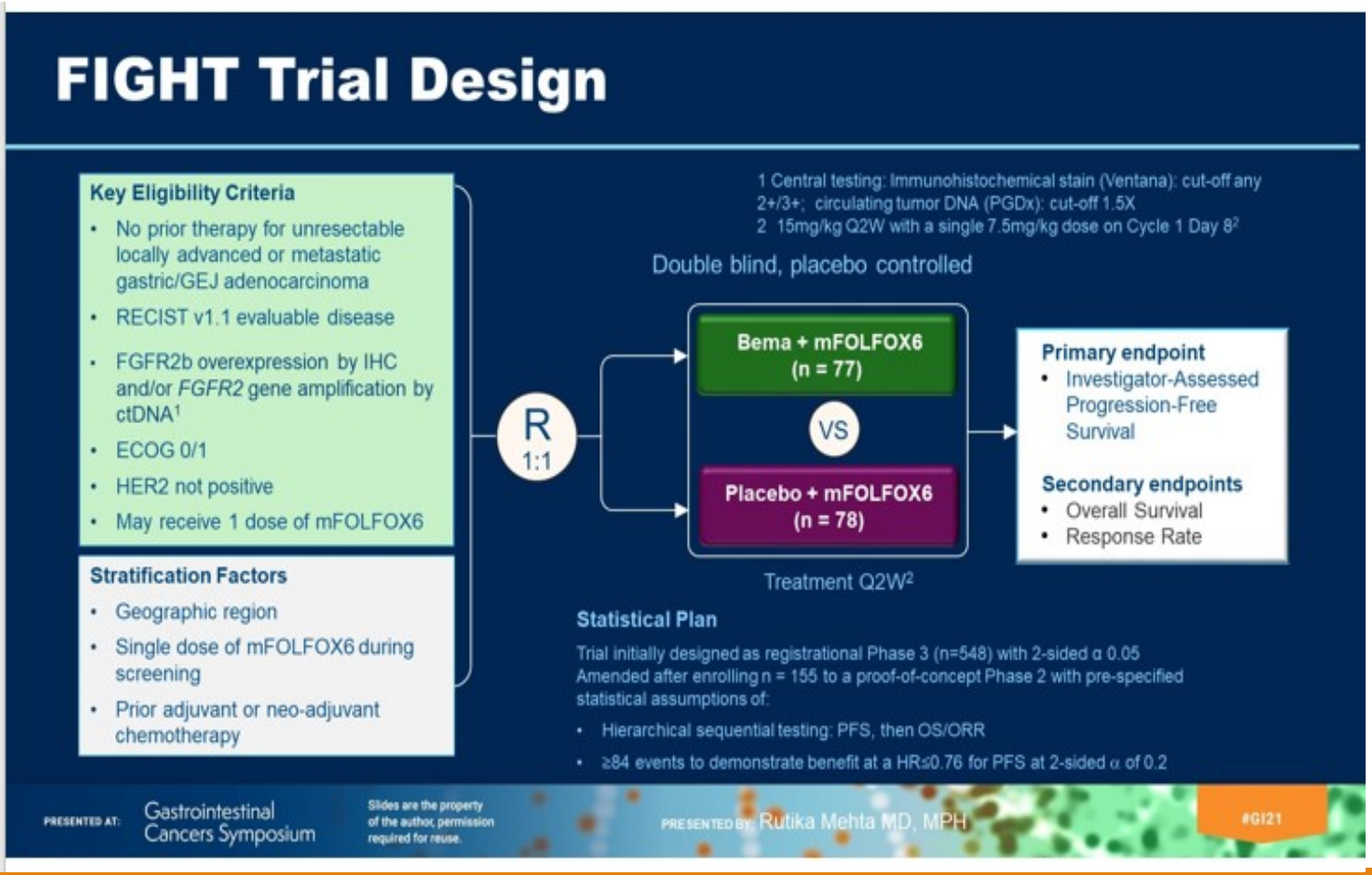


Management Stratification GE / Gastric Adenocarcinoma

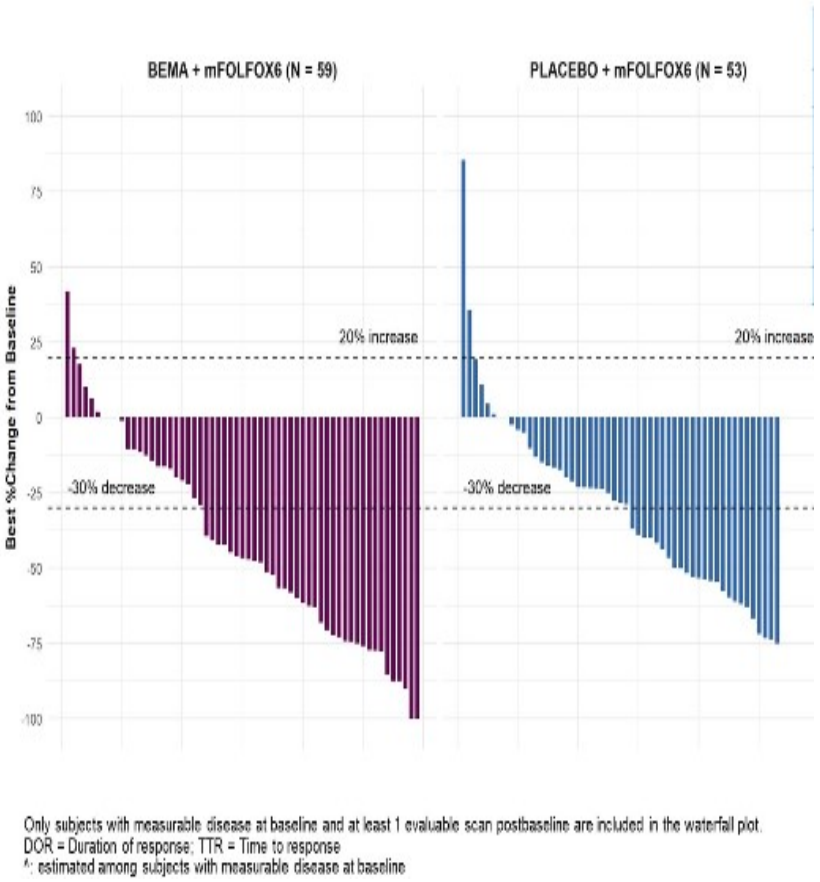


A double-blind randomized study of bemarituzumab (bema) plus mFOLFOX6 versus placebo plus mFOLFOX6 as first-line treatment for advanced gastric/gastroesophageal junction cancer (FIGHT)

Zev A Wainberg, Peter Enzinger, Yoon-Koo Kang, Kensai Yamaguchi, Shukui



FIGHT TRIAL WCS 2021



Only subjects with measurable disease at baseline and at least 1 evaluable scan postbaseline are included in the waterfall plot.
DOR = Duration of response; TTR = Time to response
^: estimated among subjects with measurable disease at baseline

Selected Adverse Events	Any Grade		Grade ≥ 3	
	Bema (N = 76)	Placebo (N = 77)	Bema (N = 76)	Placebo (N = 77)
Preferred Term	76 (100.0%)	76 (98.7%)	63 (82.9%)	57 (74.0%)
Platelet count decreased	14 (18.4%)	21 (27.3%)	1 (1.3%)	0
Aspartate aminotransferase increased	23 (30.3%)	15 (19.5%)	4 (5.3%)	2 (2.6%)
Alanine aminotransferase increased	22 (28.9%)	11 (14.3%)	2 (2.6%)	1 (1.3%)
Dry eye	20 (26.3%)	5 (6.5%)	2 (2.6%)	0

Corneal AEs occurred in 67% patients receiving Bema (24% Grade 3).
40% patients still had unresolved corneal AEs at time of analysis
Median time to resolution ~7 months

VIRTUAL 2020 ESMO congress

Nivolumab plus chemotherapy versus chemotherapy as first-line treatment for advanced gastric cancer/gastroesophageal junction cancer/esophageal adenocarcinoma: first results of the CheckMate 649 study

Markus Moehler,[1] Kohei Shitara,[2] Marcelo Garrido,[3] Pamela Salman,[4] Lin Shen,[5] Lucjan Wyrwicz,[6] Kensei Yamaguchi,[7] Tomasz Skoczylas,[8] Arinilda Campos Bragagnoli,[9] Tianshu Liu,[10] Michael Schenker,[11] Patricio Yanez,[12] Mustapha Tehfe,[13] Valerie Poulart,[14] Dana Cullen,[14] Ming Lei,[14] Kaoru Kondo,[14] Mingshun Li,[14] Jaffer A. Ajani,[15] Yelena Y. Janjigian[16]

[1]Johannes-Gutenberg University Clinic, Mainz, Germany; [2]National Cancer Center Hospital East, Kashiwa, Japan; [3]Clinica San Carlos de Apoquindo, Pontificia Universidad Católica, Chile; [4]Fundación Arturo López Pérez, Providencia, Chile; [5]Beijing Cancer Hospital, Beijing, China; [6]Klinika Onkologii i Radioterapii, Narodowy Instytut Onkologii, Warszawa, Poland; [7]Cancer Institute Hospital of JFCR, Tokyo, Japan; [8]II Klinika Chirurgii Ogólnej, Gastroenterologicznej i Nowotworów Układu Pokarmowego, Medical University of Lublin, Lublin, Poland; [9]Fundacao Pio Xii Hosp Cancer De Barretos, Barretos, Brazil; [10]Zhongshan Hospital Fudan University, Shanghai, China; [11]SF Nectarie Oncology Center, Craiova, Romania; [12]Universidad de La Frontera, Temuco, Chile; [13]Oncology Center - Centre Hospitalier de l'Universite de Montreal, Montreal, QC, Canada; [14]Bristol Myers Squibb, Princeton, NJ, USA; [15]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [16]Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY, USA

Presentation number LBA6

CheckMate 649 study design

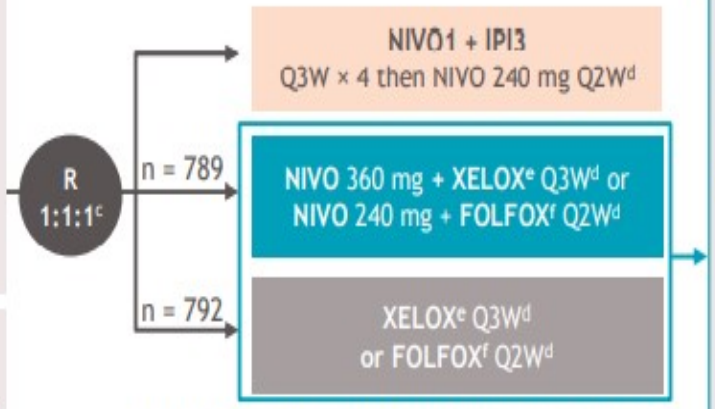
- CheckMate 649 is a randomized, open-label, phase 3 study[a]

Key eligibility criteria

- Previously untreated, unresectable, advanced or metastatic gastric/GEJ/ esophageal adenocarcinoma
- No known HER2-positive status
- ECOG PS 0-1

Stratification factors

- Tumor cell PD-L1 expression (≥ 1% vs < 1%[b])
- Region (Asia vs United States/Canada vs ROW)
- ECOG PS (0 vs 1)
- Chemo (XELOX vs FOLFOX)



N = 1581, including 955 patients (60%) with PD-L1 CPS ≥ 5

Dual primary endpoints:

- OS and PFS[g] (PD-L1 CPS ≥ 5)

Secondary endpoints:

- OS (PD-L1 CPS ≥ 1 or all randomized)
- OS (PD-L1 CPS ≥ 10)
- PFS[g] (PD-L1 CPS ≥ 10, 1, or all randomized)
- ORR[g]

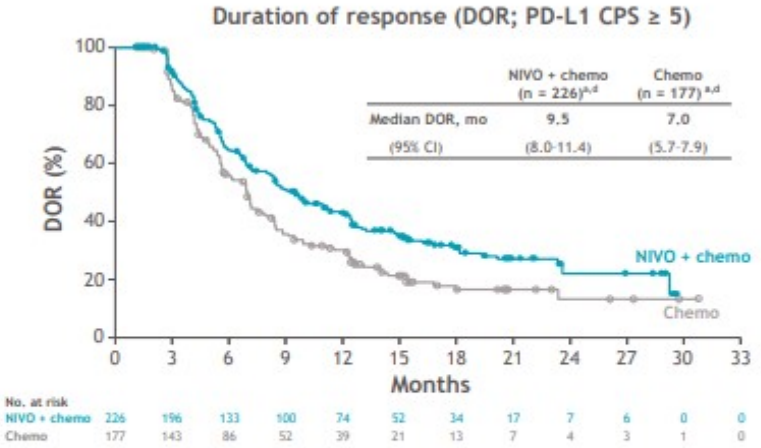
- At data cutoff (May 27, 2020), the minimum follow-up was 12.1 months[h]

[a]ClinicalTrials.gov number, NCT02872116; [b]< 1% includes indeterminate tumor cell PD-L1 expression; determined by PD-L1 IHC 28-8 pharmDx assay (Dako); [c]After NIVO + chemo arm was added and before new patient enrollment in the NIVO1+IPI3 group was closed; [d]Until documented disease progression (unless consented to treatment beyond progression for NIVO + chemo), discontinuation due to toxicity, withdrawal of consent, or study end. NIVO is given for a maximum of 2 years; [e]Oxaliplatin 130 mg/m^2 IV (day 1) and capecitabine 1000 mg/m^2 orally twice daily (days 1-14); [f]Oxaliplatin 85 mg/m^2, leucovorin 400 mg/m^2, and FU 400 mg/m^2 IV (day 1) and FU 1200 mg/m^2 IV daily (days 1-2); [g]BICR assessed; [h]Time from concurrent randomization of the last patient to NIVO + chemo vs chemo to data cutoff.

CHECKMATE 649 ESMO 2020

Response and duration of response

	PD-L1 CPS ≥ 5	
	NIVO + chemo (n = 378)[a]	Chemo (n = 391)[a]
ORR, %	60	45
95% CI	55-65	40-50
P value[b]	< 0.0001	
Best overall response,[c] %		
Complete response	12	7
Partial response	48	38
Stable disease	28	34
Progressive disease	7	11
Not evaluable	6	10
Median TTR (range), months	1.5 (0.8-10.2)	1.5 (1.0-7.1)



- ORR was higher with NIVO + chemo versus chemo, and responses were more durable

[a]Randomized patients who had target lesion measurements at baseline per BICR assessment; [b]ORR was not formally tested, the pre-specified *P* value is descriptive; [c]Percentages may not add up to 100% due to rounding; [d]Number of responders.

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Kato KN590 ESMO 2020

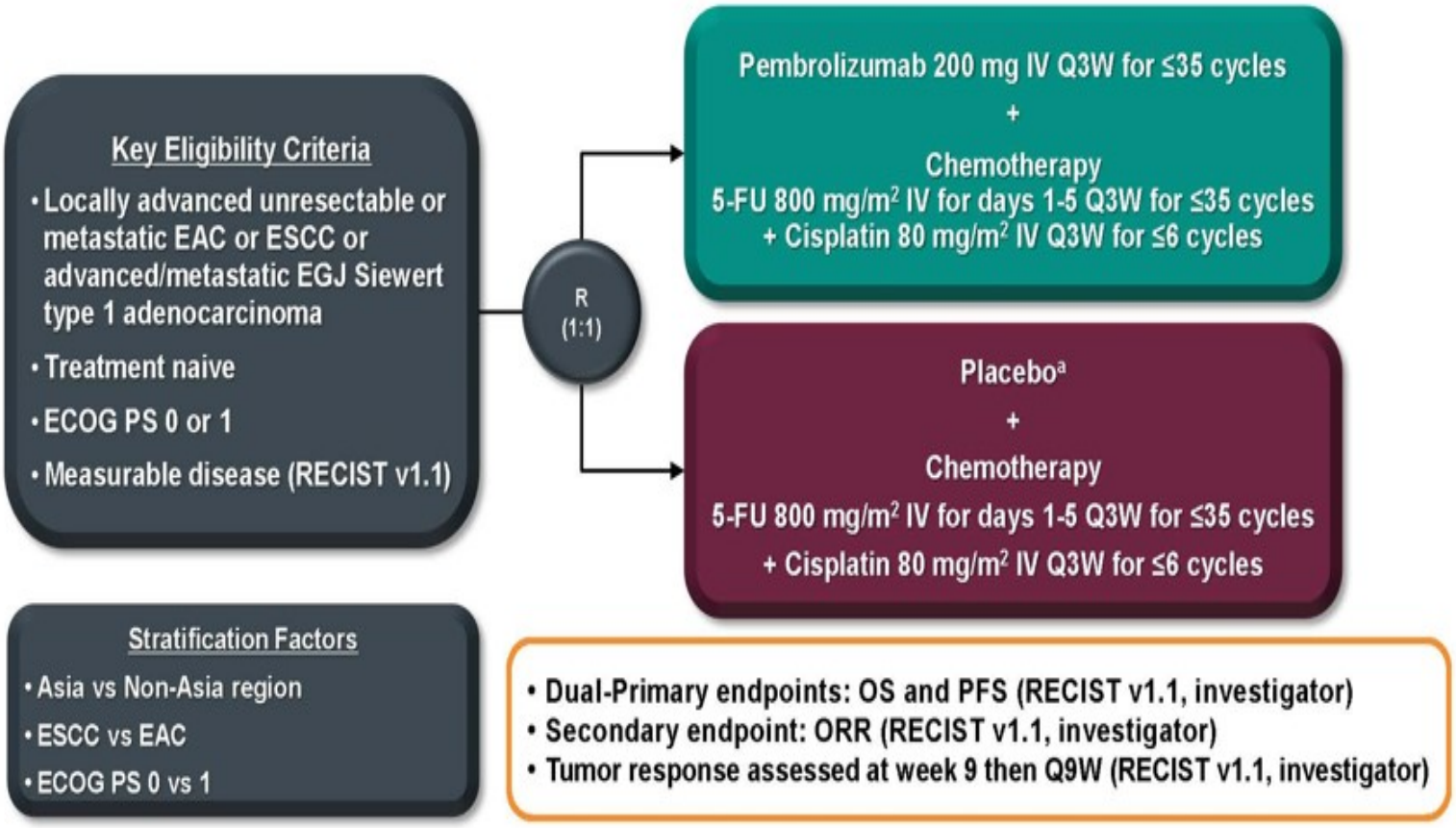
Pembrolizumab Plus Chemotherapy Versus Chemotherapy as First-Line Therapy in Patients With Advanced Esophageal Cancer: The Phase 3 KEYNOTE-590 Study

Ken Kato,[1] Jong-Mu Sun,[2] Manish A. Shah,[3] Peter Enzinger,[4] Antoine Adenis,[5] Toshihiko Doi,[6] Takashi Kojima,[6] Jean-Philippe Metges,[7] Zhigang Li,[8] Sung-Bae Kim,[9] Byoung Chul Cho,[10] Wasat Mansoor,[11] Shau-Hsuan Li,[12] Patrapim Sunpaweravong,[13] Maria Alsina Maqueda,[14] Eray Goekkurt,[15] Qi Liu,[16] Sukrut Shah,[16] Pooja Bhagia,[16] Lin Shen[17]

[1]National Cancer Center Hospital, Tokyo, Japan; [2]Samsung Medical Center, Sungkyunkwan University Seoul, Republic of Korea, [3]Weill Cornell Medical College, New York, NY, USA; [4]Dana Farber Cancer Institute, Boston, MA, USA; [5]IRCM, Inserm, Université Montpellier, ICM, Montpellier, France; [6]National Cancer Center Hospital East, Kashiwa, Japan;[7]CHU Brest – Institut de Cancerologie et d'Hematologie ARPEGO Network, Brest, France; [8]Shanghai Chest Hospital Esophageal Disease Center, Shanghai, China; [9]Asan Medical Center, Seoul, Republic of Korea; [10]Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea; [11]Christie Hospital NHS Trust, Manchester, United Kingdom; [12]Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan;[13]Prince of Songkla University Hospital, Songkhla, Thailand; [14]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [15]Hematology Oncology Practice Eppendorf, and University Cancer Center Hamburg, Hamburg, Germany; [16]Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; [17]Peking University Cancer Hospital & Institute; Beijing, China

Kato KN590 ESMO 2020

KEYNOTE-590 Study Design (NCT03189719)



[a]Saline IV Q3W for ≤35 cycles. All treatments were continued for the specified number of cycles or until disease progression, intolerable toxicity, withdrawal of consent, or physician decision; EAC, esophageal adenocarcinoma; EGJ, esophagogastric junction, ESCC, esophageal squamous cell carcinoma.

VIRTUAL 2020 ESMO congress

Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer following neoadjuvant chemoradiation therapy: first results of the CheckMate 577 study

Ronan J. Kelly,[1] Jaffer A. Ajani,[2] Jaroslaw Kuzdzal,[3] Thomas Zander,[4] Eric Van Cutsem,[5] Guillaume Piessen,[6] Guillermo Mendez,[7] Josephine Feliciano,[8] Satoru Motoyama,[9] Astrid Lièvre,[10] Hope Uronis,[11] Elena Elimova,[12] Cecile Grootscholten,[13] Karen Geboes,[14] Jenny Zhang,[15] Lili Zhu,[15] Ming Lei,[15] Kaoru Kondo,[15] James M. Cleary,[16] Markus Moehler[17]

[1]The Charles A. Sammons Cancer Center at Baylor University Medical Center, Dallas, TX, USA; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Jagiellonian University, John Paul II Hospital, Cracow, Poland; [4]University Hospital of Cologne, Cologne, Germany; [5]University Hospitals Gasthuisberg, Leuven and KULeuven, Leuven, Belgium; [6]University of Lille, Claude Huriez University Hospital, Lille, France; [7]Fundacion Favaloro, Buenos Aires, Argentina; [8]Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD, USA; [9]Akita University Hospital, Akita, Japan; [10]CHU Pontchaillou, Rennes 1 University, Rennes, France; [11]Duke Cancer Institute, Durham, NC, USA; [12]Princess Margaret Cancer Centre, Toronto, ON, Canada; [13]Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; [14]UZ Gent, Gent, Belgium; [15]Bristol Myers Squibb, Princeton, NJ, USA; [16]Dana Farber Cancer Institute, Boston, MA, USA; [17]Johannes-Gutenberg University Clinic, Mainz, Germany

Presentation number LBA9

CONCLUSIONS

1. the treatment Paradigm for gastric & Gastroesophageal cancer is an evolving Process

2. For Locally Advanced Gastric Ca/ GE adjuvant therapy still has role

3. The Alliance Trial: the better OS reaching 50.3 m with FOLFOX→FOLFOX/XRT

4. Adjuvant Nivolumab will be likely define a new standard of care in patients with residual disease after perioperative therapy & Surgery

5. Great Need for targeted Therapy against newer pathways/ receptors