# Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

## Colorectal and Gastroesophageal Cancers

**Tuesday, December 8, 2020**
**5:00 PM – 6:00 PM ET**

### Faculty

**Peter C Enzinger, MD**
**Zev Wainberg, MD, MSc**

### Moderator

**Neil Love, MD**

Year in Review 2020

# Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Sumitomo Dainippon Pharma Oncology Inc and Taiho Oncology Inc.

Year in Review 2020

# Dr Love — Disclosures

**Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies Corporation, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exelixis Inc, Foundation Medicine, Genentech, a member of the Roche Group, Genmab, Genomic Health Inc, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Guardant Health, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seagen Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, Teva Oncology, Tokai Pharmaceuticals Inc and Verastem Inc.

Year in Review 2020

# Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Year in Review 2020

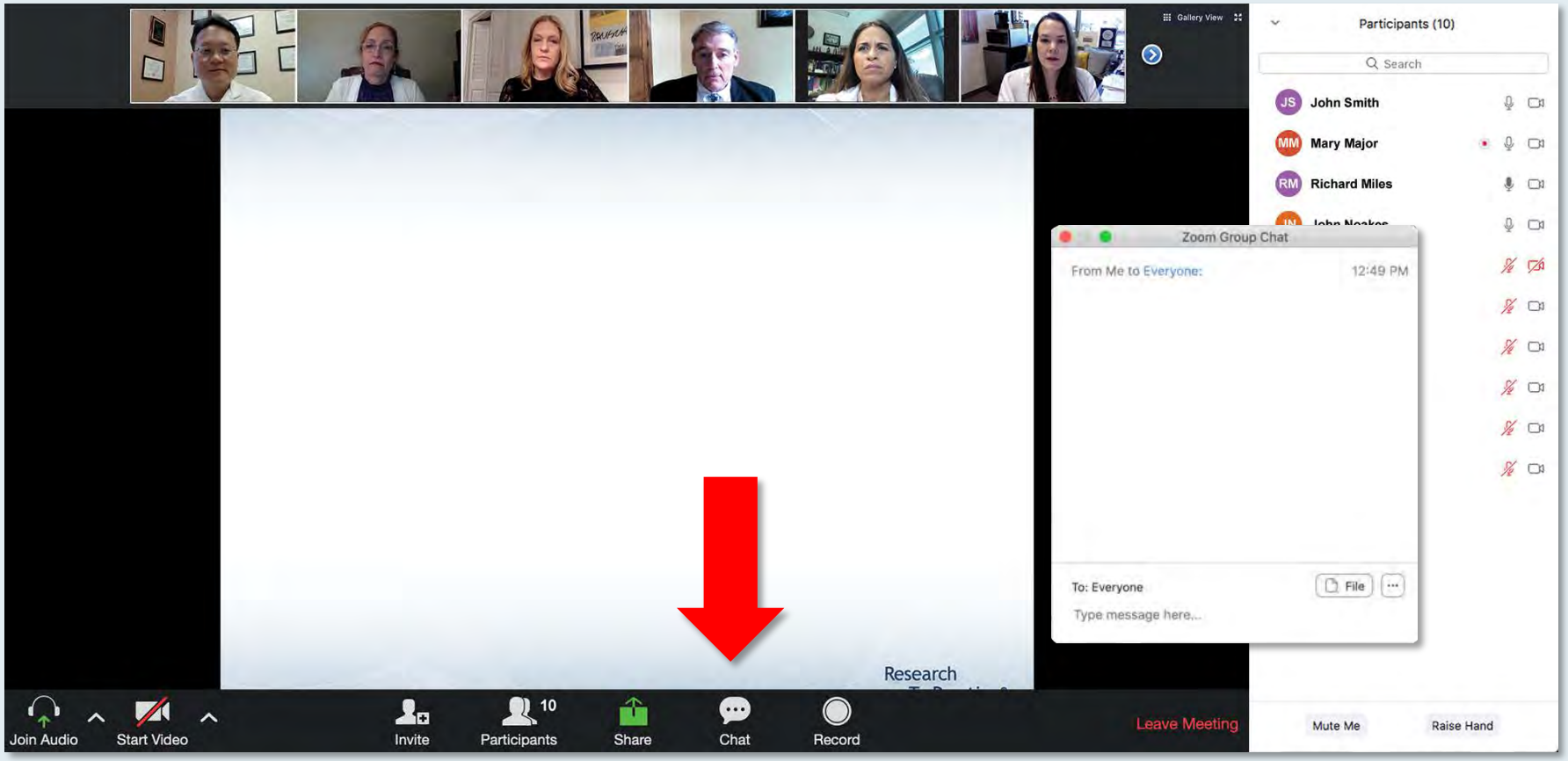
# Dr Enzinger — Disclosures

| | |
|---|---|
| **Advisory Committee and Consulting Agreements** | Astellas, AstraZeneca Pharmaceuticals LP, Celgene Corporation, Daiichi Sankyo Inc, Five Prime Therapeutics Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Taiho Oncology Inc, Takeda Oncology, Zymeworks |

# Dr Wainberg — Disclosures

| | |
|---|---|
| **Consulting Agreements** | Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Daiichi Sankyo Inc, Five Prime Therapeutics Inc, Gilead Sciences Inc, Ipsen Biopharmaceuticals Inc, Lilly, Merck, Molecular Templates |
| **Contracted Research** | Arcus Biosciences, Five Prime Therapeutics Inc, Novartis, Plexxikon Inc |
| **Data and Safety Monitoring Board/Committee** | Array BioPharma Inc, a subsidiary of Pfizer Inc, Pfizer Inc |

# We Encourage Clinicians in Practice to Submit Questions

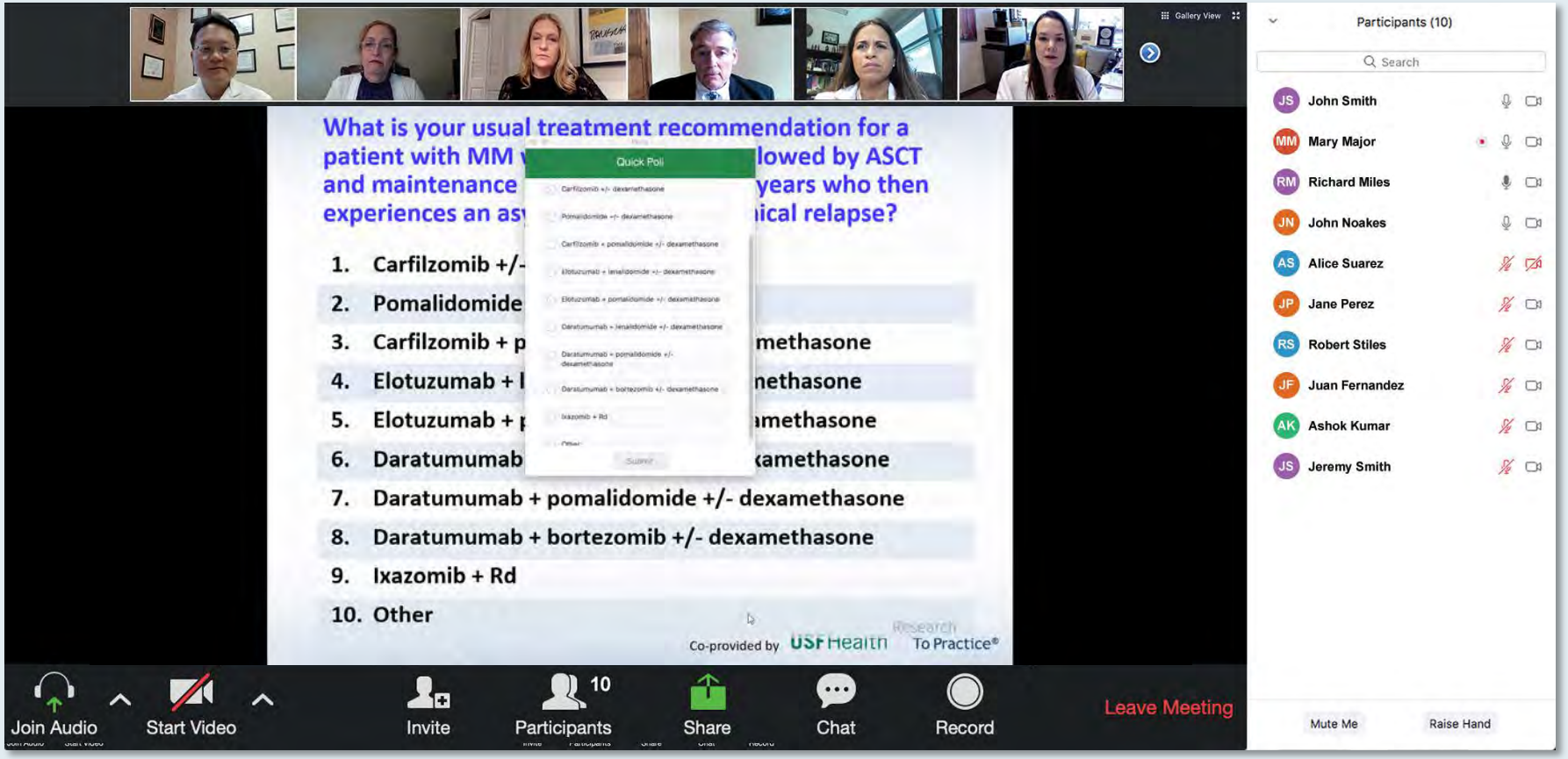



**Feel free to submit questions now before the program begins and throughout the program.**

Year in Review 2020

# Familiarizing Yourself with the Zoom Interface

## How to answer poll questions




**When a poll question pops up, click your answer choice from the available options.**

**Results will be shown after everyone has answered.**

Year in Review 2020

# Upcoming Webinars

**Wednesday, December 9, 2020**
**12:30 PM – 1:30 PM ET**

## Meet The Professor: Immunotherapy and Novel Agents in Gynecologic Cancers

**Faculty**
Gottfried E Konecny, MD

**Moderator**
Neil Love, MD

**Thursday, December 10, 2020**
**8:30 PM – 10:00 PM ET**

## Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

**Faculty**
Carey K Anders, MD
Erika Hamilton, MD
Sara Hurvitz, MD
Mark D Pegram, MD
Sara M Tolaney, MD, MPH

**Moderator**
Neil Love, MD

# Upcoming Webinars

**Friday, December 11, 2020**
**8:30 PM – 10:00 PM ET**

**Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Triple-Negative Breast Cancer**

**Faculty**
P Kelly Marcom, MD
Joyce O'Shaughnessy, MD
Hope S Rugo, MD
Professor Peter Schmid, MD, PhD

**Moderator**
Neil Love, MD

**Tuesday, December 15, 2020**
**5:00 PM – 6:00 PM ET**

Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology
**Hepatobiliary and Pancreatic Cancers**

**Faculty**
Tanios Bekaii-Saab, MD
Lipika Goyal, MD, MPhil

**Moderator**
Neil Love, MD

# Upcoming Webinars

**Wednesday, December 16, 2020**
**12:00 PM – 1:00 PM ET**

## Meet The Professor: Management of Multiple Myeloma

**Faculty**
Peter Voorhees, MD

**Moderator**
Neil Love, MD

**Wednesday, December 16, 2020**
**2:00 PM – 3:00 PM ET**

## Meet The Professor: Management of Chronic Lymphocytic Leukemia

**Faculty**
Nitin Jain, MD

**Moderator**
Neil Love, MD

*Thank you for joining us!*

*CME and MOC credit information will be emailed to each participant within 5 business days.*

Year in Review 2020

# ONCOLOGY TODAY

## WITH DR NEIL LOVE

# Management of Gastroesophageal Cancers

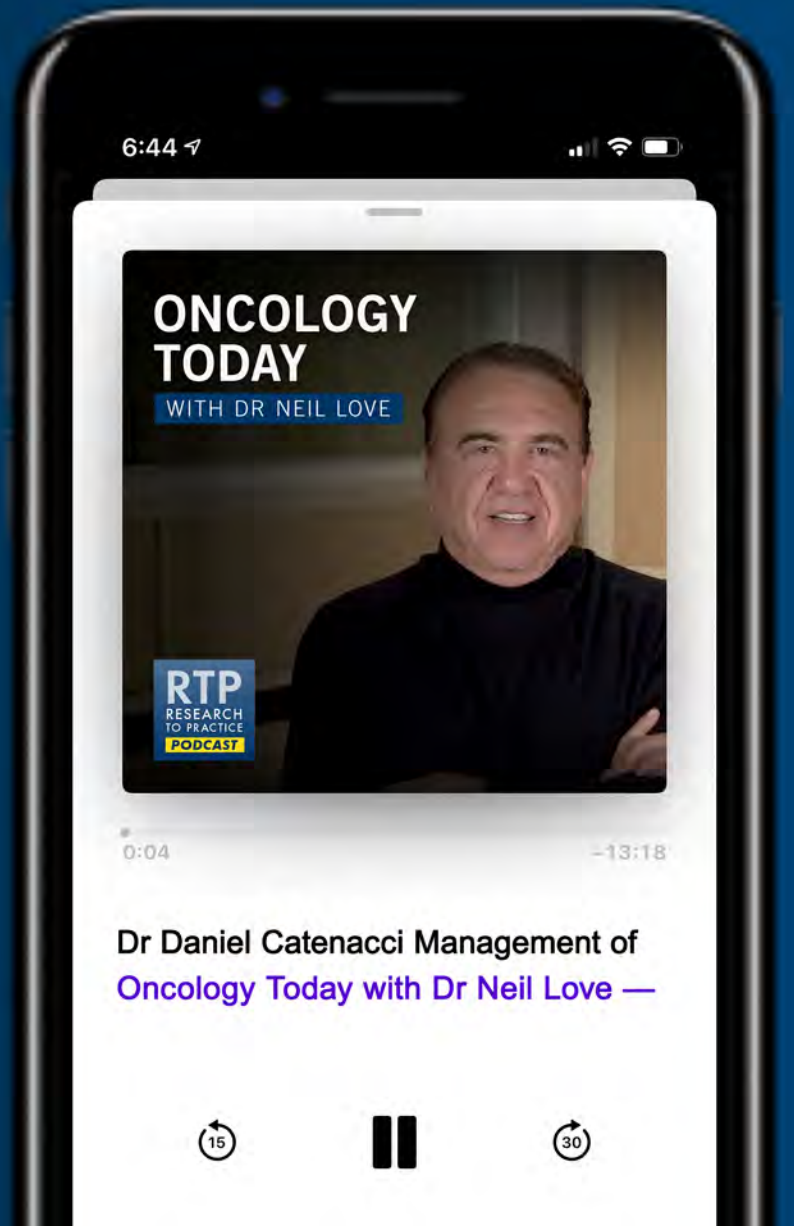

DR DANIEL CATENACCI

THE UNIVERSITY OF CHICAGO MEDICAL CENTER AND BIOLOGICAL SCIENCES


Listen on Apple Podcasts

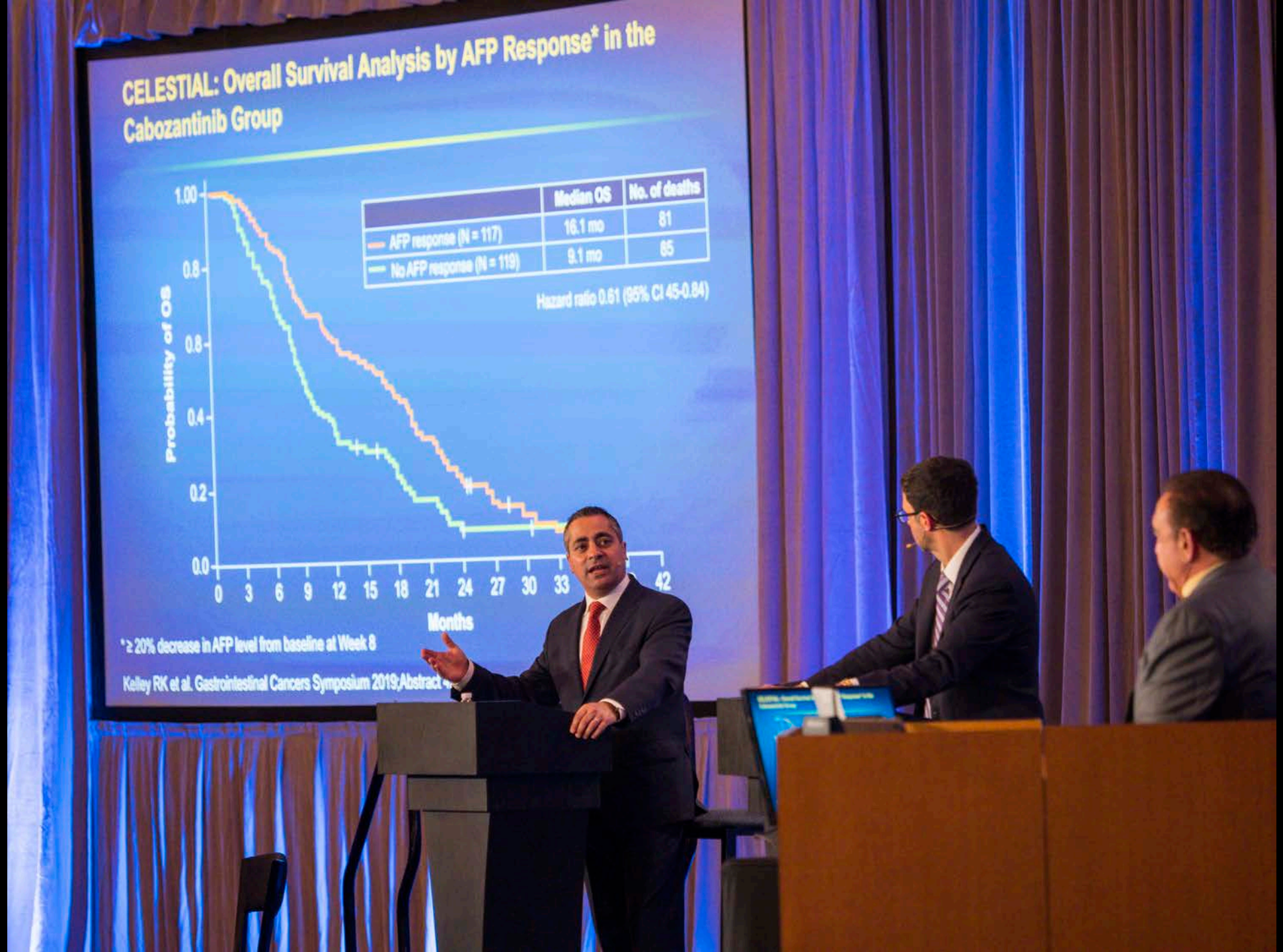
Spotify

Listen on Google Podcasts




ABDULRAHEEM QASEM
SHAWNEE MISSION, KS


What is your likely adjuvant systemic therapy recommendation for an otherwise healthy 75-year-old patient who is s/p surgical resection of pancreatic adenocarcinoma?
Gemcitabine
10%
Gemcitabine/capecitabine
37%
Gemcitabine/nab paclitaxel
15%
5-FU/LV
2%
Modified FOLFIRINOX
33%
Other


CELESTIAL: Overall Survival Analysis by AFP Response* in the Cabozantinib Group
Median OS
No. of deaths
AFP response (N = 117)
16.1 mo
81
No AFP response (N = 119)
9.1 mo
85
Hazard ratio 0.61 (95% CI 45-0.84)
Probability of OS
1.00
0.8
0.8
0.4
0.2
0.0
0 3 6 9 12 15 18 21 24 27 30 33 42
Months
* ≥ 20% decrease in AFP level from baseline at Week 8
Kelley RK et al. Gastrointestinal Cancers Symposium 2019;Abstract


What would be your most likely t
an otherwise healthy 65-year-old
progression on first-line sorafeni

# Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

## Colorectal and Gastroesophageal Cancers

**Tuesday, December 8, 2020**
**5:00 PM – 6:00 PM ET**

### Faculty

**Peter C Enzinger, MD**
**Zev Wainberg, MD, MSc**

### Moderator

**Neil Love, MD**

Year in Review 2020

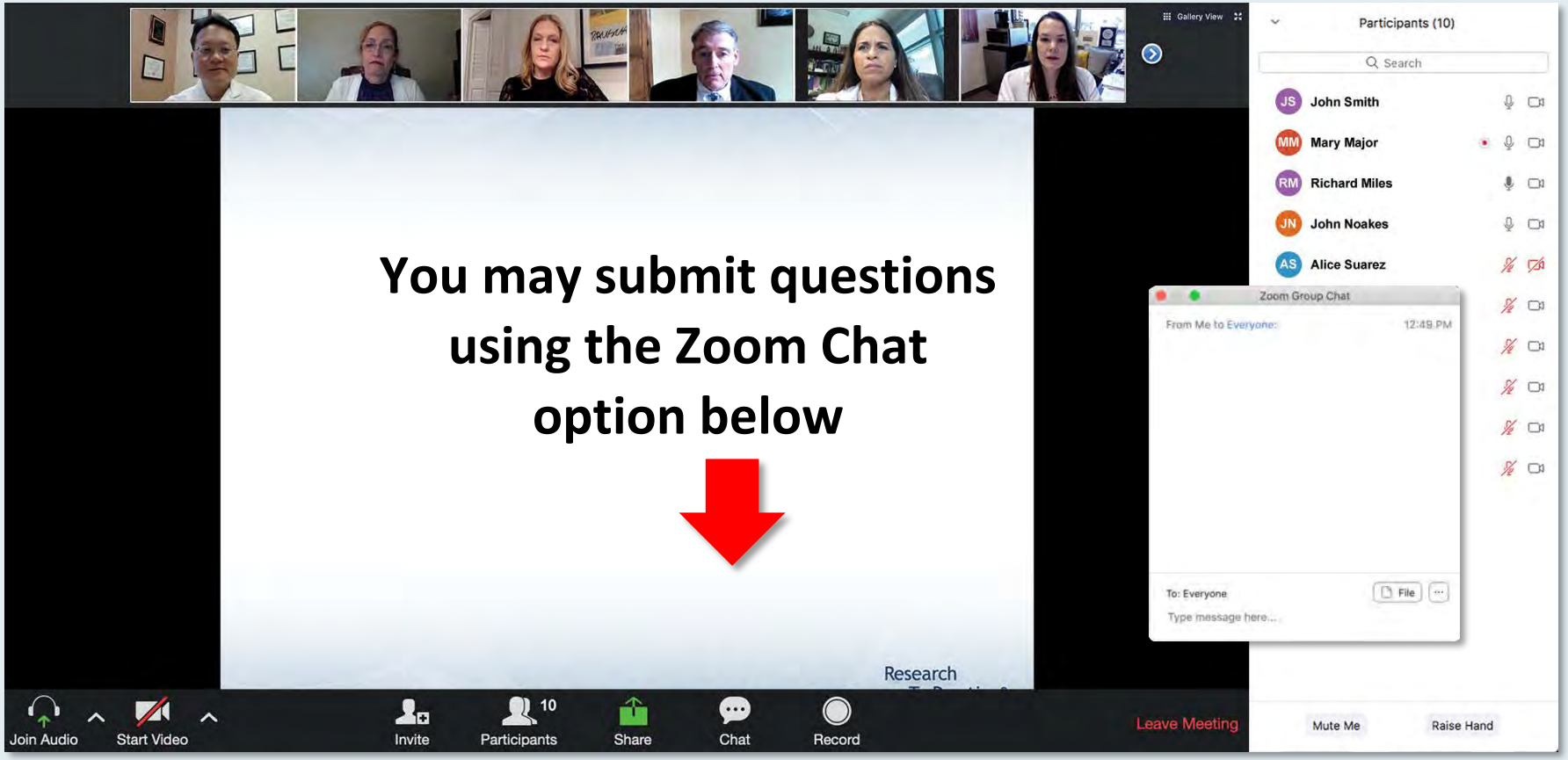
# YiR Colorectal and Gastroesophageal Cancers Faculty

**Peter C Enzinger, MD**
Director, Center for Esophageal and Gastric Cancer
Dana-Farber/Brigham and Women's Cancer Center
Institute Physician, Dana-Farber Cancer Institute
Associate Professor, Harvard Medical School
Boston, Massachusetts

**Zev Wainberg, MD, MSc**
Co-Director, GI Oncology Program
Director of Early Phase Clinical Research
Jonsson Comprehensive Cancer Center
UCLA School of Medicine
Los Angeles, California

Year in Review 2020

# We Encourage Clinicians in Practice to Submit Questions

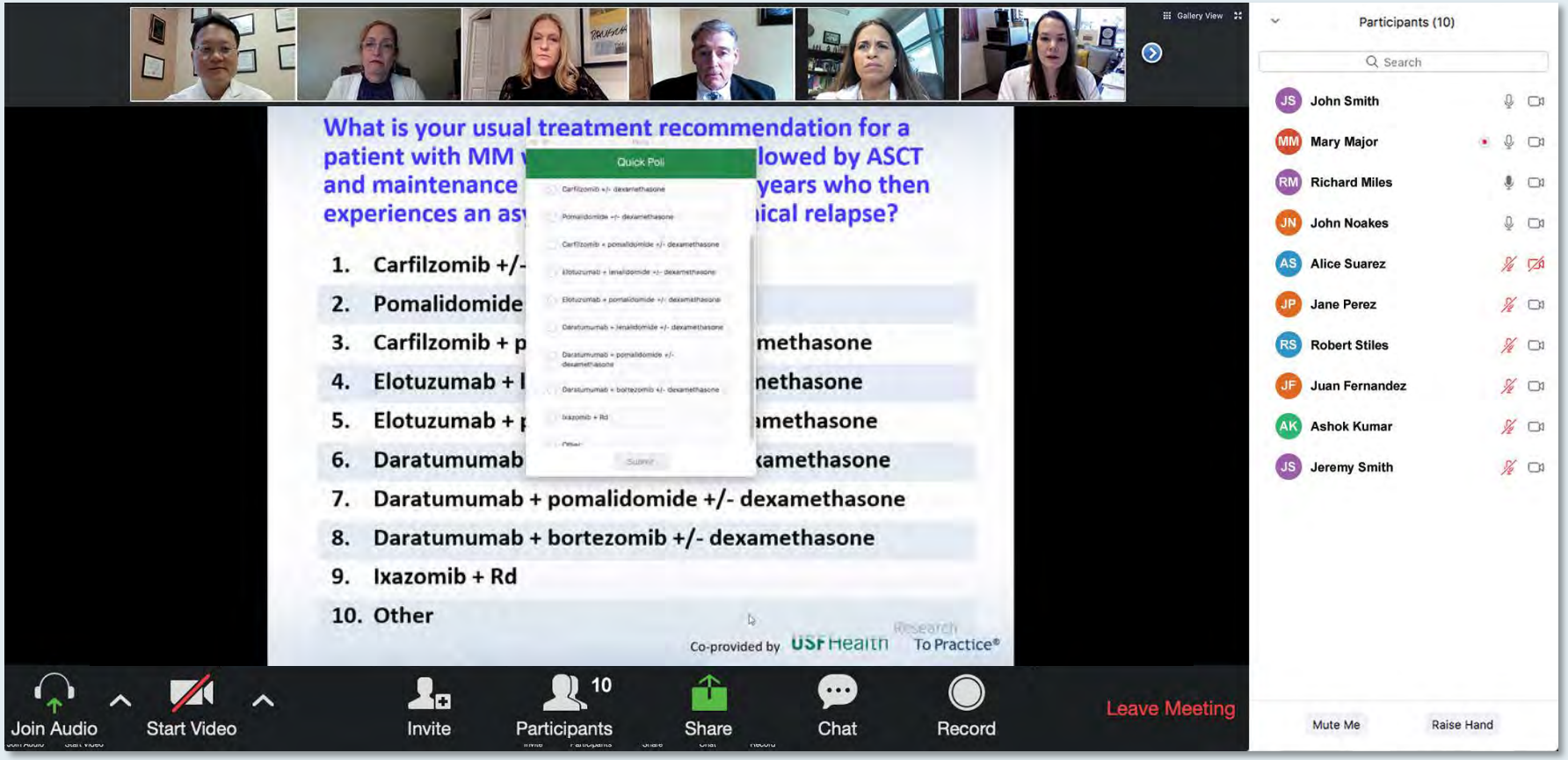



**Feel free to submit questions now before the program begins and throughout the program.**

Year in Review 2020

# Familiarizing Yourself with the Zoom Interface

## How to answer poll questions




**When a poll question pops up, click your answer choice from the available options. Results will be shown after everyone has answered.**

Year in Review 2020

# ONCOLOGY TODAY

## WITH DR NEIL LOVE

# Management of Gastroesophageal Cancers

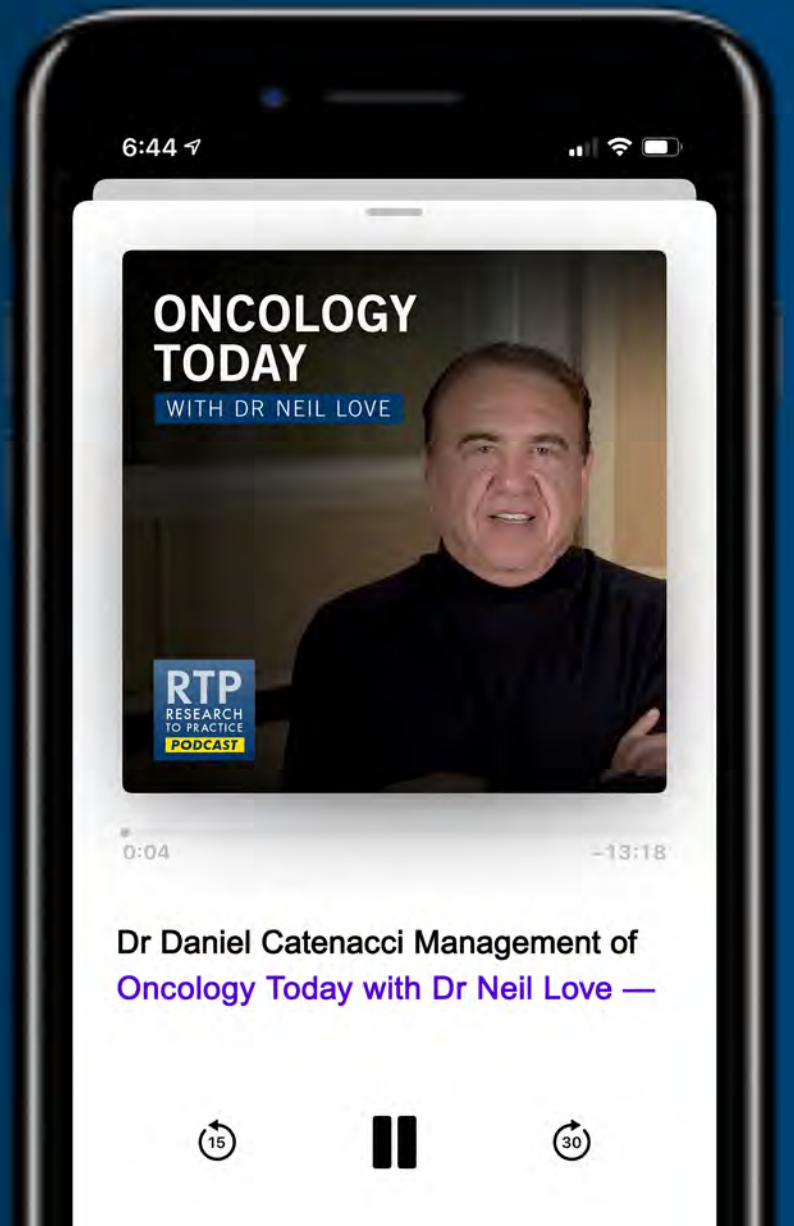

DR DANIEL CATENACCI

THE UNIVERSITY OF CHICAGO MEDICAL CENTER AND BIOLOGICAL SCIENCES


Listen on Apple Podcasts

Spotify

Listen on Google Podcasts



# *Meet The Professor*

# Immunotherapy and Novel Agents in Gynecologic Cancers

**Wednesday, December 9, 2020**
**12:30 PM – 1:30 PM ET**

## Faculty

**Gottfried E Konecny, MD**

## Moderator

**Neil Love, MD**

RTP
RESEARCH
TO PRACTICE

# Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

**Thursday, December 10, 2020**
**8:30 PM – 10:00 PM ET**

## Faculty


**Carey K Anders, MD**
**Erika Hamilton, MD**
**Sara Hurvitz, MD**
**Mark D Pegram, MD**
**Sara M Tolaney, MD, MPH**


## Moderator


**Neil Love, MD**


RTP RESEARCH TO PRACTICE

# Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Triple-Negative Breast Cancer

**Friday, December 11, 2020**
**8:30 PM – 10:00 PM ET**

## Faculty

**P Kelly Marcom, MD**
**Joyce O'Shaughnessy, MD**
**Hope S Rugo, MD**
**Professor Peter Schmid, MD, PhD**

## Moderator

**Neil Love, MD**

RTP RESEARCH TO PRACTICE

# Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

## Hepatobiliary and Pancreatic Cancers

**Tuesday, December 15, 2020**
**5:00 PM – 6:00 PM ET**

### Faculty

**Tanios Bekaii-Saab, MD**
**Lipika Goyal, MD, MPhil**

### Moderator

**Neil Love, MD**

Year in Review 2020

# *Meet The Professor*
# Management of Multiple Myeloma

**Wednesday, December 16, 2020**
**12:00 PM – 1:00 PM ET**

## Faculty

**Peter Voorhees, MD**

## Moderator

**Neil Love, MD**

RTP
RESEARCH
TO PRACTICE

# *Meet The Professor*

# Management of Chronic Lymphocytic Leukemia

**Wednesday, December 16, 2020**
**2:00 PM – 3:00 PM ET**

## Faculty

**Nitin Jain, MD**

## Moderator

**Neil Love, MD**

RTP
RESEARCH
TO PRACTICE

# Year in Review: Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology

## Colorectal and Gastroesophageal Cancers

**Tuesday, December 8, 2020**
**5:00 PM – 6:00 PM ET**

### Faculty

**Peter C Enzinger, MD**
**Zev Wainberg, MD, MSc**

### Moderator

**Neil Love, MD**

Year in Review 2020

# What is the preferred approach by clinical investigators to…

- MSI-high colorectal, gastric and esophageal cancers?
- MSS pan-RAS wild-type colorectal cancer?
- Localized gastric and esophageal cancers?
- MSS HER2-negative gastroesophageal cancer?
- MSS pan-RAS wild-type, HER2-expressing colorectal cancer?
- MSS HER2-positive gastric cancer?
- MSS pan-RAS wild-type, BRAF-mutated colorectal cancer?
- Metastatic colorectal cancer after chemotherapy and immunotherapy?

Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

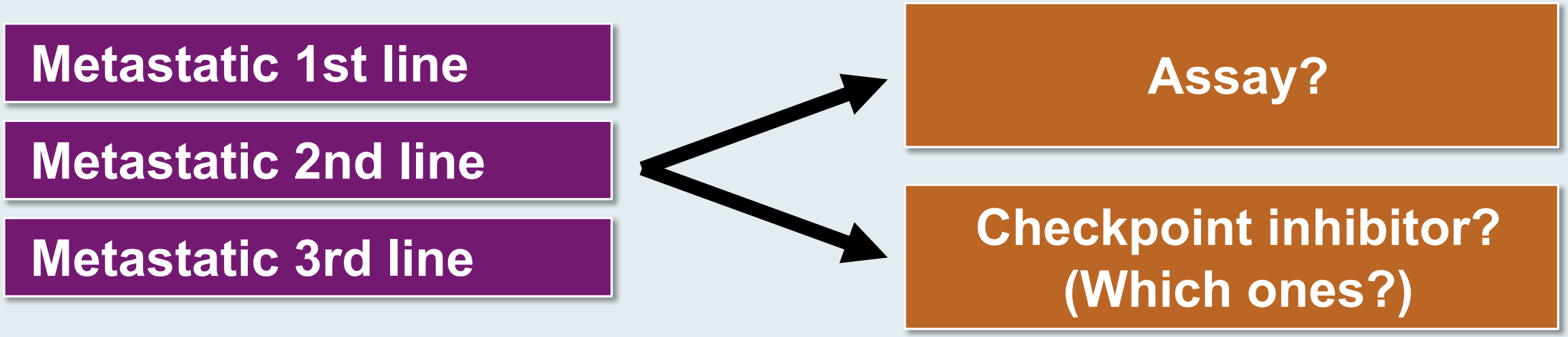
# What is the preferred approach by clinical investigators to…

- MSI-high colorectal, gastric and esophageal cancers?
- MSS pan-RAS wild-type colorectal cancer?
- Localized gastric and esophageal cancers?
- MSS HER2-negative gastroesophageal cancer?
- MSS pan-RAS wild-type, HER2-expressing colorectal cancer?
- MSS HER2-positive gastric cancer?
- MSS pan-RAS wild-type, BRAF-mutated colorectal cancer?
- Metastatic colorectal cancer after chemotherapy and immunotherapy?

Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# What is the preferred approach by clinical investigators to MSI-high colorectal, gastric and esophageal cancers?




Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

## Regulatory and reimbursement issues aside, what would be your most likely first-line treatment for a younger patient with MSI-high mCRC?

a. Pembrolizumab
b. Nivolumab
c. Ipilimumab/nivolumab
d. Chemotherapy
e. Chemotherapy + biologic
f. Chemotherapy + immunotherapy
g. Other

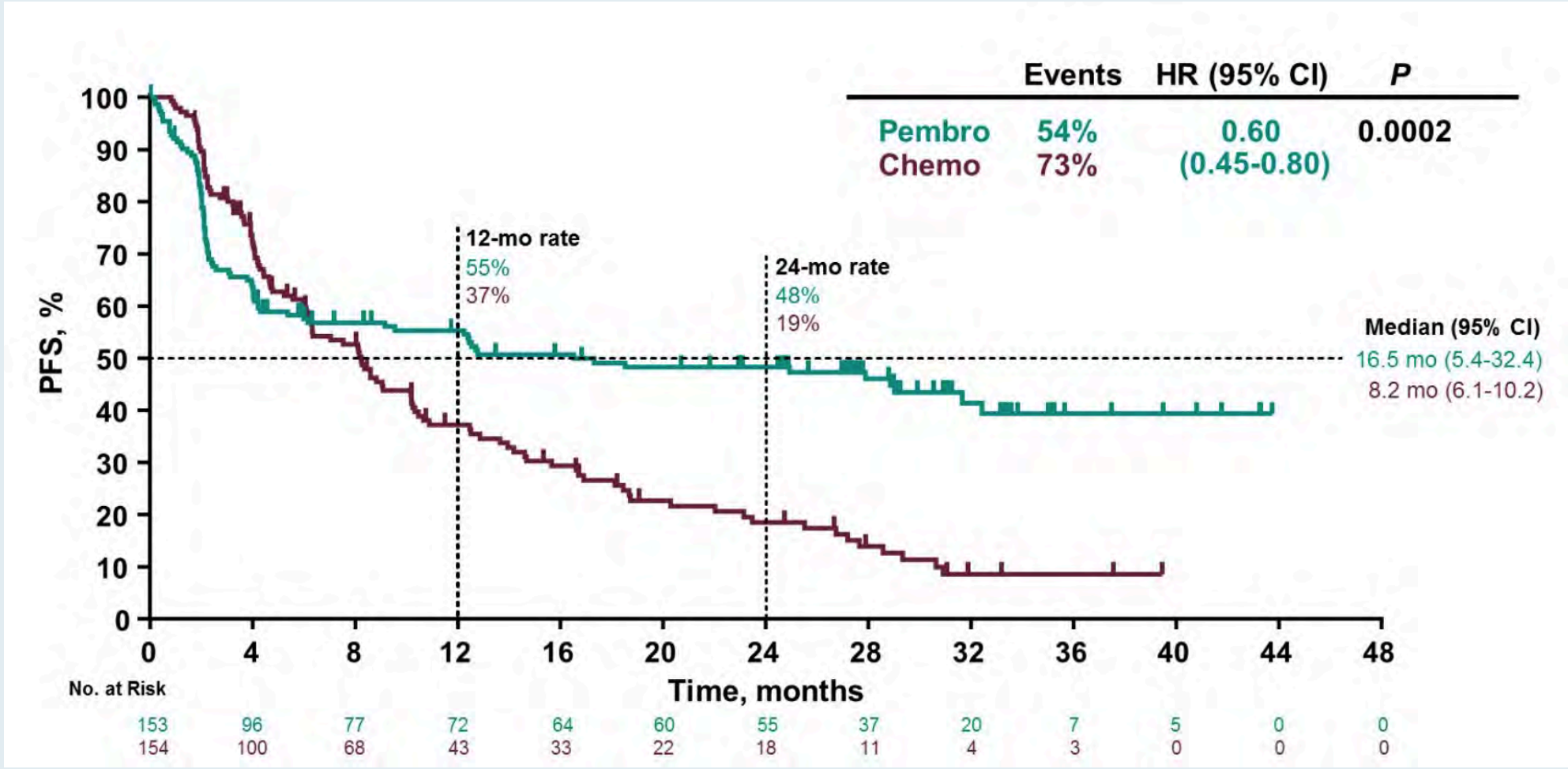
Year in Review 2020

# Pembrolizumab versus Chemotherapy for Microsatellite Instability-High/Mismatch Repair Deficient Metastatic Colorectal Cancer: The Phase 3 KEYNOTE-177 Study

Andre T et al.

ASCO 2020;Abstract LBA4.

# KEYNOTE-177: Dual-Primary Endpoint: Progression-Free Survival




**Overall survival not yet reported**

Andre T et al. ASCO 2020;Abstract LBA4.

Year in Review 2020

rapid communications

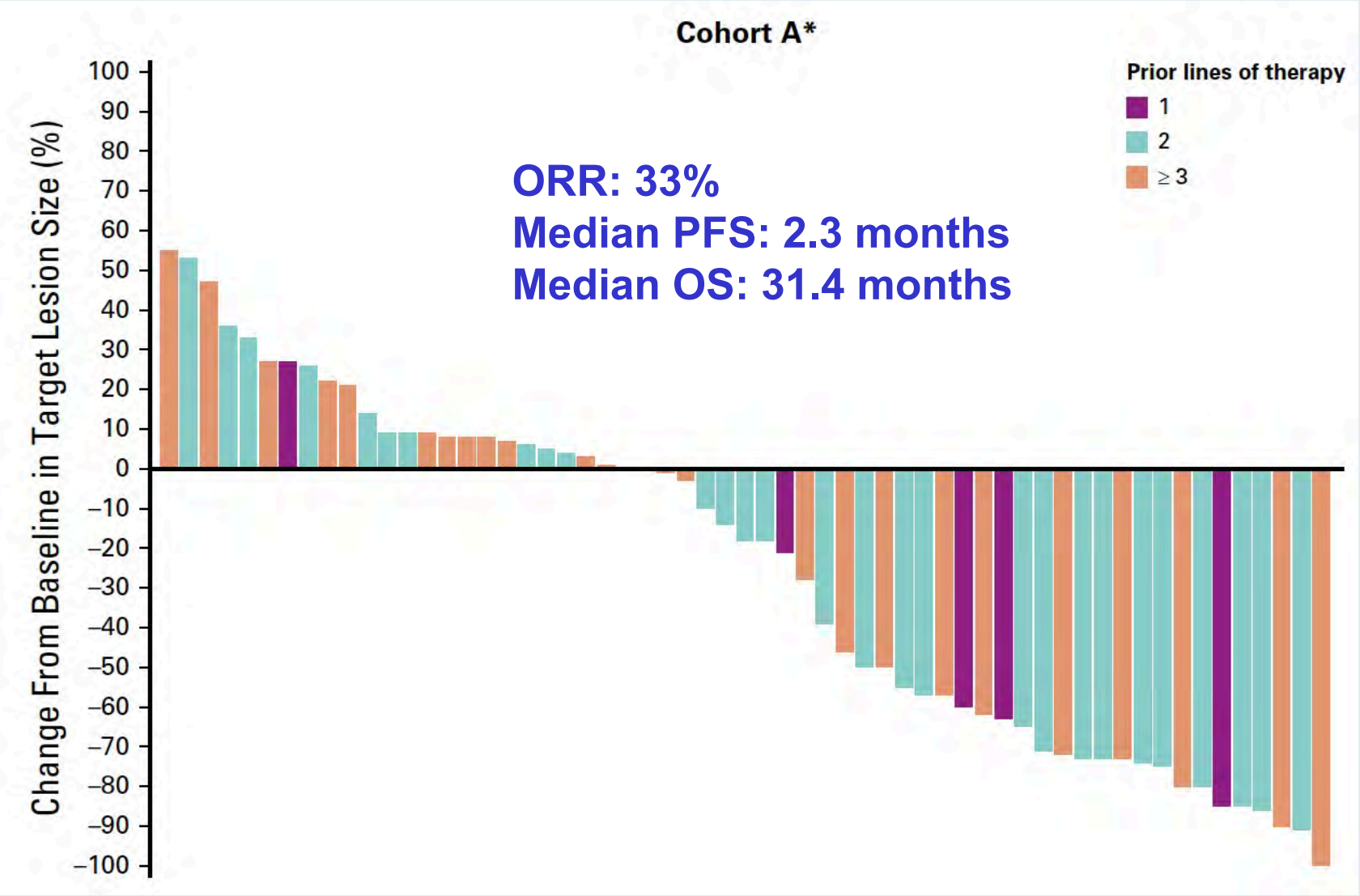
# Phase II Open-Label Study of Pembrolizumab in Treatment-Refractory, Microsatellite Instability–High/Mismatch Repair–Deficient Metastatic Colorectal Cancer: KEYNOTE-164

Dung T. Le, MD[1]; Tae Won Kim, MD[2]; Eric Van Cutsem, MD, PhD[3]; Ravit Geva, MD[4]; Dirk Jäger, MD[5]; Hiroki Hara, MD[6]; Matthew Burge, MBChB, FRACP[7]; Bert O'Neil, MD[8]; Petr Kavan, MD, PhD[9]; Takayuki Yoshino, MD[10]; Rosine Guimbaud, MD, PhD[11]; Hiroya Taniguchi, MD, PhD[12]; Elena Elez, MD, PhD[13]; Salah-Eddin Al-Batran, MD[14]; Patrick M. Boland, MD[15]; Todd Crocenzi, MD[16]; Chloe E. Atreya, MD, PhD[17]; Yi Cui, PhD[18]; Tong Dai, MD, PhD[19]; Patricia Marinello, PharmD[19]; Luis A. Diaz Jr, MD[20]; and Thierry André, MD[21]

*J Clin Oncol* 2020;38(1):11-9.

Year in Review 2020

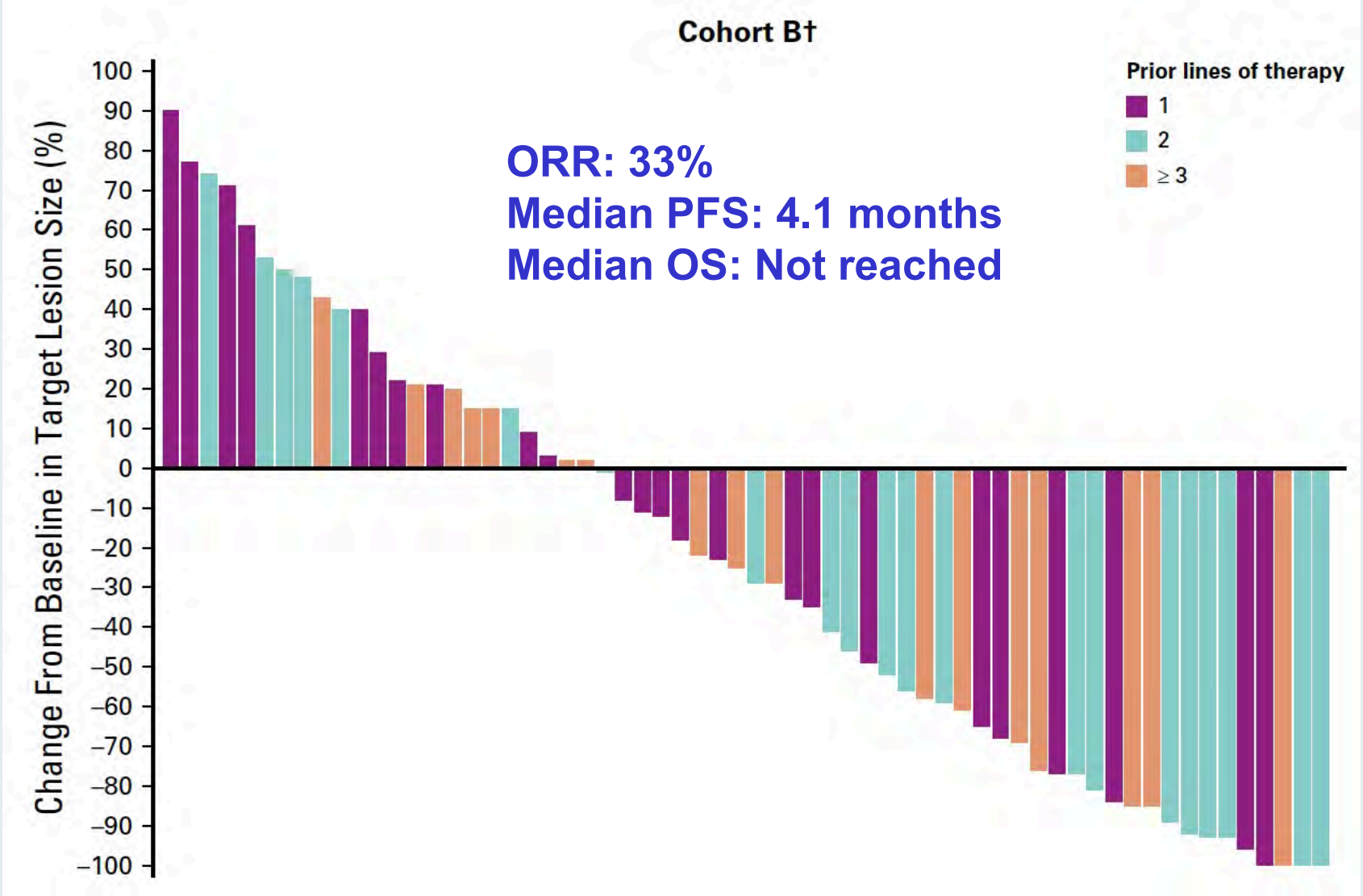
# KEYNOTE-164: Pembrolizumab in MSI-H/MRD Refractory mCRC
# Cohort A ≥2 prior lines of standard therapy




Le DT et al. *J Clin Oncol* 2020;38(1):11-9.

Year in Review 2020

# KEYNOTE-164: Pembrolizumab in MSI-H/MRD Refractory mCRC
# Cohort B ≥1 prior lines of standard therapy




Le DT et al. *J Clin Oncol* 2020;38(1):11-9.

Year in Review 2020

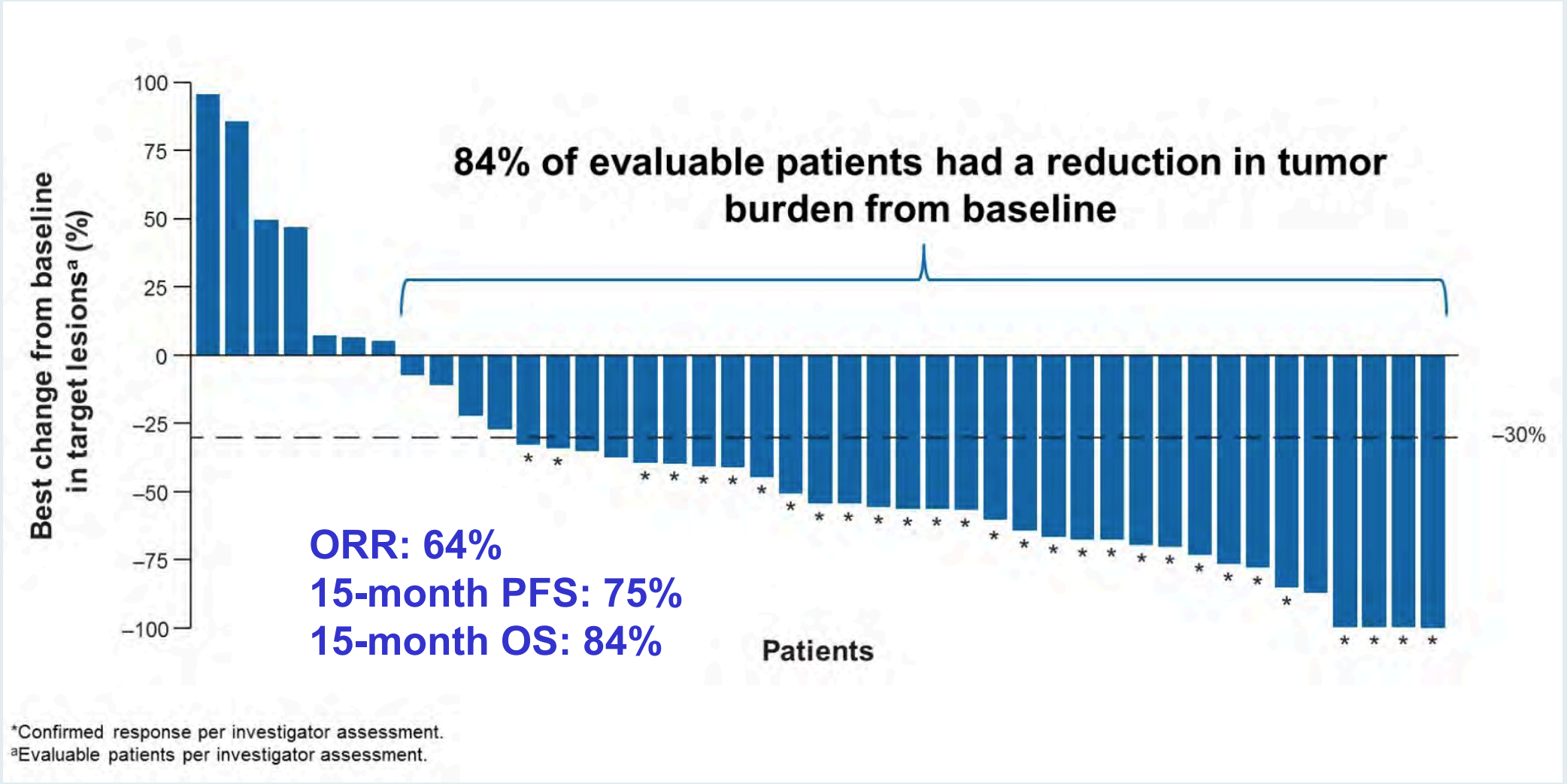
# Nivolumab plus Low-Dose Ipilimumab as First-Line Therapy in Microsatellite Instability-High/DNA Mismatch Repair Deficient mCRC: Clinical Update

Lenz H-J et al.

Gastrointestinal Cancers Symposium 2020;Abstract 11.

Year in Review 2020

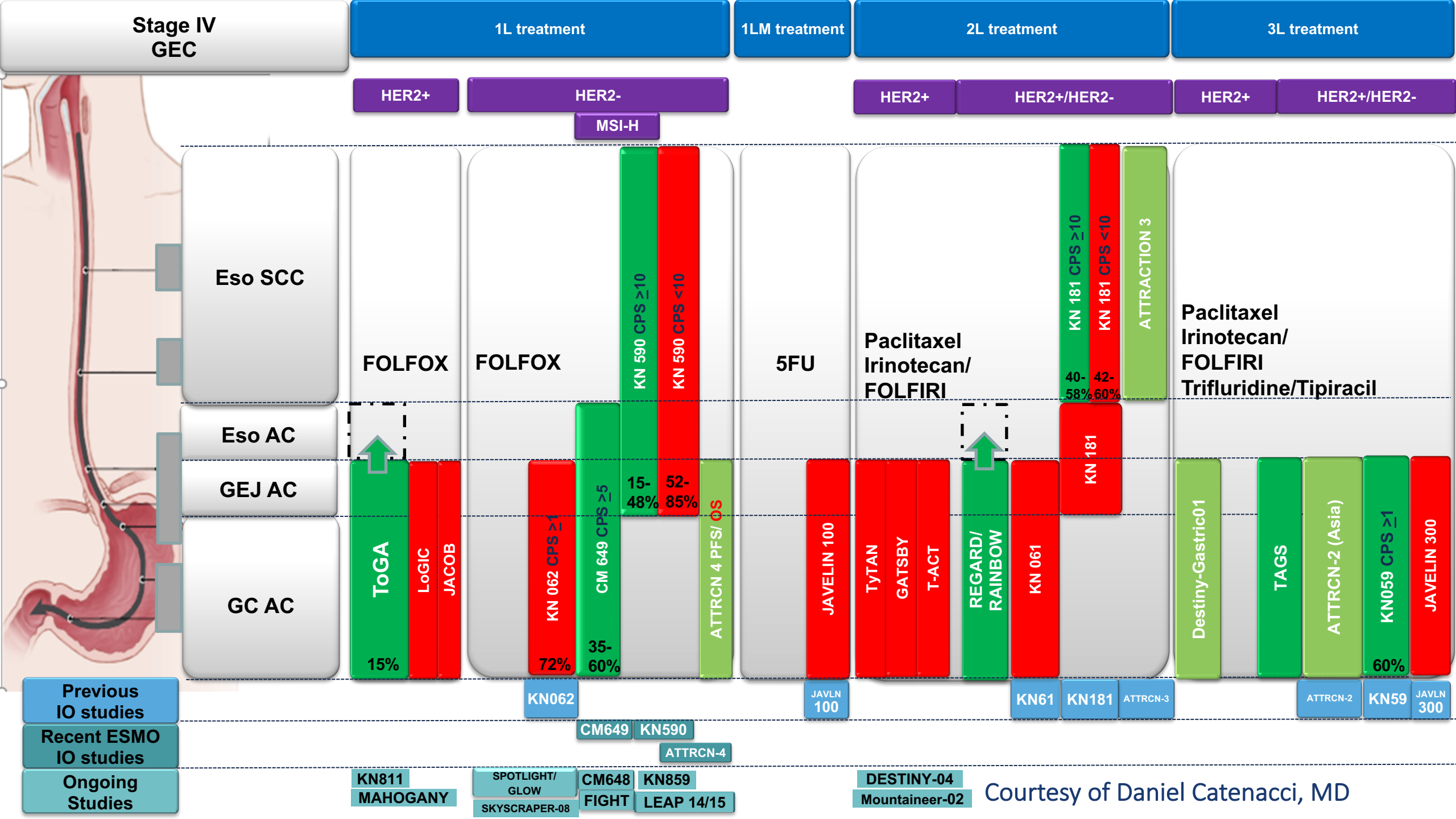
# CheckMate 142: Nivolumab/Ipilimumab as First-Line Therapy in MSI-H/dMMR mCRC




*Confirmed response per investigator assessment.
[a]Evaluable patients per investigator assessment.

Lenz H-J et al. Gastrointestinal Cancers Symposium 2020;Abstract 11.

Year in Review 2020




Courtesy of Daniel Catenacci, MD

# PD-L1 Diagnostic Antibodies

| Therapeutic Antibody /Studies | Diagnostic Antibody | Scoring System | Positivity Incidence | Comments |
|---|---|---|---|---|
| Pembrolizumab/ KEYNOTEs | 22C3 pharmDx assay | CPS Combined Positivity Score | CPS ≥1 50%-60% | • Good NPV<br>• not great PPV |
| | | Cut off - ≥1 or ≥10 (or other) | CPS≥5? ~35-40%?<br>CPS ≥10 15%-25% | • Enrich for benefit at higher cut-offs |
| Nivolumab/ CHECKMATEs\|ATTRACTIONs | 28-8 pharmDx assay | TPS[1] Tumor Positivity Score | 13.5%-25% | • Poor NPV<br>• Not enriching |
| | | Cut off - ≥1% (or other) | | |
| | | CPS Combined Positivity Score | CPS>1 ~82%<br>CPS>5 60%<br>CPS>10? | Need more data<br>Need more data<br>Enrich for benefit at higher cut-offs |

Courtesy of Daniel Catenacci, MD

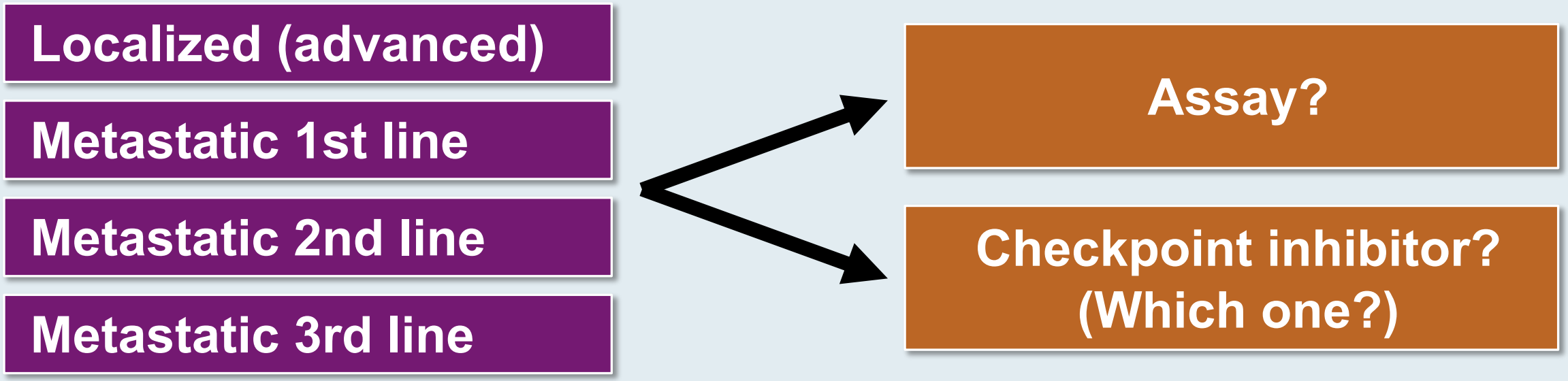
# What is the preferred approach by clinical investigators to…

- MSI-high colorectal, gastric and esophageal cancers?
- MSS pan-RAS wild-type colorectal cancer?
- Localized gastric and esophageal cancers?
- MSS HER2-negative gastroesophageal cancer?
- MSS pan-RAS wild-type, HER2-expressing colorectal cancer?
- MSS HER2-positive gastric cancer?
- MSS pan-RAS wild-type, BRAF-mutated colorectal cancer?
- Metastatic colorectal cancer after chemotherapy and immunotherapy?

Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# What is the preferred approach by clinical investigators to MSS, pan-RAS wild-type colorectal cancer?




Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# A recent randomized Phase II/III trial evaluating postoperative FOLFOX after resection of liver-only metastases showed…

a. Improvement in disease-free survival (DFS)
b. Improvement in overall survival (OS)
c. Improvement in DFS and OS
d. No clinical benefit
e. I don’t know

Year in Review 2020

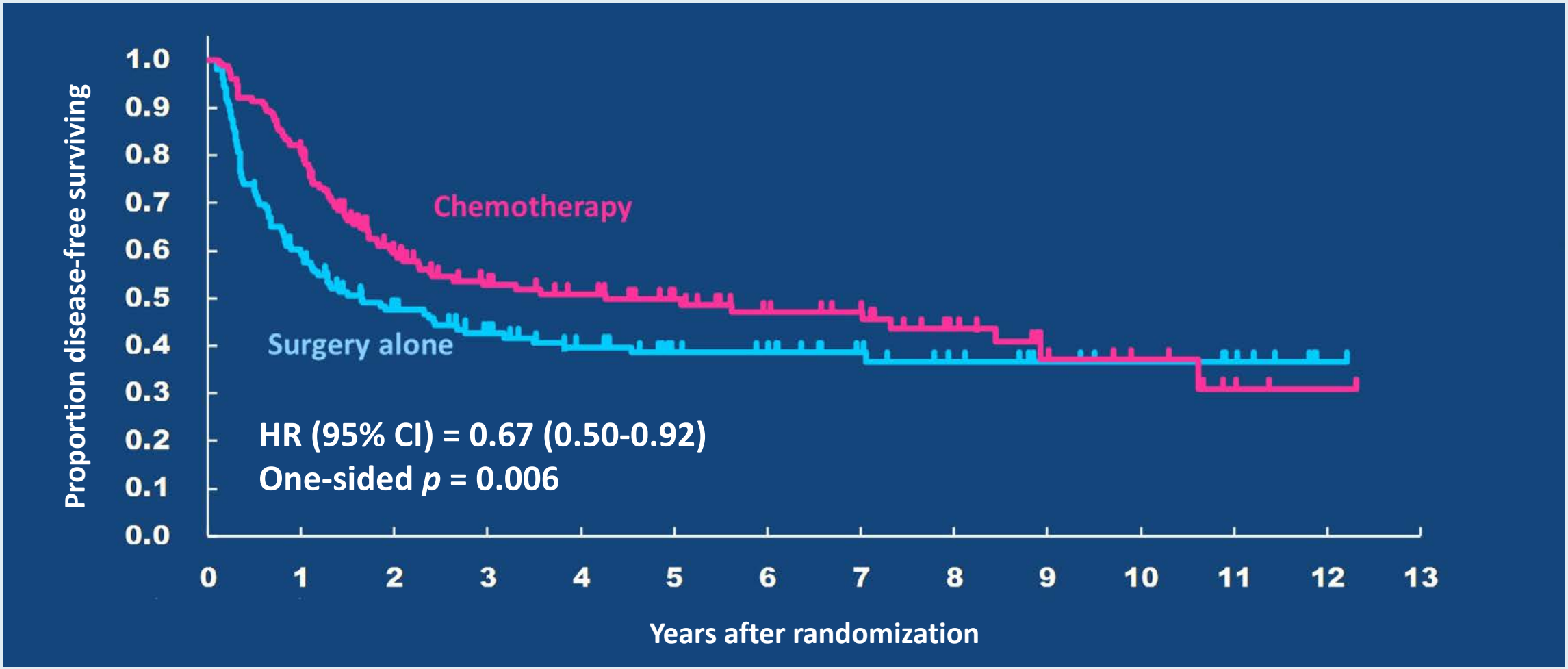
# A Randomized Phase II/III Trial Comparing Hepatectomy Followed by mFOLFOX6 with Hepatectomy Alone for Liver Metastasis from Colorectal Cancer: JCOG0603 Study

Kanemitsu Y et al.

ASCO 2020;Abstract 4005.

Year in Review 2020

# Phase II/III JCOG0603 Study: Disease-Free Survival




Kanemitsu Y et al. ASCO 2020;Abstract 4005.

original reports

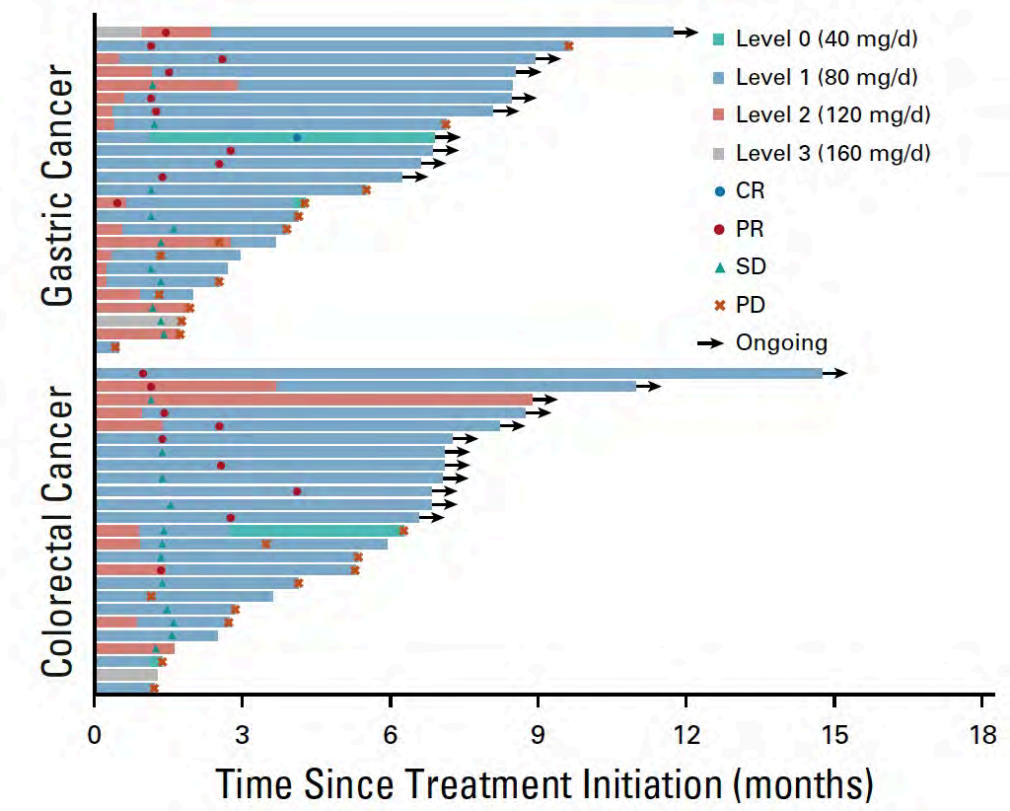
# Regorafenib Plus Nivolumab in Patients With Advanced Gastric or Colorectal Cancer: An Open-Label, Dose-Escalation, and Dose-Expansion Phase Ib Trial (REGONIVO, EPOC1603)

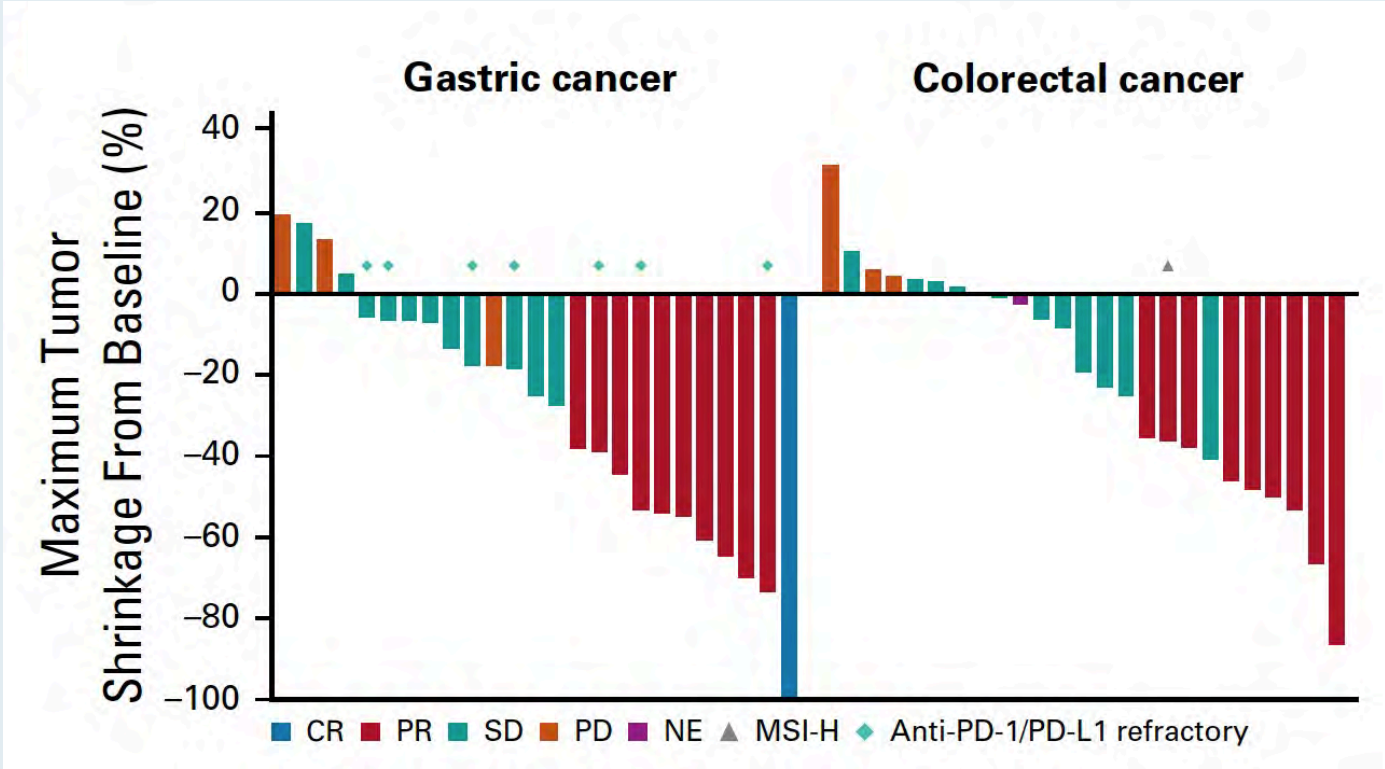
Shota Fukuoka, MD, PhD[1,2]; Hiroki Hara, MD[3]; Naoki Takahashi, MD[3]; Takashi Kojima, MD[1]; Akihito Kawazoe, MD[1]; Masako Asayama, MD[3]; Takako Yoshii, MD, PhD[3]; Daisuke Kotani, MD[1]; Hitomi Tamura, RN[4]; Yuichi Mikamoto, BPharm[4]; Nami Hirano, MLT[4]; Masashi Wakabayashi, ME[4]; Shogo Nomura, PhD[4]; Akihiro Sato, MD[4]; Takeshi Kuwata, MD, PhD[5]; Yosuke Togashi, MD, PhD[2]; Hiroyoshi Nishikawa, MD, PhD[2]; and Kohei Shitara, MD[1]

*J Clin Oncol* 2020;38(18):2053-61.

Year in Review 2020

# REGONIVO: Regorafenib plus Nivolumab in Advanced Gastric or CRC




- Three DLTs (grade 3 colonic perforation, maculopapular rash, and proteinuria) were observed with regorafenib 160 mg; none were observed with 80 or 120 mg
- During the dose-expansion part, regorafenib dose was reduced from 120 to 80 mg because of frequent maculopapular rash

Fukuoka S et al. *J Clin Oncol* 2020;38(18):2053-61.

Year in Review 2020

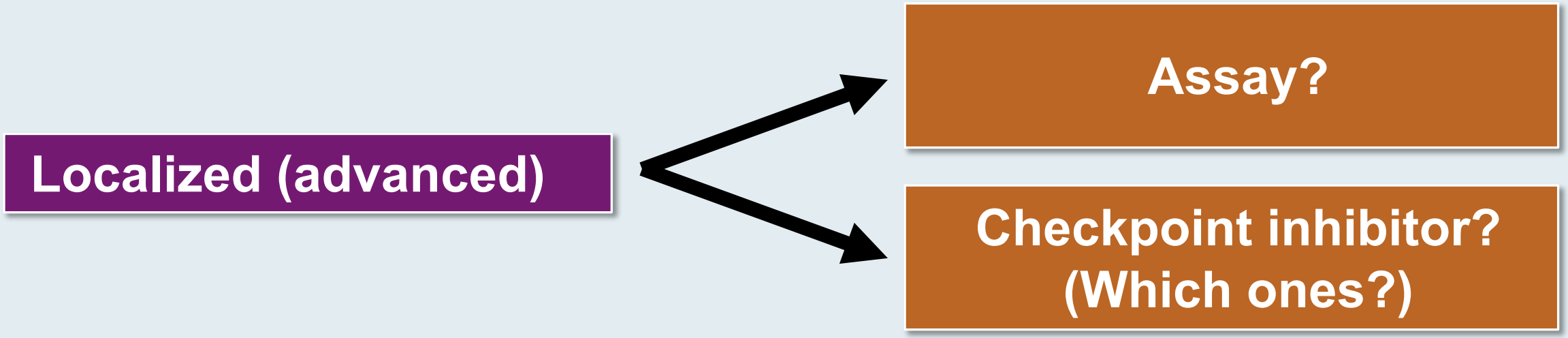
# What is the preferred approach by clinical investigators to…

- MSI-high colorectal, gastric and esophageal cancers?
- MSS pan-RAS wild-type colorectal cancer?
- Localized gastric and esophageal cancers?
- MSS HER2-negative gastroesophageal cancer?
- MSS pan-RAS wild-type, HER2-expressing colorectal cancer?
- MSS HER2-positive gastric cancer?
- MSS pan-RAS wild-type, BRAF-mutated colorectal cancer?
- Metastatic colorectal cancer after chemotherapy and immunotherapy?

Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# What is the preferred approach by clinical investigators to localized gastric and esophageal cancers?




Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# CM 577(Adj EsoSCC/EsoAC/GEJAC)

## CheckMate 577 study design

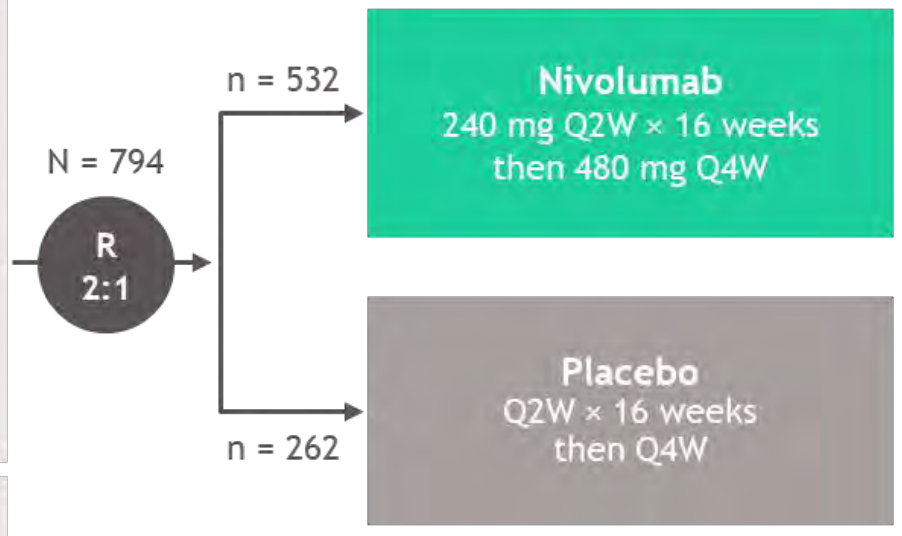
- CheckMate 577 is a global, phase 3, randomized, double-blind, placebo-controlled trial[a]

**Key eligibility criteria**

- Stage II/III EC/GEJC
- Adenocarcinoma or squamous cell carcinoma
- Neoadjuvant CRT + surgical resection (R0,[b] performed within 4-16 weeks prior to randomization)
- Residual pathologic disease
  - ≥ ypT1 or ≥ ypN1
- ECOG PS 0-1

**Stratification factors**

- Histology (squamous vs adenocarcinoma)
- Pathologic lymph node status (≥ ypN1 vs ypN0)
- Tumor cell PD-L1 expression (≥ 1% vs < 1%[c])




**Total treatment duration of up to 1 year[d]**

**Primary endpoint:**

- DFS[e]

**Secondary endpoints:**

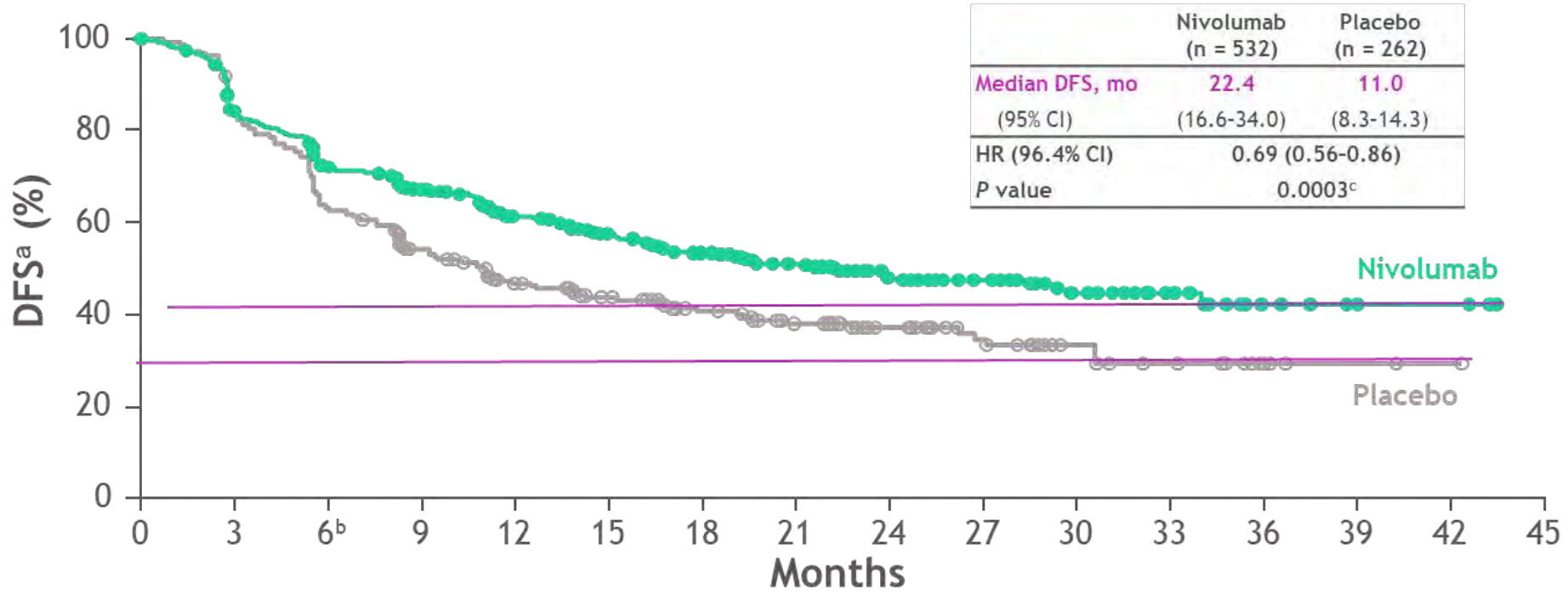
- OS[f]
- OS rate at 1, 2, and 3 years

- Median follow-up was 24.4 months (range, 6.2-44.9)[g]
- Geographical regions: Europe (38%), US and Canada (32%), Asia (13%), rest of the world (16%)

Courtesy of Daniel Catenacci, MD

# CM 577(Adj EsoSCC/EsoAC/GEJAC)

## Disease-free survival




| | Nivolumab (n = 532) | Placebo (n = 262) |
|---|---|---|
| Median DFS, mo | 22.4 | 11.0 |
| (95% CI) | (16.6-34.0) | (8.3-14.3) |
| HR (96.4% CI) | 0.69 (0.56-0.86) | |
| *P* value | 0.0003[c] | |

| No. at risk | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Nivolumab | 532 | 430 | 364 | 306 | 249 | 212 | 181 | 147 | 92 | 68 | 41 | 22 | 8 | 4 | 3 | 0 |
| Placebo | 262 | 214 | 163 | 126 | 96 | 80 | 65 | 53 | 38 | 28 | 17 | 12 | 5 | 2 | 1 | 0 |

- Nivolumab provided superior DFS with a 31% reduction in the risk of recurrence or death and a doubling in median DFS versus placebo

[a]Per investigator assessment; [b]6-month DFS rates were 72% (95% CI, 68-76) in the nivolumab arm and 63% (95% CI, 57-69) in the placebo arm; [c]The boundary for statistical significance at the pre-specified interim analysis required the *P* value to be less than 0.036.

Courtesy of Daniel Catenacci, MD

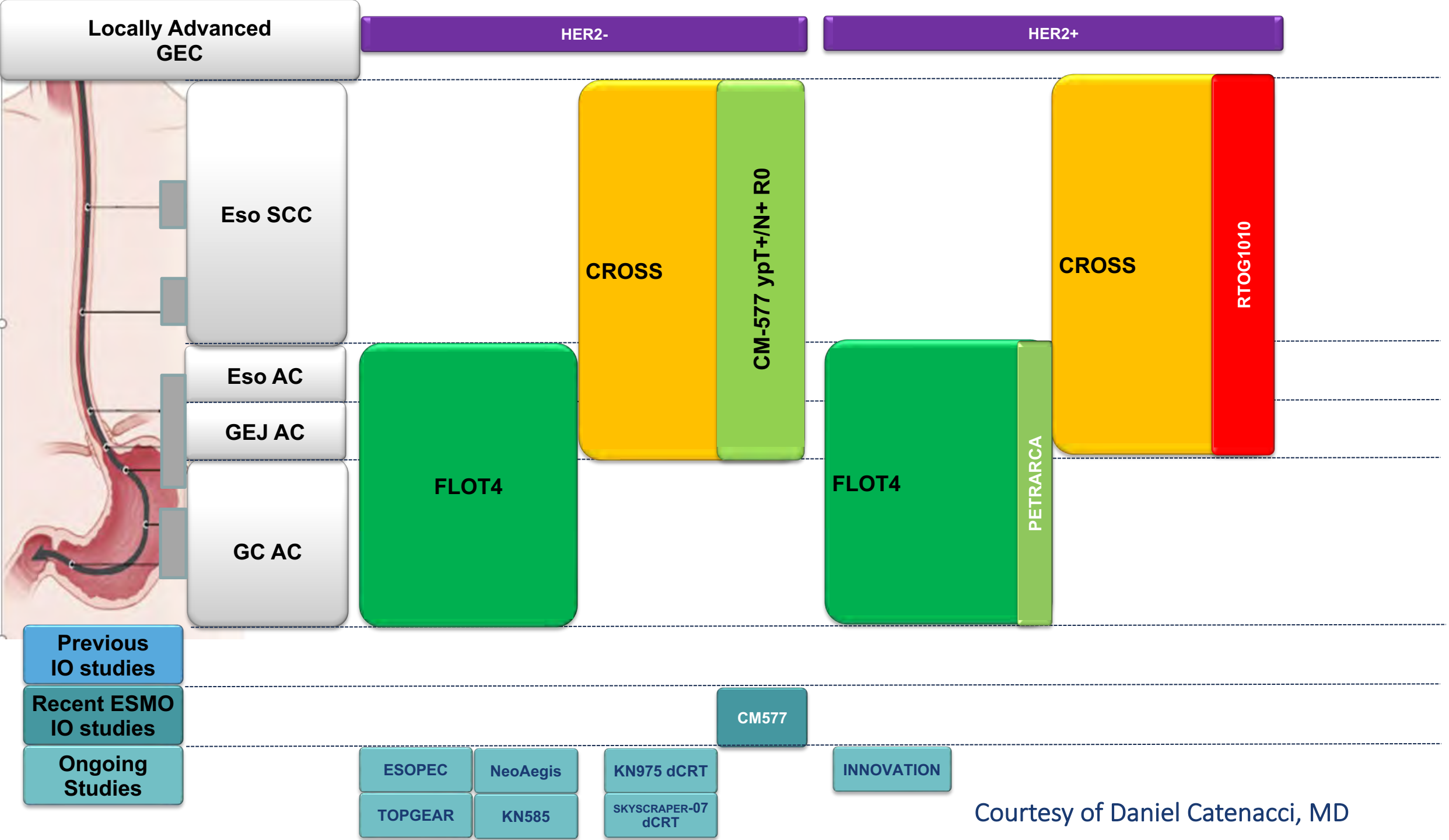
# Treatment-related adverse events with potential immunologic etiology

| Select TRAEs,[b,c] n (%) | Nivolumab[a] n = 532 | | Placebo[a] n = 260 | |
|---|---|---|---|---|
| | Any grade | Grade 3-4 | Any grade | Grade 3-4 |
| Endocrine | 93 (17) | 5 (< 1) | 6 (2) | 0 |
| Gastrointestinal | 91 (17) | 4 (< 1) | 40 (15) | 3 (1) |
| Hepatic | 49 (9) | 6 (1) | 18 (7) | 4 (2) |
| Pulmonary | 23 (4) | 6 (1) | 4 (2) | 1 (< 1) |
| Renal | 7 (1) | 1 (< 1) | 2 (< 1) | 0 |
| Skin | 130 (24) | 7 (1) | 28 (11) | 1 (< 1) |

- The majority of select TRAEs were grade 1 or 2
- Grade 3–4 select TRAEs occurred in ≤ 1% of patients in the nivolumab arm and there were no grade 5 select TRAEs
- The most common grade 3–4 select TRAEs in the nivolumab arm were pneumonitis (n = 4) and rash (n = 4) (0.8% each); in the placebo arm, these events occurred in 1 patient each (0.4%)

[a]Patients who received ≥ 1 dose of study treatment; [b]Select TRAEs are those with potential immunologic etiology that require frequent monitoring/intervention; [c]Events reported between first dose and 30 days after last dose of study drug.

Courtesy of Daniel Catenacci, MD




Courtesy of Daniel Catenacci, MD

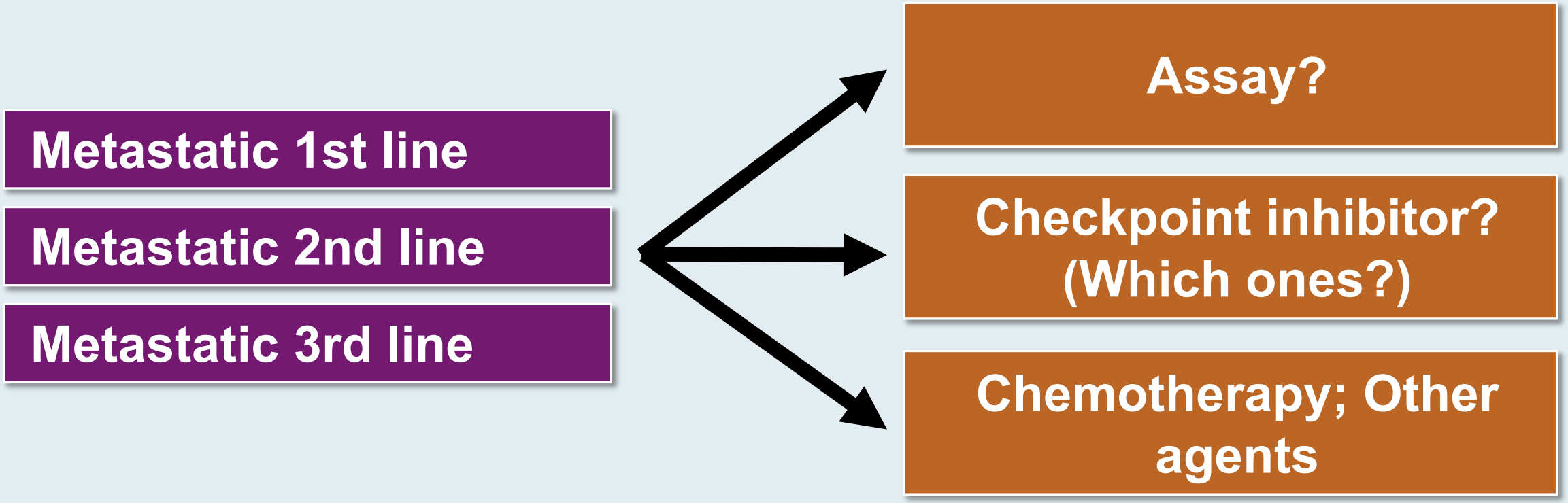
# What is the preferred approach by clinical investigators to…

- MSI-high colorectal, gastric and esophageal cancers?
- MSS pan-RAS wild-type colorectal cancer?
- Localized gastric and esophageal cancers?
- MSS HER2-negative gastroesophageal cancer?
- MSS pan-RAS wild-type, HER2-expressing colorectal cancer?
- MSS HER2-positive gastric cancer?
- MSS pan-RAS wild-type, BRAF-mutated colorectal cancer?
- Metastatic colorectal cancer after chemotherapy and immunotherapy?

Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# What is the preferred approach by clinical investigators to MSS, HER2-negative gastroesophageal adenocarcinoma?




Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

**A 65-year-old patient with locally advanced HER2-negative microsatellite-stable gastric cancer has a complete response to carboplatin/paclitaxel and radiation therapy but then develops recurrent disease 3 months later. CPS = 10. What treatment would you recommend?**

a. FOLFOX
b. Other chemotherapy
c. Pembrolizumab
d. Nivolumab
e. Other

Year in Review 2020

**What is your usual next treatment for a younger patient (PS 0) with metastatic HER2-negative, microsatellite-stable gastric cancer who has experienced disease progression on FOLFOX, paclitaxel/ramucirumab and an anti-PD-1/PD-L1 antibody?**

a. TAS-102
b. Palliative care
c. Other chemotherapy
d. Other

# Key First-Line Studies of Checkpoint Inhibitors for Gastric, GEJ and Esophageal Cancers

| Study | Setting | Randomization | Primary endpoints | Hazard ratio (*p*-value) |
|---|---|---|---|---|
| KN-062 | Metastatic gastric/ GEJ ADC | Pembro vs Pembro/chemo vs Placebo/chemo | OS (CPS ≥1) | Pembro vs chemo: 0.91 (NR)<br>Pembro + chemo vs chemo: 0.85 (0.046) |
| KN-590 | Metastatic gastric/GEJ/esophageal | Pembro + chemo vs Placebo + chemo | OS in ESCC CPS ≥10<br>OS in ESCC<br>OS in CPS ≥10<br>OS in all patients | 0.57 (<0.0001)<br>0.72 (0.0006)<br>0.62 (<0.0001)<br>0.73 (<0.0001) |
| CM-649 | Metastatic gastric/GEJ/esophageal | Nivo + chemo vs Chemo | OS (CPS ≥5) | 0.71 (<0.0001) |
| ATTRACTION-4 | Metastatic gastric/GEJ | Nivo + chemo vs Placebo + chemo | PFS (all comers)<br>OS (all comers) | 0.68 (0.0007)<br>0.90 (0.257) |

Pembro = pembrolizumab; nivo = nivolumab; ESCC = esophageal squamous cell carcinoma; CPS = combined positive score

Shitara K et al. *JAMA Oncol* 2020; Kato et al. ESMO 2020; Kelly et al. ESMO 2020; Moehler et al. ESMO 2020; Boku et al. ESMO 2020.

# Key Second-Line Studies of Checkpoint Inhibitors for Gastric, GEJ and Esophageal Cancers

| Study | Setting (second line) | Randomization | Primary endpoints | Hazard ratio (*p*-value) |
|---|---|---|---|---|
| KN-061 | Metastatic G/GEJ ADC | Pembrolizumab vs Paclitaxel | OS (CPS ≥1) | 0.81 (0.03) |
| KN-181 | Metastatic esophageal/EGJ | Pembrolizumab vs Chemo | OS (CPS ≥10)<br>OS (all SCC) | 0.69 (0.0074)<br>0.78 (0.0095) |

Fuchs CS et al. ASCO 2020;Abstract 4503; Kojima T et al. *JCO* 2020

Year in Review 2020

# TAGS: TAS-102 Gastric Study[a]

**Patients with mGC**
*(including GEJ cancer)*
- ≥2 prior regimens:
  - Fluoropyrimidine
  - Platinum
  - Taxane and/or irinotecan
  - HER2 inhibitor, if available, for HER2+ disease
  - Refractory to/intolerant of last prior therapy
- ECOG PS of 0 or 1
- Age ≥18 y (≥20 y in Japan)

**Target sample size: 500**

**R 2:1**

**FTD/TPI (TAS-102) + BSC (n=337)**
35 mg/m$^2$ BID orally on days 1–5 and 8–12 of each 28-day cycle

**Placebo + BSC (n=170)**
BID orally on days 1–5 and 8–12 of each 28-day cycle

**End points**
- Primary:
  - OS
- Key secondary:
  - PFS, safety
- Other secondary:
  - ORR
  - DCR
  - QOL
  - Time to ECOG PS ≥2

- Treatment until progression, intolerable toxicity, or patient withdrawal
- Multicenter, randomized, double-blind, placebo-controlled, phase III study
  - Stratification: ECOG PS (0 vs 1), region (Japan vs ROW), prior ramucirumab (yes vs no)
  - Sites: 18 countries, 110 sites; enrollment: February 2016 – January 2018
  - Data cutoff date: March 31, 2018
  - Target 384 events allowed detection of HR for death of 0.70 with 90% power at 1-sided type 1 error of 0.025

BID, twice daily; BSC, best supportive care; ECOG PS, Eastern Cooperative Oncology Group performance status; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; ORR, overall response rate; PFS, progression-free survival; QOL, quality of life; ROW, rest of world; [a]NCT02500043

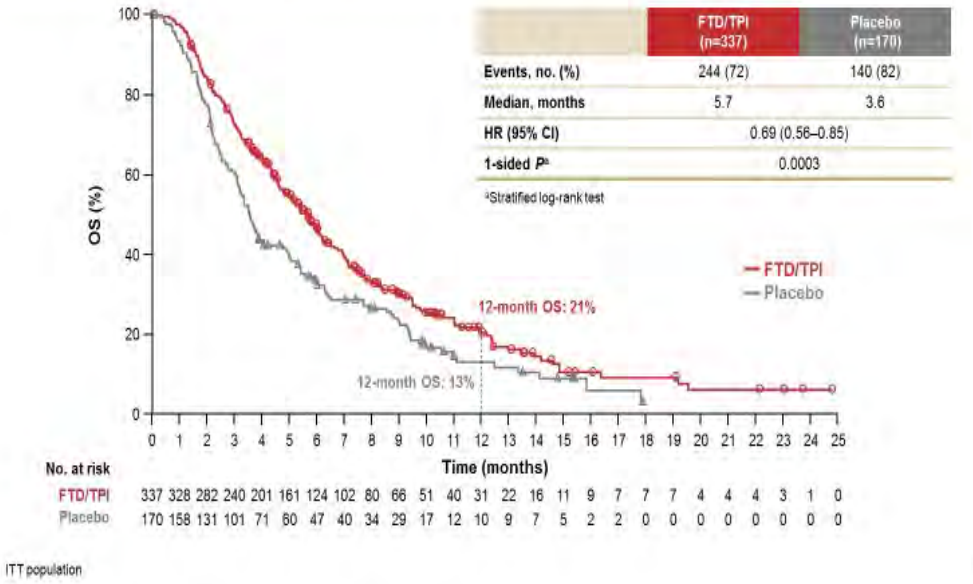


Shitara K et al. Lancet Oncol. 2018 Nov;19(11):1437-1448.

Courtesy of Peter C Enzinger, MD

# TAGS: TAS-102 vs Placebo in 3rd line Gastric Cancer

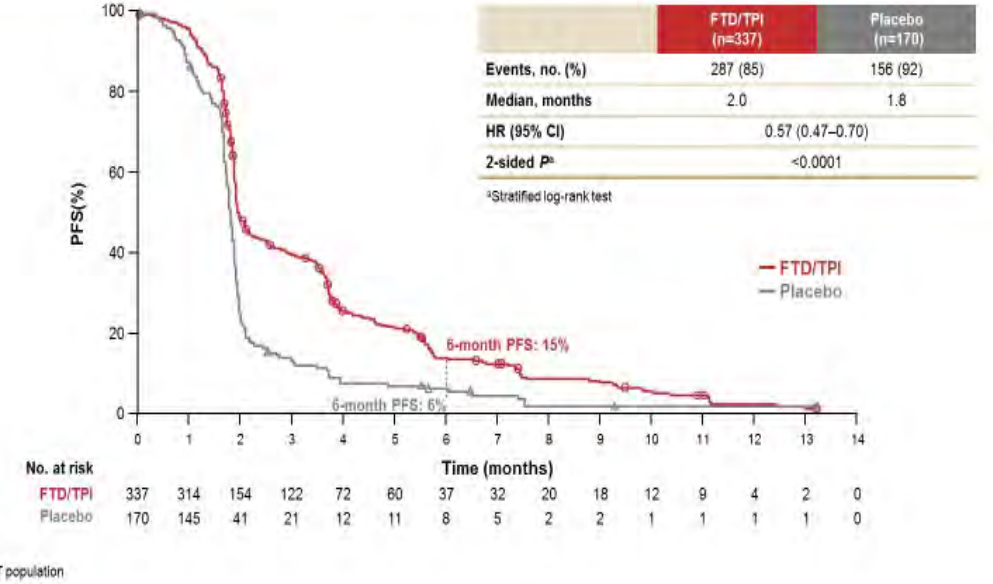
## Primary Endpoint – OS




ITT population

8

## Secondary Endpoint – PFS




ITT population

9

| AE | FTD/TPI | | Placebo | |
|---|---|---|---|---|
| | Any | Grade 3-4 | Any | Grade 3-4 |
| ANC | | 38% | | 0% |
| Diarrhea | 23% | 3% | 14% | 2% |
| Fatigue | 27% | 7% | 21% | 6% |
| Vomiting | 25% | 4% | 20% | 2% |

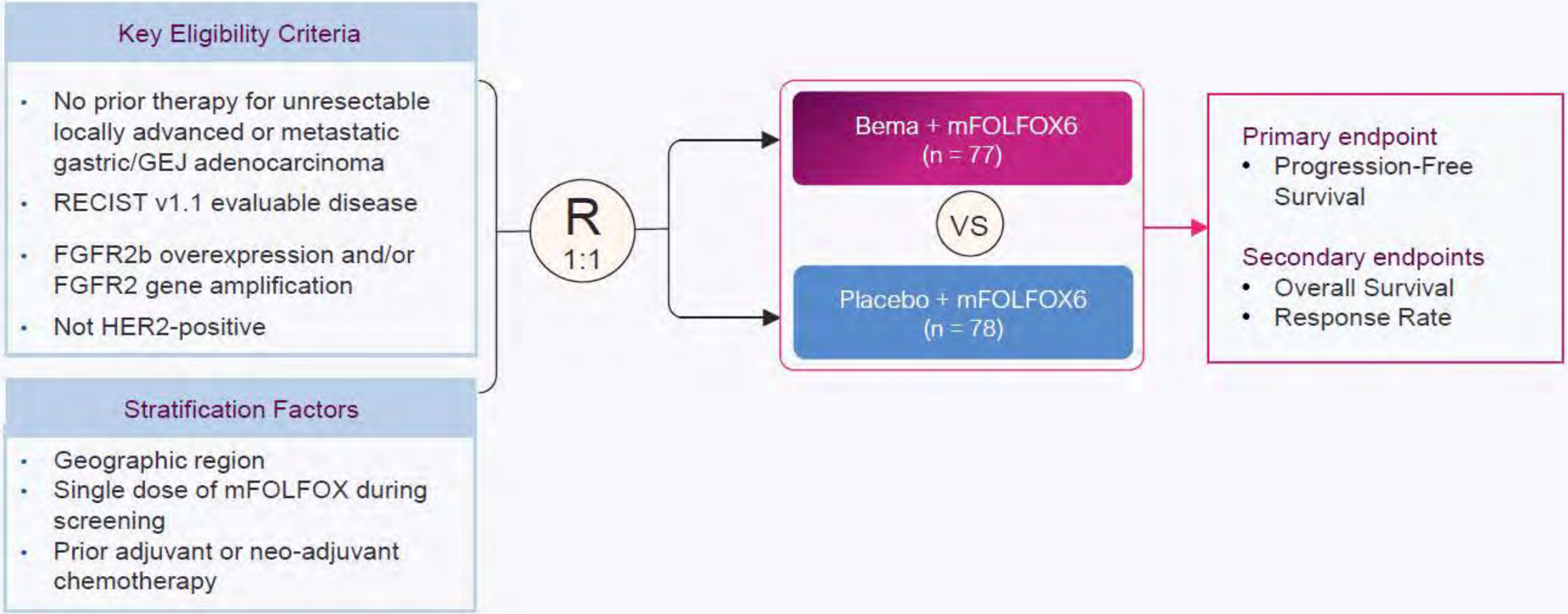


Shitara K et al. Lancet Oncol. 2018 Nov;19(11):1437-1448.

Courtesy of Peter C Enzinger, MD

# Phase II FIGHT Trial Design

## Patients Selected for FGFR2b+ Tumors (~30% of all HER2- Gastric/GEJ Cancer)




Bema = bemarituzumab (a first-in-class therapeutic antibody targeting FGFR2b)



Courtesy of Peter C Enzinger, MD

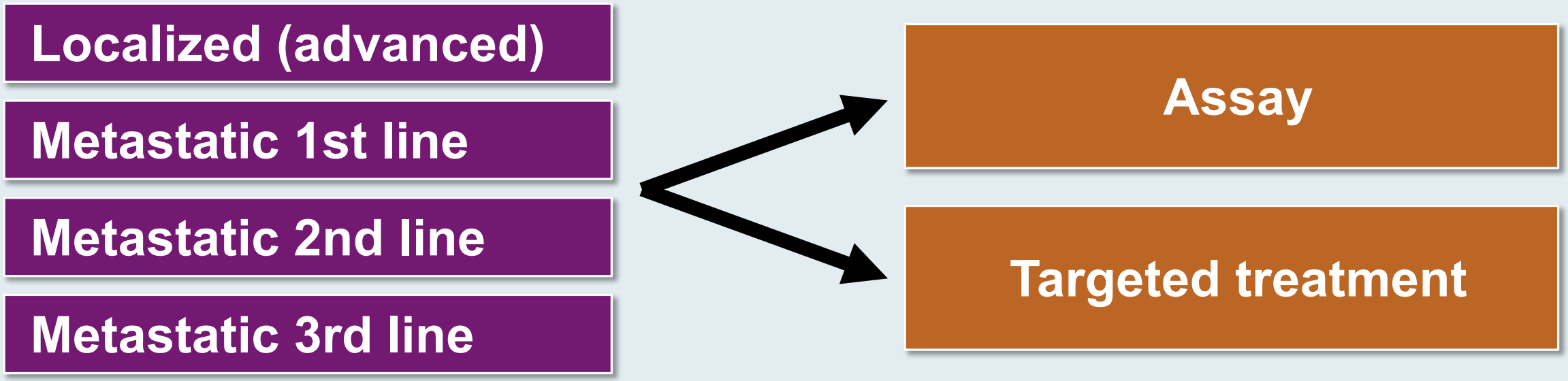
# What is the preferred approach by clinical investigators to…

- MSI-high colorectal, gastric and esophageal cancers?
- MSS pan-RAS wild-type colorectal cancer?
- Localized gastric and esophageal cancers?
- MSS HER2-negative gastroesophageal cancer?
- MSS pan-RAS wild-type, HER2-expressing colorectal cancer?
- MSS HER2-positive gastric cancer?
- MSS pan-RAS wild-type, BRAF-mutated colorectal cancer?
- Metastatic colorectal cancer after chemotherapy and immunotherapy?

Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# What is the preferred approach by clinical investigators to MSS, pan-RAS wild-type, HER2-expressing colorectal cancer?




Data sets with the potential to change clinical (and research) algorithms

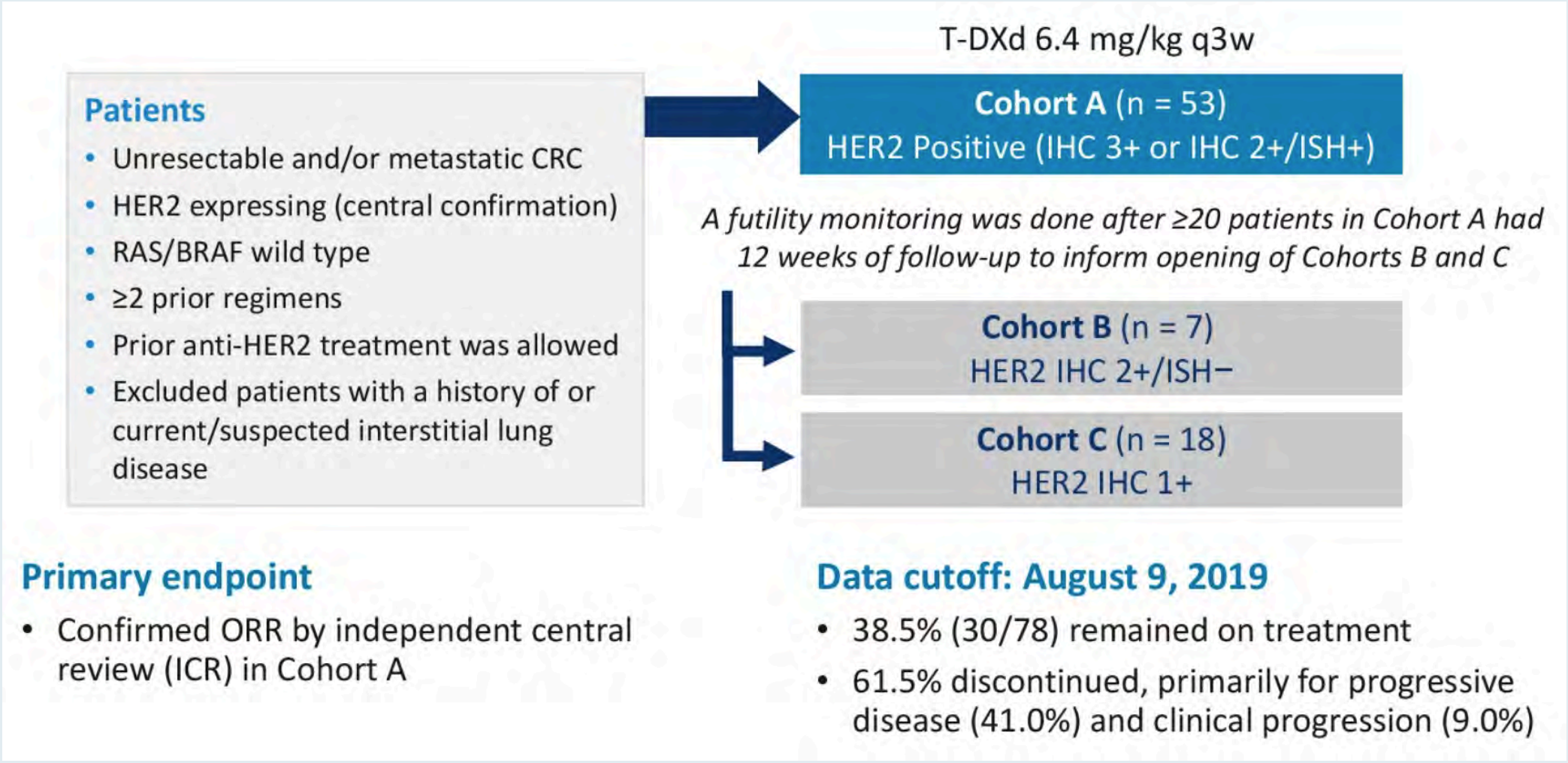
Year in Review 2020

# A Phase II, Multicenter, Open-Label Study of Trastuzumab Deruxtecan (T-DXd; DS-8201) in Patients (pts) with HER2-Expressing Metastatic Colorectal Cancer (mCRC): DESTINY-CRC01

Siena S et al.

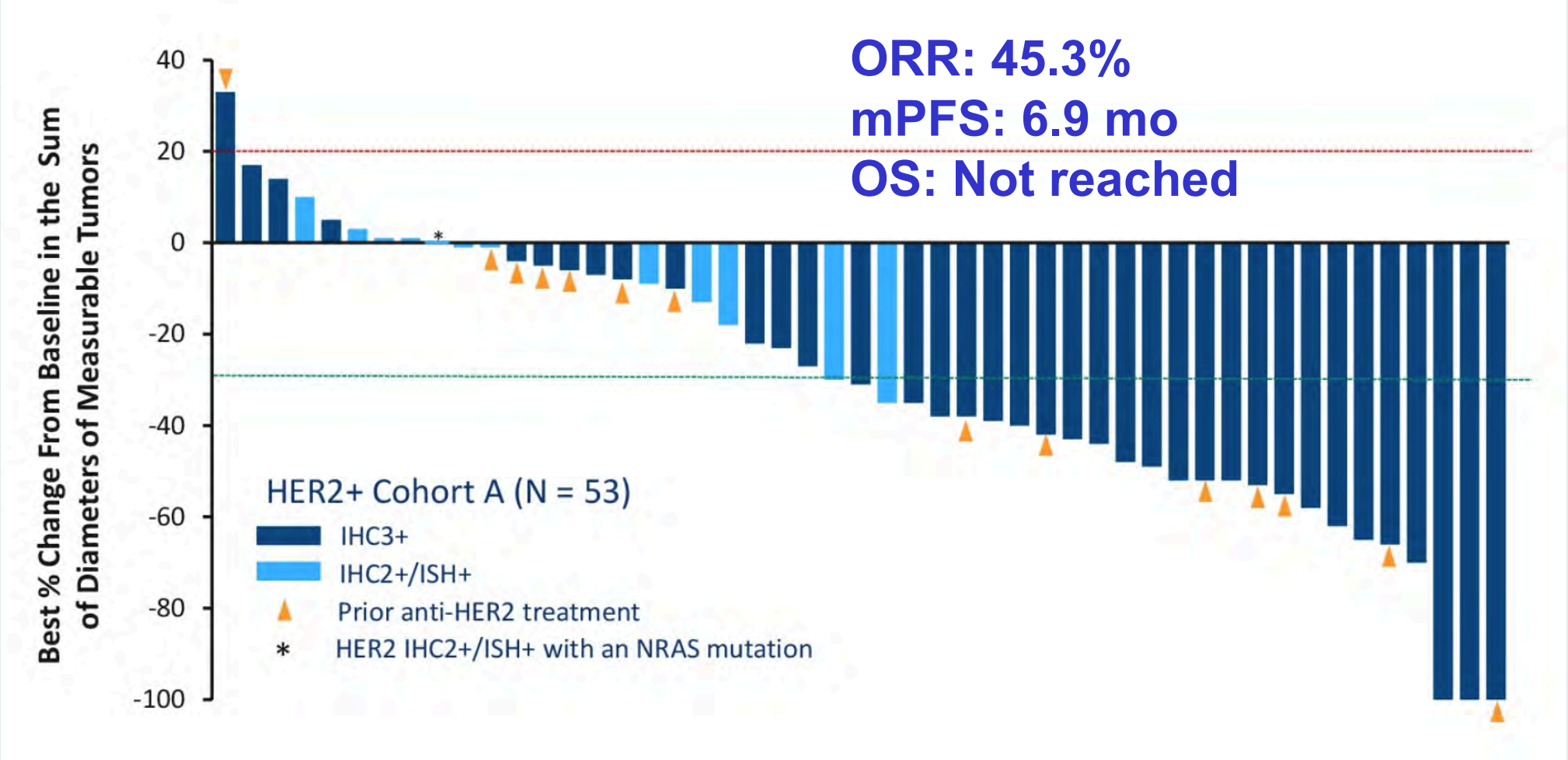
ASCO 2020;Abstract 4000.

# DESTINY-CRC01 Phase II Study Design




Siena S et al. ASCO 2020;Abstract 4000.

# DESTINY-CRC01: Best Change in Tumor Size Over Time




Siena S et al. ASCO 2020;Abstract 4000.

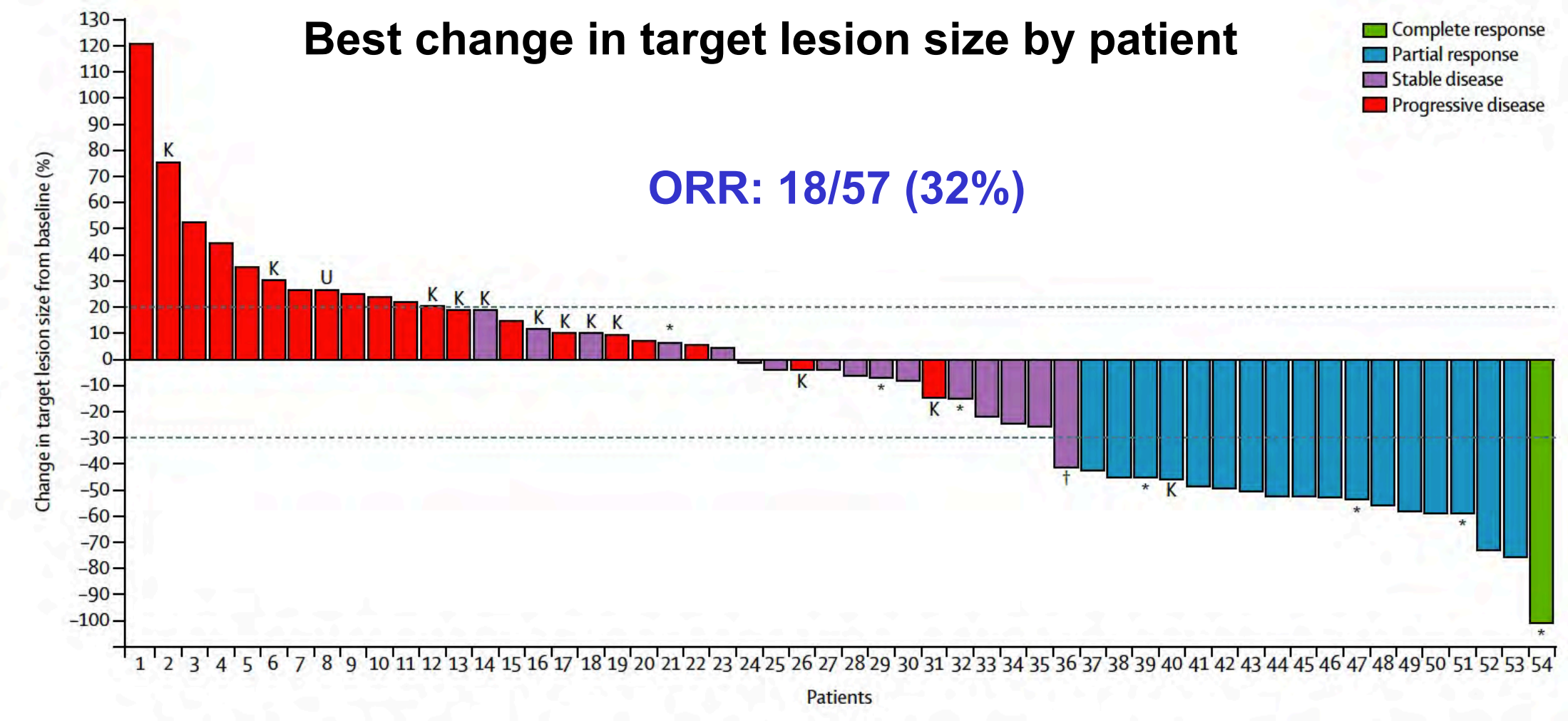
Year in Review 2020

*Lancet Oncol* 2019;20:518-30

# Pertuzumab plus trastuzumab for *HER2*-amplified metastatic colorectal cancer (MyPathway): an updated report from a multicentre, open-label, phase 2a, multiple basket study

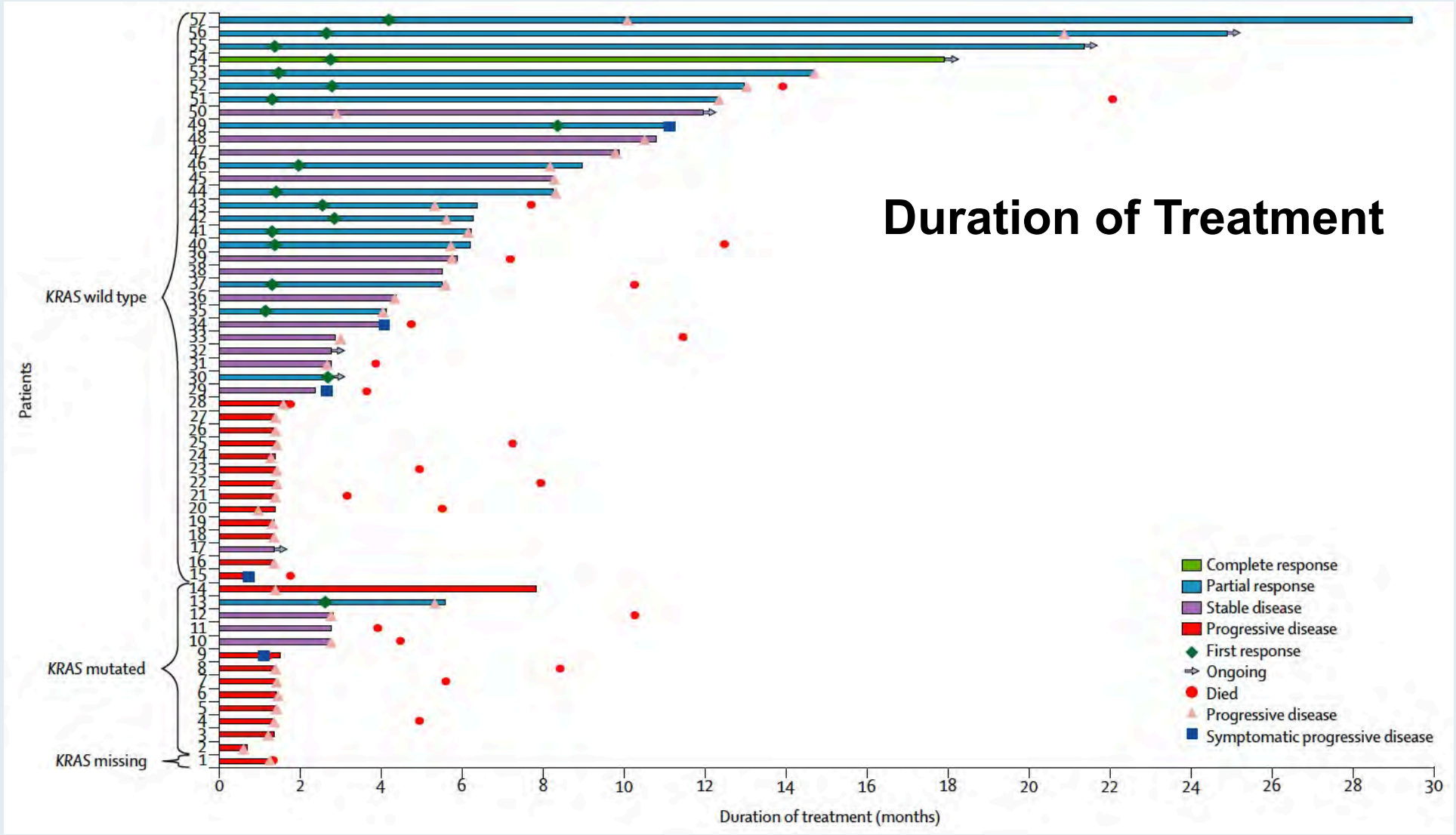
*Funda Meric-Bernstam*, Herbert Hurwitz*, Kanwal Pratap Singh Raghav, Robert R McWilliams, Marwan Fakih, Ari VanderWalde, Charles Swanton, Razelle Kurzrock, Howard Burris, Christopher Sweeney, Ron Bose, David R Spigel, Mary S Beattie, Steven Blotner, Alyssa Stone, Katja Schulze, Vaikunth Cuchelkar, John Hainsworth*

# MyPathway: Pertuzumab with Trastuzumab for HER2-Amplified mCRC




Meric-Bernstam F et al. *Lancet Oncol* 2019;20:518-30.

# MyPathway: Pertuzumab with Trastuzumab for HER2-Amplified mCRC



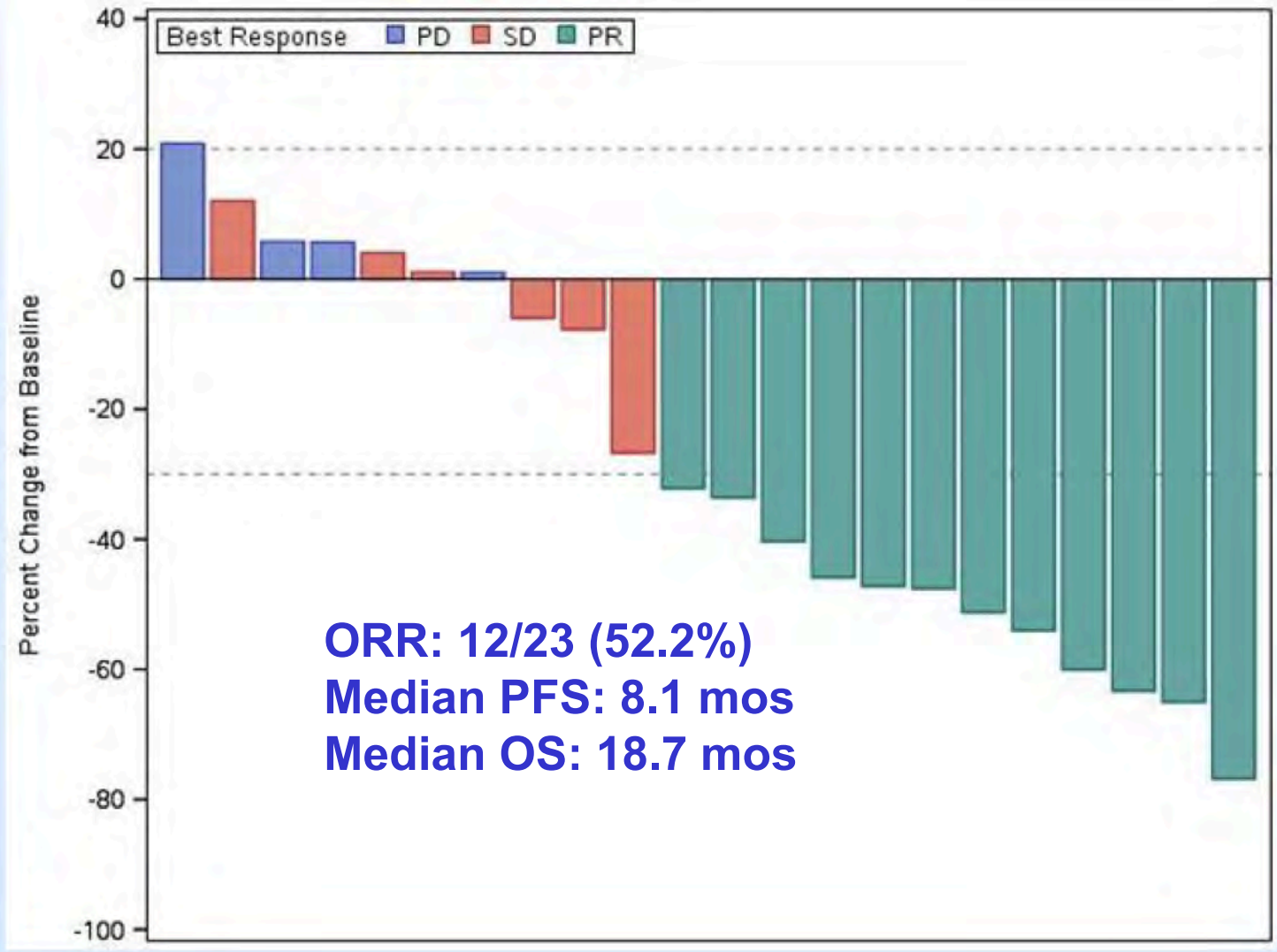

Meric-Bernstam F et al. *Lancet Oncol* 2019;20:518-30.

# Trastuzumab and Tucatinib for the Treatment of HER2 Amplified Metastatic Colorectal Cancer: Initial Results from the MOUNTAINEER Trial

Strickler JH et al.

ESMO 2019;Abstract 527PD.

# MOUNTAINEER: Response and Survival




Strickler JH et al. ESMO 2019;Abstract 527PD.

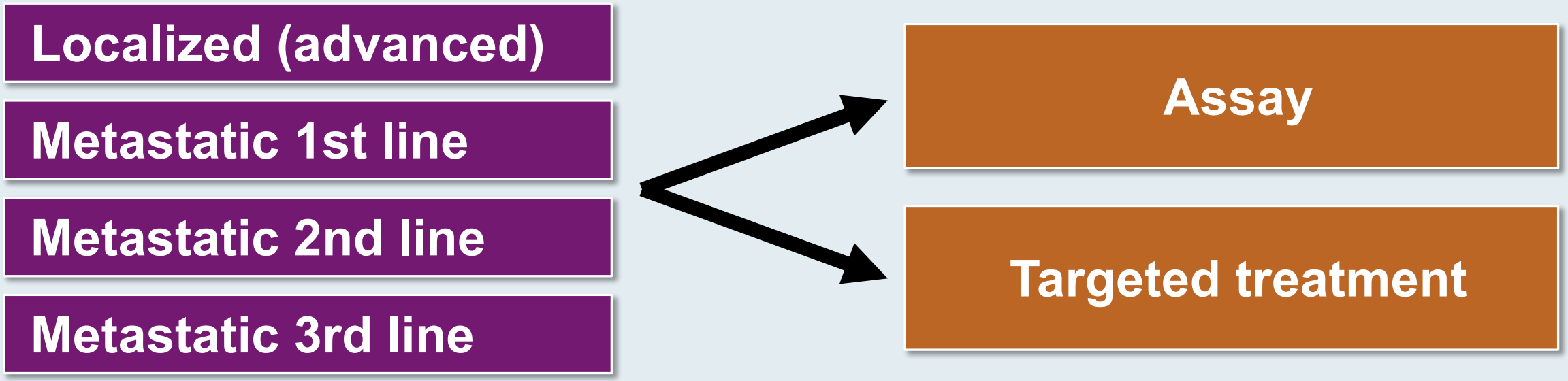
# What is the preferred approach by clinical investigators to…

- MSI-high colorectal, gastric and esophageal cancers?
- MSS pan-RAS wild-type colorectal cancer?
- Localized gastric and esophageal cancers?
- MSS HER2-negative gastroesophageal cancer?
- MSS pan-RAS wild-type, HER2-expressing colorectal cancer?
- MSS HER2-positive gastric cancer?
- MSS pan-RAS wild-type, BRAF-mutated colorectal cancer?
- Metastatic colorectal cancer after chemotherapy and immunotherapy?

Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# What is the preferred approach by clinical investigators to MSS, HER2-positive gastric cancer?




Data sets with the potential to change clinical (and research) algorithms

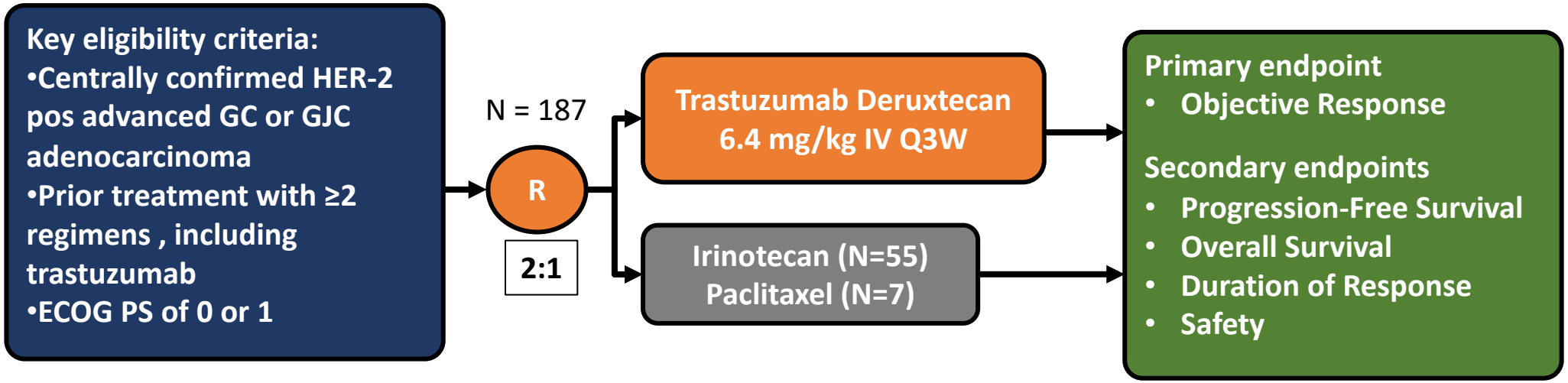
Year in Review 2020

**Regulatory and reimbursement issues aside, what third-line treatment would you recommend for a younger patient (PS 0) with metastatic HER2-positive, microsatellite-stable gastric cancer (CPS < 1) with progression on FOLFOX/trastuzumab and then paclitaxel/ramucirumab?**

a. TAS-102
b. Pembrolizumab
c. Nivolumab
d. Trastuzumab deruxtecan
e. Pertuzumab/trastuzumab
f. Tucatinib-based regimen
g. Other

Year in Review 2020

# DESTINY-Gastric01: Randomized Phase 2 Study of Trastuzumab Deruxtecan vs Chemotherapy in Patients With Trastuzumab Refractory Gastric and GEJ Adenocarcinoma

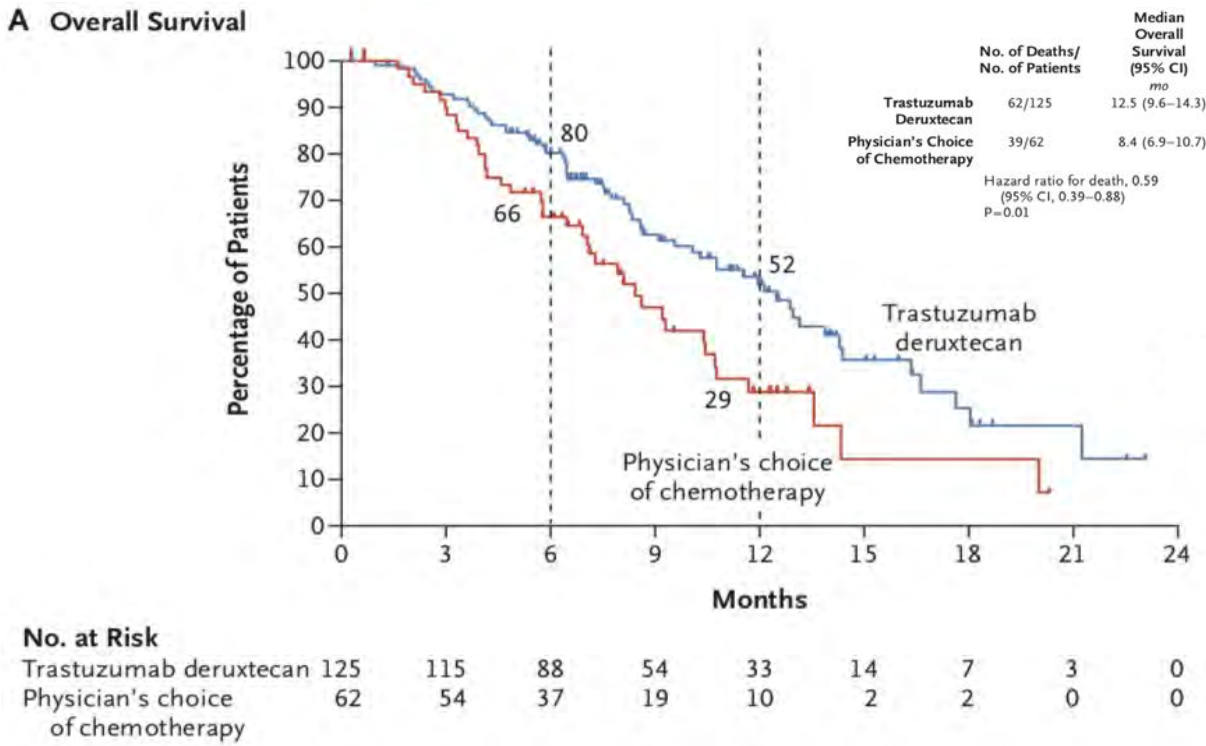


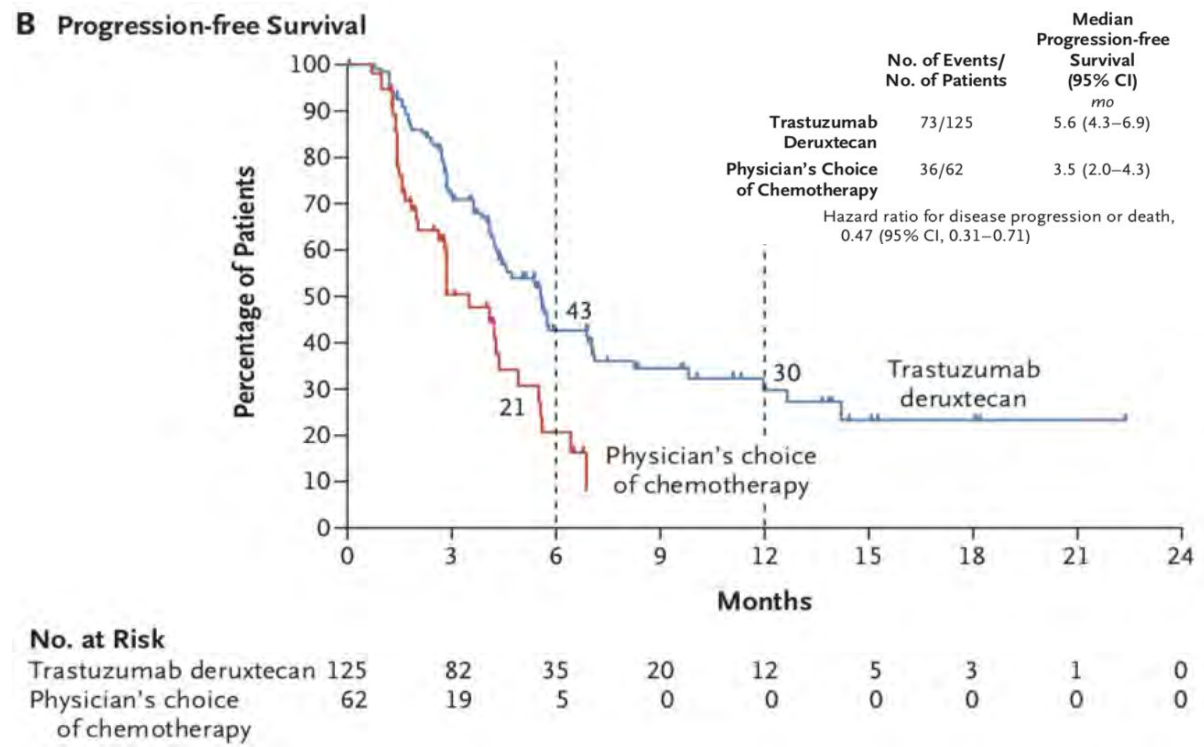



Shitara K et al. N Engl J Med 2020; 382:2419-2430.

Courtesy of Peter C Enzinger, MD

# DESTINY-Gastric01: Randomized Phase 2 Study of Trastuzumab Deruxtecan vs Chemotherapy in Patients With Trastuzumab Refractory Gastric and GEJ Adenocarcinoma



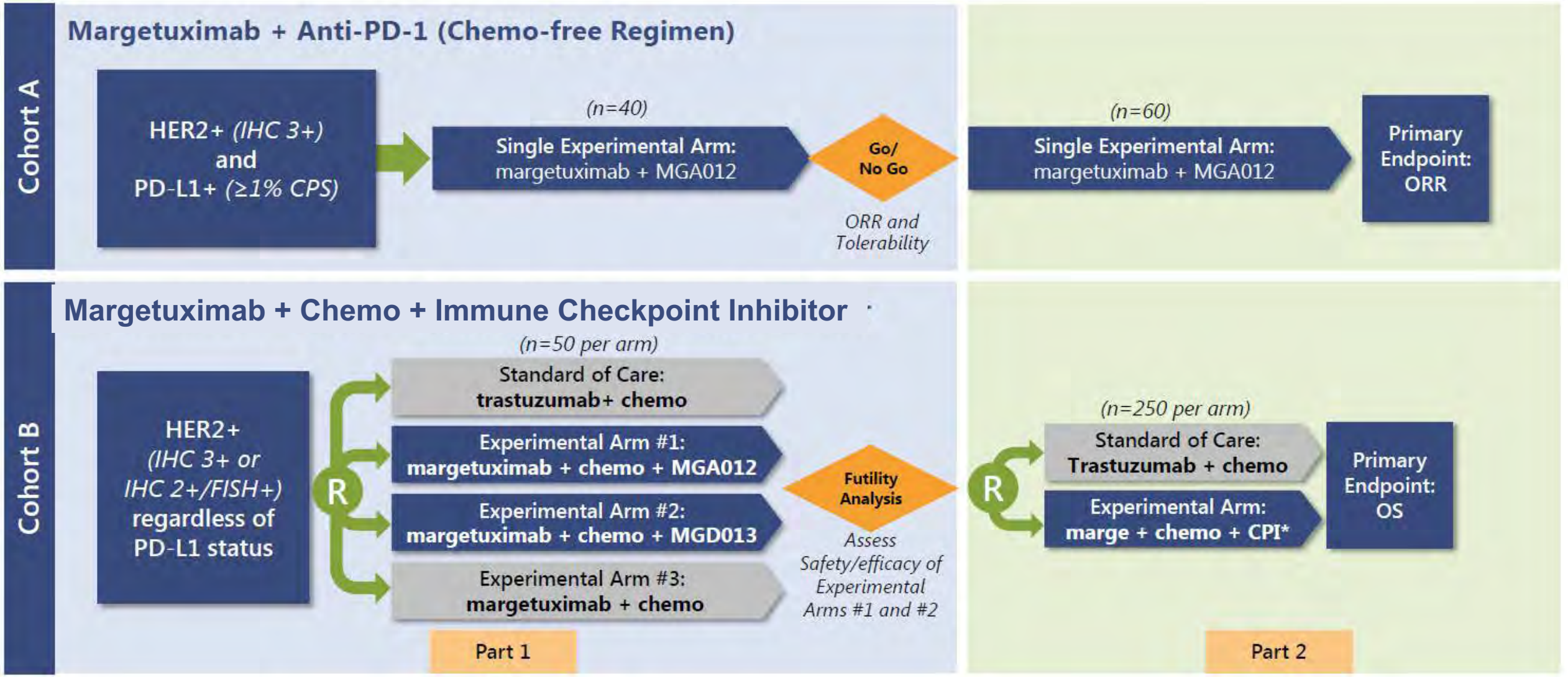






Shitara K et al. N Engl J Med 2020; 382:2419-2430.

Courtesy of Peter C Enzinger, MD

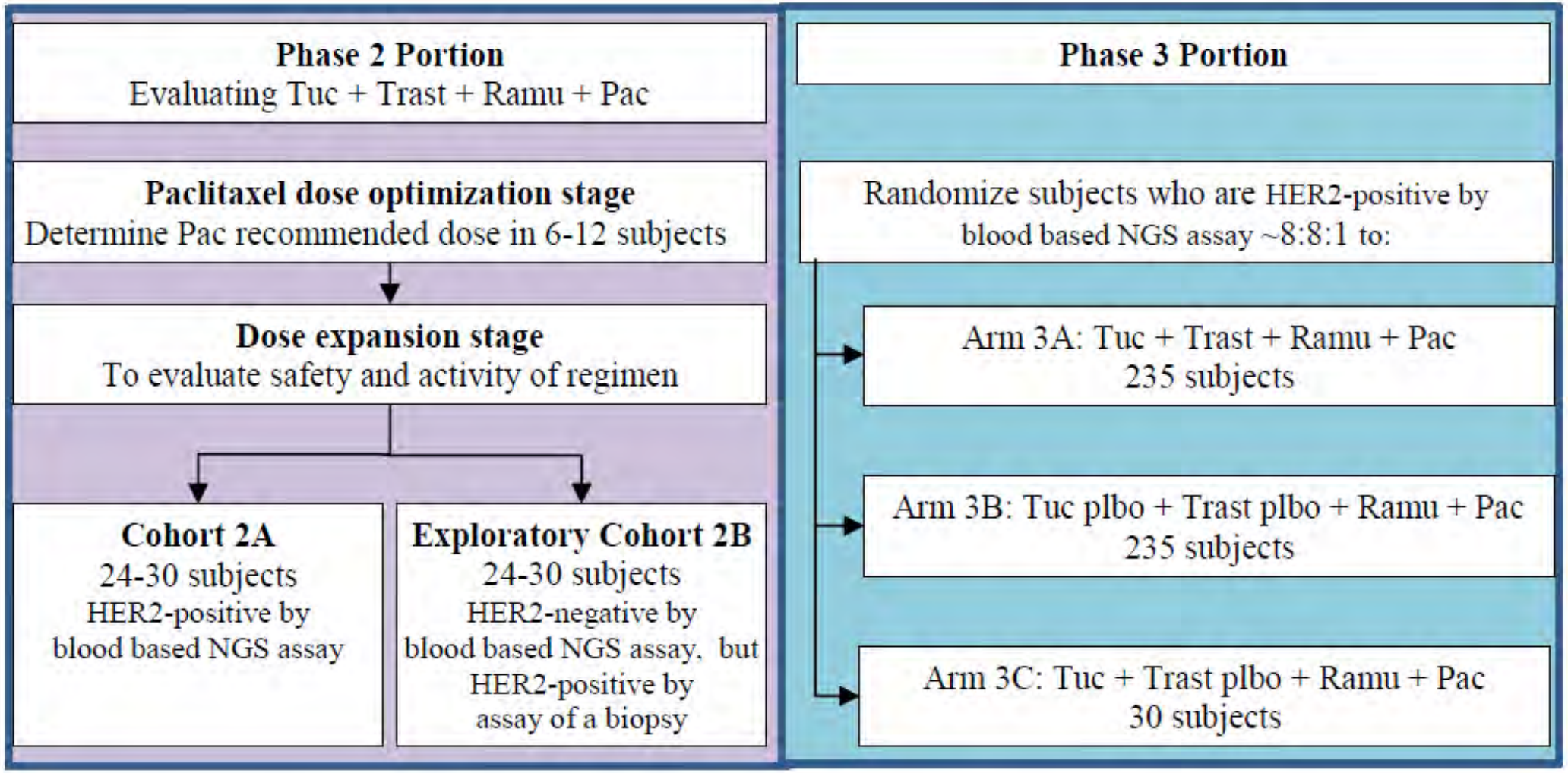
# MAHOGANY - Schema






Courtesy of Peter C Enzinger, MD

# MOUNTAINEER-02 Schema




Pac=paclitaxel; plbo=placebo; Ramu=ramucirumab; Tuc=tucatinib; Trast=trastuzumab.



Courtesy of Peter C Enzinger, MD

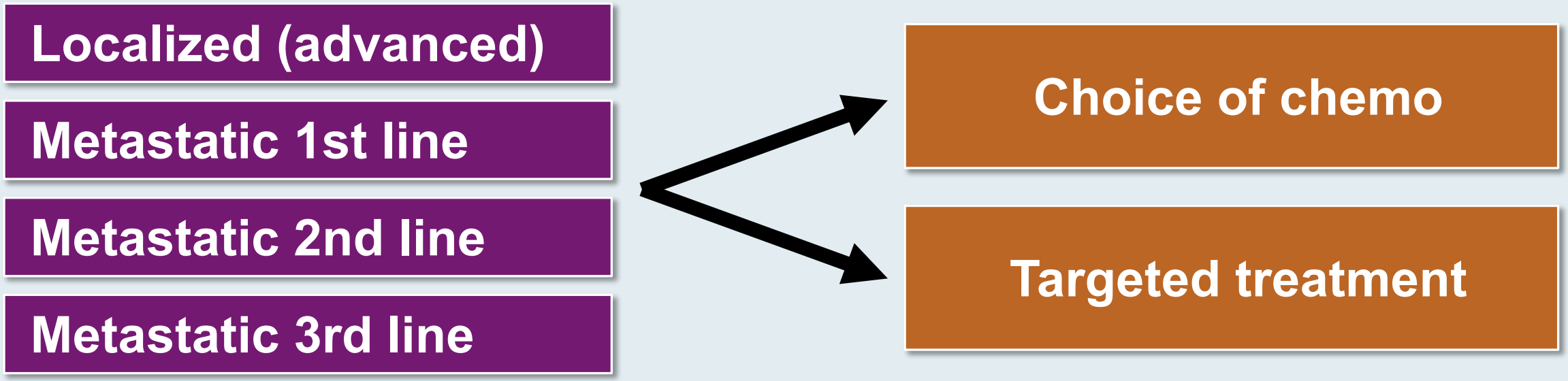
# What is the preferred approach by clinical investigators to…

- MSI-high colorectal, gastric and esophageal cancers?
- MSS pan-RAS wild-type colorectal cancer?
- Localized gastric and esophageal cancers?
- MSS HER2-negative gastroesophageal cancer?
- MSS pan-RAS wild-type, HER2-expressing colorectal cancer?
- MSS HER2-positive gastric cancer?
- MSS pan-RAS wild-type, BRAF-mutated colorectal cancer?
- Metastatic colorectal cancer after chemotherapy and immunotherapy?

Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# What is the preferred approach by clinical investigators to MSS, pan-RAS wild-type, BRAF-mutated colorectal cancer?




Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

**Regulatory and reimbursement issues aside, what would be your preferred second-line treatment for a 65-year-old patient with asymptomatic pan-RAS wild-type, MSS mCRC and a BRAF V600E mutation who experienced disease progression after FOLFIRINOX/bevacizumab?**

a. Chemotherapy
b. Chemotherapy/bevacizumab
c. Irinotecan + vemurafenib + EGFR antibody
d. Dabrafenib + trametinib + EGFR antibody
e. Encorafenib + binimetinib + EGFR antibody
f. Encorafenib + EGFR antibody
g. Other

Year in Review 2020

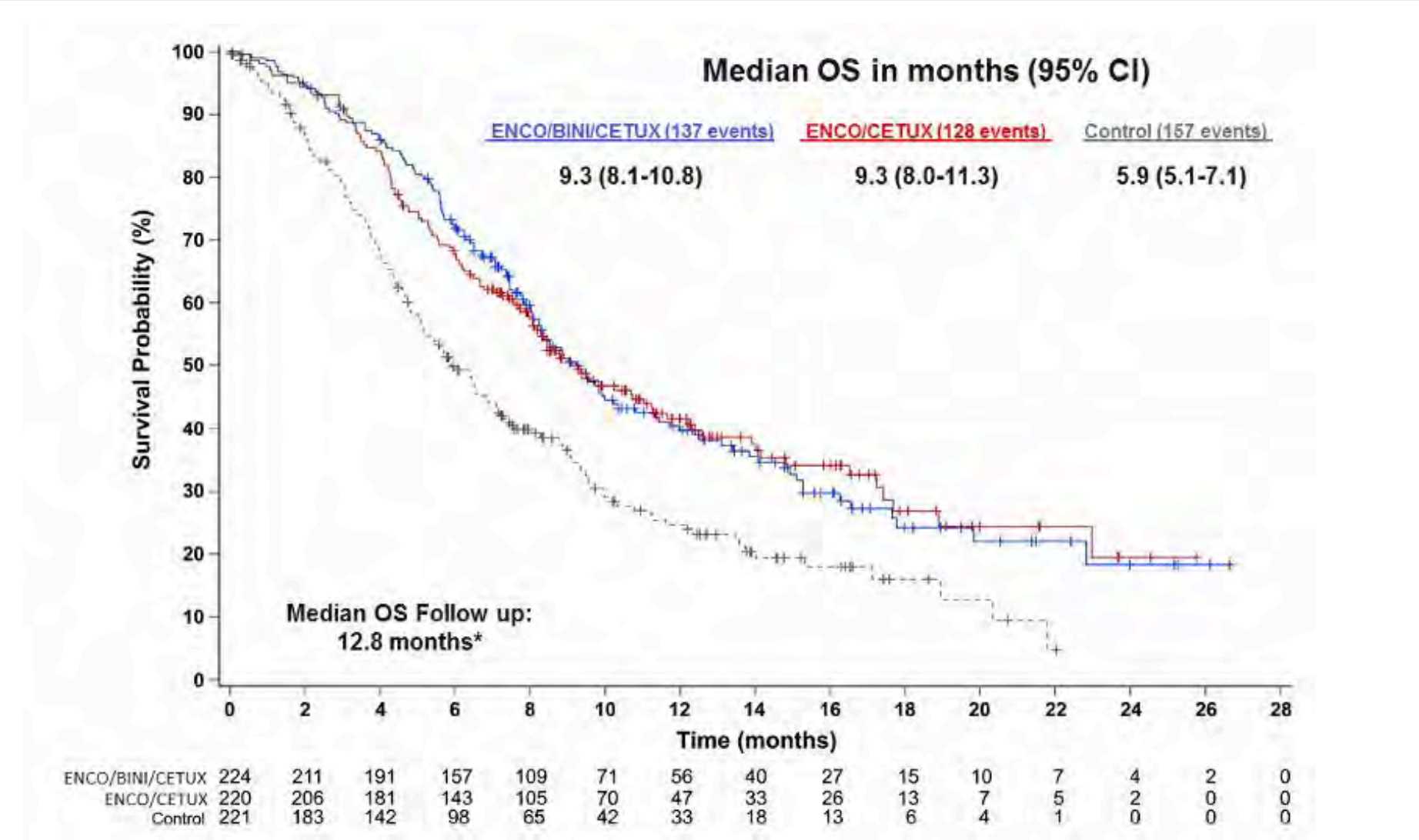
# Encorafenib plus Cetuximab with or without Binimetinib for BRAF V600E Metastatic Colorectal Cancer: Updated Survival Results from a Randomized, Three-Arm, Phase III Study versus Choice of Either Irinotecan or FOLFIRI plus Cetuximab (BEACON CRC)

Kopetz S et al.

ASCO 2020;Abstract 4001.

Year in Review 2020

# BEACON CRC: Updated Overall Survival Analysis




Kopetz S et al. ASCO 2020;Abstract 4001.

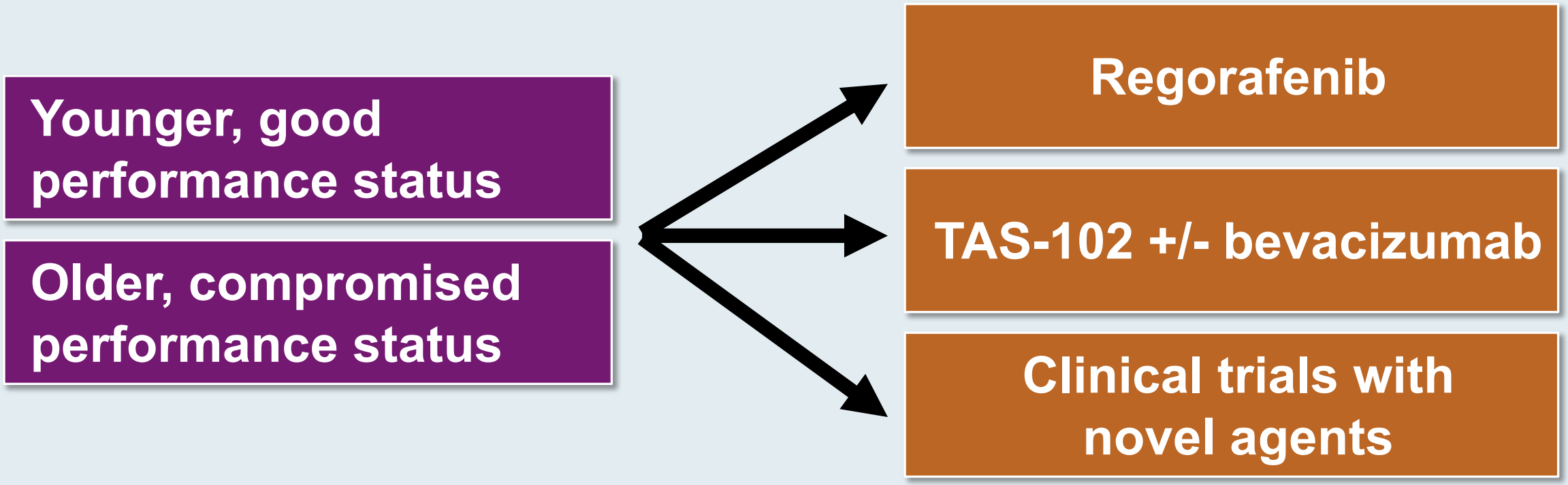
# What is the preferred approach by clinical investigators to…

- MSI-high colorectal, gastric and esophageal cancers?
- MSS pan-RAS wild-type colorectal cancer?
- Localized gastric and esophageal cancers?
- MSS HER2-negative gastroesophageal cancer?
- MSS pan-RAS wild-type, HER2-expressing colorectal cancer?
- MSS HER2-positive gastric cancer?
- MSS pan-RAS wild-type, BRAF-mutated colorectal cancer?
- Metastatic colorectal cancer after chemotherapy and immunotherapy?

Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

# What is the preferred approach by clinical investigators to metastatic colorectal cancer after chemotherapy and immunotherapy?




Data sets with the potential to change clinical (and research) algorithms

Year in Review 2020

**A 65-year-old patient with right-sided, pan-RAS wild-type, BRAF wild-type, microsatellite-stable mCRC receives first-line FOLFOX/bevacizumab and second-line FOLFIRI/bevacizumab and is now experiencing disease progression with a PS of 0. What would be your most likely third-line treatment recommendation?**

a. Cetuximab
b. Cetuximab + irinotecan
c. Panitumumab
d. Panitumumab + irinotecan
e. Regorafenib
f. TAS-102
g. Regorafenib or TAS-102 — coin flip

Year in Review 2020

# Have you or would you use TAS-102 in combination with bevacizumab outside of a clinical trial setting for a patient with mCRC?

a. I have
b. I have not but would for the right patient
c. I have not and would not

*Lancet Oncol* 2019;20(8):1070-82.

# Regorafenib dose-optimisation in patients with refractory metastatic colorectal cancer (ReDOS): a randomised, multicentre, open-label, phase 2 study

*Tanios S Bekaii-Saab, Fang-Shu Ou, Daniel H Ahn, Patrick M Boland, Kristen K Ciombor, Erica N Heying, Travis J Dockter, Nisha L Jacobs, Boris C Pasche, James M Cleary, Jeffrey P Meyers, Rodwige J Desnoyers, Jeannine S McCune, Katrina Pedersen, Afsaneh Barzi, E Gabriela Chiorean, Jeffrey Sloan, Mario E Lacouture, Heinz-Josef Lenz, Axel Grothey*

# ReDOS: Summary of Outcomes

| | Dose escalation (n = 54) | Standard dosing (n = 62) |
|---|---|---|
| **Primary endpoint** | | |
| Proportion completing 2 cycles, initiating cycle 3 | 23/54 (43%) | 16/62 (26%) |
| **Select Grade 3/4 adverse events** | | |
| Fatigue | 13% | 18% |
| Hand-foot skin reaction | 15% | 16% |
| Hypertension | 7% | 15% |
| **Efficacy** | | |
| Median OS | 9.8 mo | 6.0 mo |
| | HR: 0.72, $p = 0.12$ | |
| Median PFS | 2.8 mo | 2.0 mo |
| | HR: 0.84, $p = 0.38$ | |

Bekaii-Saab TS et al. *Lancet Oncol* 2019;20(8):1070-82.

*Lancet Oncol* 2020;21(3):412-20.

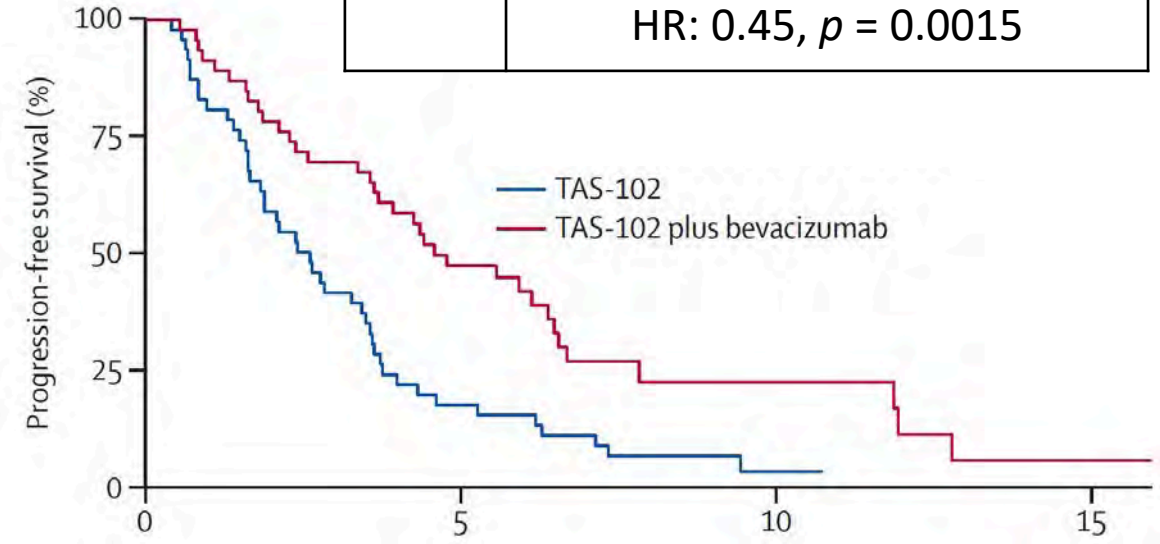
# TAS-102 with or without bevacizumab in patients with chemorefractory metastatic colorectal cancer: an investigator-initiated, open-label, randomised, phase 2 trial

*Per Pfeiffer, Mette Yilmaz, Sören Möller, Daniela Zitnjak, Merete Krogh, Lone Nørgård Petersen, Laurids Østergaard Poulsen, Stine Braendegaard Winther, Karina Gravgaard Thomsen, Camilla Qvortrup*

# TAS-102 with or without Bevacizumab in Refractory mCRC

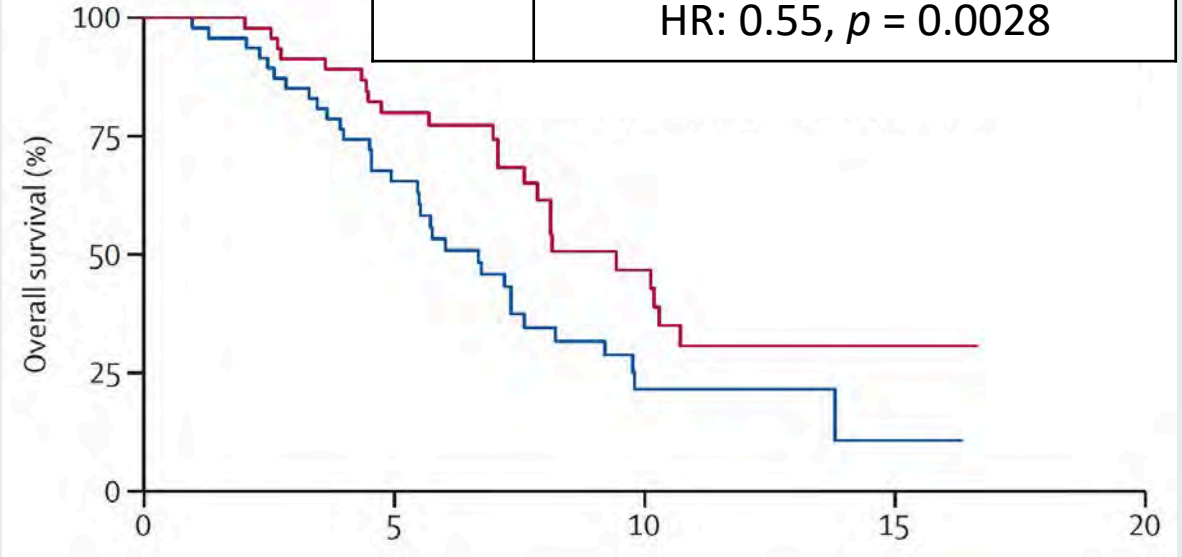
## Progression-Free Survival and Overall Survival

| | TAS-102 (n = 47) | TAS-102/Bev (n = 46) |
|---|---|---|
| mPFS | 2.6 mo | 4.6 mo |
| | HR: 0.45, $p$ = 0.0015 | |




Time since randomization (months)

| | TAS-102 (n = 47) | TAS-102/Bev (n = 46) |
|---|---|---|
| mOS | 6.7 mo | 9.4 mo |
| | HR: 0.55, $p$ = 0.0028 | |




Time since randomization (months)

Pfeiffer P et al. *Lancet Oncol* 2020;21(3):412-20.

Year in Review 2020

Comment

*Lancet Oncol* 2020;21(3):412-20.

# TAS-102 plus bevacizumab: a new standard for metastatic colorectal cancer?

*Ann Oncol* 2020;31(9):1160-8.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ORIGINAL ARTICLE

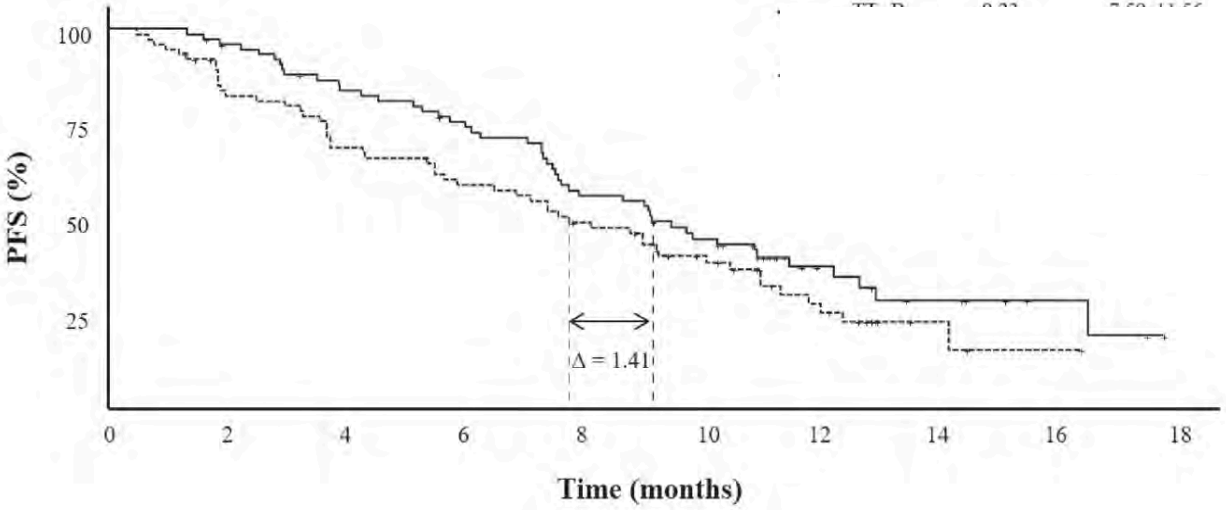
# Trifluridine/tipiracil plus bevacizumab in patients with untreated metastatic colorectal cancer ineligible for intensive therapy: the randomized TASCO1 study☆

E. Van Cutsem[1*], I. Danielewicz[2], M. P. Saunders[3], P. Pfeiffer[4], G. Argilés[5], C. Borg[6], R. Glynne-Jones[7], C. J. A. Punt[8], A. J. Van de Wouw[9], M. Fedyanin[10], D. Stroyakovskiy[11], H. Kroening[12], P. Garcia-Alfonso[13], H. Wasan[14], A. Falcone[15], A. Kanehisa[16], A. Egorov[16], P. Aubel[16], N. Amellal[16] & V. Moiseenko[17]

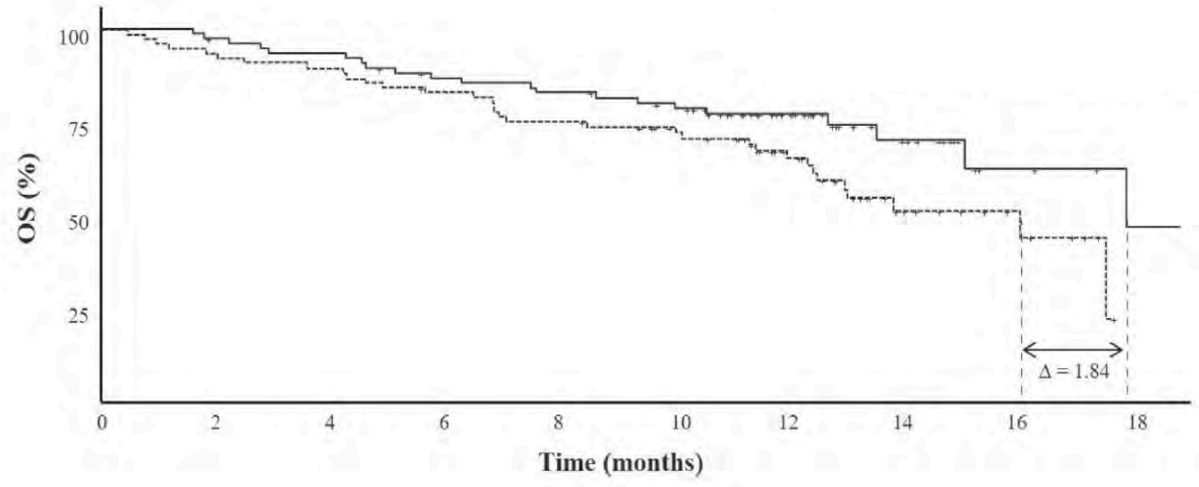
Year in Review 2020

# TASCO1: TAS-102 plus Bevacizumab for Untreated mCRC Ineligible for Intensive Therapy

| | Cape/Bev (n = 76) | TAS-102/Bev (n = 77) |
|---|---|---|
| mPFS | 7.8 mo | 9.2 mo |
| | HR: 0.71 | |




| | Cape/Bev (n = 76) | TAS-102/Bev (n = 77) |
|---|---|---|
| mOS | 16.2 mo | 18.0 mo |
| | HR: 0.56 | |




Van Cutsem E et al. *Ann Oncol* 2020;31(9):1160-8.

# Factors Associated with Effectiveness of Trifluridine/Tipiracil versus Regorafenib in Patients with Pretreated mCRC

Grell P et al.

Gastrointestinal Cancers Symposium 2020;Abstract 137.

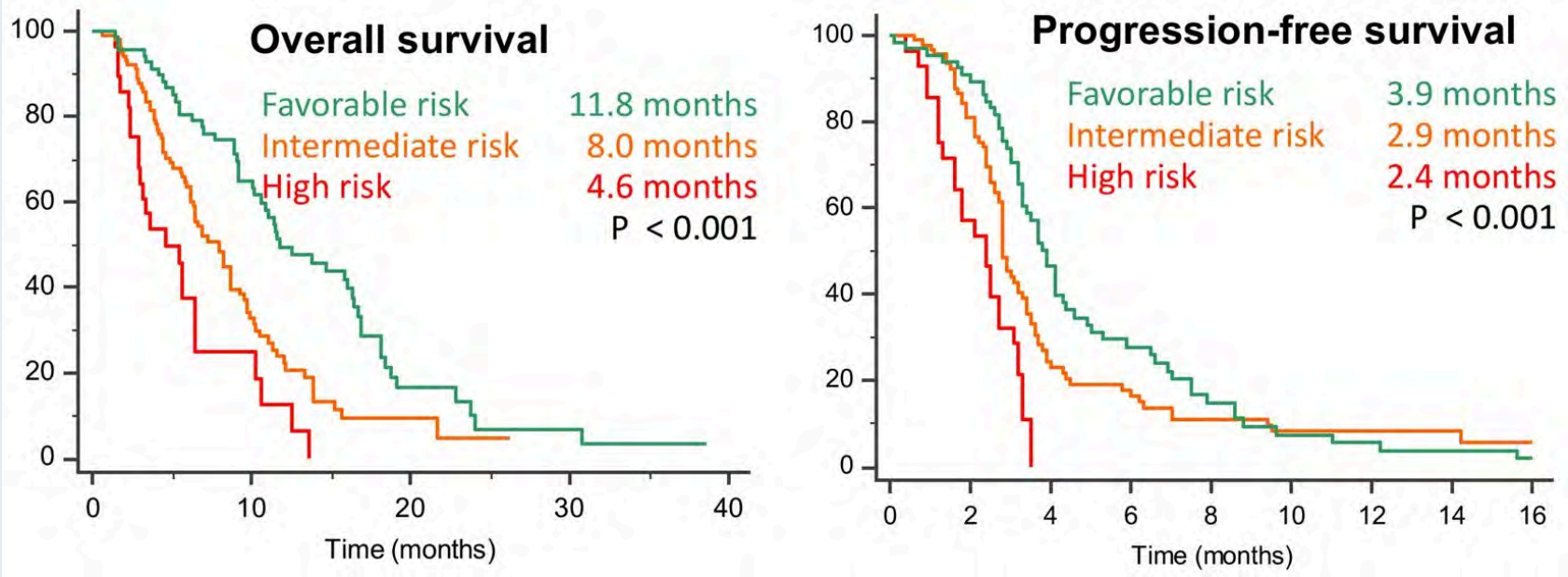
# Factors Significantly Associated with Longer OS in Patients with Previously Treated mCRC Who Received TAS-102 or Regorafenib

**Factors significantly associated with longer OS:**

- Time ≥24 months from diagnosis of mCRC
- Time ≥3 months from 5FU or capecitabine in TAS-102, anti-VEGF in regorafenib
- ECOG PS 0 versus 1
- Normal baseline CRP level
- Baseline WBC <8 x $10^9$/L

**TASREG prognostic scoring system (1 point each)**

- High risk (0 to 1)
- Intermediate risk (2 to 3)
- Favorable risk (≥4)




Grell P et al. Gastrointestinal Cancers Symposium 2020;Abstract 137.

Year in Review 2020

# Factors Significantly Associated with Longer OS in Patients with Previously Treated mCRC Who Received TAS-102 or Regorafenib

**Factors significantly associated with longer OS in TAS-102-treated patients**

- Grade ≥2 neutropenia (HR: 0.34)

**Factors significantly associated with longer OS in regorafenib-treated patients**

- Normal baseline LDH (HR: 0.40)
- No liver metastases (HR: 0.45)
- Nonsynchronous disease (HR: 0.40)

Grell P et al. Gastrointestinal Cancers Symposium 2020;Abstract 137.

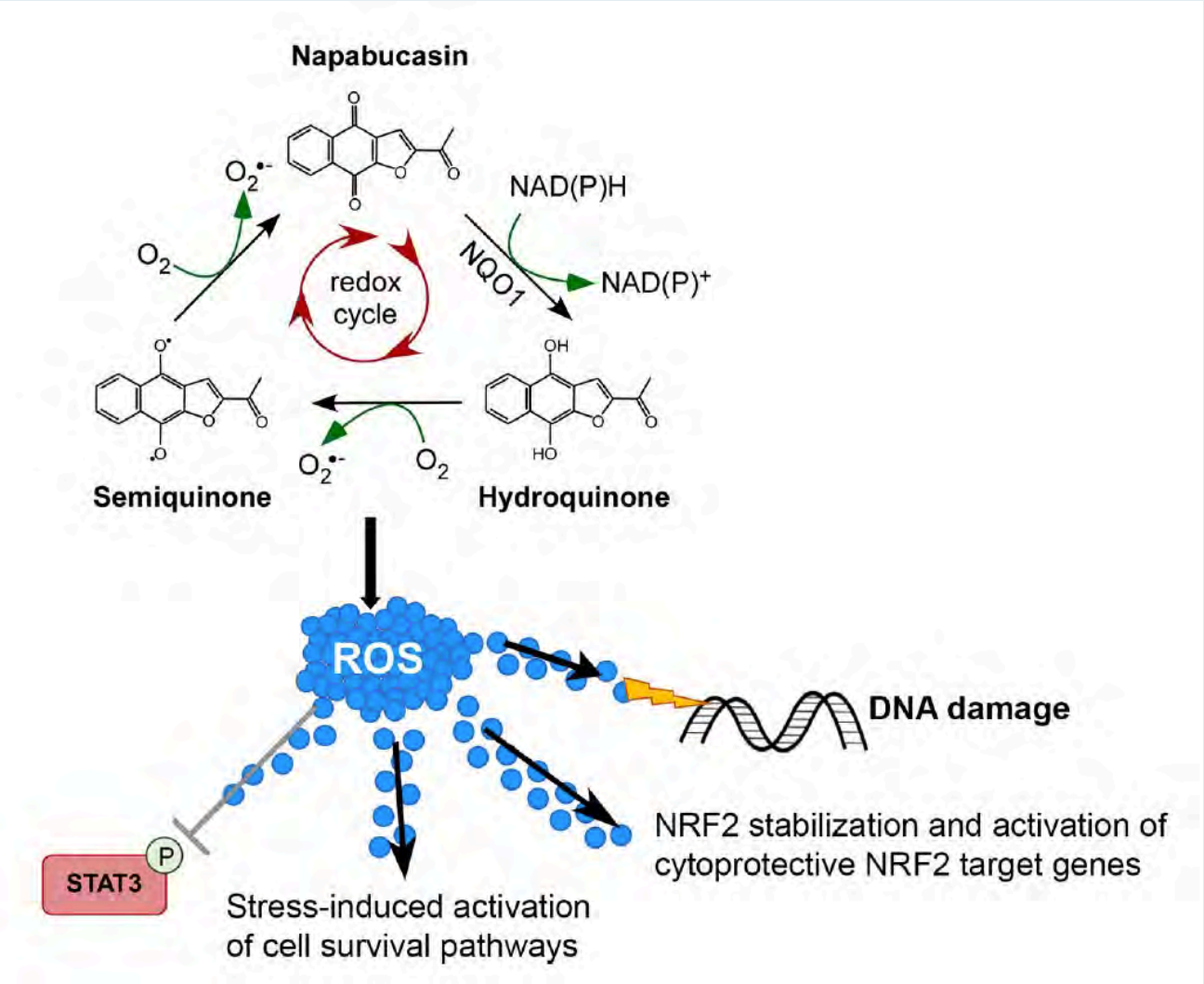
Year in Review 2020

*Clin Cancer Res* 2019;25(23):7162-74

# Bioactivation of napabucasin triggers reactive oxygen species–mediated cancer cell death

Fieke E M Froeling[1,2,3,6], Manojit Mosur Swamynathan[1,7], Astrid Deschênes[1], Iok In Christine Chio[1,2,4], Erin Brosnan[1,2], Melissa A Yao[1,2,8], Priya Alagesan[1,2], Matthew Lucito[1,2], Juying Li[5], An-Yun Chang[5], Lloyd C Trotman[1], Pascal Belleau[1], Youngkyu Park[1,2], Harry A Rogoff[5,*], James D Watson[1,*], David A Tuveson[1,2,*]

# Proposed Mechanism of Action of Napabucasin




Froeling FEM et al. *Clin Cancer Res* 2019;25(23):7162-74.

Year in Review 2020

# *Meet The Professor*

# Immunotherapy and Novel Agents in Gynecologic Cancers

**Wednesday, December 9, 2020**
**12:30 PM – 1:30 PM ET**

## Faculty

**Gottfried E Konecny, MD**

## Moderator

**Neil Love, MD**

RTP
RESEARCH
TO PRACTICE

*Thank you for joining us!*

*CME and MOC credit information will be emailed to each participant within 5 business days.*

Year in Review 2020