

Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Colorectal Cancer (Part 3 of a 3-Part Series)

**Thursday, February 11, 2021
5:00 PM – 6:00 PM ET**

Faculty

**Kristen K Ciombor, MD, MSCI
Eric Van Cutsem, MD, PhD**

Moderator

Neil Love, MD

Faculty



Kristen K Ciombor, MD, MSCI
Assistant Professor of Medicine
Division of Hematology/Oncology
Vanderbilt-Ingram Cancer Center
Nashville, Tennessee



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Professor of Medicine
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Commercial Support

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Dr Love — Disclosures

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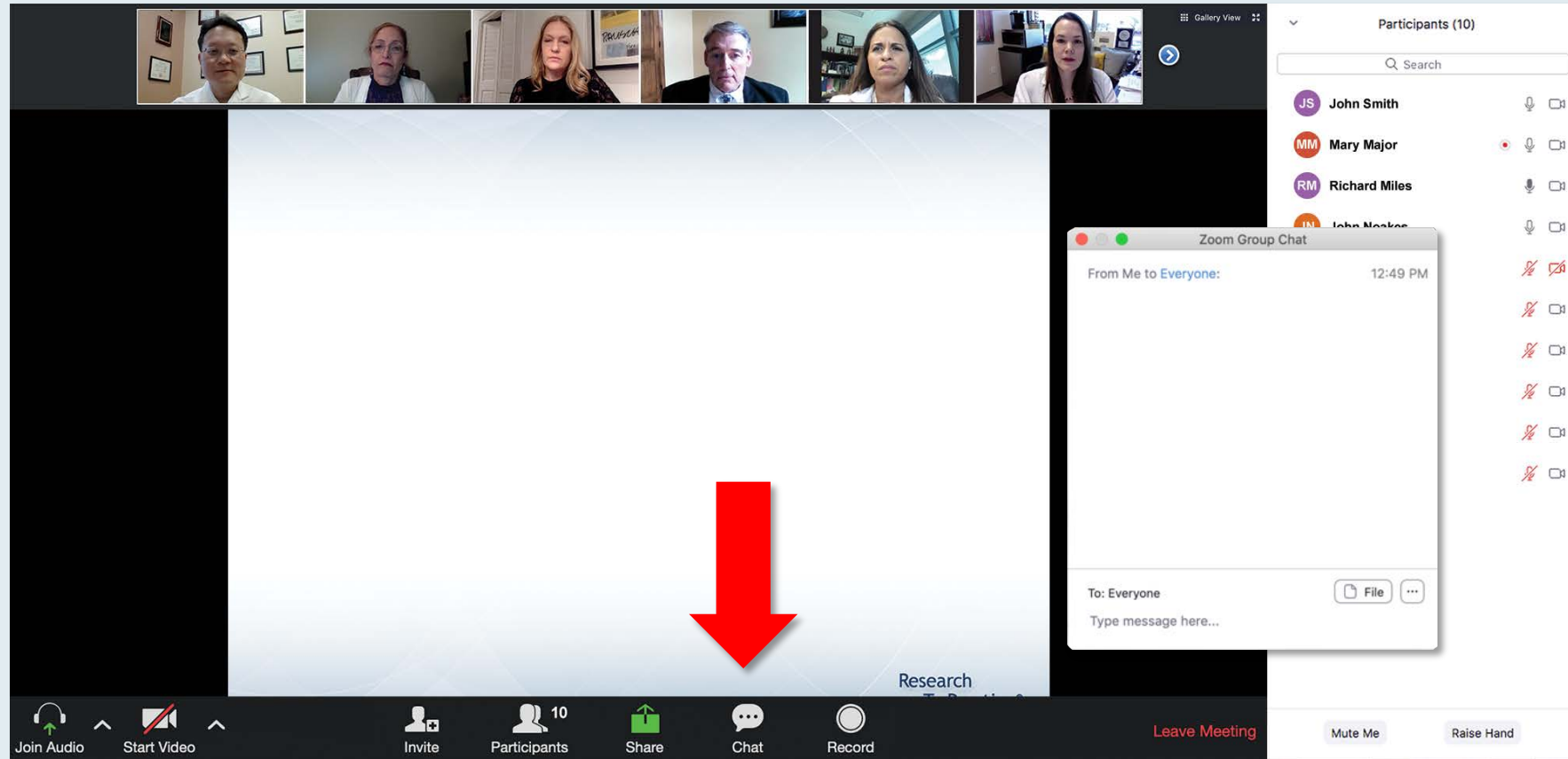
Dr Ciombor — Disclosures

Consulting Agreements	Merck, Natera Inc
Contracted Research	Array BioPharma Inc, a subsidiary of Pfizer Inc, Bristol-Myers Squibb Company, Calithera Biosciences, Daiichi Sankyo Inc, Incyte Corporation, Merck, NuCana, Pfizer Inc

Prof Van Cutsem — Disclosures

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Contracted Research	Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Ipsen Biopharmaceuticals Inc, Lilly, Merck KGaA, Merck Sharp & Dohme Corp, Novartis, Roche Laboratories Inc, Servier

We Encourage Clinicians in Practice to Submit Questions



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

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1. Carfilzomib +/- dexamethasone
2. Pomalidomide +/- dexamethasone
3. Carfilzomib + pomalidomide +/- dexamethasone
4. Elotuzumab + lenalidomide +/- dexamethasone
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7. Daratumumab + pomalidomide +/- dexamethasone
8. Daratumumab + bortezomib +/- dexamethasone
9. Ixazomib + Rd
10. Other

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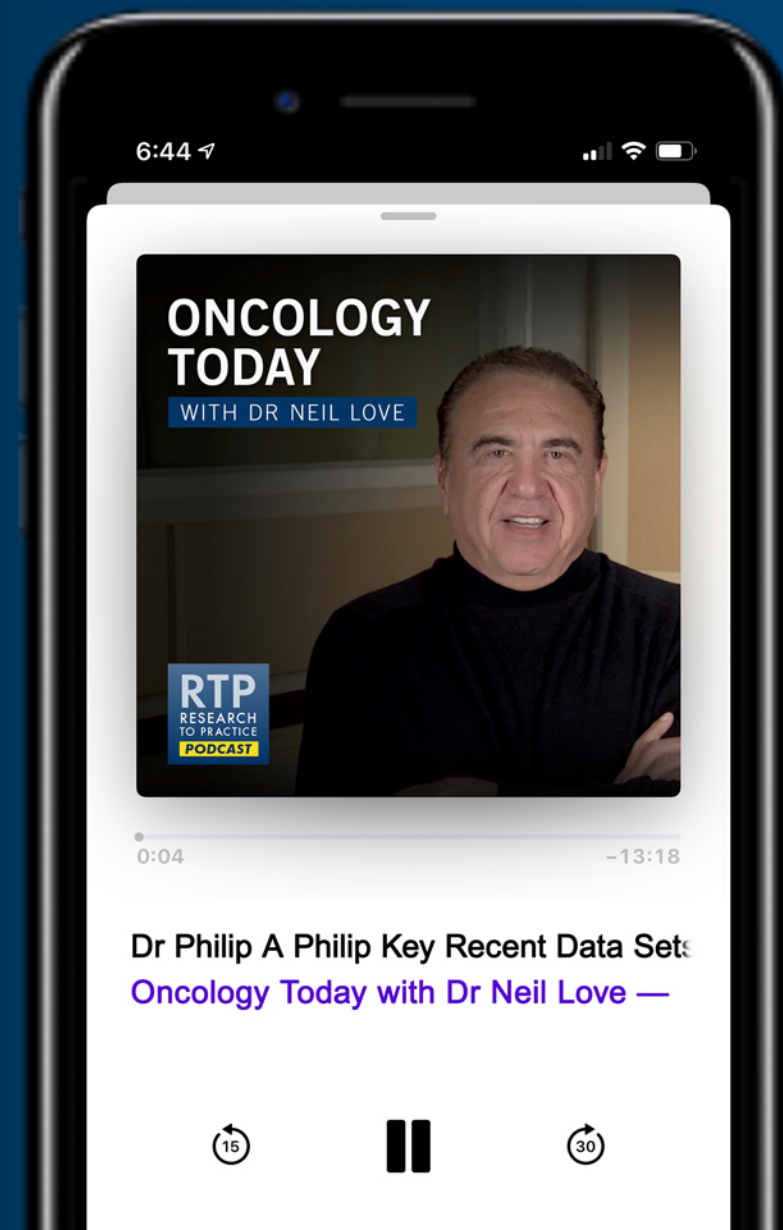
ONCOLOGY TODAY

WITH DR NEIL LOVE

Key Recent Data Sets in Gastrointestinal Cancers



DR PHILIP A PHILIP
KARMANOS CANCER INSTITUTE
WAYNE STATE UNIVERSITY





A 65-year-old woman with ER-positive, HER2-negative, node-negative breast cancer has developed multiple initially asymptomatic bone metastases 3 years after starting adjuvant tamoxifen. Which endocrine-based treatment would you most likely recommend?

Fulvestrant	25%
Tamoxifen	15%
Other endocrine therapy	10%
Exemestane + letrozole	5%
Exemestane + toremifene	5%
Exemestane + toremifene	5%
Exemestane + toremifene	5%
Exemestane + toremifene	5%
Exemestane + toremifene	5%
Exemestane + toremifene	5%
Other	5%

Exemestane + letrozole

Current Concepts and Recent Advances in Oncology

Real World Oncology Rounds

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8:30 AM – 4:30 PM ET

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Robert Dreicer, MD, MS

Justin F Gainor, MD

Sara Hurvitz, MD

Ian E Krop, MD, PhD

John M Pagel, MD, PhD

Alexander Perl, MD

Daniel P Petrylak, MD

Philip A Philip, MD, PhD, FRCP

Paul G Richardson, MD

Mitchell R Smith, MD, PhD

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**8:30 AM — Chronic Lymphocytic
Leukemia and Lymphomas**

John Pagel, Mitchell Smith

9:30 AM — Multiple Myeloma

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1:15 PM — Gastrointestinal Cancers

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**3:30 PM — Acute Myeloid Leukemia
and Myelodysplastic Syndromes**

Courtney DiNardo, Alexander Perl

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Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

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What Clinicians Want to Know: Understanding the Factors Affecting the Optimal Diagnosis and Management of Ovarian Cancer

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Kathleen Moore, MD

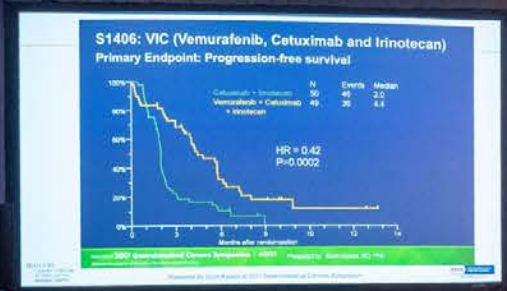
David M O'Malley, MD

Moderator

Neil Love, MD

Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.





THE Evaluation button to complete
credit for your participation.

and at the conclusion of the activity.



















Doublet with GSPR	75%	22 months	Coxon, ABCO '16
Verapamil + pertuzumab	75%	22 months	Nagar et al. ASCO '16
Verapamil + atezolizumab	75%	22 months	Tanner et al. ASCO '16
Ercorfenib + atezolizumab [R]	75%	42 months	Tanner et al. ESMO '16
Dabrafenib + pertuzumab	75%	34 months	Abeyaratne, ABCO '16
Triple with GSPR			
Verapamil + atezolizumab + trastuzumab [R]	75%	42 months	Kaplan, ABCO '17
Ercorfenib + trastuzumab + atezolizumab [R]	75%	42 months	Tanner, ESMO '16
Dabrafenib + trastuzumab + pertuzumab	75%	41 months	Abeyaratne, ABCO '16
Ercorfenib + atezolizumab	75%		Tanner et al. ESMO '16

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Quick Poll

What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

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2. Pomalidomide +/- dexamethasone
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9. Ixazomib + Rd
10. Other

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Participants (10)

Name	Microphone	Video
JS John Smith	On	On
MM Mary Major	On	On
RM Richard Miles	On	On
JN John Noakes	On	On
AS Alice Suarez	Off	Off
JP Jane Perez	Off	Off
RS Robert Stiles	Off	Off
JF Juan Fernandez	Off	Off
AK Ashok Kumar	Off	Off
JS Jeremy Smith	Off	Off

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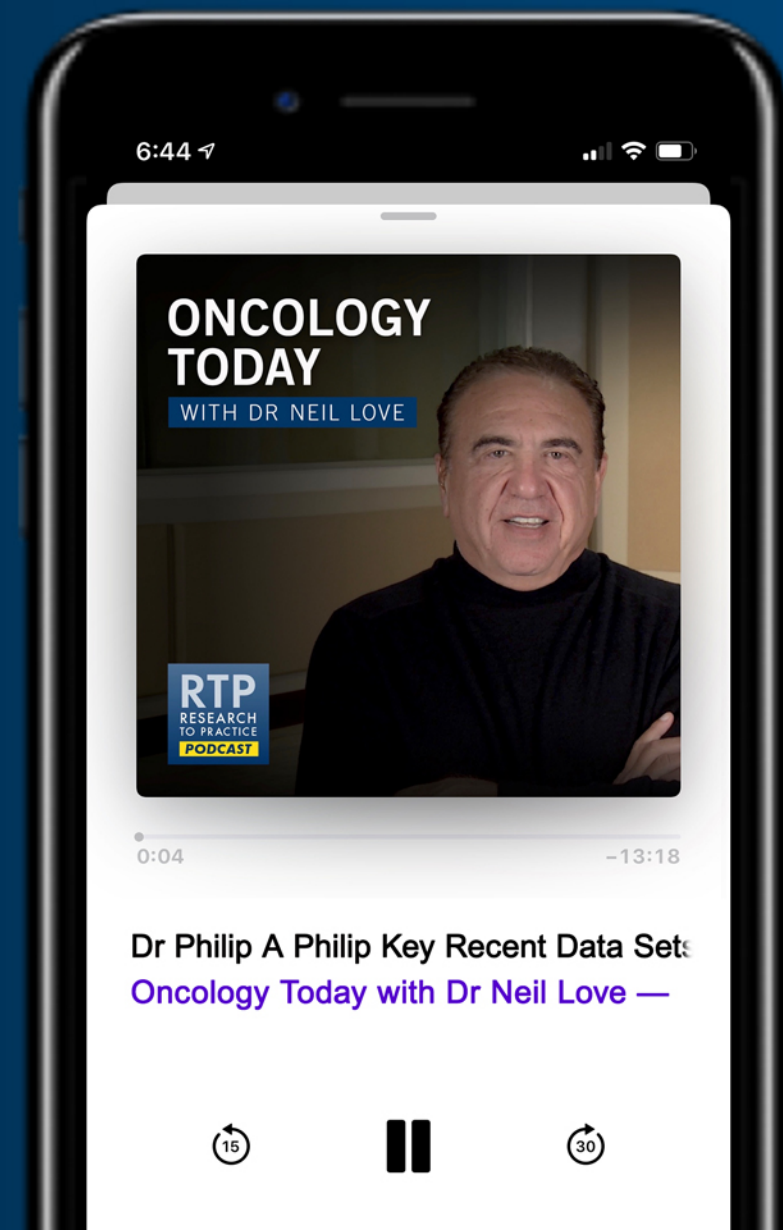
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Warren S Brenner, MD
Lynn Cancer Institute
Boca Raton, Florida



Margaret Deutsch, MD
Duke Cancer Center Raleigh
Raleigh, North Carolina



Gigi Chen, MD
Diablo Valley Oncology and
Hematology Medical Group
Pleasant Hill, California



Justin Peter Favaro, MD, PhD
Oncology Specialists of Charlotte
Charlotte, North Carolina



Mamta Choksi, MD
Florida Cancer Specialists and
Research Institute
New Port Richey, Florida

Agenda

Case 1 – Dr Brenner: 65-yo woman; MSS TMB 11, KRAS G13B mutation, right-sided mCRC

Case 2 – Dr Chen: 62-yo woman; MSI-H, TMB-high mCRC; responds to pembrolizumab → pneumonitis

GI Cancers Journal Club – Part 1: KEYNOTE-177, CHECKMATE 142

Case 3 – Dr Favaro: 55-yo woman; mCRC, KRAS/BRAF mutations, currently on TAS-102/bevacizumab

Case 4 – Dr Brenner: 70-yo woman; MSI-H mCRC; PD-L1-positive, BRAF V600E and sBRCA1 mutations

GI Cancers Journal Club – Part 2: TASC01, ctDNA in mCRC with BRAF V600E Mutation

Case 5 – Dr Deutsch: 65-yo man; relapsed mCRC, asymptomatic with rising CEA off treatment

Case 6 – Dr Choksi: 34-yo single mother of 2 minor children; extensively treated mCRC

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Case Presentation – Dr Brenner: 65-year-old woman with right-sided, MSS mCRC with TMB 11 mut/Mb and a KRAS G13B mutation



Warren S Brenner, MD

- Diagnosed with metastatic cecal adenocarcinoma invading transmurally into segment of small bowel
 - Positive lymph nodes: 8 of 17
 - Tumor implants with involvement of small bowel mesentery, omentum, liver and probable lung
- 11/2020: Surgery due to bowel obstruction
- NGS: MSS | KRAS G13B | TMB: 11 muts/Mb | UGT1A: heterozygous gene polymorphism
- 12/2020: FOLFIRINOX with pegfilgrastim support

Questions

- Should FOLFIRINOX be the standard of care for patients with right-sided colon cancer, or should we use FOLFOX, FOLFIRI or would another agent/regimen be better?
- Would you recommend patients be tested for the UGT1A gene polymorphism before using irinotecan?
- Would you consider using pembrolizumab given the TMB >10? If so, where would you sequence it in her treatment?

Case Presentation – Dr Chen: A 62-year-old woman with MSI-high, TMB-high mCRC



Gigi Chen, MD

- History of Stage IIB Hodgkin's lymphoma over 15 years ago
 - Treated with ABVD → involved-field radiation
- 2018: Screening colonoscopy reveals low-grade carcinoma
 - Left colectomy pathology: pT3N1c sigmoid colon cancer
- 10/2019: Adjuvant mFOLFOX x 12 completed
- 5/2020: Disease progression – bilateral lung nodules, left infrahilar mass
 - CT guided biopsy reveals adenocarcinoma consistent with colon primary
- NGS: MSI-high | TMB: 88 muts/Mb
- 7/2020: Single-agent pembrolizumab
 - Cycle 4: slight progression | Cycle 8: partial response; SOB – evidence of pneumonitis
- Pembrolizumab held

Questions

- How long do we see a delayed response to immunotherapy in colon cancer? Is it safe to resume pembrolizumab after a course of steroids?
- Would the faculty recommend dose and/or frequency adjustment of pembrolizumab?

Regulatory and reimbursement issues aside, what would be your most likely first-line treatment for a younger patient with microsatellite instability (MSI)-high metastatic colorectal cancer (mCRC)?

1. Pembrolizumab
2. Nivolumab
3. Ipilimumab/nivolumab
4. Chemotherapy
5. Chemotherapy + biologic agent
6. Chemotherapy + immunotherapy
7. Other

	Anti-PD-L1			Anti-PD-1	
	4 trials Atezolizumab	6 trials Durvalumab	4 trials Avelumab	15 trials Nivolumab	15 trials Pembrolizumab
Ph1	+ Cobimetinib + bevacizumab ¹	+ Cabozantinib ⁵ + Selumetinib ± tremelimumab ⁶		+ Regorafenib ¹⁴	+ Maraviroc ²⁷ + Romidepsin ± chemotherapy ²⁸ + Grapiprant ²⁹ + Binimetinib ³⁰ + Pemetrexed + oxaliplatin ⁴⁰
Ph1/2	+ Imprime PGG + bevacizumab or isatuximab or selicrelumab + bevacizumab vs regorafenib ²		+ Regorafenib ¹⁰	+ Regorafenib ¹⁵ + Copanlisib ¹⁶ + ONC201 ¹⁷ + Binimetinib ± ipilimumab ¹⁸ + GO-004 GRT-C901/GRT-R902 ± ipilimumab ²³ + Guadecitabine ²⁶	+ Epacadostat + azacitidine/INCB057643/ INCB059872 ³¹ + Poly-ICLC ³² + Napabucasin ³³ + Regorafenib ³⁴ + EDP1503 ³⁵ + Birinapant ⁴¹ + Entinostat ³⁹
Ph2	+ Bevacizumab + chemotherapy ³ + Bevacizumab + chemotherapy ⁴	+ Trametinib ⁷ + Azacitidine ⁸ + Monalizumab ⁹	+ Cetuximab + chemotherapy ¹¹ + eFT508 ¹² + Cetuximab + FOLFOX ¹³	+ Relatlimab ¹⁹ + Panitumumab + ipilimumab ²⁰ + Ipilimumab ²¹ + BNC105 or BBI608 ²² + BNC105 or napabucasin ²⁴ + Ipilimumab + temozolomide ²⁵	+ Navarixin ³⁶ + Vicriviroc ³⁷ + Bevacizumab + capecitabine ³⁸

1. NCT02876224; 2. NCT03555149; 3. NCT03721653; 4. NCT03698461; 5. NCT03539822; 6. NCT02586987; 7. NCT03428126; 8. NCT02811497; 9. NCT02671435; 10. NCT03475953; 11. NCT03608046; 12. NCT03258398; 13. NCT03174405; 14. NCT03712943; 15. NCT03406871; 16. NCT03711058; 17. NCT03791398; 18. NCT03271047; 19. NCT03642067; 20. NCT03442569; 21. NCT03693846; 22. NCT03647839; 23. NCT03639714; 24. NCT03647839; 25. NCT03832621; 26. NCT03576963; 27. NCT03274804; 28. NCT02512172; 29. NCT03658772; 30. NCT03374254; 31. NCT02959437; 32. NCT02834052; 33. NCT02851004; 34. NCT03657641; 35. NCT03775850; 36. NCT03473925; 37. NCT03631407; 38. NCT03396926; 39. NCT02437136; 40. NCT03626922; 41. NCT02587962. ClinicalTrials.gov searched in June 2019. Studies may include combinations with additional agents.

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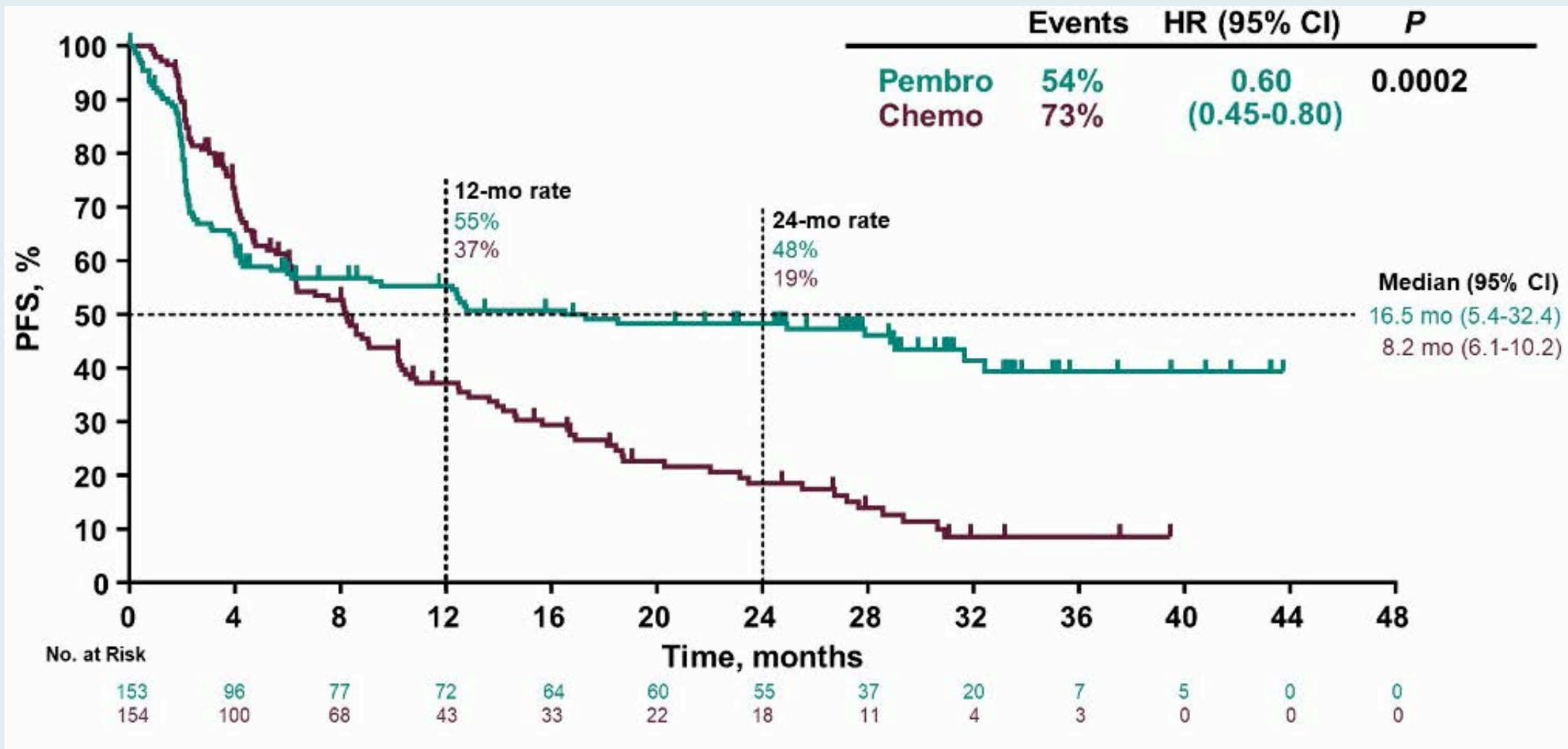
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KEYNOTE-177: Phase 3 Randomized Study of Pembrolizumab Versus Chemotherapy for Microsatellite Instability-High Advanced Colorectal Cancer

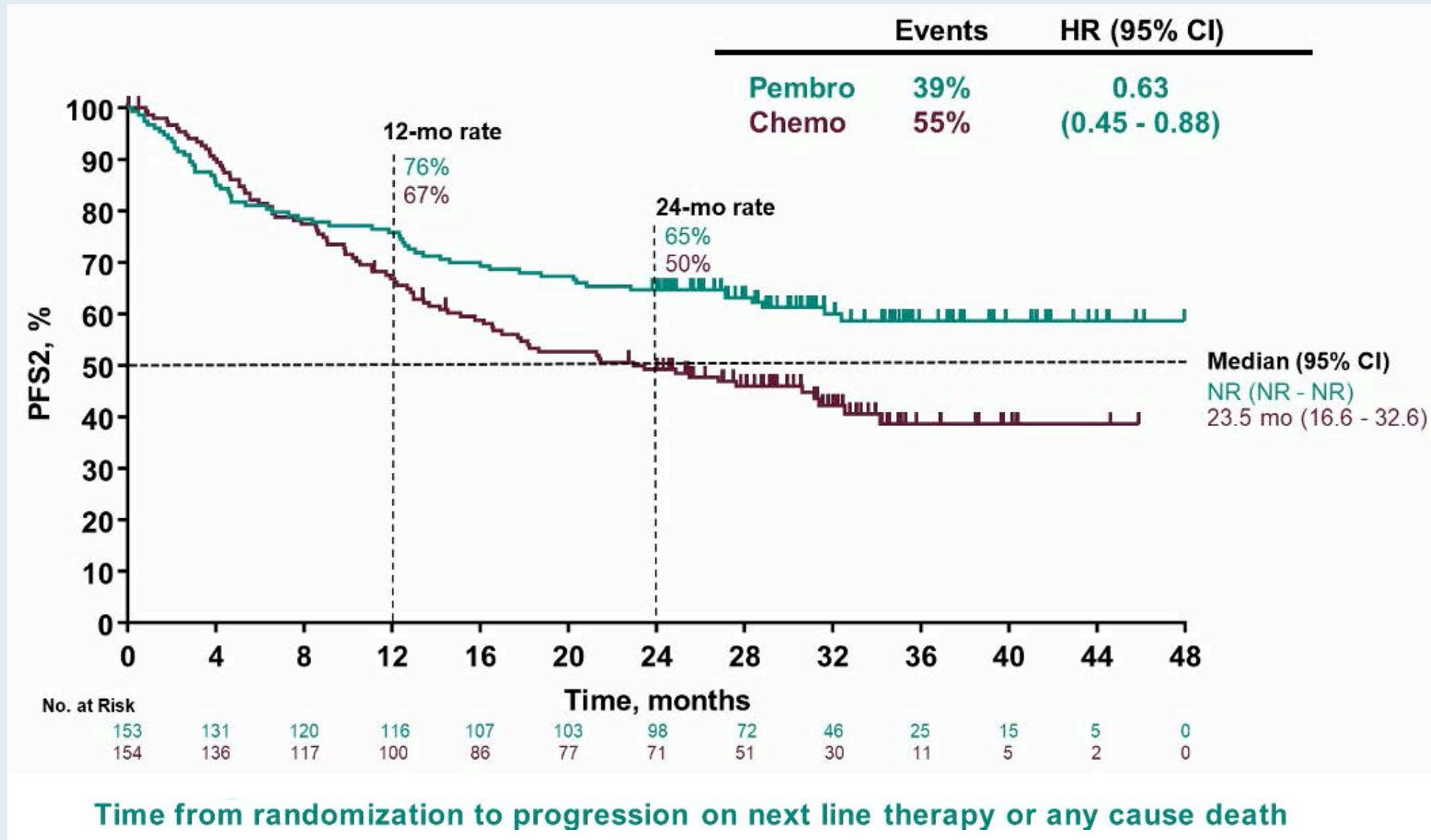
Kai-Keen Shiu,¹ Thierry André,² Tae Won Kim,³ Benny Vittrup Jensen,⁴ Lars Henrik Jensen,⁵ Cornelis Punt,⁶ Denis Smith,⁷ Rocio Garcia-Carbonero,⁸ Manuel Benavides,⁹ Peter Gibbs,¹⁰ Christelle de la Fouchardiere,¹¹ Fernando Rivera,¹² Elena Elez,¹³ Johanna Bendell,¹⁴ Dung T. Le,¹⁵ Takayuki Yoshino,¹⁶ Ping Yang,¹⁷ Mohammed Farooqui,¹⁸ Patricia Marinello,¹⁸ and Luis A. Diaz Jr¹⁹

¹University College Hospital, NHS Foundation Trust, London, United Kingdom; ²Sorbonne Université and Hôpital Saint Antoine, Paris, France; ³Asan Medical Center, University of Ulsan, Seoul, Republic of Korea; ⁴Herlev and Gentofte Hospital, Herlev, Denmark; ⁵University Hospital of Southern Denmark, Vejle, Denmark; ⁶Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, Netherlands; ⁷Bordeaux University Hospital, Bordeaux, France; ⁸Hospital Universitario 12 de Octubre, Ima12, CNIO, UCM, Madrid, Spain; ⁹Hospital Regional Universitario de Malaga, Malaga, Spain; ¹⁰Western Health, St Albans, Australia; ¹¹Léon Bérard Center, Lyon, France; ¹²Hospital Universitario Marques de Valdecilla, IDIVAL, Santander, Spain; ¹³Vall d'Hebron Institute of Oncology, Barcelona, Spain; ¹⁴Sarah Cannon Research Institute, Nashville, TN, USA; ¹⁵Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, USA; ¹⁶National Cancer Center Hospital East, Kashiwa, Japan; ¹⁷MSD China, Beijing, China; ¹⁸Merck & Co., Inc. Kenilworth, NJ, USA; ¹⁹Memorial Sloan Kettering Cancer Center, New York, NY, USA

KEYNOTE-177: Progression-Free Survival



KEYNOTE-177: Progression-Free Survival 2



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 Overman¹⁵

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Abstract Number 58

CheckMate 142: Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg – First-Line Cohort Design

- CheckMate 142 is an ongoing, multicohort, nonrandomized phase 2 trial evaluating the efficacy and safety of NIVO-based therapies in patients with mCRC^a

- Histologically confirmed metastatic or recurrent CRC
- MSI-H/dMMR per local laboratory
- No prior treatment for metastatic disease

NIVO3 Q2W
+
IPI1 Q6W^b

Primary endpoint:

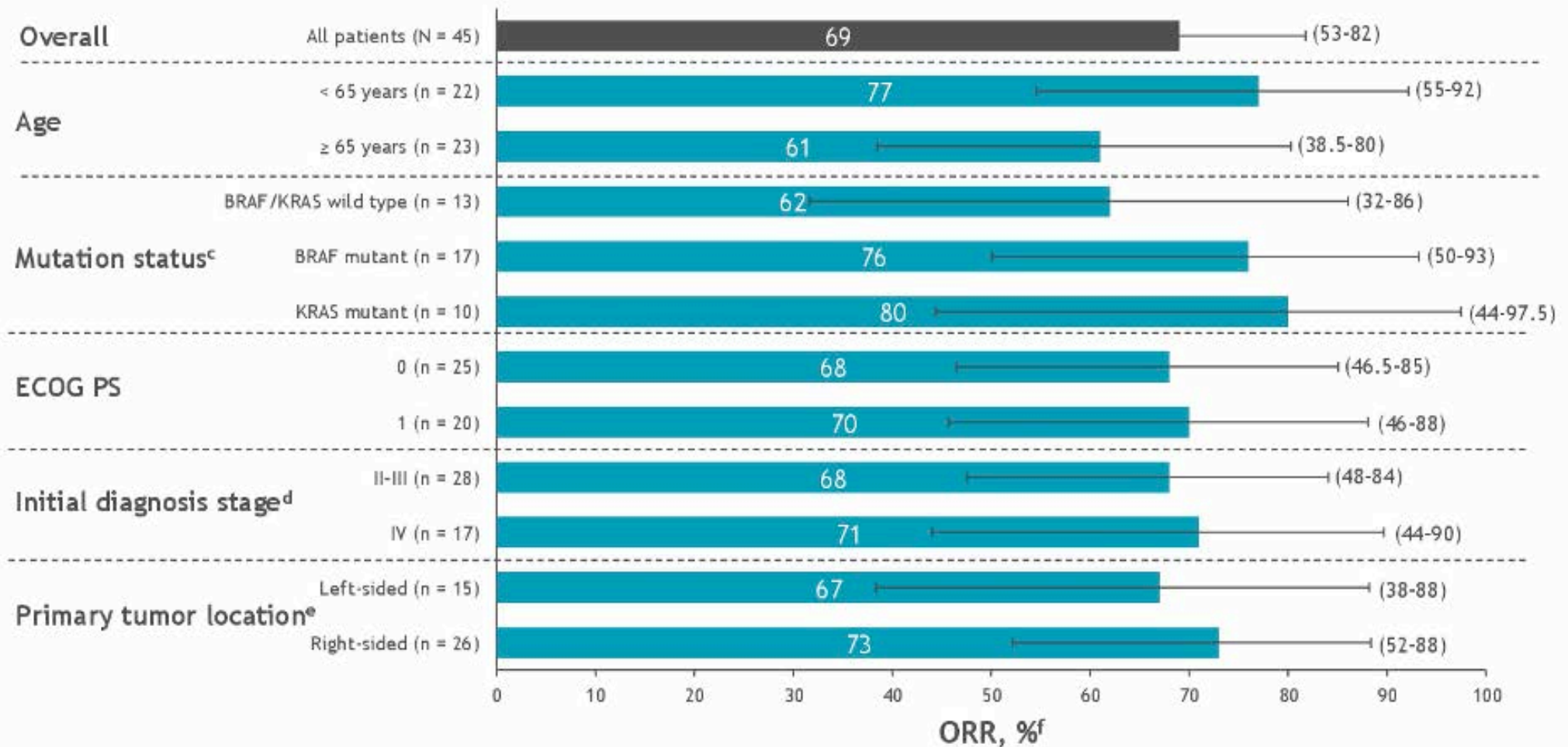
- ORR per investigator assessment (RECIST v1.1)

Other key endpoints:

- ORR per BICR, DCR,^c DOR, PFS, OS, and safety

- At data cutoff (October 2019), the median duration of follow-up was 29.0 months (range, 24.2-33.7)^d

CheckMate 142: Objective Response Rate by Subgroup



- ORR was generally similar across evaluated subgroups and consistent with that of the overall study population

Microsatellite Instability in Colorectal Cancer: An analysis of the National Cancer Database.

Kamelah Abushalha¹,
Sawsan Abulaimoun²,
Sarah J Aurit², Erin
Jenkins², Peter T.
Silberstein²

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Borders, Amman, Jordan;

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PRESENTED BY: Kamelah Abushalha

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Author Conclusions: *“In settings where resources are scarce and universal testing is not possible, there is a benefit from MSI testing in **female patients, those with right-sided colon cancer, mucinous adenocarcinoma, and medullary carcinoma.**”*

Agenda

Case 1 – Dr Brenner: 65-yo woman; MSS TMB 11, KRAS G13B mutation, right-sided mCRC

Case 2 – Dr Chen: 62-yo woman; MSI-H, TMB-high mCRC; responds to pembrolizumab → pneumonitis

GI Cancers Journal Club – Part 1: KEYNOTE-177, CHECKMATE 142

Case 3 – Dr Favaro: 55-yo woman; mCRC, KRAS/BRAF mutations, currently on TAS-102/bevacizumab

Case 4 – Dr Brenner: 70-yo woman; MSI-H mCRC; PD-L1-positive, BRAF V600E and sBRCA1 mutations

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Case 5 – Dr Deutsch: 65-yo man; relapsed mCRC, asymptomatic with rising CEA off treatment

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Case Presentation – Dr Favaro: A woman in her mid-50s with mCRC – KRAS, BRAF mutations



Justin Peter Favaro, MD, PhD

- Initially treated with FOLFOX/bevacizumab → disease progression
- Treated with FOLFIRI/bevacizumab → disease progression
- Treated with BRAF inhibitor → rapid disease progression
- Regorafenib intolerant
- Progressive disease → radiation therapy
- Recently initiated therapy with TAS-102 + bevacizumab
 - Tolerating regimen well

Questions

- Would the faculty consider incorporating lower dose TAS-102 plus bevacizumab for patients with heavily pretreated disease?
- Is this a good approach for patients who want to explore other treatment options?

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

1. I have
2. I have not but would for the right patient
3. I have not and would not

Case Presentation – Dr Brenner: A 70-year-old woman with PD-L1-positive, MSI-H mCRC with a BRAF V600E tumor mutation and a somatic BRCA1 mutation



Warren S Brenner, MD

- 1/2019: FOLFOX + bevacizumab – discordant response
- 4/2019: FOLFOXIRI + bevacizumab → progression
- 7/2019: Nivolumab/ipilimumab initiated
- 9/2019: Nivolumab/ipilimumab completed → single-agent nivolumab
- 12/2019: Panhypopituitarism, treated with low-dose prednisone
- 1/2020: Nivolumab re-initiated
 - Patient currently in CR, tolerating treatment well

Questions

- How would the faculty sequence immunotherapy and a BRAF inhibitor in a patient with a BRAF mutation and a microsatellite instability-high tumor?
- When should we consider dual checkpoint inhibitor treatment?
- When do we stop immunotherapy in patients who are in CR after receiving immunotherapy?

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, microsatellite stable (MSS) mCRC and a BRAF V600E mutation who experienced disease progression after FOLFIRINOX/bevacizumab?

1. Chemotherapy
2. Chemotherapy/bevacizumab
3. Irinotecan + vemurafenib + EGFR antibody
4. Dabrafenib + trametinib + EGFR antibody
5. Encorafenib + binimetinib + EGFR antibody
6. Encorafenib + EGFR antibody
7. Other

Patients with mCRC

- Histologically confirmed mCRC
- PD during or after therapy with fluoropyrimidine, irinotecan, oxaliplatin and EGFR-inhibitor (RAS wildtype), prior bevacizumab was optional
- ECOG PS 0–1
- Enrollment between Aug 2017 and Sept 2018

RANDOMIZATION

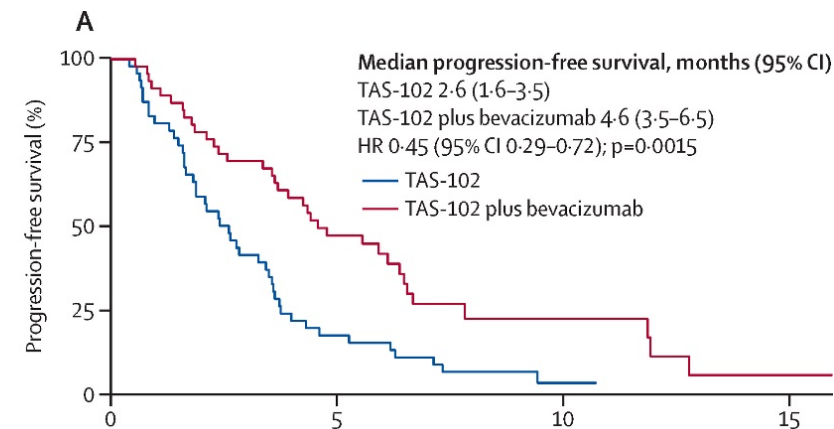
N=80

N=41

Arm A
FTD/TPI 35 mg/m² orally twice daily on days 1–5 and 8–12 of a 28-day treatment cycle

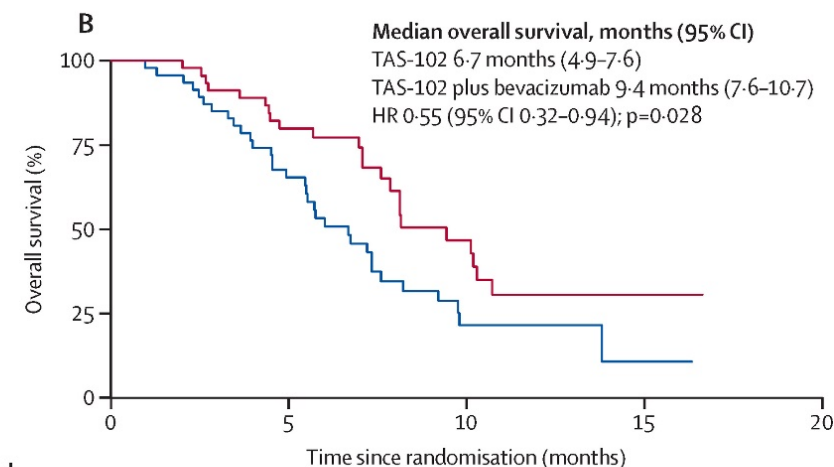
N=39

Arm B
Same dose of FTD/TPI (as Arm A), with bevacizumab 5 mg/kg on day 1 and day 15



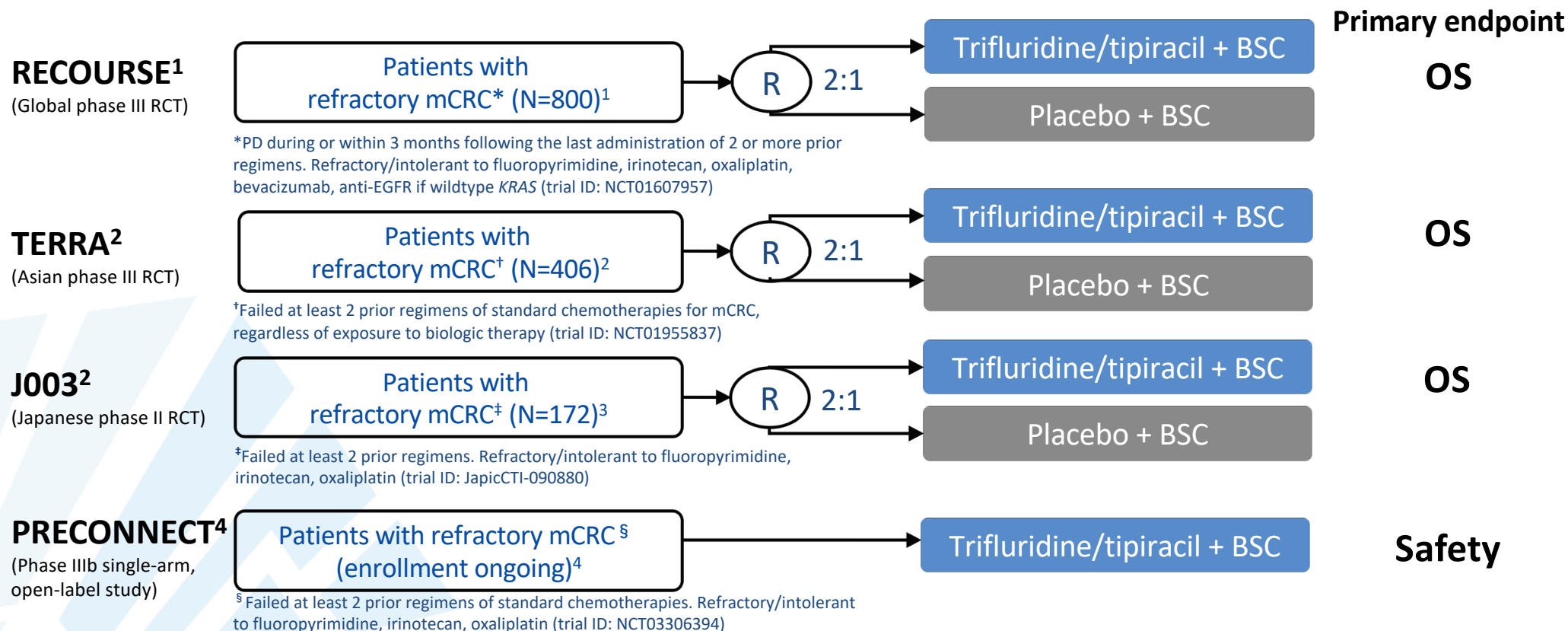
Number at risk
(number censored)
TAS-102
TAS-102 plus bevacizumab

Time (months)	0	5	10	15
TAS-102	47 (38)	8 (6)	1 (0)	0
TAS-102 plus bevacizumab	46 (24)	20 (8)	5 (3)	1



Number at risk
(number censored)
TAS-102
TAS-102 plus bevacizumab

Time (months)	0	5	10	15	20
TAS-102	47 (16)	29 (16)	6 (1)	1 (0)	0
TAS-102 plus bevacizumab	46 (9)	34 (10)	12 (4)	2 (0)	0



1. Mayer RJ, Van Cutsem E et al. N Engl J Med 2015;372:1909–19; 2. Xu J, et al. J Clin Oncol 2018;36:350–8; 3. Yoshino T, et al. Lancet Oncol 2012;13:993–1001;

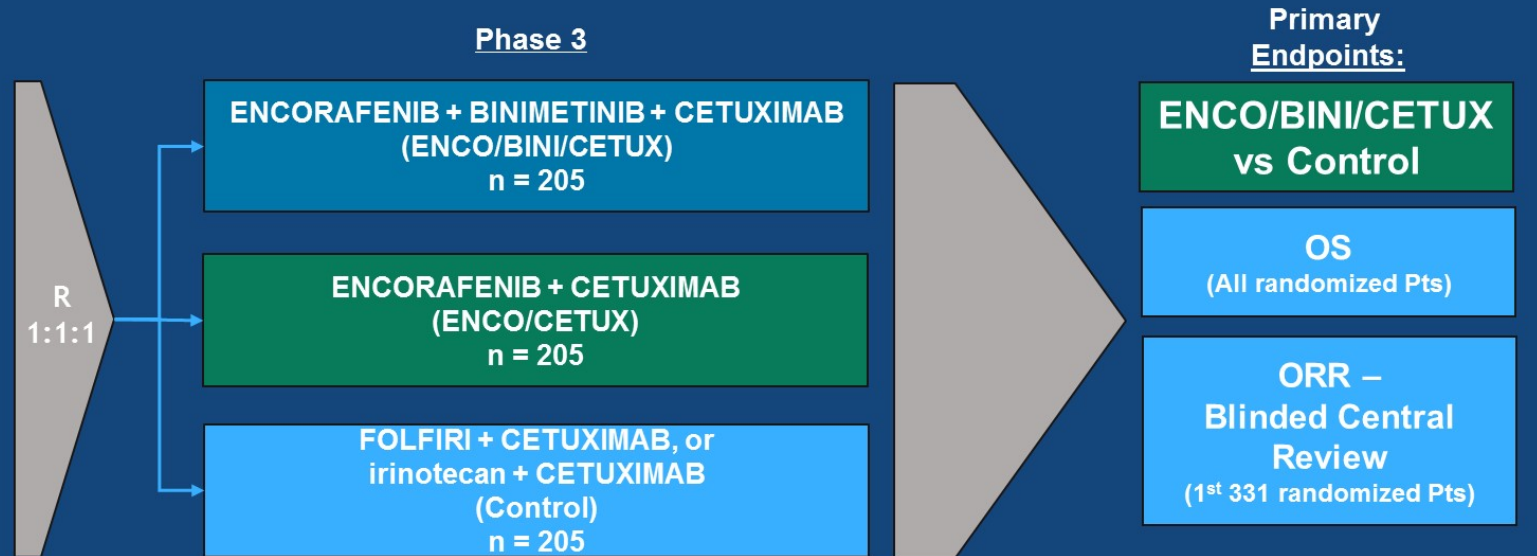
4. Falcone A, ...Van Cutsem E et al. WCGIC 2018 (Oral and Poster Presentation). Abstract O-013

Indication	Treatments	Phase	Study status
mCRC, 1L	Trifluridine/tipiracil + bevacizumab vs capecitabine + bevacizumab (TASC01)	Randomized Phase II	Recruitment completed
mCRC, 1L	Trifluridine/tipiracil + bevacizumab vs capecitabine + bevacizumab (SOLSTICE)	Randomized Phase III	Recruiting
mCRC, 2L	Trifluridine/tipiracil + oxaliplatin + bevacizumab or nivolumab	Phase I	In progress
mCRC, 2L	Trifluridine/tipiracil + irinotecan	Phase I	Recruitment completed
mCRC, 3/4L	Trifluridine/tipiracil + nivolumab	Phase II	In progress
mCRC, 3L	Trifluridine/tipiracil ± bevacizumab (SUNLIGHT)	Randomized Phase III	Recruiting
mCRC 3L	PRECONNECT	Phase IIIb	Results available
mCRC, pretreated	Tas-102 + nintedanib Tas-102 + panitumumab	Phase I/II	In progress

Phase III BEACON CRC Trial

Study Design

Patients with *BRAF* V600E-mutant 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: ENCO/CETUX vs Control and ENCO/BINI/CETUX vs ENCO/CETUX - OS & ORR, PFS, Safety, QOL

Post hoc Updated Analysis: includes 6 months of additional follow-up since cut off for primary analysis

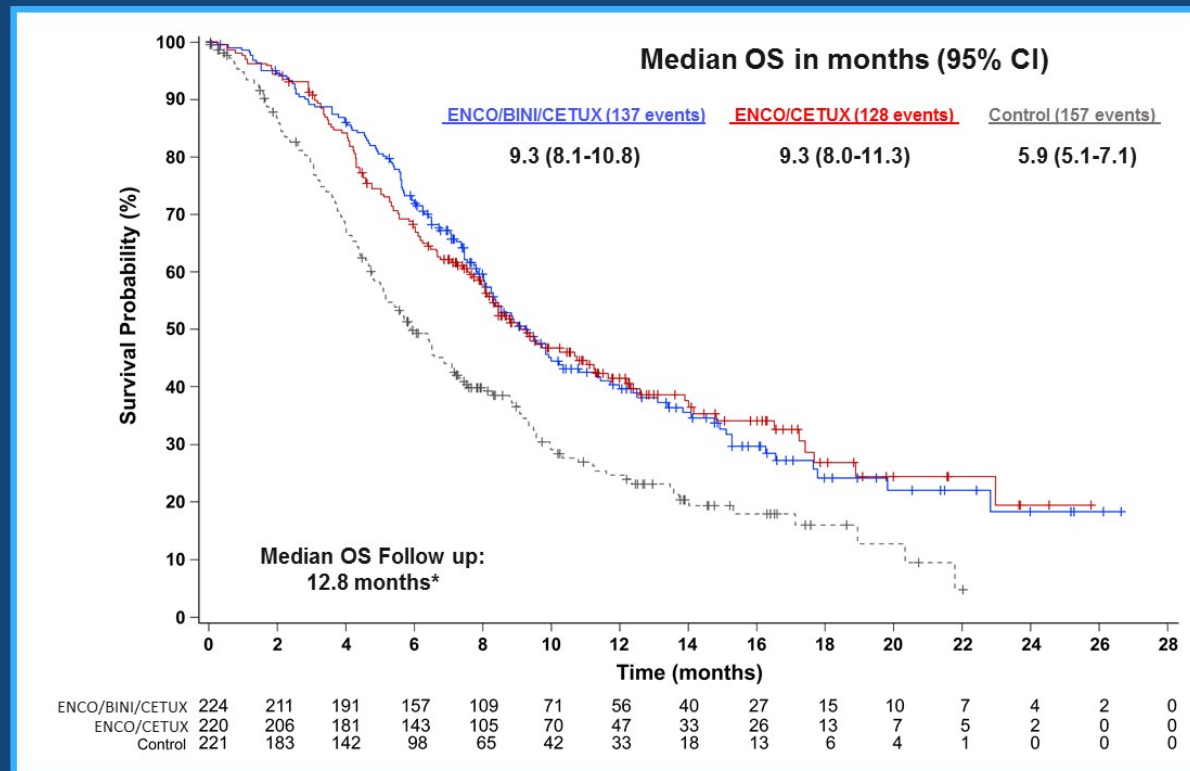
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PRESENTED BY: Scott Kopetz, MD, PhD

BEACON CRC

Updated Overall Survival: ENCO/BINI/CETUX vs ENCO/CETUX vs Control



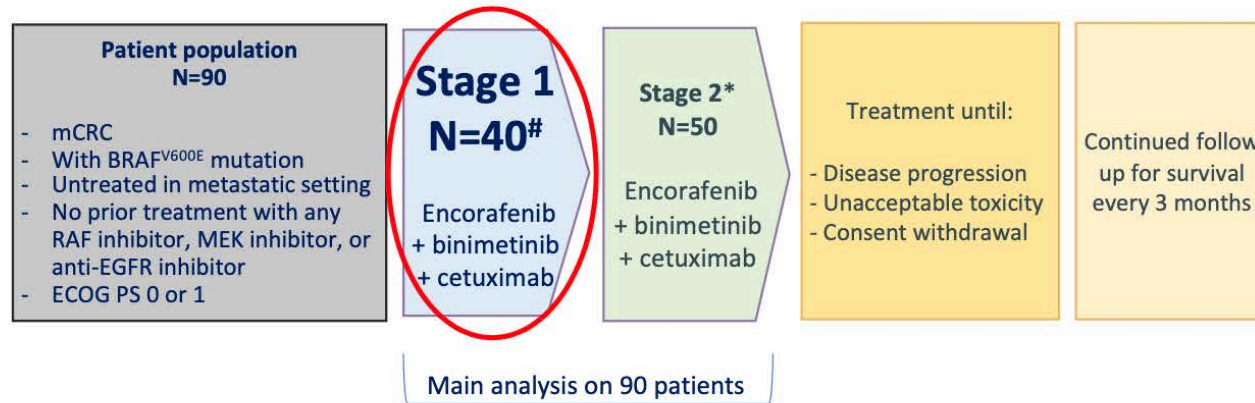
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PRESENTED BY: Scott Kopetz, MD, PhD

ANCHOR CRC, Phase 2 study in FIRST LINE BRAF^{V600E} mCRC

2-STAGE DESIGN¹



Primary objective & endpoint: confirmed ORR (investigator assessed)

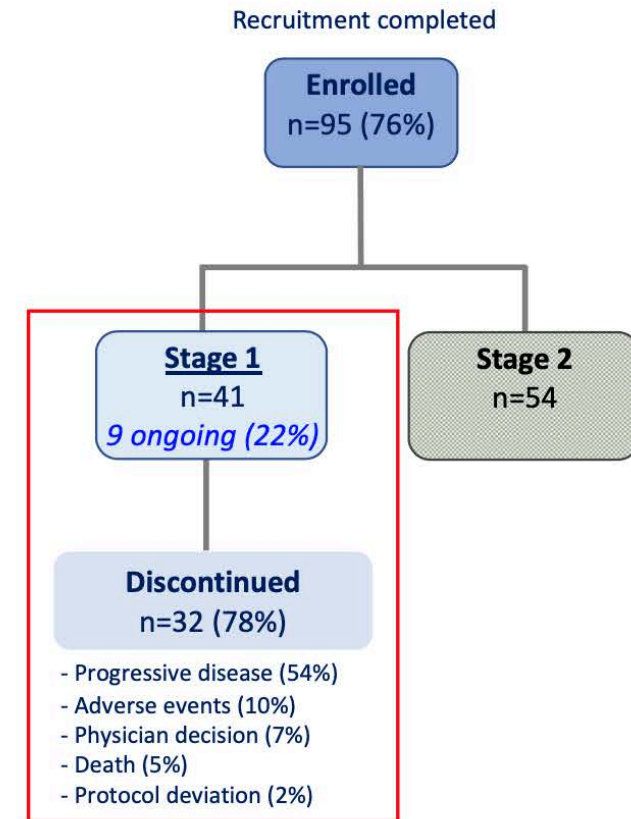
Secondary endpoints: PFS, OS, Safety, QoL, PK

1. Grothey A, et al. *Annals Oncol.* 2019;30(suppl 4):P-400

[#]Futility analysis

*Stage 2 enrolment only after ≥ 12 responses observed in stage 1

cORR=confirmed objective response rate, OS=overall survival, PK=pharmacokinetics, PFS=progression free survival, QoL=quality of life



Cut-off date: 06-Feb-2020

Note: the data have not been fully cleaned due to Covid-19 pandemic.

Agenda

Case 1 – Dr Brenner: 65-yo woman; MSS TMB 11, KRAS G13B mutation, right-sided mCRC

Case 2 – Dr Chen: 62-yo woman; MSI-H, TMB-high mCRC; responds to pembrolizumab → pneumonitis

GI Cancers Journal Club – Part 1: KEYNOTE-177, CHECKMATE 142

Case 3 – Dr Favaro: 55-yo woman; mCRC, KRAS/BRAF mutations, currently on TAS-102/bevacizumab

Case 4 – Dr Brenner: 70-yo woman; MSI-H mCRC; PD-L1-positive, BRAF V600E and sBRCA1 mutations

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Case 6 – Dr Choksi: 34-yo single mother of 2 minor children; extensively treated mCRC

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Phase II study evaluating trifluridine/tipiracil + bevacizumab and capecitabine + bevacizumab in first-line unresectable metastatic colorectal cancer (mCRC) patients who are non-eligible for intensive therapy (TASCO1): results of the final analysis on the overall survival.

Presenter: Eric Van Cutsem, MD, PhD

University Hospital Gasthuisberg, Leuven, Belgium

Abstract Number: 14

Author Group: Eric Van Cutsem, Iwona Danielewicz, Mark P. Saunders, Per Pfeiffer, Guillem Argilés, Christophe Borg, Rob Glynne-Jones, Cornellis J. A. Punt, Agnes J. Van de Wouw, Mikhail Fedyanin, Danil Stroyakovskiy, Hendrik Kroening, Pilar García-Alfonso, Harpreet Wasan, Alfredo Falcone, Paul Aubel, Anton Egorov, Nadia Amellal, Vladimir Moiseenko

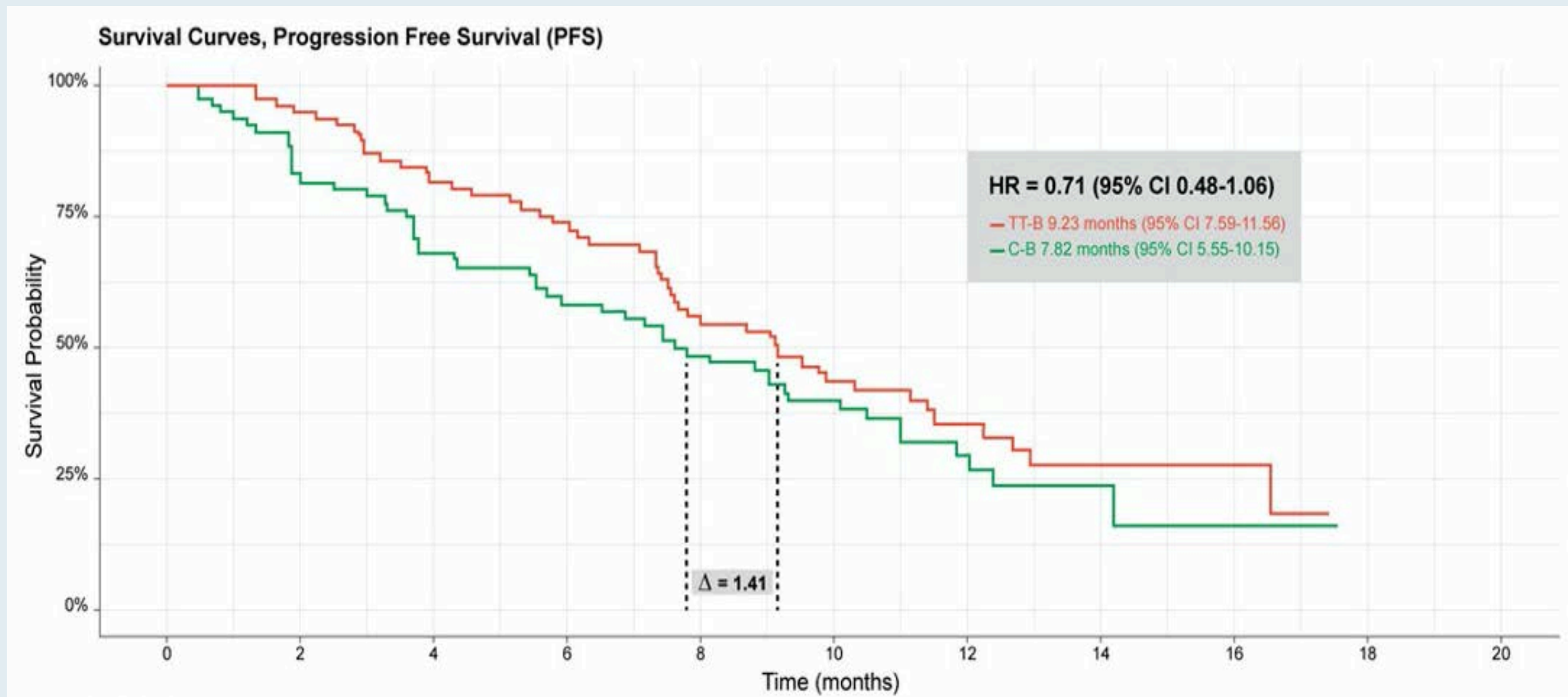
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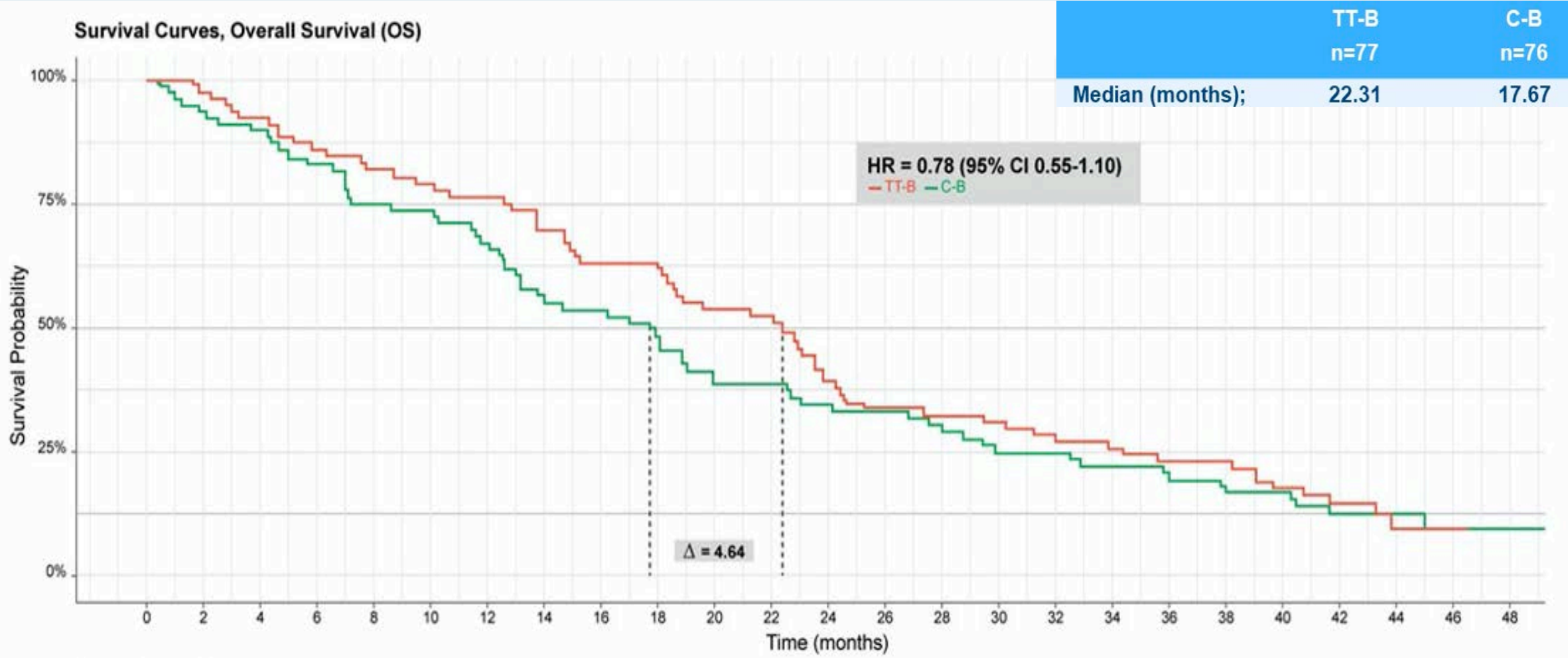
TASCO1: Progression-Free Survival (Primary Endpoint)



TT-B = TAS-102 + bevacizumab; C-B = capecitabine + bevacizumab

Van Cutsem E et al. Gastrointestinal Cancers Symposium 2021;Abstract 14.

TASCO1: Overall Survival (Secondary Endpoint)



Utility of Circulating Tumor DNA in the Clinical Management of Patients with BRAF^{V600E} Metastatic Colorectal Cancer

Morris VK et al.

Gastrointestinal Cancers Symposium 2021;Abstract 119.

Utility of ctDNA in Management of mCRC with BRAF V600E Mutation

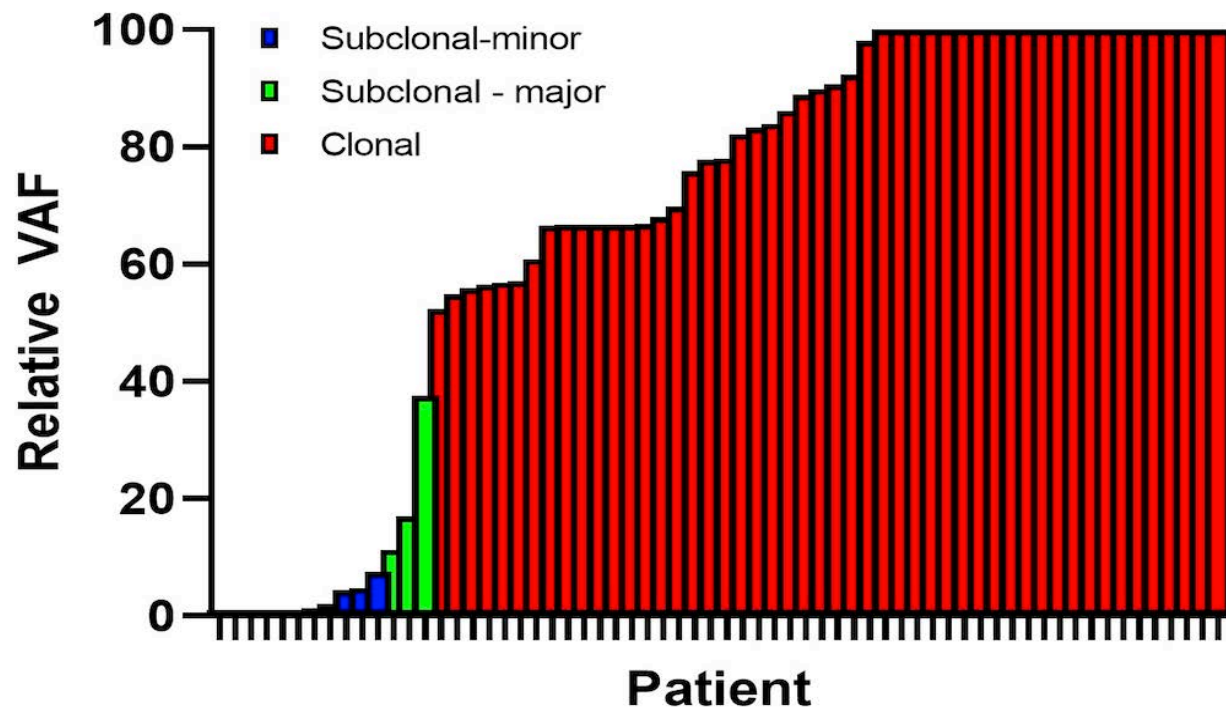


Figure 2: Distribution of relative VAF according to clonal status demonstrate high rate of clonal alterations.

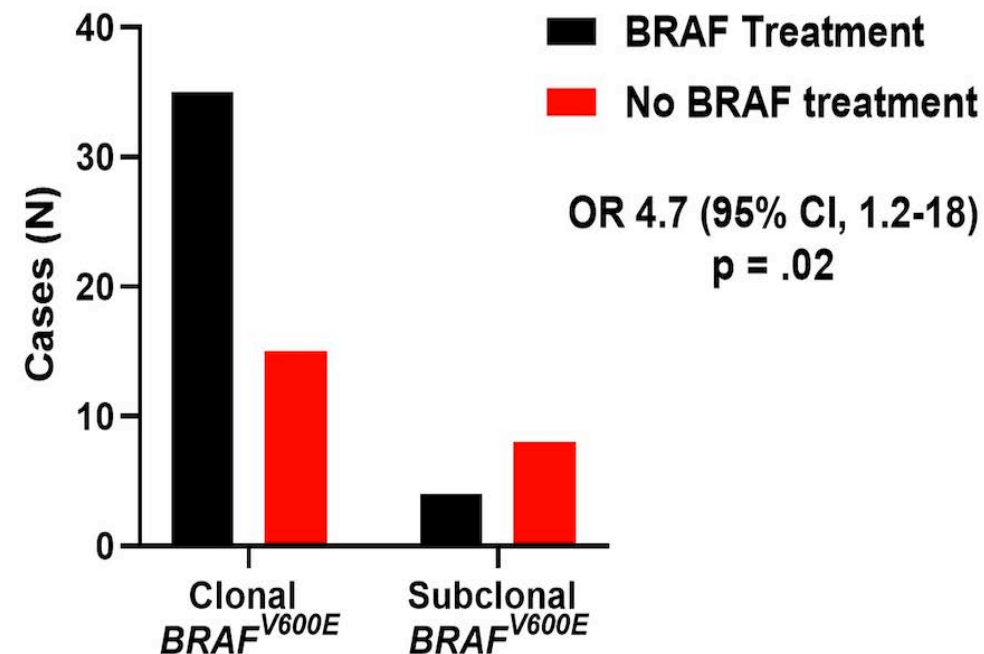


Figure 4: Patients with clonal $BRAF^{V600E}$ mCRC were more likely (70% vs 33%) to receive targeted therapies against the $BRAF^{V600E}$ oncoprotein than when subclonal $BRAF^{V600E}$ mutations were detected.

Utility of ctDNA in Management of mCRC with BRAF V600E Mutation

Conclusions

- Use of ctDNA to characterize clonality of a *BRAF*^{V600E} mutation according to relative VAF may help to identify patients with *BRAF*^{V600E} mCRC appropriate for matched targeted therapies in this setting.
- The overwhelming majority of patients with minor subclonal *BRAF*^{V600E} mutations had received prior anti-EGFR for *KRAS/NRAS/BRAF*^{wild-type} mCRC. This presumed acquired mechanism of resistance in the ctDNA may inform on the discordance noted between FFPE and ctDNA cases in matched patients.
- Given upcoming frontline clinical trials for *BRAF*^{V600E} mCRC which require early identification of a *BRAF*^{V600E} mutation prior to treatment initiation, use of ctDNA to identify *BRAF*^{V600E} mutations is a convenient and feasible approach in early management of mCRC.

Circulating tumor DNA analysis

Assessment of recurrence risk, benefit of adjuvant therapy, and early relapse detection after treatment in colorectal cancer patients.

Presented by: Tenna Vesterman Henriksen, PhD-student,
Aarhus University & Department of Molecular Medicine, Aarhus University Hospital

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ctDNA Analysis and Summary

	n	Univariable analysis		Multivariable analysis	
		HR (95% CI)	P-value	HR (95% CI)	P-value
CEA PostOP	175	1.3 (0.56-3.2)	0.524		
CEA PostACT	99	1.4 (0.44-4.2)	0.596		
CEA Longitudinal	197	4.9 (3.2-15)	<0.0001	1.8 (0.77 - 4.0)	0.184
ctDNA Longitudinal	197	95.7 (28-322)	<0.0001	80.55 (23.1 - 281)	<0.0001

1. Patients with ctDNA detected immediately after surgery had high risk of recurrence
2. Longitudinal monitoring increased the predictive power of ctDNA
3. Molecular recurrence (ctDNA) was detected a median of 8 months before radiological detection of recurrence
4. Longitudinal testing with ctDNA outperformed CEA in RFS prediction

Global BRAF Testing Practices in Metastatic Colorectal Cancer

Kopetz S et al.

Gastrointestinal Cancers Symposium 2021;Abstract 128.

Author Conclusions: *“BRAF testing has global variability, impacting tx decisions. Increased awareness and routine testing may lead to informed decisions regarding targeted therapies, such as encorafenib plus cetuximab where approved, in patients with BRAF V600E-mutant mCRC.”*

Agenda

Case 1 – Dr Brenner: 65-yo woman; MSS TMB 11, KRAS G13B mutation, right-sided mCRC

Case 2 – Dr Chen: 62-yo woman; MSI-H, TMB-high mCRC; responds to pembrolizumab → pneumonitis

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Case Presentation – Dr Deutsch: A 65-year-old man with mCRC and biochemical relapse (rising CEA) after FOLFIRI



Margaret Deutsch, MD

- 11/2016: Diagnosed with rectosigmoid colon cancer – T4N2
 - Concurrent renal cell carcinoma
- Former IV drug user | Hepatitis C positive
- Neoadjuvant RT and infusional 5-FU → resection → adjuvant FOLFOX
- 3/2019: FOLFIRI x 4 complicated by neutropenia
- 1/2021: CT reveals 1 cm obturator lymph node with no other evidence of disease
 - Rising CEA

Questions

- What criteria would the faculty employ to determine timing of resumption of chemotherapy for a patient with rising CEA and no significant symptoms or measurable disease to follow on imaging?
- What treatment would be appropriate when resuming therapy given disease interval?

Case Presentation – Dr Choksi: A 34-year-old woman with heavily pretreated mCRC; single mother of minor children



Mamta Choksi, MD

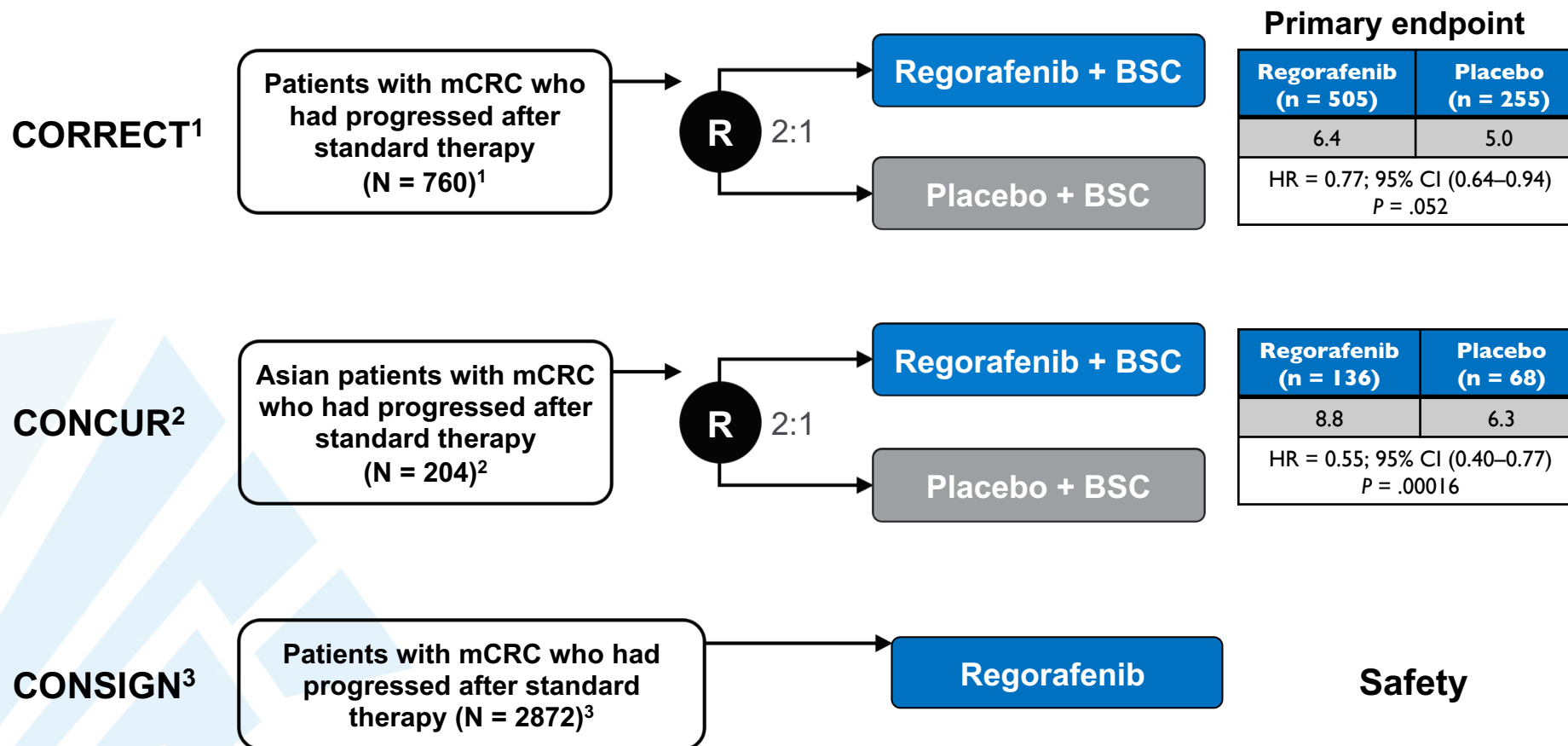
- Required multiple hospitalizations since diagnosis in December 2019
- Required multiple paracenteses in last 4 months
- NGS: MSS | TMB low | No targetable mutations
- Currently recovering from most recent surgery
- **Plan:** Irinotecan + cetuximab upon recovery

Questions

- Why do the faculty think we are seeing more and more young patients with Stage IV colon cancer these days? Is it something environmental? Is it something genetic? Could it be food or habit related?
- How can we best treat these types of patients?

A 65-year-old patient with right-sided, pan-RAS wild-type, BRAF wild-type, MSS 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?

1. Cetuximab
2. Cetuximab + irinotecan
3. Panitumumab
4. Panitumumab + irinotecan
5. Regorafenib
6. TAS-102
7. Regorafenib or TAS-102 — coin flip



1. Grothey A, Van Cutsem E, et al. Lancet. 2013;381:303-312; 2. Li J, et al. Lancet Oncol. 2015;16:619-629; 3. Van Cutsem E, et al. The Oncologist 2019; 2:185-192.

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

Dose escalation arm

Standard dose group

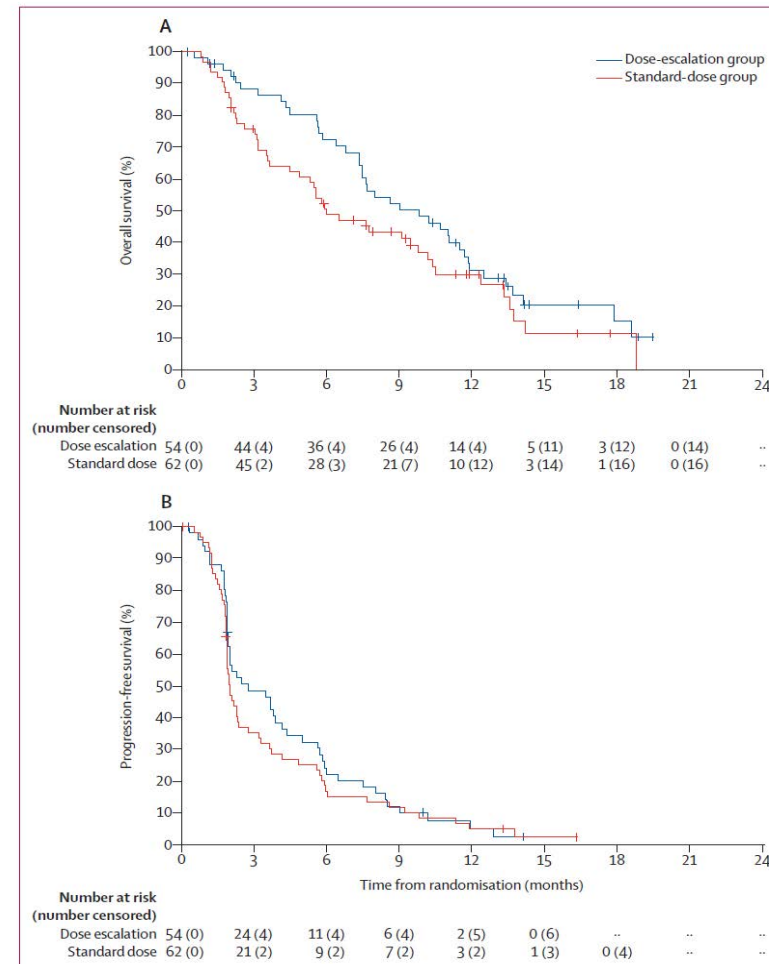
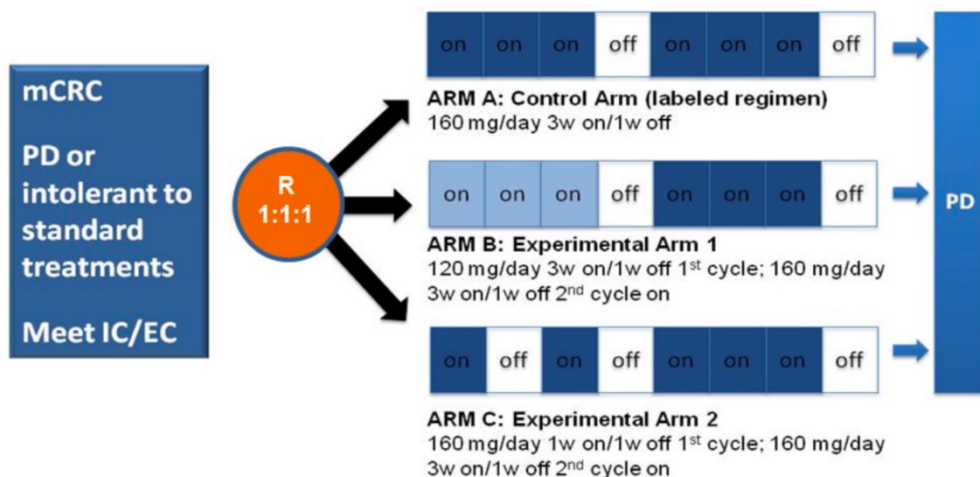


Figure 2: Overall survival (A) and progression-free survival (B) in the dose-escalation and standard-dose groups. Censored patients are marked on the curves with a cross.



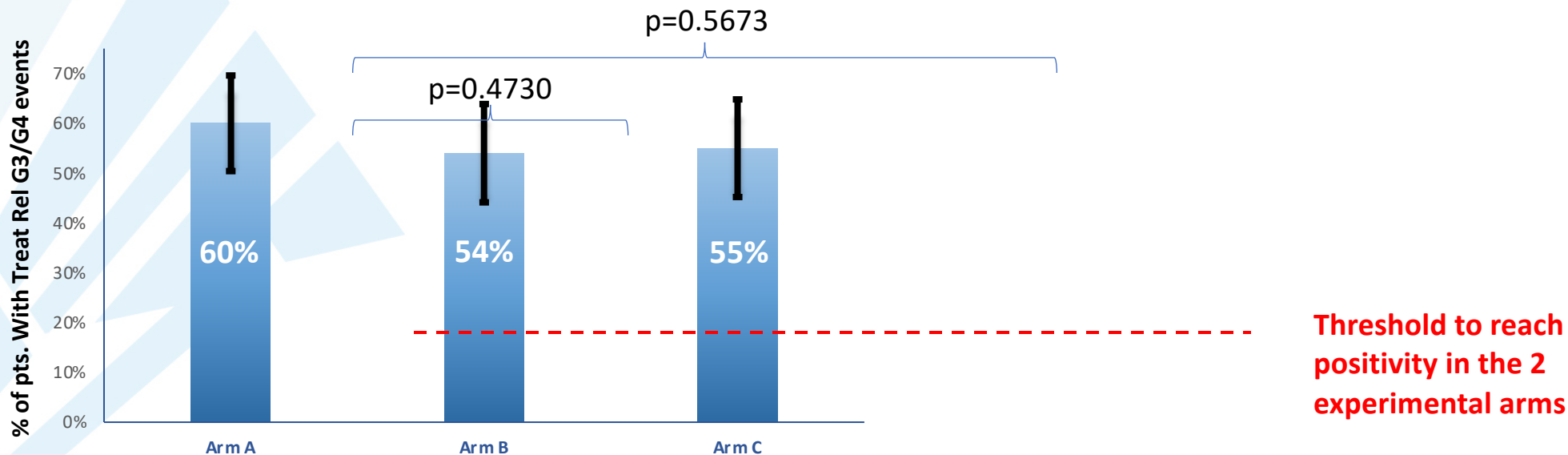
Primary endpoint:

- **Safety** :% of patients having G3/G4 AEs during the entire course of the treatment

Secondary endpoints:

- OS
- PFS
- % of Patients starting C3 on each arm
- Dose intensity
- DCR

Primary Endpoint: Pts having G3/G4 AEs during treatment course



As of 3/2/2020, 28 patients were treated

Patients

- Histologically confirmed refractory CRC
- MMR proficient.
- Failed/ intolerant to standard chemotherapy.

Phase I

N= 12

Nivolumab
240mg IV q2wk
and regorafenib
according to dose
escalation of
80mg, 120 mg or
160mg 21 days on
7 days off

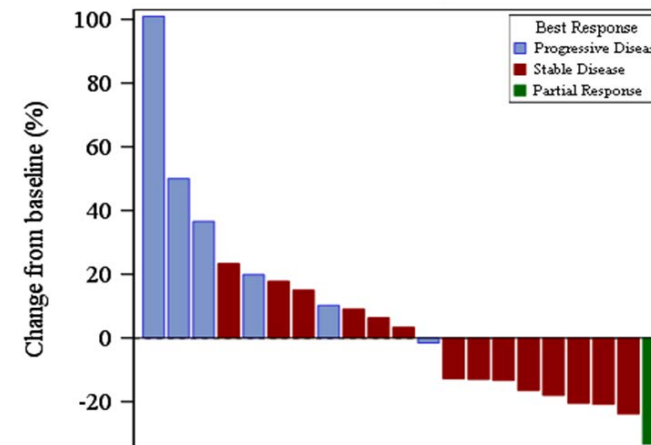
Expanded Cohort

N=16(goal=40)

Nivolumab
240mg IV
Q2wk for 16 wks then
480 mg q4wk and dose
of regorafenib based on
MTD

Best Overall Response	N = 21
CR	0
PR (unconfirmed)	1 (4.8%)
SD	14 (66.7%)
DCR	15 (71.4%)
PD	6 (28.6%)

7 patients were not evaluable for RR (3 DLTs, 3 consent withdrawal and 1 clinical progression)



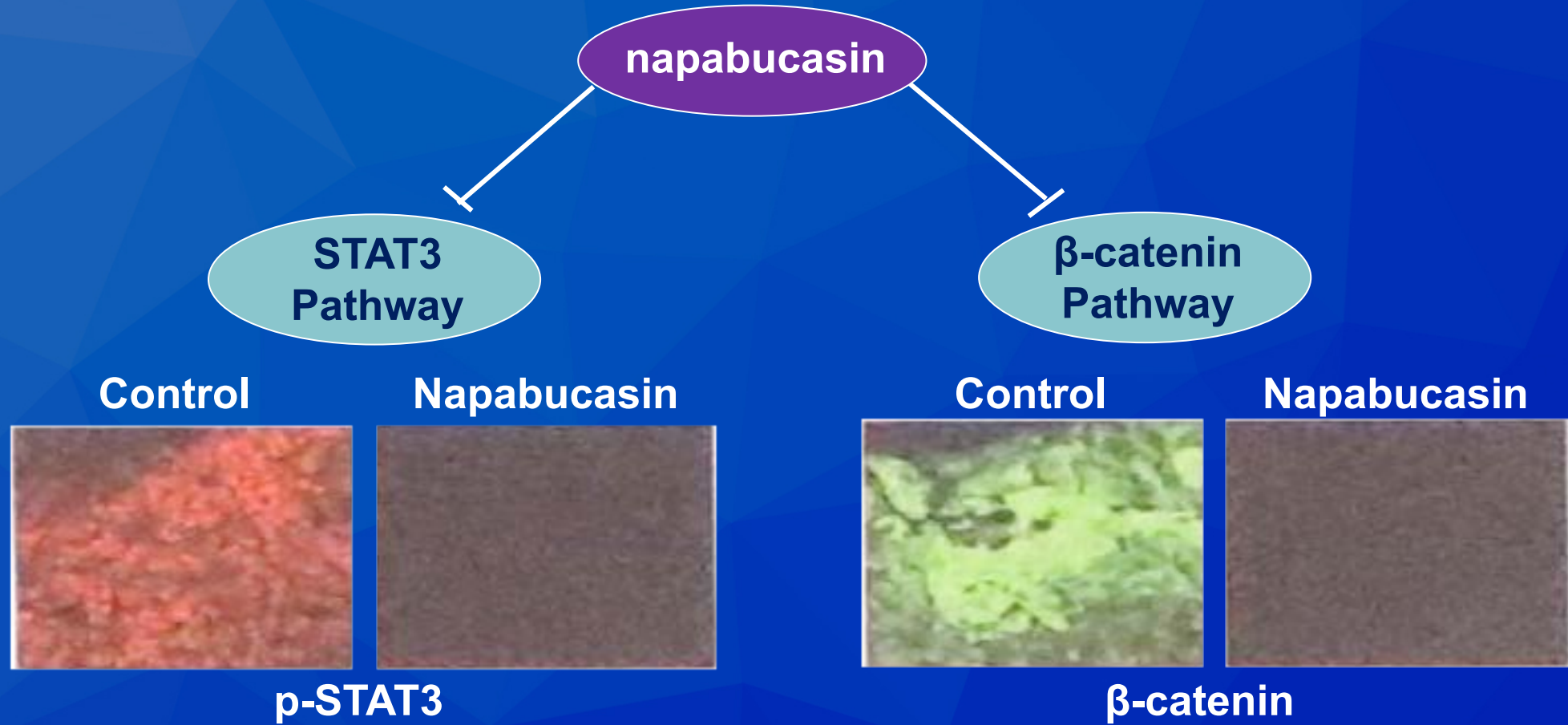
❖ **Appealing combinations:**

- ✓ Interesting phase 2 study: trifluridine/tipiracil + bevacizumab
- ✓ Exploring other combinations e.g.
 - ❑ Cobimetinib + atezolizumab
 - ❑ Regorafenib + nivolumab
 - ❑ IO combinations + TKI

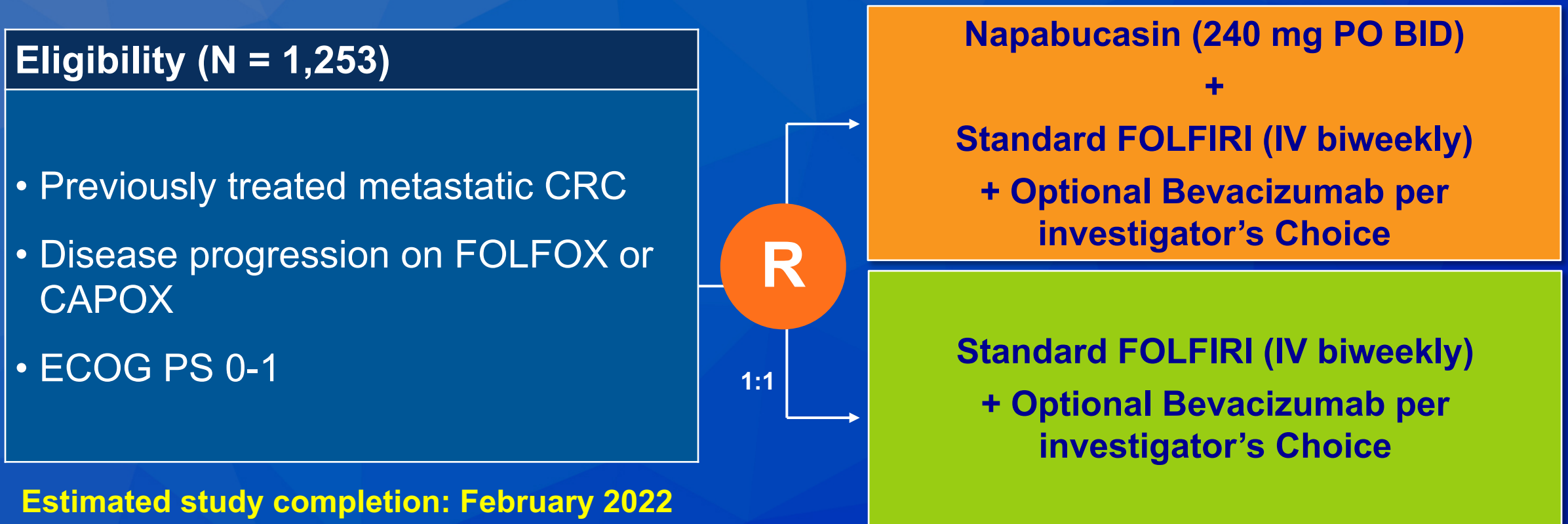
❖ **New drugs:**

- ✓ Napabucasin
- ✓ CAR-T-cells
- ✓

Napabucasin – A First-in-Class Cancer Stemness Inhibitor



Ongoing Phase III CanStem303C Trial Design



Primary endpoint: Overall survival in general population

Secondary endpoints include OS and PFS in predefined biomarker-positive (nuclear beta-catenin and/or pSTAT3-positive) subpopulation, PFS in general population, objective response rate, safety and quality of life



DESTINY-CRC01 Study Design

An open-label, multicenter, phase 2 study (NCT03384940)

Patients

- Unresectable and/or metastatic CRC
- HER2 expressing (central confirmation)
- RAS/BRAF wild type
- ≥ 2 prior regimens
- Prior anti-HER2 treatment was allowed
- Excluded patients with a history of or current/suspected interstitial lung disease

T-DXd 6.4 mg/kg q3w

Cohort A (n = 53)

HER2 Positive (IHC 3+ or IHC 2+/ISH+)

A futility monitoring was done after ≥ 20 patients in Cohort A had 12 weeks of follow-up to inform opening of Cohorts B and C

Cohort B (n = 7)

HER2 IHC 2+/ISH-

Cohort C (n = 18)

HER2 IHC 1+

Primary endpoint

- Confirmed ORR by independent central review (ICR) in Cohort A

Data cutoff: August 9, 2019

- 38.5% (30/78) remained on treatment
- 61.5% discontinued, primarily for progressive disease (41.0%) and clinical progression (9.0%)

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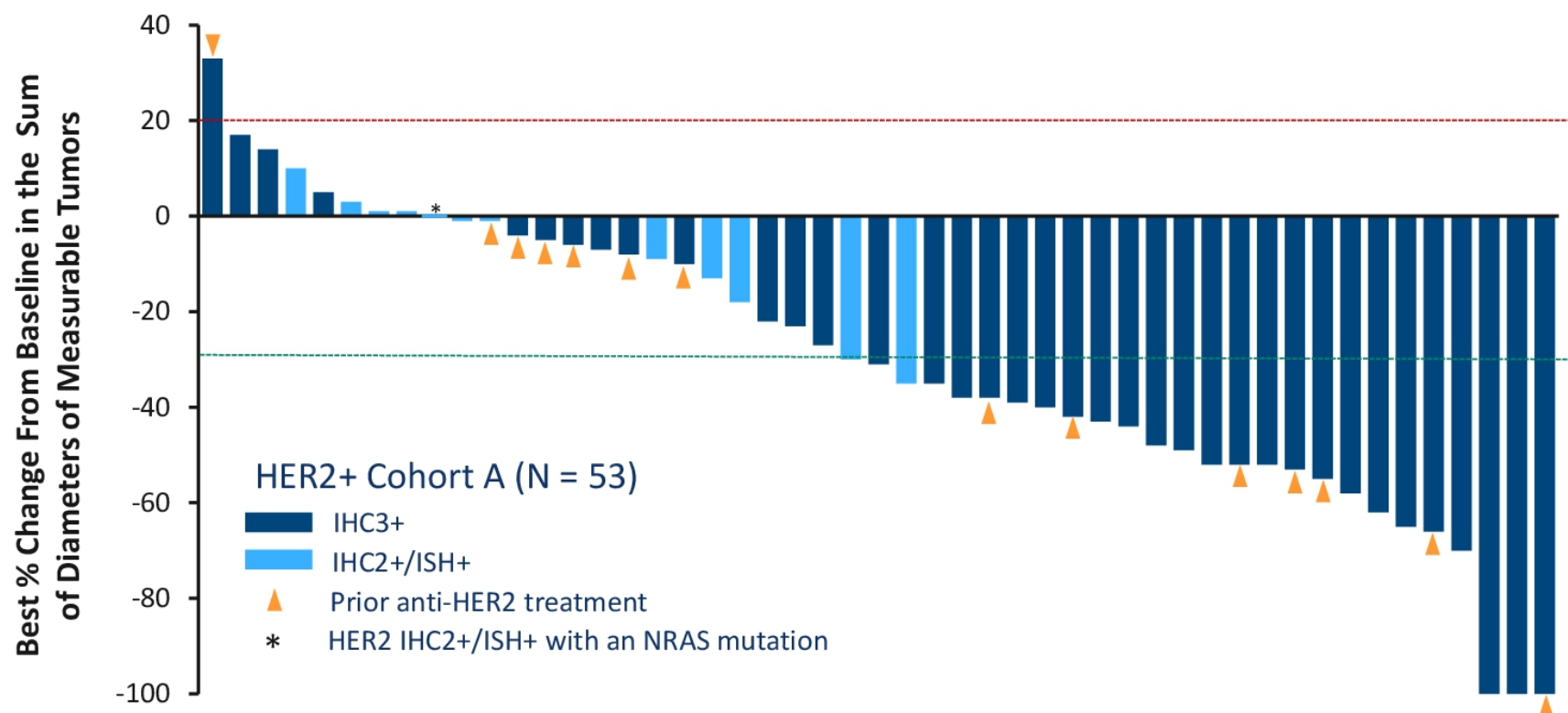
PRESENTED BY: Prof Salvatore Siena; Università degli Studi di Milano, Milan, Italy; salvatore.siena@unimi.it

3



DESTINY-CRC01 Cohort A

Best Change in Tumor Size



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PRESENTED BY: Prof Salvatore Siena; Università degli Studi di Milano, Milan, Italy; salvatore.siena@unimi.it

7



AEs of Special Interest: Interstitial Lung Disease

All Patients (N = 78)						
Preferred Term, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial Lung Disease	0	2 (2.6)	1 (1.3)	0	2 (2.6)	5 (6.4)

Among the 5 total events:

- Median time to investigator-reported onset was 80 days (range, 22-132)
- 5 of 5 patients with grade ≥ 2 ILD received corticosteroids
- 2 patients recovered, 1 did not recover (later died due to disease progression), and 2 died
- In the 2 fatal cases, onset was from 40-126 days, both received steroids as part of treatment, and death occurred 6-18 days after diagnosis

Protocol recommendations: Monitor for symptoms. Hold T-DXd and start steroids as soon as ILD is suspected

Drug related; ILD was determined by an Independent ILD Adjudication Committee based on 44 preferred terms.

One additional grade 5 ILD case in Cohort B was reported after the data cutoff. This case was adjudicated after data cutoff as drug-related ILD.

Agenda

Case 1 – Dr Brenner: 65-yo woman; MSS TMB 11, KRAS G13B mutation, right-sided mCRC

Case 2 – Dr Chen: 62-yo woman; MSI-H, TMB-high mCRC; responds to pembrolizumab → pneumonitis

GI Cancers Journal Club – Part 1: KEYNOTE-177, CHECKMATE 142

Case 3 – Dr Favaro: 55-yo woman; mCRC, KRAS/BRAF mutations, currently on TAS-102/bevacizumab

Case 4 – Dr Brenner: 70-yo woman; MSI-H mCRC; PD-L1-positive, BRAF V600E and sBRCA1 mutations

GI Cancers Journal Club – Part 2: TASCO1, ctDNA in mCRC with BRAF V600E Mutation

Case 5 – Dr Deutsch: 65-yo man; relapsed mCRC, asymptomatic with rising CEA off treatment

Case 6 – Dr Choksi: 34-yo single mother of 2 minor children; extensively treated mCRC

GI Cancers Journal Club – Part 3: GARNET, ICI Combinations, LEAP-005, MORPHEUS, alloSHRINK

A Delayed Path to Diagnosis:

Findings from young-onset colorectal
cancer patients and survivors.

Laura Porter, MD

Medical Affairs Senior Consultant



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Critical Findings

- Young-onset CRC patients are diagnosed at late stages due to multiple challenges around the lack of information or misinformation.
- There is a need for education of the general public and physicians on the signs and symptoms of CRC in those below the screening age.
- Many of the critical issues that occur during treatment, fatigue, emotional and sexual health and financial worries persist after treatment has ended.
- The survey had certain limitations, including gender bias (89% female) and race/ethnicity bias (90% White/Caucasian). The Alliance plans to increase its outreach and enhance diversity among participants in future surveys.

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PRESENTED BY: Laura Porter, MD

#G121

Safety and efficacy of anti-PD-1 antibody dostarlimab in patients (pts) with mismatch repair-deficient (dMMR) solid cancers: Results from GARNET study

Thierry André¹, Dominique Berton², Giuseppe Curigliano³, Susan L. Ellard⁴, Jose Manuel Trigo Perez⁵, Hendrik-Tobias Arkenau⁶, Cyril Abdeddaim⁷, Victor Moreno⁸, Wei Guo⁹, Ellie Im⁹, Naureen Starling¹⁰

¹Sorbonne University and Saint-Antoine Hospital, Paris, France; ²GINECO & Institut de Cancerologie de l'Ouest, Centre René Gauducheau, Saint-Herblain, France; ³Division of Early Drug Development for Innovative Therapies, IEO, European Institute of Oncology IRCCS, and University of Milano, Milan, Italy; ⁴BC Cancer-Kelowna, British Columbia, Canada; ⁵Medical Oncology Department, Hospital Ramón y Cajal, Madrid, Spain; ⁶Sarah Cannon Research Institute UK Limited, London, UK; ⁷Centre de Lutte Contre le Cancer-Centre Oscar Lambret, Lille, France; ⁸START Madrid-FJD, Fundación Jiménez Díaz Hospital, Madrid, Spain; ⁹GlaxoSmithKline, Waltham, MA, USA; ¹⁰ Royal Marsden Hospital NHS Foundation Trust, London and Surrey, UK

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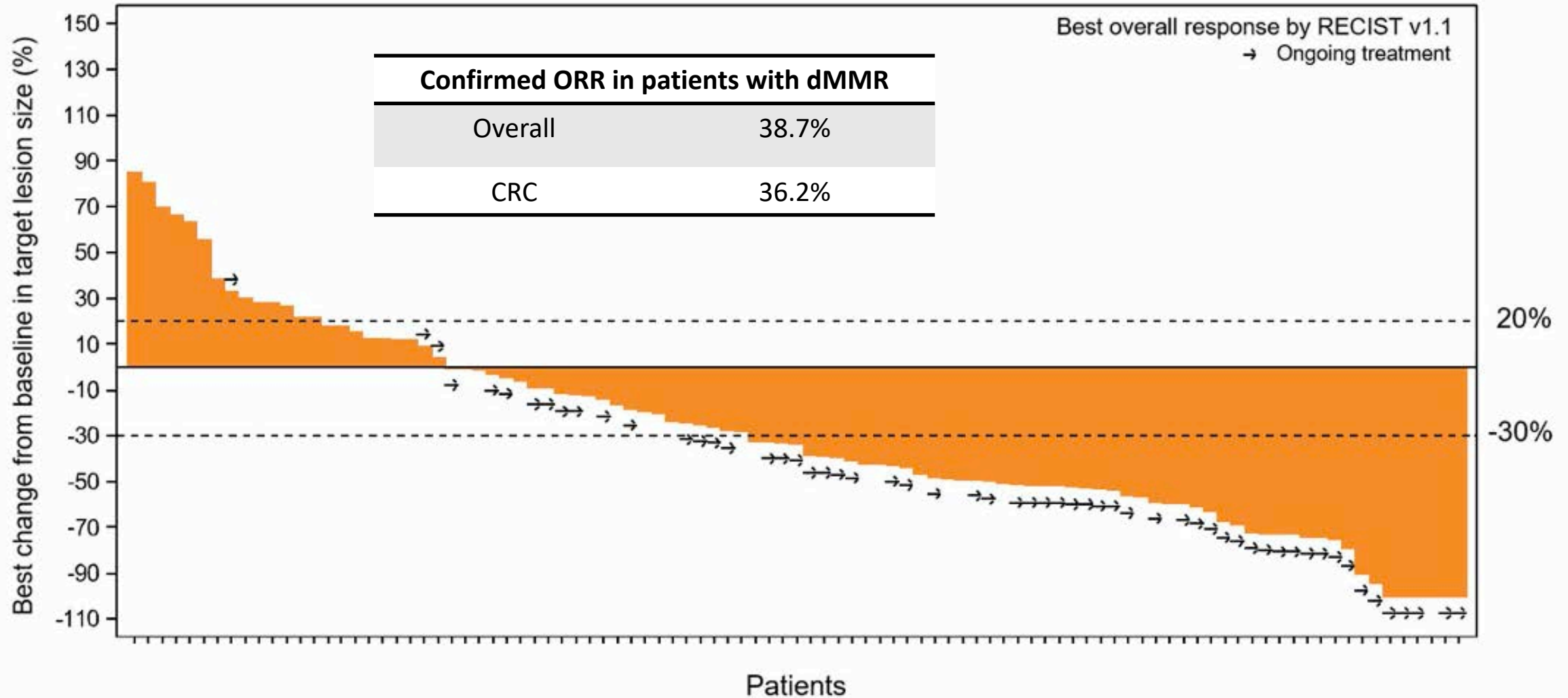
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GARNET: Response and Best Change from Baseline in Target Lesion Size



GARNET: Conclusions

- Majority of patients were enrolled with advanced disease that had progressed on prior therapy with limited treatment options
 - These represent patients with a high unmet need
- Convenient schedule of administration (Q3W for 4 cycles then Q6W)
- Dostarlimab demonstrated durable antitumor activity in a cohort of patients with locally determined dMMR CRC and non-CRC solid tumors
 - Majority of this cohort were GI tumors (93.4% were GI tumors, 65% were CRC tumors)
 - Responses were seen across all tumor types
- No new safety signals were detected and most TRAEs were low grade
 - Only 3.5% of patients discontinued dostarlimab due to a TRAE
 - Grade ≥ 3 TRAEs occurred in 12 (8%) of patients
 - No deaths were attributed to dostarlimab
- Cohort is open for further enrollment
 - Follow-up is ongoing and will be reported at future data cuts
 - Data for the whole cohort with dMMR and MSI determination centrally will be reported in the future

Phase II study of ipilimumab, nivolumab, and panitumumab in patients with *KRAS/NRAS/BRAF* wild-type, microsatellite stable metastatic colorectal cancer

Michael S. Lee, Patrick J. Loehrer, Iman Imanirad, Stacey A. Cohen, Kristen Ciombor, Dominic T. Moore, Cheryl A. Carlson, Hanna K. Sanoff, Autumn J. McRee

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Nivolumab/Ipilimumab/Panitumumab: Response and Tolerability

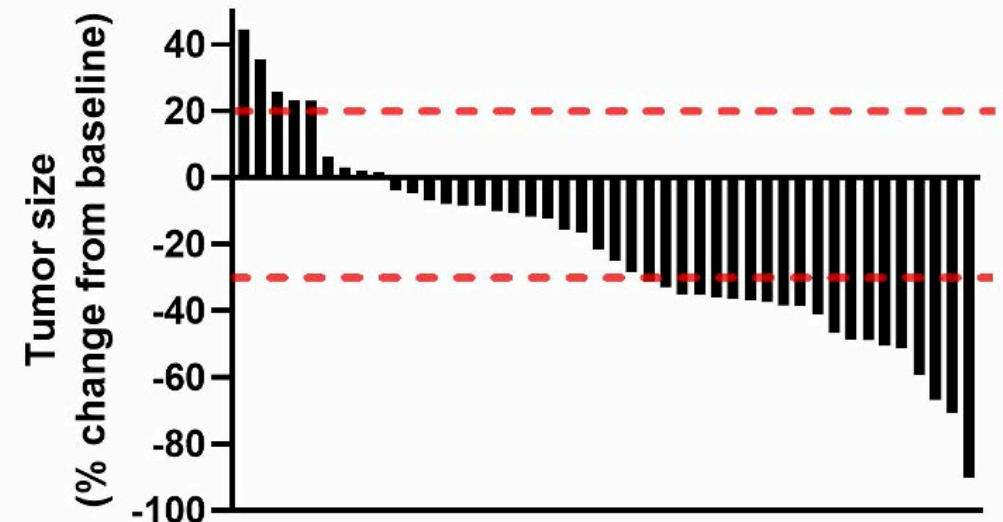
Primary endpoint: Response rate at 12 weeks

Response	% of evaluable subjects (Number) (n=49 evaluable)
Complete Response	0% (0)
Partial Response	35% (17)
Stable Disease	43% (21)
Progression *	22% (11)

We prespecified that **17** 12-week responders would merit further investigation
Therefore the study met its primary endpoint

Toxicity	% (number)
Hypomagnesemia	11% (6)
Rash acneiform	11% (6)
Lipase increased	9% (5)
Amylase increased	7% (4)
ALT increased	5% (3)
AST increased	5% (3)
Diarrhea	5% (3)
Hypophosphatemia	5% (3)
Rash - maculopapular	5% (3)

Best response (confirmed or unconfirmed)



Phase II study of pembrolizumab plus capecitabine and bevacizumab in microsatellite stable (MSS) metastatic colorectal cancer (mCRC): interim analysis

Authors: Andrea Bocobo, Renee Wang, Spencer C. Behr, Julia Carnevale, Pelin Cinar, Eric A. Collisson, Lawrence Fong, Wesley Kidder, Andrew Ko, Pallav K. Kolli, Megan K. Kennedy, Angela Laffan, Sheila Lindsay, Sneha Nalla, Gabriel P. Schwartz, Julia Whitman, Patricia Zendejas, Li Zhang, Katherine Van Loon, Chloe E. Atreya

University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center

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PRESENTED BY: Andrea Bocobo

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Pembrolizumab with Capecitabine/Bevacizumab for MSS mCRC

Table 5: Radiographic Response by RECIST 1.1

	Total N = 29
Evaluable by RECIST 1.1, n (%)	24 (83%) ¹
Best response by RECIST 1.1, n (%)	
Partial response	2 (8%)
Stable disease	14 (59%)
Progressive disease	8 (33%)

¹ 5 patients were unevaluable by RECIST 1.1 at the 12/07/2020 data cutoff; 4 patients discontinued treatment due to clinical progression prior to restaging; 1 patient had not yet completed restaging scans.

- Combination of **pembrolizumab with capecitabine and bevacizumab** was found to be **tolerable** with an **expected toxicity profile** in **MSS mCRC** patients.
- With **2 responses**, the study met interim analysis criteria to continue accrual.
- Tissue and blood-based immune correlatives are planned.

Table 4: Adverse Events (AEs)

Treatment-related AEs	Total (N = 26) ¹ n (%)	
	Grades 1-2 ²	Grade ≥ 3
Patients with any treatment-related AEs	25 (96%)	10 (38%) ³
Fatigue	17 (65%)	0 (0%)
Palmar-plantar erythrodysesthesia	16 (62%)	0 (0%)
Nausea	11 (42%)	0 (0%)
Rash	10 (38%)	0 (0%)
Mucositis	8 (31%)	0 (0%)
Diarrhea	8 (31%)	1 (4%)
Anorexia	8 (31%)	0 (0%)
Skin hyperpigmentation	8 (31%)	0 (0%)
Vomiting	7 (27%)	0 (0%)
Dry skin	7 (27%)	0 (0%)
Constipation	6 (23%)	0 (0%)
Immune-related AEs	Grades 1-2	Grade ≥ 3
Patients with any immune-related AEs ⁴	5 (19%)	0 (0%)
Rash	3 (12%)	0 (0%)
Hypothyroidism	2 (8%)	0 (0%)
Adrenal insufficiency	1 (4%)	0 (0%)
Diarrhea	1 (4%)	0 (0%)

LEAP-005: A Phase II Multicohort Study of Lenvatinib plus Pembrolizumab in Patients with Previously Treated Selected Solid Tumors — Results from the Colorectal Cancer Cohort

Gomez-Roca C et al.

Gastrointestinal Cancers Symposium 2021;Abstract 94.

LEAP-005: Results from the Colorectal Cancer Cohort

Efficacy	N = 32
Overall response rate	22%
Disease control rate	47%
Median duration of response	Not reached
Median progression-free survival	2.3 months
Median overall survival	7.5 months

Author Conclusions: *“In pts with previously treated advanced non–MSI-H/pMMR colorectal cancer, lenvatinib plus pembro demonstrated promising antitumor activity and a manageable safety profile. Enrollment in the colorectal cohort was expanded to 100 pts”.*

Phase Ib/II open-label, randomized evaluation of efficacy and safety of atezolizumab + isatuximab vs regorafenib in MORPHEUS-colorectal cancer

Jayesh Desai,¹ Marwan Fakih,² Katrina Pedersen,³ Yong Sang Hong,⁴ Neil H. Segal,⁵ Simon Allen,⁶ Lorna Bailey,⁷ Christelle Lenain,⁸ Danny Lu,⁹ Pakeeza Sayyed,⁸ Jochen Schulze,⁸ Michael Cecchini,¹⁰

¹Peter MacCallum Cancer Centre, Victoria, Australia; ²City of Hope National Medical Center, Duarte, CA, USA; ³Washington University School of Medicine, St. Louis, MO, USA; ⁴Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; ⁵Memorial Sloan Kettering Cancer Center, New York, NY, USA; ⁶Genentech, Inc., South San Francisco, CA, USA; ⁷Roche Products Limited, Welwyn, UK; ⁸F. Hoffmann-La Roche AG, Basel, Switzerland; ⁹Hoffmann-La Roche Limited, Mississauga, Canada; ¹⁰Yale Cancer Center, New Haven, CT, USA.

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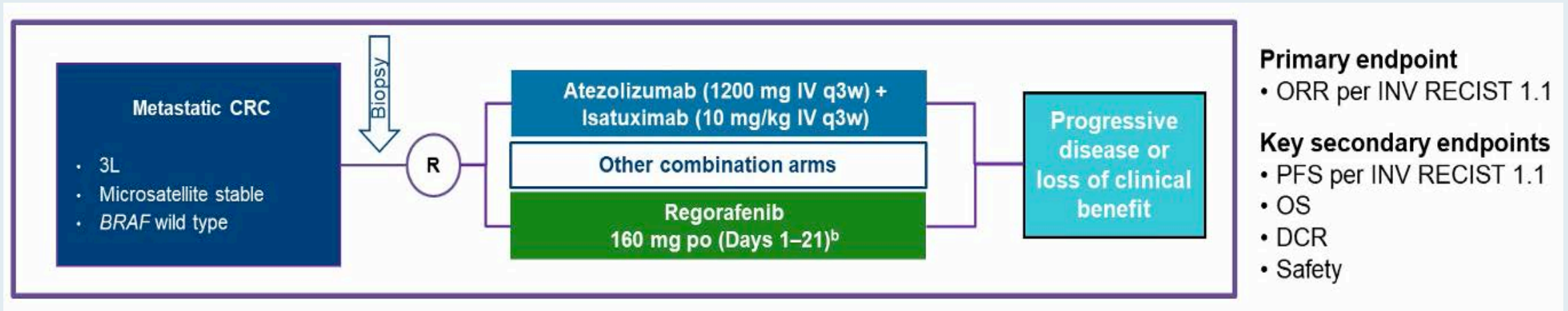
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Presented By Jayesh Desai at 2021 Gastrointestinal Cancers Symposium

MORPHEUS: Study Design and Conclusions



Conclusions

- The atezolizumab + isatuximab combination was well tolerated, with a manageable safety profile
 - The safety profile for this treatment arm was consistent with the known safety profile of the individual study treatments, and no new safety signals were observed
- The atezolizumab + isatuximab combination did not show increased clinical activity compared with regorafenib
- Overall, no correlation was observed between the biomarker data and efficacy

Updated Data from the alloSHRINK Phase 1 First-in-Human Study Evaluating CYAD-101, an Innovative Non-Gene-Edited Allogeneic CAR-T, in Metastatic Colorectal Cancer

Hans Prenen, Jeroen Dekervel, Alain Hendlisz, Sébastien Anguille, Awada Ahmad, Emilie Cerf, Caroline Lonez, Eytan Breman, Marie-Sophie Dheur, Erik Alcantar-Orozco, David E. Gilham, Anne Flament, Frédéric F. Lehmann, Eric Van Cutsem



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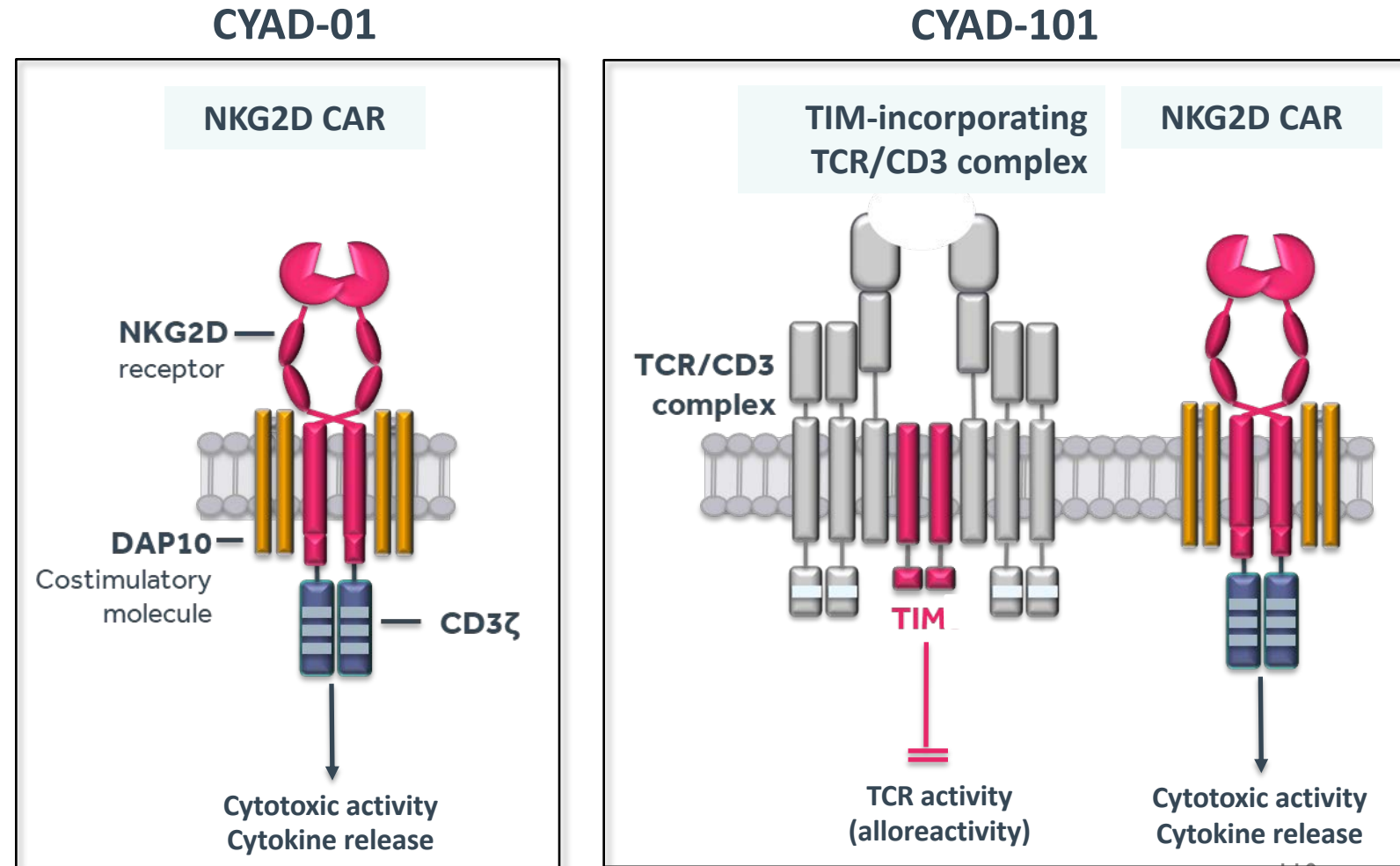
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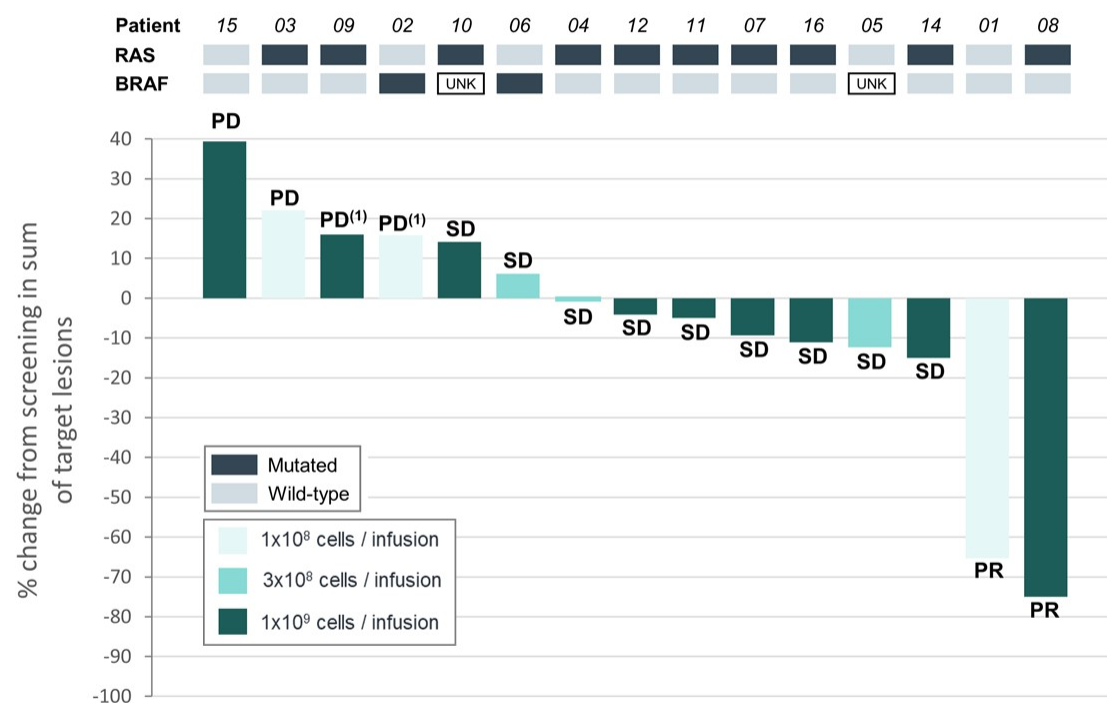
Two NKG2D CAR T-cells: autologous CYAD-01 and allogeneic CYAD-101

- **NKG2D** is an activating receptor expressed on natural killer (NK) cells which binds up to eight ligands expressed on a broad range of malignancies and absent in normal tissues
- **CYAD-01** are **autologous** (patient's own cells) NKG2D-CD3 ζ chimeric antigen receptor (CAR) T-cells
- **CYAD-101** are **allogeneic** (healthy donor-derived) NKG2D-CD3 ζ CAR T-cells co-expressing a TCR inhibitory molecule (TIM) to reduce the alloreactivity



Updated data from the alloSHRINK Phase 1 First-in-Human Study evaluating CYAD-101, an innovative Non-Gene-Edited Allogeneic CAR-T, in mCRC

Results – change of target lesions



PR: Partial response; SD: Stable disease; PD: Progressive disease; UNK: Unknown. (1) Progression of non-target lesions.

The information herein is based on currently available data and is subject to updates.

- At the highest CYAD-101 dose level (n = 9), **6 patients** have shown some evidence of **tumor control** by RECIST 1.1 criteria
- The **median progression free-survival** is **3.94 months** (range: 1.2-8.1 months)
- The **overall survival** is **10.58 months** (range: 1.9-18.7 months)

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PRESENTED BY: Hans Prenen, University Hospital Antwerp

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alloSHRINK: Phase I Study of the Non-Gene-Edited Allogeneic CAR T-Cell Agent CYAD-101 in mCRC

CONCLUSIONS

- At the highest CYAD-101 dose level, six of nine patients have shown some evidence of tumor control by RECIST 1.1 criteria.
- Within this limited dataset, in the patients achieving SD or PR, there was evidence of new T-cell clones entering the hyper-expanded TCR repertoire post-treatment. Moreover, an interesting elevation of Luminex score was observed in the patient with durable partial response after first and second infusions of CYAD-101.
- Pre-clinical studies^{2,3} have shown that CAR T-cell treatment employing the NKG2D receptor-based CAR utilizes both direct anti-tumor activity and elicits the host endogenous immune response. Our observations imply that modulation of the endogenous immune response may be an important mechanism of action of CYAD-101 in mCRC patients. Further testing will be pursued in the on-going expansion phase of the alloSHRINK clinical study to confirm our findings.
- The clinical evaluation of CYAD-101 with therapeutic modalities possessing complementary mechanisms of action, such as checkpoint inhibitors, is strongly warranted and is now being pursued in the KEYNOTE-B79 clinical study due to initiate in 2021.

Second Primary Colorectal Cancer (SPCRC) in Patients with Sporadic Deficient Mismatch Repair (dMMR) Colorectal Cancer (CRC)

Alidina A et al.

Gastrointestinal Cancers Symposium 2021;Abstract 45.

SPCRC in Patients with Sporadic dMMR CRC

Characteristics of SPCRC Cases

	Primary dMMR, n = 11	Primary pMMR, n = 27	P value
SPCRC site			
Right	4 (36%)	7 (26%)	0.49
Left	6 (56%)	13 (48%)	
Rectum	1 (9%)	7 (26%)	
SPCRC MMR status			
dMMR	7 (64%)	7 (26%)	0.019
pMMR	2 (16%)	17 (63%)	
Unknown	2 (16%)	3 (11%)	
SPCRC stage I-III	10 (91%)	22 (81%)	0.65
SPCRC screen detected	8 (73%)	20 (74%)	1

Conclusions:

Patients with an initial dMMR CRC were older and more often had a right sided primary.

Patients with sporadic dMMR CRC had an elevated risk of SPCRC compared to those with a pMMR CRC.

If further data confirms this elevated SPCRC risk, increased colonoscopic surveillance of patients presenting with an initial sporadic dMMR cancer could be considered, where clinically appropriate.

Current Concepts and Recent Advances in Oncology

Real World Oncology Rounds

**A Daylong Clinical Summit Hosted in Partnership with
North Carolina Oncology Association (NCOA) and
South Carolina Oncology Society (SCOS)**

Saturday, February 13, 2021

8:30 AM – 4:30 PM ET

Saturday, February 13, 2021

**8:30 AM — Chronic Lymphocytic
Leukemia and Lymphomas**

John Pagel, Mitchell Smith

9:30 AM — Multiple Myeloma

Paul Richardson, Peter Voorhees

10:45 AM — Genitourinary Cancers

Robert Dreicer, Daniel Petrylak

11:45 AM — Lung Cancer

Justin Gainor, Heather Wakelee

Saturday, February 13, 2021

1:15 PM — Gastrointestinal Cancers

Philip Philip, Eric Van Cutsem

2:15 PM — Breast Cancer

Sara Hurvitz, Ian Krop

**3:30 PM — Acute Myeloid Leukemia
and Myelodysplastic Syndromes**

Courtney DiNardo, Alexander Perl

Thank you for joining us!

***CME credit information will be emailed
to each participant within 3 business days.***