Year in Review: Clinical Investigator Perspectives on the Most Relevant New Data Sets and Advances in Oncology Colorectal Cancer Wednesday, April 19, 2023 5:00 PM – 6:00 PM ET

> Faculty Pashtoon M Kasi, MD, MS Wells A Messersmith, MD

> > Moderator Neil Love, MD



Faculty



Pashtoon M Kasi, MD, MS Director, Colon Cancer Research Director, Liquid Biopsy Research Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine Englander Institute for Precision Medicine Division of Hematology and Medical Oncology NewYork-Presbyterian Hospital/Weill Cornell Medicine New York, New York



MODERATOR Neil Love, MD Research To Practice Miami, Florida



Wells A Messersmith, MD Chief Medical Officer, Oncology Services Professor and Head, Division of Medical Oncology University of Colorado Cancer Center Aurora, Colorado



We Encourage Clinicians in Practice to Submit Questions



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



Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys





ONCOLOGY TODAY WITH DR NEIL LOVE

Management of Gastroesophageal Cancers



DR MANISH SHAH WEILL CORNELL MEDICINE









Dr Manish Shah – Management of Gas Oncology Today with Dr Neil Love —

(15)

What I Tell My Patients: Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Cervical and Endometrial Cancer Wednesday, April 26, 2023 11:15 AM – 12:45 PM CT (12:15 PM – 1:45 PM ET) Faculty Paula J Anastasia, MN, RN, AOCN Michael J Birrer, MD, PhD Jennifer Filipi, MSN, NP Brian M Slomovitz, MD

Breast Cancer Wednesday, April 26, 2023 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)

Faculty Jamie Carroll, APRN, MSN, CNP Virginia Kaklamani, MD, DSc Joyce O'Shaughnessy, MD Ronald Stein, JD, MSN, NP-C, AOCNP **Diffuse Large B-Cell Lymphoma Thursday, April 27, 2023** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)

Faculty Christopher R Flowers, MD, MS Amy Goodrich, CRNP Robin Klebig, APRN, CNP, AOCNP Matthew Lunning, DO

Chronic Lymphocytic Leukemia Thursday, April 27, 2023 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)

Faculty John N Allan, MD Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC Corinne Hoffman, MS, APRN-CNP, AOCNP Adam S Kittai, MD

What I Tell My Patients: Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

HER2-Targeted Antibody-Drug Conjugates Thursday, April 27, 2023 6:00 PM – 7:30 PM CT (7:00 PM – 8:30 PM ET) Faculty

Lyudmila A Bazhenova, MD Kelly EH Goodwin, MSN, RN, ANP-BC Virginia Kaklamani, MD, DSc Caroline Kuhlman, MSN, APRN-BC Alexis N McKinney, MSN, AGNP-BC Zev Wainberg, MD, MSc

Hepatobiliary Cancers Friday, April 28, 2023 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)

Faculty

Ahmed Omar Kaseb, MD, CMQ Blanca Ledezma, MSN, NP, AOCNP Daneng Li, MD Amanda K Wagner, APRN-CNP, AOCNP **Ovarian Cancer Friday, April 28, 2023** 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)

Faculty Courtney Arn, CNP David M O'Malley, MD Richard T Penson, MD, MRCP Jaclyn Shaver, MS, APRN, CNP, WHNP

Lung Cancer

Friday, April 28, 2023 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)

Faculty Stephen V Liu, MD Tara Plues, APRN, MSN Jillian Thompson, MSN, ANP-BC, AOCNP Anne S Tsao, MD, MBA

What I Tell My Patients: Faculty Physicians and Nurses Discuss Patient Education About New Treatments and Clinical Trials

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Acute Myeloid Leukemia, Myelodysplastic Syndromes and Myelofibrosis Saturday, April 29, 2023 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)

Faculty

Ilene Galinsky, NP Daniel A Pollyea, MD, MS Additional faculty to be announced Prostate Cancer Saturday, April 29, 2023 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET) Faculty

Neeraj Agarwal, MD, FASCO Kathy D Burns, RN, MSN, AGACNP-BC, OCN Susan K Roethke, MSN, CRNP, AOCNP, ANP-BC Sandy Srinivas, MD

Beyond The Guidelines: Urologic Oncology Investigators Provide Perspectives on the Optimal Management of Urothelial Bladder Cancer Part 1 of a 2-Part CME Satellite Symposium Series Held in Conjunction with the American Urological Association Annual Meeting 2023 (AUA2023) **Sunday, April 30, 2023** 8:00 AM - 10:00 AM CT (9:00 AM - 11:00 AM ET) Faculty Sia Daneshmand, MD Joshua J Meeks, MD, PhD Matthew Milowsky, MD J Alfred Witjes, MD, PhD **Moderator Arlene Siefker-Radtke, MD**

Beyond The Guidelines: Urologic Oncology Investigators Provide Perspectives on the Optimal Management of Prostate Cancer Part 2 of a 2-Part CME Satellite Symposium Series Held in Conjunction with the American Urological Association Annual Meeting 2023 (AUA2023) **Sunday, April 30, 2023** 6:00 PM - 8:00 PM CT (7:00 PM - 9:00 PM ET) Faculty Himisha Beltran, MD **Stephen J Freedland, MD** Fred Saad, MD **Neal D Shore, MD Moderator** Matthew R Smith, MD, PhD

Year in Review: Clinical Investigator **Perspectives on the Most Relevant New Data Sets** and Advances in Oncology A Multitumor CME/MOC-Accredited Live Webinar Series **Hepatobiliary Cancers Thursday, May 4, 2023** 5:00 PM - 6:00 PM ET **Faculty** Ghassan Abou-Alfa, MD, MBA **Richard S Finn, MD Moderator**

Neil Love, MD



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Commercial Support

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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.



Dr Kasi — Disclosures

Consulting Agreements	AstraZeneca Pharmaceuticals LP, BostonGene, Daiichi Sankyo Inc, Delcath Systems Inc, DoMore Diagnostics, Eisai Inc, Exact Sciences Corporation, Foundation Medicine, Illumina, Incyte Corporation, Lilly, Merck Sharp & Dohme LLC, Natera Inc, NeoGenomics, QED Therapeutics, SAGA Diagnostics AB, Seagen Inc, Servier Pharmaceuticals LLC, Taiho Oncology Inc, Tempus
Scientific Advisory Board Member	Elicio Therapeutics
Stock Options/Ownership — Public Company	Elicio Therapeutics (Angion Biomedica Corp)



Dr Messersmith — Disclosures

Consulting Agreements	Cardiff Oncology, Istari Oncology	
Contracted Research	ALX Oncology, AStar EDDC, BeiGene Ltd, CanBas Co Ltd, Exelixis Inc, Fate Therapeutics, Pfizer Inc, PureTech Health, Mirati Therapeutics Inc, Rascal Therapeutics	
Data and Safety Monitoring Board/Committee	Amgen Inc, QED Therapeutics, Zymeworks Inc	
Unpaid Advisory Board	Pfizer Inc, Takeda Pharmaceuticals USA Inc	
Nonrelevant Financial Relationship	Criterium	



Other Therapeutic Considerations in Colorectal Cancer

Pashtoon Kasi, MD, MS Director, Colon Cancer Research Director, Precision Medicine Research for Liquid Biopsies

pmk4001@med.cornell.edu

🈏 @pashtoonkasi



Englander Institute for Precision Medicine Sandra and Edward Meyer Cancer Center





Cancer Center

Targeted Therapy for Colorectal Cancer



Wells A Messersmith, MD

- Cercek A et al. PD-1 blockade in mismatch repair-deficient, locally advanced rectal cancer. N Engl J Med 2022;386(25):2363-76.
- Chalabi M et al. Neoadjuvant immune checkpoint inhibition in locally advanced MMRdeficient colon cancer: The NICHE-2 study. ESMO 2022; Abstract LBA7.
- Ludford K et al. **Neoadjuvant pembrolizumab** in localized microsatellite instability high/deficient mismatch repair solid tumors. *J Clin Oncol* 2023;[Online ahead of print].
- Diaz LA Jr et al. **Pembrolizumab** versus chemotherapy for microsatellite instability-high or mismatch repair-deficient **metastatic** colorectal **cancer (KEYNOTE-177):** Final analysis of a randomised, open-label, phase 3 study. *Lancet Oncol* 2022;23(5):659-70.
- Overman MJ et al. Nivolumab (NIVO) ± ipilimumab (IPI) in patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Five-year follow-up from CheckMate 142. ASCO 2022;Abstract 3510.



Wells A Messersmith, MD (continued)

- Kopetz S et al. Quality of life with **encorafenib** plus **cetuximab** with or without **binimetinib** treatment in patients with **BRAF V600E-mutant metastatic** colorectal cancer: Patient-reported outcomes from **BEACON CRC**. *ESMO Open* 2022;7(3):100477.
- Tabernero J et al. BREAKWATER safety lead-in (SLI): Encorafenib (E) + cetuximab (C) + chemotherapy (chemo) for BRAFV600E metastatic colorectal cancer (mCRC). ESMO 2022;Abstract LBA26.
- Strickler JH et al. MOUNTAINEER: Open-label, phase 2 study of tucatinib in combination with trastuzumab for HER2-positive metastatic colorectal cancer (SGNTUC-017). ESMO World Congress on Gastrointestinal Cancer 2022;Abstract LBA-2.
- Strickler JH et al. Additional analyses of MOUNTAINEER: A phase II study of tucatinib and trastuzumab for HER2-positive mCRC. ESMO 2022;Abstract LBA27.
- Yaeger R et al. Adagrasib with or without cetuximab in colorectal cancer with mutated KRAS G12C. N Engl J Med 2023;388(1):44-54.



Wells A Messersmith, MD (continued)

 Kuboki Y et al. Sotorasib in combination with panitumumab in refractory KRAS G12Cmutated colorectal cancer: Safety and efficacy for phase Ib full expansion cohort. ESMO 2022;Abstract 3150.



Pashtoon M Kasi, MD

- Cohen SA et al. Real-world monitoring of **circulating tumor DNA** reliably **predicts cancer recurrence** in patients with resected **stages I-III** colorectal cancer. ESMO 2022;Abstract 319MO.
- Kotani D et al. **Molecular residual disease** and efficacy of **adjuvant chemotherapy** in patients with colorectal cancer. *Nat Med* 2023;29(1):127-34.
- Tie J et al. **Circulating tumor DNA** analysis guiding **adjuvant** therapy in **Stage II** colon cancer. *N Engl J Med* 2022;386(24):2261-72.
- Morris VK et al. Treatment of **metastatic** colorectal cancer: ASCO guideline. *J Clin Oncol* 2023;41(3):678-700.
- Yoshino T et al. Panitumumab (PAN) plus mFOLFOX6 versus bevacizumab (BEV) plus mFOLFOX6 as first-line treatment in patients with RAS wild-type (WT) metastatic colorectal cancer (mCRC): Results from the phase 3 PARADIGM trial. ASCO 2022;Abstract LBA1.



Pashtoon M Kasi, MD (continued)

- Cremolini C et al. Modified FOLFOXIRI plus panitumumab (mFOLFOXIRI/PAN) versus mFOLFOX6/PAN as initial treatment of patients with unresectable RAS and BRAF wild-type metastatic colorectal cancer (mCRC): Results of the phase III randomized TRIPLETE study by GONO. ASCO 2022;Abstract LBA3505.
- Martinelli E et al. Evidence of therapeutic effectiveness of third-line cetuximab rechallenge in appropriately selected patients: Findings from long-term follow-up of CRICKET and CAVE trials. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract O-7.
- Tabernero J et al. Trifluridine/tipiracil plus bevacizumab for third-line treatment of refractory metastatic colorectal cancer: The phase 3 randomized SUNLIGHT study. Gastrointestinal Cancers Symposium 2023;Abstract 4.



Pashtoon M Kasi, MD (continued)

- Taieb J et al. Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer: Final results from the phase IIIb single-arm PRECONNECT study by duration of therapy. BMC Cancer 2023;23(1):94.
- Dasari NA et al. FRESCO-2: A global phase III multiregional clinical trial (MRCT) evaluating the efficacy and safety of fruquintinib in patients with refractory metastatic colorectal cancer. ESMO 2022;Abstract LBA25.
- Burnett H et al. Impact of regorafenib dose optimization on comparative outcomes in the treatment of relapsed/refractory metastatic colorectal cancer (mCRC). ESMO 2022;Abstract 400P.



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DPYD Testing: Time to Put Patient Safety First

Sharyn D. Baker, PharmD, PhD¹; Susan E. Bates, MD²; Gabriel A. Brooks, MD³; William L. Dahut, MD⁴; Robert B. Diasio, MD⁵; Wafik S. El-Deiry, MD, PhD⁶; William E. Evans, PharmD⁷; William D. Figg, PharmD, MBA⁸; Dan L. Hertz, PharmD, PhD⁹; J. Kevin Hicks, PharmD, PhD¹⁰; Suneel Kamath, MD¹¹; Pashtoon Murtaza Kasi, MD¹²; Todd C. Knepper, PharmD¹⁰; Howard L. McLeod, PharmD¹³; Peter H. O'Donnell, MD¹⁴; Mary V. Relling, PharmD⁷; Michelle A. Rudek, PharmD, PhD¹⁵; Tristan M. Sissung, PhD⁸; D. Max Smith, PharmD¹⁶; Alex Sparreboom, PhD¹; Sandra M. Swain, MD¹⁶; and Christine M. Walko, PharmD¹⁰



J Clin Oncol 2023;[Online ahead of print].

2021;20(6):961-74

MOLECULAR CANCER THERAPEUTICS | REVIEW

Innate Immune Checkpoint Inhibitors: The Next Breakthrough in Medical Oncology?

Robert W. Lentz¹, Meryl D. Colton², Siddhartha S. Mitra³, and Wells A. Messersmith¹



Trial in Progress: A Phase II Study (with Safety Run-In) of Evorpacept (ALX148), Cetuximab, and Pembrolizumab in Patients with Refractory Mircrosatellite Stable Metastatic Colorectal Cancer (AGICC-ALX148 21CRC01, NCT05167409)

Lentz RW et al.

Gastrointestinal Cancers Symposium 2023; Abstract TPS257.



Evorpacept: Structure and Mechanism of Action





Lentz RW et al. Gastrointestinal Cancers Symposium 2023; Abstract TPS257.

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MODULE 8: KRAS G12C-Mutant CRC — Dr Messersmith



ASCO Guidelines for mCRC

• Morris VK et al. Treatment of **metastatic** colorectal cancer: ASCO guideline. *J Clin Oncol* 2023;41(3):678-700.



7 key practice questions



1. For patients with previously untreated, initially unresectable mCRC who are candidates for chemotherapy plus bevacizumab, is <u>doublet</u> (folinic acid, FU, and oxaliplatin [FOLFOX], or folinic acid, FU, and irinotecan [FOLFIRI]) or <u>triplet</u> (folinic acid, FU, oxaliplatin, and irinotecan [FOLFOXIRI]) cytotoxic chemotherapy recommended?

2a. In the first-line setting, are outcomes for patients with microsatellite instabilityhigh (MSI-H) or deficient mismatch repair (dMMR) mCRC improved with pembrolizumab immunotherapy versus chemotherapy with or without bevacizumab or cetuximab?

2b. Is pembrolizumab recommended as later-line therapy for patients with microsatellite stable (MSS) or proficient mismatch repair (pMMR) mCRC and high tumor mutational burden (TMB = 10 mutations/ Mb)?

3. For patients with treatment-naive **<u>RAS wild-type mCRC</u>**, are anti–epidermal growth factor receptor (EGFR) antibodies (ie, panitumumab and cetuximab) recommended for patients with right-sided or left-sided primary tumors?

Morris VK et al. Treatment of metastatic colorectal cancer: ASCO guideline. J Clin Oncol 2023;41(3):678-700.

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7 key practice questions



4. For patients with previously treated **<u>BRAF V600E– mutant</u>** mCRC, does treatment with encorafenib plus cetuximab result in better outcomes compared with chemotherapy plus targeted therapy?

5. For patients with colorectal **peritoneal metastases**, are outcomes improved with cytoreductive surgery (CRS) with or without hyperthermic intraperitoneal chemotherapy (HIPEC) plus chemotherapy, compared with chemotherapy alone?

6. For patients with <u>unresectable liver-limited mCRC</u>, are liver-directed therapies stereotactic body radiation therapy (SBRT) and selective internal radiation therapy (SIRT) recommended?

7. For patients with mCRC and potentially curable one constraints with mCRC and potentially curable one constraints are constrained and potentially curable on the constraints are constrained and constraints are constrained and constraints are constraints and constraints are constrai

Morris VK et al. Treatment of metastatic colorectal cancer: ASCO guideline. J Clin Oncol 2023;41(3):678-700.

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Checkpoint Inhibitors for Microsatellite Instability-High and Microsatellite-Stable CRC

- Cercek A et al. **PD-1 blockade** in mismatch repair-deficient, **locally advance**d rectal cancer. *N Engl J Med* 2022;386(25):2363-76.
- Chalabi M et al. **Neoadjuvan**t immune checkpoint inhibition in **locally advanced** MMRdeficient colon cancer: The **NICHE-2** study. ESMO 2022;Abstract LBA7.
- Ludford K et al. **Neoadjuvant pembrolizumab** in localized microsatellite instability high/deficient mismatch repair solid tumors. *J Clin Oncol* 2023;[Online ahead of print].
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- Overman MJ et al. Nivolumab (NIVO) ± ipilimumab (IPI) in patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Five-year follow-up from CheckMate 142. ASCO 2022;Abstract 3510.



Dual Blockade in dMMR/MSI-H rectal cancer

NICHE-2 study design

Investigator-initiated, non-randomized multicenter* study



specimen-Circulating tumor DNA dynamics

Courtesy of Wells A Messersmith, MD

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Chalabi, ESMO 2022
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Major pathologic response in 95% of patients; 67% pCR







Courtesy of Wells A Messersmith, MD





Safety and efficacy analogous to approved anti-PD-1 mAbs^{3,4}

- > 650 patients treated; 8 ongoing trials / 2 completed
- Complete blocker of PD-1-PD-L1/2 interactions
- Enhanced T cell activation and effector function

1. El-Khoueiry AB. SITC 2021 Annual Meeting. Poster #479. 2. Waight et al. Cancer Cell. 2018;33(6): 1033-1047. 3. O'Malley, et al. Gynecol Oncol. 2021; 163: 274-280. 4. O'Malley et al, J Clin Oncol. 2022; 40(7): 762-771.

El-Khoueiry A. Botensilimab, a novel innate/adaptive immune activator, plus balstilimab (anti-PD-1) for metastatic heavily pretreated microsatellite stable colorectal cancer. Courtesy of Pashtoon M Kasi, MD, MS

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MODULE 8: KRAS G12C-Mutant CRC — Dr Messersmith



Circulating Tumor DNA (ctDNA) in CRC

- Cohen SA et al. **Real-world monitoring** of circulating tumor DNA **reliably predicts cancer recu**rrence in patients with **resected stages I-III** colorectal cancer. ESMO 2022;Abstract 319MO.
- Kotani D et al. **Molecular residual disease** and efficacy of **adjuvant chemotherapy** in patients with colorectal cancer. *Nat Med* 2023;29(1):127-34.
- Tie J et al. Circulating tumor DNA analysis guiding adjuvant therapy in Stage II colon cancer. N Engl J Med 2022;386(24):2261-72.





Courtesy of Pashtoon M Kasi, MD, MS

ctDNA: Dawn of a New Era

LocationAvailable On DemandTimeSat, Jun 4, 2022 | 9:00 AM - 10:30 AM EDTTrack(s)Special Sessions



Liquid Biopsies (ctDNA) in Clinic for Colorectal Cancer



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Malla M, Loree JM, Kasi PM, Parikh AR. Using Circulating Tumor DNA in Colorectal Cancer: Current and Evolving Practices. J Clin Oncol. 2022 Aug 20;40(24):2846-2857. PMID: 35839443.



Tumor-informed Platforms Versus **Tumor-agnostic** (tumor-uninformed or plasma-only) Platforms



Courtesy of Pashtoon M Kasi, MD, MS

Kasi PM. ctDNA Assays: Exploring Their Clinical Use in Oncology Care. January 2022. ASCO Daily News.







Courtesy of Pashtoon M Kasi, MD, MS

Kasi PM. ctDNA Assays: Exploring Their Clinical Use in Oncology Care. January 2022. ASCO Daily News.

The NEW ENGLAND JOURNAL of MEDICINE

Conclusion/Key Takeaways

- A ctDNA-guided approach to the treatment of stage II colon cancer <u>reduced adjuvant</u> <u>chemotherapy use</u> without compromising recurrence-free survival.
- <u>Real-world utility especially in</u> <u>stage-II colon cancer where</u> <u>the ctDNA is positive</u>.



Tie J et al. Circulating tumor DNA analysis guiding adjuvant therapy in Stage II colon cancer. N Engl J Med 2022;386(24):2261-72.

Courtesy of Pashtoon M Kasi, MD, MS

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Later-Line Treatment of mCRC

- Tabernero J et al. Trifluridine/tipiracil plus bevacizumab for third-line treatment of refractory metastatic colorectal cancer: The phase 3 randomized SUNLIGHT study. Gastrointestinal Cancers Symposium 2023;Abstract 4.
- Taieb J et al. Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer:
 Final results from the phase IIIb single-arm PRECONNECT study by duration of therapy. BMC Cancer 2023;23(1):94.
- Dasari NA et al. **FRESCO-2**: A global **phase III** multiregional clinical trial (MRCT) evaluating the efficacy and safety of **fruquintinib** in patients with refractory **metastatic** colorectal cancer. ESMO 2022;Abstract LBA25.
- Burnett H et al. Impact of **regorafenib dose optimization** on comparative outcomes in the treatment of relapsed/refractory **metastatic** colorectal cancer (mCRC). ESMO 2022;Abstract 400P.



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Conclusion/Key Takeaways

- TAS-102+BEV or FTD/TPI+BEV represents a new standard of care.
 - 3rd line or postprogression on maintenance CAPE+BEV for those getting triplet+biologic.
- PFS and OS very meaningful.
- <u>Was already in use</u> since NCCN guideline inclusion in 2022.



Kasi PM et al. Colorectal Cancer. Lancet Oct 2019. Cancer. Lancet Oct 2019.

10. Burnett H et al. Impact of regorafenib dose optimization on comparative outcomes in the treatment of relapsed/refractory metastatic colorectal cancer (mCRC). ESMO 2022;Abstract 400P.

Courtesy of Pashtoon M Kasi, MD, MS

Conclusion/Key Takeaways

- TAS-102 or FTD/TPI and now with the recent SUNLIGHT DATA on this oral systemic therapy with BEV patients rarely have to come off due to toxicity.
- <u>Chemotherapy-induced</u>
 <u>neutropenia</u> not
 necessarily an adverse issue.



EGFR

VEGF

OX

IRI

5-FU

TAS

REG

Months since stard treatment Months versus 55 months; Log-rank P-value < 0.0001 for patients who activities of the stard treatment (CIN) ≥ grade 2 CTCAE (red line – 69 patients (32.9 months; versus 2.0 months; versus 2.0

Kasi PM. BMC Cancer. 2016. PMID: 27412464.



🔰 @pashtoonkasi

RETi

HER2i

NTRK

BRAFi

Immuno

therapy

Kasi PM et al. Colorectal Cancer. Lancet Oct 2019.

10. Burnett H et al. Impact of regorafenib dose optimization on comparative outcomes in the treatment of relapsed/refractory metastatic colorectal cancer (mCRC). ESMO 2022;Abstract 400P.

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Anti-HER2 Treatment for CRC

- Strickler JH et al. MOUNTAINEER: Open-label, phase 2 study of tucatinib in combination with trastuzumab for HER2-positive metastatic colorectal cancer (SGNTUC-017). ESMO World Congress on Gastrointestinal Cancer 2022; Abstract LBA-2.
- Strickler JH et al. Additional analyses of MOUNTAINEER: A phase II study of tucatinib and trastuzumab for HER2-positive mCRC. ESMO 2022; Abstract LBA27.





Primary analysis of MOUNTAINEER: A phase 2 study of tucatinib and trastuzumab for HER2-positive mCRC

John H. Strickler, Andrea Cercek, Salvatore Siena, Thierry Andre, Kimmie Ng, Eric Van Cutsem, Christina Wu, Andrew Scott Paulson, Joleen M. Hubbard, Andrew L. Coveler, Christos Fountzilas, Adel Kardosh, Pashtoon Murtaza Kasi, Heinz-Josef Lenz, Kristen Ciombor, Elena Elez, David L. Bajor, Michael Stecher, Wentao Feng, Tanios S. Bekaii-Saab

European Society of Medical Oncology World Congress on Gastrointestinal Cancer. Jun 29-Jul 2, 2022. Abstract LBA-2

Courtesy of Wells A Messersmith, MD

Tucatinib + Trastuzumab: Change in Tumor Size



CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

Data cutoff: 28 Mar 2022

Courtesy of Wells A Messersmith, MD

Strickler, ESMO 2022

MOUNTAINEER-03: Global, Randomised, Open-Label, Phase 3 Trial



a Stratification: Primary tumor sidedness, liver metastases; b Levoleucovorin may be given in place of leucovorin; c Alpha-controlled

1L, first line; BICR, blinded independent central review; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; mCRC, metastatic colorectal cancer; mFOLFOX6, 5-fluorouracil, leucovorin, and oxaliplatin; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomisation; RAS, rat sarcoma virus; RECIST, Response Evaluation Criteria in Solid Tumors. https://clinicaltrials.gov/ct2/show/NCT05253651

Strickler, ESMO 2022

Agenda

Introduction

MODULE 1: ASCO Guidelines for Metastatic Colorectal Cancer (mCRC) — Dr Kasi MODULE 2: Checkpoint Inhibitors for MSI-H and MSS CRC — Dr Messersmith MODULE 3: Circulating Tumor DNA (ctDNA) in CRC — Dr Kasi

MODULE 4: Later-Line Treatment of mCRC — Dr Kasi

MODULE 5: Anti-HER2 Treatment for CRC — Dr Messersmith

MODULE 6: EGFR Antibodies for CRC — Dr Kasi

MODULE 7: Targeted Treatment of BRAF-Mutant CRC — Dr Messersmith

MODULE 8: KRAS G12C-Mutant CRC — Dr Messersmith



EGFR Antibodies for CRC

- Yoshino T et al. Panitumumab (PAN) plus mFOLFOX6 versus bevacizumab (BEV) plus mFOLFOX6 as firstline treatment in patients with RAS wild-type (WT) metastatic colorectal cancer (mCRC): Results from the phase 3 PARADIGM trial. ASCO 2022;Abstract LBA1.
- Cremolini C et al. Modified FOLFOXIRI plus panitumumab (mFOLFOXIRI/PAN) versus mFOLFOX6/PAN as initial treatment of patients with unresectable RAS and BRAF wild-type metastatic colorectal cancer (mCRC): Results of the phase III randomized TRIPLETE study by GONO. ASCO 2022; Abstract LBA3505.
- Martinelli E et al. Evidence of therapeutic effectiveness of third-line cetuximab rechallenge in appropriately selected patients: Findings from long-term follow-up of CRICKET and CAVE trials. ESMO World Congress on Gastrointestinal Cancer 2022;Abstract O-7.



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MODULE 8: KRAS G12C-Mutant CRC — Dr Messersmith



Targeted Treatment of BRAF-Mutant CRC

- Kopetz S et al. Quality of life with **encorafenib** plus **cetuximab** with or without **binimetinib** treatment in patients with BRAF V600E-mutant **metastatic** colorectal cancer: Patient-reported outcomes from **BEACON CRC**. *ESMO Open* 2022;7(3):100477.
- Tabernero J et al. BREAKWATER safety lead-in (SLI): Encorafenib (E) + cetuximab (C) + chemotherapy (chemo) for BRAFV600E metastatic colorectal cancer (mCRC). ESMO 2022;Abstract LBA26.



What is next for BRAF MT mCRC?



Not a comprehensive list....

Courtesy of Wells A Messersmith, MD

Enrolling

Completed

Agenda

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MODULE 1: ASCO Guidelines for Metastatic Colorectal Cancer (mCRC) — Dr Kasi MODULE 2: Checkpoint Inhibitors for MSI-H and MSS CRC — Dr Messersmith MODULE 3: Circulating Tumor DNA (ctDNA) in CRC — Dr Kasi MODULE 4: Later-Line Treatment of mCRC — Dr Kasi MODULE 5: Anti-HER2 Treatment for CRC — Dr Messersmith MODULE 6: EGFR Antibodies for CRC — Dr Kasi

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KRAS G12C-Mutant CRC

- Yaeger R et al. **Adagrasib** with or without **cetuximab** in colorectal cancer with mutated KRAS G12C. *N Engl J Med* 2023;388(1):44-54.
- Kuboki Y et al. Sotorasib in combination with panitumumab in refractory KRAS G12Cmutated colorectal cancer: Safety and efficacy for phase Ib full expansion cohort. ESMO 2022;Abstract 3150.



Appendix



ORIGINAL ARTICLE

Treatment modalities and long-term outcomes of hepatic hemangioendothelioma in the United States

Christof Kaltenmeier¹, Silvia Stacchiotti², Alessandro Gronchi³, Gonzalo Sapisochin⁴, Hao Liu¹, Eishan Ashwat¹, Vikraman Gunabushanam¹, Dheera Reddy¹, Ann Thompson¹, David Geller¹, Samer Tohme¹, Amer Zureikat¹ & Michele Molinari¹

¹Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, USA, ³Department of Cancer Medicine, ³Departmento of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, and ⁴Department of Surgery, University of Toronto, Toronto, Canada



HPB

HPB (Oxford) 2022;24(10):1688-96.

MOUNTAINEER: Global, Open-Label, Phase 2 Trial



MOUNTAINEER began as a US Investigator-Sponsored Trial and initially consisted of a single cohort (Cohort A) and was expanded globally to include patients randomised to receive tucatinib + trastuzumab (Cohort B) or tucatinib monotherapy (Cohort C)

Data cut-off for current analysis, March 28, 2022

a Each treatment cycle is 21 days; b Patients remained on therapy until evidence of radiographic or clinical progression, unacceptable toxicity, withdrawal of consent, or study closure; c Stratification: Left sided tumor primary vs other; d Patients were allowed to cross over and receive tucatinib and trastuzumab if they experienced radiographic progression at any time point or if they had not achieved a PR or CR by week 12; e Patients had HER2+ tumors as defined by one or more protocol required local tests: IHC 3+ (n=46), amplification by ISH (n=36), or amplification by NGS (n=69)

2L+, second line and later; BICR, blinded independent central review; BID, twice a day; C1D1, cycle 1 day 1; CR, complete response; DOR, duration of response; HER2, human epidermal growth receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; mAb, monoclonal antibody; mCRC, metastatic colorectal cancer; NGS, next-generation sequencing; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PO, orally; Q3W, every 3 weeks; PR, partial response; R, randomisation; RAS, rat sarcoma virus; RECIST, Response Evaluation Criteria in Solid Tumors; US, United States; VEGF, vascular endothelial growth factor.

Courtesy of Wells A Messersmith, MD

Strickler, ESMO 2022

https://clinicaltrials.gov/ct2/show/NCT03043313

Tucatinib + Trastuzumab: Efficacy Outcomes

	Tucatinib + Trastuzumab
	Cohorts A+B
Responses	n=84
Best overall response per BICR ^a , n (%)	
CR	3 (3.6)
PR	29 (34.5)
SD ^b	28 (33.3)
PD	22 (26.2)
Not available ^c	2 (2.4)
cORR per BICR, % (95% CI) ^d	38.1 (27.7, 49.3)
cORR per Investigator, % (95% CI) ^d	42.9 (32.1, 54.1)
Median time to objective response per BICR ^e , months (range)	2.1 (1.2, 9.8)
DCR ^f per BICR, n (%)	60 (71.4)
Median DOR per BICR, months (95% CI)	12.4 (8.5, 20.5)

a Confirmed best overall response assessed per RECIST 1.1; b Includes SD and non-CR/non-PD; c Includes patients with no post-baseline response assessment and patients whose disease assessments are not evaluable; d Two-sided 95% exact confidence interval, computed using the Clopper-Pearson method (1934); e Time from the start of study treatment (Cohort A) or date of randomisation (Cohort B) to the first documentation of objective response (CR or PR that is subsequently confirmed); f Defined as sum of CR, PR, and SD

BICR, blinded independent central review; cORR, confirmed objective response rate; CR, complete response; DCR, disease control rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease. Courtesy of Wells A Messersmith, MD

Strickler, ESMO 2022

Data cutoff: 28 Mar 2022

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Cervical and Endometrial Cancer

Wednesday, April 26, 2023 11:15 AM – 12:45 PM CT (12:15 PM – 1:45 PM ET) Faculty Paula J Anastasia, MN, RN, AOCN Michael J Birrer, MD, PhD Jennifer Filipi, MSN, NP Brian M Slomovitz, MD

Breast Cancer Wednesday, April 26, 2023 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)

Faculty

Jamie Carroll, APRN, MSN, CNP Virginia Kaklamani, MD, DSc Joyce O'Shaughnessy, MD Ronald Stein, JD, MSN, NP-C, AOCNP **Diffuse Large B-Cell Lymphoma Thursday, April 27, 2023** 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)

Faculty Christopher R Flowers, MD, MS Amy Goodrich, CRNP Robin Klebig, APRN, CNP, AOCNP Matthew Lunning, DO

Chronic Lymphocytic Leukemia Thursday, April 27, 2023 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)

Faculty John N Allan, MD Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC Corinne Hoffman, MS, APRN-CNP, AOCNP Adam S Kittai, MD

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

HER2-Targeted Antibody-Drug Conjugates Thursday, April 27, 2023 6:00 PM – 7:30 PM CT (7:00 PM – 8:30 PM ET) Faculty

Lyudmila A Bazhenova, MD Kelly EH Goodwin, MSN, RN, ANP-BC Virginia Kaklamani, MD, DSc Caroline Kuhlman, MSN, APRN-BC Alexis N McKinney, MSN, AGNP-BC Zev Wainberg, MD, MSc

Hepatobiliary Cancers Friday, April 28, 2023 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)

Faculty

Ahmed Omar Kaseb, MD, CMQ Blanca Ledezma, MSN, NP, AOCNP Daneng Li, MD Amanda K Wagner, APRN-CNP, AOCNP **Ovarian Cancer** Friday, April 28, 2023 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET)

Faculty Courtney Arn, CNP David M O'Malley, MD Richard T Penson, MD, MRCP Jaclyn Shaver, MS, APRN, CNP, WHNP

Lung Cancer

Friday, April 28, 2023 6:00 PM – 8:00 PM CT (7:00 PM – 9:00 PM ET)

Faculty Stephen V Liu, MD Tara Plues, APRN, MSN Jillian Thompson, MSN, ANP-BC, AOCNP Anne S Tsao, MD, MBA

What I Tell My Patients: Expert Insights into Patient Education on New Treatments and Clinical Trial Participation

Fifteenth Annual RTP Symposium Series Held During the Annual ONS Congress

Acute Myeloid Leukemia, Myelodysplastic Syndromes and Myelofibrosis Saturday, April 29, 2023 6:00 AM – 7:30 AM CT (7:00 AM – 8:30 AM ET)

Faculty

Ilene Galinsky, NP Daniel A Pollyea, MD, MS Additional faculty to be announced Prostate Cancer Saturday, April 29, 2023 12:15 PM – 1:45 PM CT (1:15 PM – 2:45 PM ET) Faculty

Neeraj Agarwal, MD, FASCO Kathy D Burns, RN, MSN, AGACNP-BC, OCN Susan K Roethke, MSN, CRNP, AOCNP, ANP-BC Sandy Srinivas, MD

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.

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

