Investigator Perspectives on the Current Utility of Validated and Emerging Biomarkers to Guide Treatment Decision-Making for Patients with Metastatic Colorectal Cancer

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematologists-oncologists, hematology-oncology fellows and other healthcare providers involved in the treatment of gastrointestinal cancers.

OVERVIEW OF ACTIVITY

Cancer of the colon or rectum is the fourth most frequently diagnosed cancer and the second most common cause of cancer-related death in the United States. In the year 2019, it is estimated that 145,600 people will be diagnosed with colon or rectal cancer in the United States, representing a continued decline over the past few decades thought to be related to improvements in detection and treatment.

Published results from ongoing trials continually lead to the emergence of new therapeutic targets and regimens, thereby altering management algorithms, and in order to offer optimal patient care, including the option of clinical trial participation, the practicing medical oncologist must be well informed of these advances. To bridge the gap between research and patient care, this program features a roundtable discussion with 2 leading gastrointestinal oncology investigators. By providing access to the latest scientific developments and the perspectives of experts in the field, this CME activity assists medical oncologists with the formulation of up-to-date management strategies.

LEARNING OBJECTIVES

- Coordinate comprehensive biomarker analysis for patients diagnosed with metastatic colorectal cancer (mCRC), and use this information to guide evidence-based care.
- Develop an understanding of the prognostic and predictive implications of tumor sidedness, and use this information to counsel patients regarding guideline-endorsed therapeutic options.
- Consider patient and disease characteristics, including primary tumor location and potentially targetable genetic abnormalities (eg, BRAF, HER2) to inform the selection of first- and later-line therapy for mCRC.
- Communicate the benefits and risks of approved anti-VEGF, anti-EGFR and other systemic therapies to patients with newly diagnosed and progressive mCRC, and develop an evidence-based algorithm for sequencing these available options.
- Appraise the recent FDA approvals of nivolumab, pembrolizumab and the combination of nivolumab/ipilimumab for patients with microsatellite instability-high or mismatch repair-deficient mCRC, and appropriately integrate these agents into current nonresearch treatment algorithms.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

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AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2.25 Medical Knowledge MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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MODERATOR — **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, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech, Genmab, Genomic Health Inc, Gilead Sciences Inc, Guardant Health, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite Pharma Inc, 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, Seattle Genetics, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, Teva Oncology, Tokai Pharmaceuticals Inc and Tolero Pharmaceuticals.

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Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 11 or later, Firefox 56 or later, Chrome 61 or later, Safari 11 or later, Opera 48 or later
Adobe Flash Player 27 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

Last review date: May 2019

Expiration date: May 2020

Select Publications

Amanam I et al. **Lower tumor mutational burden (TMB) and hepatic metastases may predict for lack of response to PD-1 blockade in MSI-H metastatic colorectal cancer (MCRC).** *Proc ESMO* 2018;**Abstract 535P**.

Arnold D et al. **Prognostic and predictive value of primary tumour side in patients with RAS wild-type metastatic colorectal cancer treated with chemotherapy and EGFR directed antibodies in six randomized trials.** *Ann Oncol* 2017;28(8):1713-29.

Battaglin F et al. **Microsatellite instability in colorectal cancer: Overview of its clinical significance and novel perspectives.** *Clin Adv Hematol Oncol* 2018;16(11):735-45.

Boeckx N et al. **The predictive value of primary tumor location in patients with metastatic colorectal cancer: A systematic review.** *Crit Rev Oncol Hematol* 2018;121:1-10.

Cohen R et al. **Assessment of local clinical practice for testing of mismatch repair deficiency in metastatic colorectal cancer: The need for new diagnostic guidelines prior to immunotherapy.** *Proc ESMO* 2018;**Abstract 537P**.

Cremolini C et al. **FOLFOXIRI plus bevacizumab versus FOLFIRI plus bevacizumab as first-line treatment of patients with metastatic colorectal cancer: Updated overall survival and molecular subgroup analyses of the open-label, phase 3 TRIBE study.** *Lancet Oncol* 2015;16(13):1306-15.

Das RK et al. **Causal modeling of CALGB/SWOG 80405 (Alliance) identifies primary (1°) side-related angiogenic drivers of metastatic colorectal cancer (mCRC).** *Proc ESMO* 2018;**Abstract 458PD**.

Dienstmann R et al. **Molecular subtypes and the evolution of treatment decisions in metastatic colorectal cancer.** *Am Soc Clin Oncol Educ Book* 2018;(38):231-8.

Heinemann V et al. **Somatic DNA mutations, tumor mutational burden (TMB), and MSI status: Association with efficacy in patients (pts) with metastatic colorectal cancer (mCRC) of FIRE-3 (AIO KRK-0306).** *Proc ASCO* 2018;**Abstract 3591**.

Hoyer L, Schmidt N. **Verification of guideline conform mCRC treatment with EGFR inhibitors with real world evidence data from EU5 countries.** *Proc ESMO* 2018;**Abstract 489P**.

Innocenti F et al. **Mutational analysis of patients with colorectal cancer in CALGB/SWOG 80405 identifies new roles of microsatellite instability and tumor mutational burden for patient outcome.** *J Clin Oncol* 2019;[Epub ahead of print].

Jeong JH et al. **HER2 amplification and cetuximab efficacy in patients with metastatic colorectal cancer harboring wild-type RAS and BRAF.** *Clin Colorectal Cancer* 2017;16(3):e147-52.

Kopetz S et al. **Randomized trial of irinotecan and cetuximab with or without vemurafenib in BRAF-mutant metastatic colorectal cancer (SWOG 1406).** Gastrointestinal Cancers Symposium 2017;**Abstract 520**.

Le DT et al. **PD-1 blockade in tumors with mismatch repair deficiency.** *N Engl J Med* 2015;372(26):2509-20.

Lee JJ, Chu E. **Recent advances in the clinical development of immune checkpoint blockade therapy for mismatch repair proficient (pMMR)/non-MSI-H metastatic colorectal cancer.** *Clin Colorectal Cancer* 2018;17(4):258-73.

Lenz HJ et al. **Durable clinical benefit with nivolumab (NIVO) plus low-dose ipilimumab (IPI) as first-line therapy in microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC).** *Proc ESMO* 2018;**Abstract LBA18_PR**.

Lenz HJ et al. **Impact of consensus molecular subtyping (CMS) on overall survival (OS) and progression free survival (PFS) in patients with metastatic colorectal cancer (mCRC): Analysis of CALGB/SWOG 80405 (Alliance).** *Proc ASCO* 2017;**Abstract 3511**.

Loree JM et al. **Classifying colorectal cancer by tumor location rather than sidedness highlights a continuum in mutation profiles and consensus molecular subtypes.** *Clin Cancer Res* 2018;24(5):1062-72.

Loupakis F et al. **Impact of primary tumour location on efficacy of bevacizumab plus chemotherapy in metastatic colorectal cancer.** *Br J Cancer* 2018;119(12):1451-5.

Loupakis F et al. **Primary tumor location as a prognostic factor in metastatic colorectal cancer.** *J Natl Cancer Inst* 2015;107(3):dju427.

Marginean EC, Melosky B. **Is there a role for programmed death ligand-1 testing and immunotherapy in colorectal cancer with microsatellite instability? Part I — Colorectal cancer: Microsatellite instability, testing, and clinical implications.** *Arch Pathol Lab Med* 2018;142(1):17-25.

Marginean EC, Melosky B. **Is there a role for programmed death ligand-1 testing and immunotherapy in colorectal cancer with microsatellite instability? Part II — The challenge of programmed death ligand-1 testing and its role in microsatellite instability-high colorectal cancer.** *Arch Pathol Lab Med* 2018;142(1):26-34.

Select Publications

Morano F et al. **Negative hyper-selection of RAS wild-type (wt) metastatic colorectal cancer (mCRC) patients randomized to first-line FOLFOX plus panitumumab (pan) followed by maintenance therapy with either 5FU/LV plus pan or single-agent pan: Translational analyses of the VALENTINO study.** *Proc ESMO* 2018;**Abstract LBA22**.

Normanno N et al. **RAS testing of liquid biopsy correlates with the outcome of metastatic colorectal cancer patients treated with first-line FOLFIRI plus cetuximab in the CAPRI-GOIM trial.** *Ann Oncol* 2018;29(1):112-8.

Ou SI et al. **Liquid biopsy to identify actionable genomic alterations.** *Am Soc Clin Oncol Educ Book* 2018;(38):978-97.

Overman MJ et al. **Durable clinical benefit with nivolumab plus ipilimumab in DNA mismatch repair-deficient/microsatellite instability-high metastatic colorectal cancer.** *J Clin Oncol* 2018;36(8):773-9.

Overman MJ et al. **Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): An open-label, multicentre, phase 2 study.** *Lancet Oncol* 2017;18(9):1182-191.

Parikh A et al. **Prolonged response to HER2-directed therapy in a patient with HER2-amplified, rapidly progressive metastatic colorectal cancer.** *J Natl Compr Canc Netw* 2017;15(1):3-8.

Rich TA et al. **RET rearrangements may arise following anti-EGFR therapy in advanced colorectal cancer.** *Proc ESMO* 2018;**Abstract 482P**.

Ross JS et al. **Targeting HER2 in colorectal cancer: The landscape of amplification and short variant mutations in ERBB2 and ERBB3.** *Cancer* 2018;124(7):1358-73.

Sartore-Bianchi A et al. **Dual-targeted therapy with trastuzumab and lapatinib in treatment-refractory, KRAS codon 12/13 wild-type, HER2-positive metastatic colorectal cancer (HERACLES): A proof-of-concept, multicentre, open-label, phase 2 trial.** *Lancet Oncol* 2016;17(6):738-46.

Schirripa M et al. **Biomarker-driven and molecular targeted therapies for colorectal cancers.** *Semin Oncol* 2018;45(3):124-32.

Sclafani F. **PD-1 inhibition in metastatic dMMR/MSI-H colorectal cancer.** *Lancet Oncol* 2017;18(9):1141-2.

Sepulveda AR et al. **Molecular biomarkers for the evaluation of colorectal cancer: Guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and the American Society of Clinical Oncology.** *J Clin Oncol* 2017;35(13):1453-86.

Seufferlein T et al. **A novel biomarker combination and its association with resistance to chemotherapy combinations with bevacizumab: First results of the PERMAD trial.** *Proc ESMO* 2018;**Abstract 474P**.

Shaikh T et al. **Mismatch repair deficiency (dMMR) testing in patients with colorectal cancer and nonadherence to testing guidelines in young adults.** *JAMA Oncol* 2018;4(2):e173580.

Siena S et al. **Final results of the HERACLES trial in HER2-amplified colorectal cancer.** *Proc AACR* 2017;**Abstract CT005**.

Stintzing S et al. **Impact of BRAF and RAS mutations on first-line efficacy of FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab: Analysis of the FIRE-3 (AIO KRK-0306) study.** *Eur J Cancer* 2017;79:50-60.

Sunakawa Y et al. **Gene mutation status in circulating tumor DNA (ctDNA) and first-line FOLFOXIRI plus bevacizumab (bev) in metastatic colorectal cancer (mCRC) harboring RAS mutation.** *Proc ESMO* 2018;**Abstract 543P**.

Tejpar S et al. **Prognostic and predictive relevance of primary tumor location in patients with RAS wild-type metastatic colorectal cancer: Retrospective analyses of the CRYSTAL and FIRE-3 trials.** *JAMA Oncol* 2017;3(2):194-201.

Van Cutsem E et al. **BEACON CRC study safety lead-in: Assessment of the BRAF inhibitor encorafenib + MEK inhibitor binimetinib + anti-epidermal growth factor receptor antibody cetuximab for BRAFV600E metastatic colorectal cancer.** *Proc ESMO World Congress on Gastrointestinal Cancer* 2018;**Abstract O-027**.

Venook AP et al. **Impact of primary (1°) tumor location on overall survival (OS) and progression-free survival (PFS) in patients (pts) with mCRC: Analysis of CALGB/SWOG 80405 (Alliance).** *Proc ASCO* 2016;**Abstract 3504**.

Wei XL et al. **The clinical and biomarker association of programmed death ligand 1 and its spatial heterogeneous expression in colorectal cancer.** *J Cancer* 2018;9(23):4325-33.