Colorectal Cancer Update

Issue 1, 2019

(Video Program)

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 death among all neoplasms in the United States. In the year 2018, it is estimated that 140,250 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, *Colorectal Cancer Update* uses one-on-one discussion with 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

- Consider comprehensive biomarker analysis for patients diagnosed with colorectal cancer (CRC), and use this information to guide evidence-based care.
- Develop a long-term care plan for individuals diagnosed with metastatic CRC (mCRC), considering patient and disease characteristics, including biomarker profile, tumor location, prior systemic therapy, symptomatology and personal goals of treatment.
- Recall the recent FDA approvals of anti-PD-1 and anti-CTLA-4 antibodies for microsatellite instability-high or mismatch repair-deficient mCRC, and appropriately integrate these agents into current treatment algorithms.
- Describe ongoing research to validate or identify additional biomarkers predictive of response to immune checkpoint inhibitors in mCRC, and use this information to guide trial design and future clinical practice.
- Recall new data with investigational agents demonstrating promising activity in CRC, and use this information to refer appropriate patients for participation in ongoing trials.

ACCREDITATION STATEMENT

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CREDIT DESIGNATION STATEMENT

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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 1.75 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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HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should review the CME information, watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/CCU119/Video/CME**. The corresponding audio program is available as an alternative at **ResearchToPractice.com/CCU119**.

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

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Advisory Committee: Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Celgene Corporation, Lilly, Merck KGaA, Darmstadt, Germany, Merck Sharp & Dohme Corp, Novartis, Roche Laboratories Inc, Servier; **Paid Research:** Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Ipsen Biopharmaceuticals Inc, Lilly, Merck, Merck KGaA, Darmstadt, Germany, Novartis, Roche Laboratories Inc, Servier.

EDITOR — **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 Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech, 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, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, 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 Inc, Teva Oncology and Tokai Pharmaceuticals Inc.

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This activity is supported by educational grants from Bayer HealthCare Pharmaceuticals, Lilly and Taiho Oncology Inc.

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: January 2019

Expiration date: January 2020

Select Publications

Andre T et al. **Nivolumab + ipilimumab combination in patients with DNA mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) metastatic colorectal cancer (mCRC): First report of the full cohort from CheckMate-142.** Gastrointestinal Cancers Symposium 2018;**Abstract 553**.

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.

Bardelli A et al. **Plasma *HER2 (ERBB2)* copy number to predict response to HER2-targeted therapy in metastatic colorectal cancer.** *Proc ASCO* 2018;**Abstract 3506**.

Bekaii-Saab TS et al. **Regorafenib dose optimization study (ReDOS): Randomized phase II trial to evaluate dosing strategies for regorafenib in refractory metastatic colorectal cancer (mCRC) — An ACCRU Network study.** Gastrointestinal Cancers Symposium 2018;**Abstract 611**.

Bendell J et al. **Phase Ib/II study of cancer stemness inhibitor napabucasin in combination with FOLFIRI +/- bevacizumab (bev) in metastatic colorectal cancer (mCRC) patients (pts).** ESMO World Congress on Gastrointestinal Cancer 2017;**Abstract LBA-003**.

Corcoran RB et al. **Combined BRAF, EGFR, and MEK inhibition in patients with *BRAF*^{V600E}-mutant colorectal cancer.** *Cancer Discov* 2018;8(4):428-43.

Diaz LA et al. **Keynote-177: Phase 3, open-label, randomized study of first-line pembrolizumab (Pembro) versus investigator-choice chemotherapy for mismatch repair-deficient (dMMR) or microsatellite instability-high (MSI-H) metastatic colorectal carcinoma (mCRC).** Gastrointestinal Cancers Symposium 2018;**Abstract TPS877**.

Grothey A et al. **Fluoropyrimidine (FP) + bevacizumab (BEV) + atezolizumab vs FP/BEV in BRAFwt metastatic colorectal cancer (mCRC): Findings from Cohort 2 of MODUL — A multicentre, randomized trial of biomarker-driven maintenance treatment following first-line induction therapy.** *Proc ESMO* 2018;**Abstract LBA19**.

Hamauchi S et al. **Neutropenia as a predictive factor in metastatic colorectal cancer treated with TAS-102.** *Clin Colorectal Cancer* 2017;16(1):51-7.

Jones JC et al. **$^{Non\text{-}V600}$ BRAF mutations define a clinically distinct molecular subtype of metastatic colorectal cancer.** *J Clin Oncol* 2017;35(23):2624-30.

Le DT et al. **KEYNOTE-164: Pembrolizumab for patients with advanced microsatellite instability high (MSI-H) colorectal cancer.** *Proc ASCO* 2018;**Abstract 3514**.

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

Lemery S et al. **First FDA approval agnostic of cancer site — When a biomarker defines the indication.** *N Engl J Med* 2017;377(15):1409-12.

Lenz H 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**.

Lesniewski-Kmak K et al. **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 primary analysis.** *Proc ESMO World Congress on Gastrointestinal Cancer* 2018;**Abstract O-022**.

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):1182-91.

Salem ME et al. **Clinicopathological differences and survival outcomes with first-line therapy in patients with left-sided colon cancer and rectal cancer: Pooled analysis of 2879 patients from AGITG (MAX), COIN, FOCUS2, OPUS, CRYSTAL and COIN-B trials in the ARCAD database.** *Eur J Cancer* 2018;103:205-13.

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

Tabernero J et al. **Phase Ia and Ib studies of the novel carcinoembryonic antigen (CEA) T-cell bispecific (CEA CD3 TCB) antibody as a single agent and in combination with atezolizumab: Preliminary efficacy and safety in patients with metastatic colorectal cancer (mCRC).** *Proc ASCO* 2017;**Abstract 3002**.

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**.

Select Publications

Van Cutsem E et al. **Regorafenib for patients with metastatic colorectal cancer who progressed after standard therapy: Results of the large, single-arm, open-label phase IIIb CONSIGN study.** *Oncologist* 2018;[Epub ahead of print].

Van Cutsem E et al; RECOURSE Study Group. **The subgroups of the phase III RECOURSE trial of trifluridine/tipiracil (TAS-102) versus placebo with best supportive care in patients with metastatic colorectal cancer.** *Eur J Cancer* 2018;90:63-72.

Van Cutsem E, Dekervel J. **Not all BRAF-mutant metastatic colorectal cancers are identical: Distinct clinical consequences of $^{non\text{-}V600}$BRAF mutations.** *J Clin Oncol* 2017(23):2598-9.

Van Cutsem E et al. **ESMO consensus guidelines for the management of patients with metastatic colorectal cancer.** *Ann Oncol* 2016;27(8):1386-422.

Xu J et al. **Results of a randomized, double-blind, placebo-controlled, phase III trial of trifluridine/tipiracil (TAS-102) monotherapy in Asian patients with previously treated metastatic colorectal cancer: The TERRA study.** *J Clin Oncol* 2018;36(4):350-58.