

Cost-Effectiveness of New and Emerging Treatment Options for the Treatment of Metastatic Colorectal Cancer

Jennifer Zadlo, PharmD, BCOP

The Impact of Metastatic Disease on CRC

In the United States, colon cancer and rectal cancer are the third most common form of cancer in both men and women. An estimated 140,250 new cases of colorectal cancer (CRC) are expected to be diagnosed in this country in 2018, including 75,610 cases in men and 64,640 in women. In addition, 50,630 deaths are expected from CRC in the same year, totaling 27,390 deaths among men and 23,240 deaths among women. Overall, CRC is expected to comprise 9% of the total new cancer cases in the male population in the United States and 7% of all cancers in women, along with 8% of all cancer deaths for both genders.¹

While the overall number of cases of CRC and deaths from the disease have been steadily decreasing since the early 1990s, the actual incidence of CRC is increasing in people younger than 50 years. The number of expected deaths has risen likely because of the very poor prognosis for people who are diagnosed with metastatic CRC (mCRC) from initial presentation.² Approximately 21% of patients with CRC are diagnosed with metastatic spread upon initial diagnosis, and another 50% to 60% of all patients who presented with earlier stage CRC will eventually develop metastases. A staggering 80% to 90% of these patients will have unresectable liver metastases.³ Advances in systemic therapies have improved overall survival for patients with mCRC. These may include combining multiple approaches and therapies, ranging from surgery to chemotherapy and targeted biologic treatments. That said, patterns of treatment choice and resulting medical care usage and costs can differ depending upon the phase of mCRC and other factors impacting patient care and healthcare usage.^{4,5}

The Cost Implications of mCRC

The economic costs associated with CRC and its management generally vary by many factors, including stage of disease at diagnosis, patient age, the observation time included in an individual analysis (specified time period vs lifetime costs), types of medical services included, and the overall scope of the costs considered in an investigation. Data in general have been complex to assess and compare because there can be substantial heterogeneity across

ABSTRACT

Cancer of the colon and rectum is now the third most common form of cancer in the United States in both women and men. Approximately 21% of patients with colorectal cancer (CRC) are diagnosed with metastatic spread upon initial presentation, and 50% to 60% of all patients with earlier stage CRC will eventually develop metastases. Advances in systemic therapies have improved overall survival for patients with metastatic CRC (mCRC), but with an increasing cost burden on the healthcare system. Patterns of treatment choice and resulting medical care usage and costs can differ depending on patient-specific characteristics, impacting overall patient care and healthcare usage. The economic burden associated with CRC and its management is affected by several factors, including stage of disease at diagnosis, patient age, time period studied, oncologic therapy choice, and point of view. Available data assessing cost impact have recently been emerging; however, they are complex to interpret given the substantial heterogeneity among study population and the types and duration of analyses.

Am J Manag Care. 2018;24(7):S118-S124

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TABLE. Costs and Healthcare Utilization Associated with Metastatic Colorectal Cancer^{4,5,7,8}

Author	Study Design	Time Frame	Outcomes
Paramore et al	Retrospective case control study: 2795 mCRC cases matched to 699 non-mCRC controls (age, sex, geographic region, and duration of plan enrollment)	Claims data: 1998-2004	3 phases of disease, cost per month ^a : <ul style="list-style-type: none"> • Diagnostic phase: \$12,205 • Treatment phase: \$4722 • Death phase: \$12,328
Song et al	Retrospective analysis to assess patterns of medical care in 6675 patients with newly diagnosed mCRC	Claims data: January 2004-July 2009	3 phases of disease, cost per month ^a : <ul style="list-style-type: none"> • Diagnostic phase: \$16,895 • Treatment phase: \$8891 • Death phase: \$27,554
Chastek et al	Retrospective review that assessed costs and usage of 589 patients with mCRC: grouped as newly diagnosed patients with mCRC versus those who were initially diagnosed with nonmetastatic CRC and developed metastatic disease later, but by the time of study enrollment	4 years of data from the Oncology Management Registry	Mean unadjusted total cost per patient studied (medical + pharmaceutical costs): \$252,200. Highest contributors: <ul style="list-style-type: none"> • Mean cost of outpatient hospital visits: \$71,334 • Mean inpatient hospitalization costs: \$58,124 (accounted for one-third of the \$176,135 unadjusted mean cost for medical services) • Mean chemotherapy costs: \$31,112 • Mean biologic agent cost: \$38,276

CRC indicates colorectal cancer; mCRC, metastatic colorectal cancer.

^aThese phases were defined as: diagnostic phase, covering the first (index) month after initial diagnosis and up to 2 months following the index month; treatment phase, covered all subsequent months after diagnosis until the death phase (if death occurred); death phase, covered 3 months of follow-up, including 2 months before the patient's death and the month of death.

studies and in the factors and variables included in each of those individual analyses. However, comparisons of data within a health organization and between different systems can assist clinicians in better comprehending the potential significance of differences in cancer care policies and how they affect costs and clinical management. In addition, understanding the extent to which such data can be compared is crucial for economic evaluations of all aspects of cancer care, including therapeutic interventions.⁶

A MEDLINE literature search for cost-effectiveness of mCRC treatment in the United States was conducted. One early study by Paramore et al retrospectively studied use patterns and healthcare costs for patients with newly diagnosed mCRC, reviewing assessments of claims data from selected US health insurance plans. Details of this study are highlighted in the **Table**.^{4,5,7,8} This analysis showed that the incremental cost difference in the follow-up period averaged \$97,031 more for mCRC cases than for those in the control arm. Notable cost drivers in this analysis were hospitalizations (\$37,369) and specialist visits (\$34,582), including chemotherapy administration. Approximately 40% of the 672 patients in the phase analysis experienced a fatal event during follow-up. Mean and median monthly costs increased during the study period, unrelated to any particular disease phase. The investigators concluded that the overall economic burden of mCRC is substantial for patients insured by commercial health plans in this country, and that costs of care have increased significantly in recent years.⁷ It is noteworthy that this study included claims data from 1998 through 2004, making the application of these results limited. Several therapies

currently used in the treatment of mCRC were FDA approved late during this time, or after this study was conducted. Oxaliplatin was FDA approved in 2002, and both bevacizumab and cetuximab were FDA approved in February of 2004. Although this study demonstrated the substantially increasing economic impact of mCRC, most patients would likely not have received treatment with the newer, more costly agents that are currently considered standard of care. Caution should be exercised when extrapolating these results to current day.

Song et al also performed an analysis to assess patterns of medical care in patients with newly diagnosed mCRC. Patients in this study were selected from a sizeable US insurance claims database. These patients were observed from their initial diagnosis until death, disenrollment, or end of the study period, whichever occurred first. Patterns of medical care were analyzed via different (and mutually exclusive) service categories, including outpatient, inpatient, emergency department, outpatient pharmacy, chemotherapy, and biologic therapy. Data measured estimated aggregate and category costs monthly. Details of the study are summarized in the **Table**. While the treatment phase was the least expensive, it also had the longest duration, with a mean 16.4 months, compared with the diagnostic and death phases at 2.8 months and 2.4 months, respectively. Inpatient care was the highest cost component in both the diagnostic phase, accounting for 41.7% of costs, and the death phase at 71.4% of costs. However, inpatient care accounted for only 17.9% of total care costs for patients in the treatment phase. In contrast, outpatient care was the leading cost driver in

the treatment phase, accounting for 45% of total costs. In terms of actual treatments, biologic agents contributed 7.7%, 17.6%, and 4.1% of costs for the diagnostic, treatment, and death phases, respectively, versus chemotherapy, which accounted for 11.5%, 15.6%, and 2.9% of costs in the diagnosis, treatment, and death phases, respectively. Overall, the study demonstrated notable differences in the patterns and costs related to healthcare usage in different phases of mCRC management.⁴

Additional variables also have an impact on healthcare costs and usage in patients with mCRC. A review by Chastek et al assessed costs and usage by initial CRC stage upon diagnosis and the number of treatment lines received by patients with mCRC. Details of this study are listed in the Table. Linked healthcare claims from a US health insurance database were incorporated into this analysis to delineate both healthcare costs and patient characteristics. A 4-year estimate of total healthcare costs stratified by disease stage and patient characteristics was the key endpoint, with follow-up terminated by patient death, insurance plan disenrollment, or study conclusion. Overall, estimated 4-year total costs showed that CRC stage at diagnosis and the number of lines of treatment a patient received after metastasis were substantial cost drivers. Variables associated with a statistically significant ($P < .05$) cost included gender, patient age group, and comorbidity index score following development of metastases. Total overall 4-year costs were greatest among patients who presented initially with mCRC and lowest among those with stage 3 disease who later developed metastatic spread.⁵

These studies demonstrate the substantial heterogeneity that exists across studies evaluating healthcare costs associated with the treatment of mCRC, making it difficult to draw meaningful comparisons and conclusions. These studies demonstrate the continually rising high costs associated with this disease, in addition to the need for structured studies evaluating costs across healthcare organizations.

Cost-Effectiveness of Treatments: Delineating Differences in Therapies Used

Systemic therapy with chemotherapy plus biologic therapy or targeted therapy remains the backbone for treatment of mCRC. Chemotherapy usually consists of a fluoropyrimidine backbone with 5-fluorouracil (5-FU) or capecitabine, in combination with irinotecan or oxaliplatin. Over the course of several decades, these chemotherapy combinations have increased patient survival from a meager 1 month to 21 months.^{9,10} However, more recent advances in mCRC therapy have been driven by the introduction of monoclonal antibodies (mAbs) as additional first-line treatments in combination with chemotherapy or in second-line or later treatment lines. Two major classes of mAbs exist: those that inhibit tumor growth by interference with angiogenesis through blockade of vascular

endothelial growth factor (VEGF) and those that inhibit tumor growth by interference with cell signaling, including blocking signal transduction through epidermal growth factor receptor (EGFR).¹¹ Currently used mAbs for the treatment of mCRC include the anti-VEGF agents bevacizumab, ziv-aflibercept, and ramucirumab, and the anti-EGFR-targeted drugs cetuximab and panitumumab. The latter are specifically indicated for the subgroup of patients with mCRC and Kirsten ras oncogene (*KRAS*) wild-type (WT) tumors.^{3,11-13} Regorafenib is a small-molecule inhibitor that blocks several signaling pathways, including VEGF. According to current National Comprehensive Cancer Network (NCCN) guidelines, regorafenib may also be given as treatment for mCRC.³ In more recent years, trifluridine-tipiracil, pembrolizumab, and nivolumab have also been approved by the FDA for use in patients with mCRC.¹⁴ The immunotherapy agents nivolumab and pembrolizumab are currently used in a specific subset of patients with mCRC with microsatellite instability-high (MSI-high) or mismatch repair deficiency (dMMR).¹⁵ While these newer targeted therapies represent significant breakthroughs in the treatment of mCRC, their application can elevate treatment costs substantially. It is vital to assess the economic impact of these targeted treatments along with their clinical effectiveness. This is important not only for appropriate stratification of patients for therapy, but also to support price negotiations and reimbursement decisions.¹¹ In general, study designs for cost-effectiveness include cost-effectiveness analysis and cost utility analysis. Life-years gained (LYG) and quality-adjusted life-years (QALYs), an index value combining gained additional lifetime along with quality of life during that gained lifetime, comprise the most commonly used benefit measures. The overriding purpose of these health economic evaluations is to compare differences in costs and benefits between alternative interventions and/or treatments.^{11,16}

There are many variables evaluated within a cost-effectiveness study that can be analyzed in multiple ways, depending on the viewpoint taken, and may be related to individual drugs or lines of therapy. The variables may be confined to certain therapeutic time periods or may assess lifetime treatment costs. For example, Shankaran et al investigated the clinical effectiveness and incremental lifetime costs associated with the use of bevacizumab in older patients with mCRC. A total of 4414 patients were stratified by the type of treatment used, specifically no chemotherapy, chemotherapy alone, or chemotherapy plus bevacizumab. Mean lifetime costs were derived from Medicare claims for all services provided between diagnosis and the end of follow-up. Of patients studied, 15% received bevacizumab for first-line management. This agent was associated with improved survival but only for those patients who received treatment for more than 1 month. Both median and mean survival were longest in the chemotherapy plus bevacizumab cohort, with a median survival of 19.4 months and a mean survival of 28.0 months compared with patients who solely received chemotherapy

(median survival of 15.1 months and mean survival of 22.9 months). The mean lifetime per-patient costs were \$143,284 with combination chemotherapy and bevacizumab compared with \$111,280 for chemotherapy alone. Overall, treatment with bevacizumab and chemotherapy was associated with a 5.1-month increase in mean survival along with a \$32,004 increase in mean lifetime treatment costs. This calculated to an incremental cost of \$75,303 per LYG. These results suggested that bevacizumab was clinically effective in this older population with costs that fell into an acceptable level in the United States of between \$50,000 and \$150,000 per QALY.¹⁷

More recently, another study led by Shankaran used data from the phase 3 FIRE-3 clinical trial to assess clinical and economic trade-offs associated with first-line treatment of patients with KRAS-WT mCRC.¹⁸ The FIRE-3 trial was an open-label, randomized, multicenter trial conducted in Germany and Austria of patients with mCRC receiving folinic acid and leucovorin plus 5-FU plus irinotecan (FOLFIRI) plus bevacizumab versus FOLFIRI plus cetuximab.¹⁹ A cost-effectiveness model was used to project survival and lifetime costs of chemotherapy with those regimens. Incremental cost-effectiveness ratios (ICERs) were assessed in terms of LYG. It is important to note that patients with extended RAS mutations were included in this trial. Results demonstrated that patients who received first-line cetuximab achieved 5.7 months LYG costing \$46,266, for an ICER of \$97,223 per life-year or \$122,610 per QALY compared with patients in the bevacizumab cohort. For extended RAS-WT patients, the ICER was \$77,339 per life-year (\$99,584/QALY). Cetuximab treatment was determined to be cost-effective approximately 80.3% of the time. However, it must be noted that this was based on a “willingness-to-pay” threshold of \$150,000 per LYG and that actual numbers surrounding value of care in this respect have varied over the years, with \$50,000 per QALY being an original benchmark and others suggested between \$110,00 and \$160,000 per QALY based on more current US per-capita income.^{18,20} Overall, based on FIRE-3 data, cetuximab has an ICER of \$86,487 per LYG when compared with bevacizumab, which is potentially important when considering first-line therapy in patients with mCRC.¹⁸

Graham et al performed another economic analysis of cetuximab, this time comparing cetuximab and panitumumab, both anti-EGFR therapies used for the treatment of mCRC in RAS-WT patients. Graham and colleagues compared costs and cost-effectiveness of subsequent-line therapy using cetuximab versus panitumumab in patients with KRAS-WT mCRC following failure of prior chemotherapy.²¹ The ASPECCT trial was a phase 3, randomized, multicenter study conducted in North America, South America, Europe, Asia, Africa, and Australia of patients who received either cetuximab or panitumumab for chemotherapy-refractory mCRC.²² Data from the ASPECCT trial were used in this economic analysis; Graham et al performed a cost-minimization analysis and developed a model to assess cost-effectiveness of each of the mAbs used as monotherapy,

assuming equivalent efficacy based on progression-free survival from the trial.²¹ The cost-effectiveness model also included physician visits, monitoring for disease progression, best supportive care, and end-of-life costs. Results showed lower projected costs for patients treated with panitumumab compared with cetuximab, with a projected overall savings of 16.5% (\$9468) per each patient who received panitumumab. The incremental cost per QALY gained also showed panitumumab therapy to be less expensive, although the outcomes with this drug were only slightly better than those seen with cetuximab per the clinical trial data.²¹

Previous lines of therapy may also impact the cost-effectiveness of subsequent lines. A study by Woldemichael et al examined how the cost-effectiveness of second-line chemotherapy varied by the first-line treatment regimens used in elderly patients with mCRC. In this review of 11,000 patients with mCRC in the Medicare population, mean incremental survival was 6.7 months for those who received second-line therapy. However, survival varied between 4 months and 9 months, depending on whether 5-FU with or without leucovorin, irinotecan, oxaliplatin, or other agents were used as part of first-line treatment. The incremental cost associated with second-line treatment was \$60,231 but ranged between \$55,368 and \$71,211, depending on the first-line treatment course. ICERs per LYG associated with the receipt of second-line treatment were \$97,368, \$110,621, \$130,689, and \$247,951 when irinotecan, 5-FU/leucovorin, oxaliplatin, and all other combinations, respectively, were administered in first-line treatment. The investigators concluded that when therapies are administered in a sequential manner, cost-effectiveness of second-line therapy depended on what was actually administered during first-line treatment.¹⁰

Data surrounding newer therapies beyond bevacizumab, cetuximab, and panitumumab are sparser at this time, especially for treatments used for third-line therapies and beyond. One cost-effectiveness study used clinical data from the RECURSE and CORRECT trials.²³ The RECURSE trial was a phase 3, randomized, placebo-controlled, double-blind, multicenter, international study conducted in Japan, the United States, Europe, and Australia of trifluridine/tipiracil versus placebo for refractory mCRC.²⁴ CORRECT was a phase 3, randomized, placebo-controlled, double-blind, multicenter, international study conducted in 16 different countries in North America, Europe, Asia, and Australia of regorafenib plus placebo versus best supportive care plus placebo in patients with refractory mCRC.²⁵ The cost-effectiveness study by Bullement et al, performed in the United Kingdom, demonstrated that the use of trifluridine/tipiracil was associated with a 0.27 incremental LYG compared with just best supportive care, which corresponds to a 0.17 QALY gain.²³ The incremental cost of treatment with trifluridine/tipiracil was £8479 (approximately US \$11,363 at the time of publication), resulting in an incremental cost-effectiveness ratio of £51,194 (US \$68,605) per QALY gained.²³

Of great importance in the use of these targeted therapies is considering the economic burden of common adverse events (AEs) associated with their use in treating mCRC. Fu et al performed an analysis to determine hospitalization costs of AEs associated with use of mAbs (bevacizumab, cetuximab, or panitumumab) for mCRC. The main outcomes in this study included the length of stay (LOS) and hospitalization costs based on 2010 US dollars for AEs identified upon patient discharge. Results demonstrated that gastrointestinal (GI) perforation incurred the longest median LOS, totaling 11.5 days in terms of hospitalizations. Other notable AEs included wound-healing complications (LOS 7 days), followed by arterial thromboembolism (5.5 days), venous thromboembolism (4 days), and heart failure (also 4 days). GI perforations resulted in the highest inpatient cost per event with a mean cost of \$66,224 and median cost of \$34,027, followed by arterial thromboembolism (mean \$40,992 and median \$18,587), wound-healing complications (mean \$36,440 and median \$21,163), interstitial lung disease (mean \$26,705 and median \$19,111), and acute myocardial infarction (mean \$22,395 and median \$15,223). Skin toxicity led to a cost of \$6475 and median cost of \$6110 with hypertension also creating lower costs overall at a mean cost of \$14,108 and median cost of \$6047. Overall, the study showed that costs associated with treatment-related AEs can vary substantially; however, cost data such as this could be applied to economic assessment of head-to-head comparisons of the agents used in treatment for mCRC.²⁶

A more recent study by Latremouille-Viau and colleagues assessed patients with mCRC treated with chemotherapy or targeted therapies using data from administrative claims databases from 2009 to 2014. This study included 4158 patients with 1 or more mCRC treatment episodes. The adjusted monthly total cost difference delineated by categories of AE found that the costliest AEs per month, in descending order, were hematologic events (\$1480 monthly costs), respiratory AEs (\$1253 monthly), endocrine/metabolic events (\$1213 monthly), central nervous system AEs (\$1136 monthly), and cardiovascular events (\$1036 monthly).²⁷

Despite the amount of data related to cost-effectiveness of cancer therapy, it is still extremely difficult to actually assign a “value” to any type of cancer care.^{28,29} The definition of value itself is arbitrary and may vary due to type of healthcare system, patient population, or even by country.^{28,29} In response to this concern, the American Society of Clinical Oncology (ASCO) worked to develop a formula to determine the value of care based on the concept that the cost of a given intervention should relate to its benefit to the patient. ASCO created a value framework for those with advanced malignant disease, creating a clinical benefit score encompassing aspects related to survival, a therapy toxicity score, along with palliation and treatment-free intervals to calculate a net health benefit. A summary assessment of the cost of the therapy (drug acquisition cost and a calculated actual patient cost or co-pay based

on healthcare coverage) was also taken into consideration. This framework is considered an iterative process and an ongoing effort, and ASCO welcomes comment on it from all interested parties.²⁹

Of note, ASCO is just 1 example of an organization with the development of a formula to determine value-based cancer care. The NCCN has implemented evidence-based blocks into their treatment guidelines, the European Society for Medical Oncology has developed their Magnitude of Clinical Benefit Scale (ESMO-MCBS), and Memorial Sloan Kettering Cancer Center has developed the DrugAbacus tool to help guide clinicians in providing valuable cancer care.³⁰

Patient Care and Shared Decision Making to Optimize Outcomes

With the ever-evolving development of new therapies for the treatment of mCRC, patient care considerations must remain in the forefront of therapy. Along with increased effectiveness of new agents, so also increased are the costs of these new and emerging agents. Currently, more than 40,000 new patients are treated for mCRC annually in the United States. New therapies must be evaluated not only for their clinical efficacy, but also for the convenience of administration, how their use affects patient and caregiver schedules and lifestyles, along with the potential AEs associated with therapy, as noted earlier.²¹

Many patients with cancer of any type want more detailed information about their diagnosis, treatment options, and prognosis, and they want to be active participants in decision making about their therapy.³¹ However, data have demonstrated that as many as one-third of patients with cancer have misunderstood the information they receive.^{31,32} For example, if patients misunderstand their prognosis, polarized decisions about treatment options can be made that can impede optimal management. One study of patients with advanced malignant disease found that most overestimated their life expectancy post-diagnosis and 59% were overly optimistic overall about their prognosis. Patients who thought they were going to live for at least 6 months were more likely to be in favor of receiving life-extending therapy over best supportive care compared with those who believed there was at least a 10% chance that they would not survive until that 6-month mark. Essentially, patient understanding of their chance for survival can seriously impact therapy choices.^{31,33}

Shared decision making (SDM) is a process that enables clinicians and their patients to participate jointly in making health decisions.^{34,35} In this process, the patients and clinicians discuss treatment options and their benefits and risks, and consider a patient's values, preferences, and circumstances surrounding their management. SDM allows scientific evidence and patient preferences to be incorporated together into a collaborative discussion that will increase patient knowledge, risk perception surrounding therapy

choices, and patient-clinician communication overall. Conflict surrounding both the use of clinical testing and treatment choice can then be reduced.³⁴ SDM is now a critical aspect of cancer treatment and management. The key factors for effective SDM include³⁵:

- Determination of the situations in which SDM is critical
- Acknowledgment of the decision to the patient
- Description of the treatment options, including risks, benefits, and uncertainty associated with each potential choice
- Elicitation of patient preferences and values
- Agreement on a plan for the next steps in the decision-making process

It must be emphasized that SDM is not a 1-step process. Truly incorporating SDM into clinical decision making requires multiple steps and visits. The typical components of SDM surrounding therapy over the course of a series of office visits would include³⁶:

- **Choice talk:** The clinician offers (and justifies) the different choices for therapy but checks for the patient's reaction and defers closure on a decision
- **Option talk:** The clinician lists the options for therapy in more detail, including their risks and benefits to generate a dialogue with the patient and offers decision aids (DAs), summarizing the various options and checking for patient misconceptions about them
- **Decision talk:** The clinician and patient focus on eliciting a patient preference and moving to a therapy decision, also offering a review of the process leading to that decision to arrive at closure

DAs can have the potential to assist clinicians and patients to navigate complex management choices in mCRC. One study by Leigh et al used an oncologist-designed take-home booklet and accompanying audio DA to assist patients with mCRC who were considering first-line chemotherapy. A total of 107 of 207 patients received this DA, and they demonstrated a greater increase in understanding of their treatment options and their risks and benefits along with prognosis compared with a control group who did not receive the DA. The investigators concluded that use of a DA such as this can improve informed consent surrounding therapy for mCRC.³¹

More recently, Fu et al conducted a survey of patients with advanced CRC who were undergoing or who had completed one chemotherapy regimen. Patients were initially asked to rate the importance of 15 therapy-related AEs that may arise from chemotherapy or biological therapy as they related to treatment decision making. Patients then identified the top 5 AEs that would most impact them and elucidated their preferences for treatment in hypothetical mCRC treatment case studies. Results demonstrated that patients clearly identified serious AEs, including stroke, myocardial infarction, and GI perforation, as key drivers in their therapy decision making. However, they also showed a lower willingness

to tolerate symptom-related events related to therapy, including pain, fatigue, and depression. Patients' willingness to tolerate these therapy-associated AEs substantially highlights a need for improved clinician-patient communication surrounding the risks and benefits of the various therapies available for mCRC to truly achieve collaborative and optimal decisions for individualized therapy and management plans.³⁷

Conclusions

While the continuous development of new therapies for mCRC has revolutionized treatment of the disease, they have arrived with an increasing cost burden on the healthcare system. Patterns of treatment choice, medical care usage, and cost differences depend on therapies chosen, as well as patient and health system characteristics that impact overall patient management and healthcare usage. Overall, it is difficult to generalize an actual value of any particular cancer therapy. However, estimates can be attempted by measuring clinical benefits and risks of treatment in addition to cost. It is most important to focus on shared decision management between clinician and patient in selecting therapy options that offer clinical benefit, while avoiding unmanageable cost burden for the patient. Such shared-decision processes benefit patient confidence in care, overall management, and ultimately, patient outcomes. ■

Author affiliation: Clinical Pharmacy Specialist, Gastrointestinal Medical Oncology, Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, TX.

Funding source: This activity is supported by an educational grant from Taiho Oncology, Inc.

Author disclosure: Dr Zadlo has no relevant financial relationships with commercial interests to disclose.

Authorship information: Concept and design, drafting of the manuscript, and critical revision of the manuscript for important intellectual content.

Address correspondence to: JLZadlo@mdanderson.org.

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