

Performance Improvement Strategies in Colorectal Cancer Audio Conference June 15, 2010

OLIVIA FRITZ: Welcome to the Community of Practice Teleconference with colorectal cancer (CRC) experts Dr. Thomas Cartwright and Dr. John Marshall. I am Olivia Fritz, your moderator for today's discussion. This teleconference is being recorded. However, resale of the content is prohibited.

During today's call, you will have an opportunity to discuss ways to overcome CRC-related process barriers and voice questions or comments to help other clinicians improve CRC patient care. This activity has been developed as part of the American Medical Association (AMA)-standardized, CME initiative Performance Improvement Strategies in Colorectal Cancer, for which Drs. Cartwright and Marshall have served as faculty experts. Details about this initiative will be discussed during today's teleconference.

I am pleased to now introduce to you Dr. Cartwright and Dr. Marshall. Dr. Cartwright is co-chairman of the US Oncology GI research committee and a medical oncologist in private practice in Ocala, Florida. Dr. Marshall is Professor of Medicine and Oncology and Chief of the Division of Hematology/Oncology at Georgetown University. Dr. Marshall also serves as Associate Director of Clinical Research at Lombardi Comprehensive Cancer Center in Washington DC. Dr. Marshall?

DR. JOHN MARSHALL: Thank you very much for that nice introduction, and thanks to you all for joining Dr. Cartwright and me for this brief call to give you some background on our activity and then also to answer any questions you may have; some good questions have already been submitted.

So let me welcome you to our Community of Practice Forum for CRC. The goal of our audioconference is to bring us



together, those of us who are interested in the care of patients and who focus on CRC, to both discuss the advances in the care of these patients, but also to focus on processes or systems of care to ensure that we're all providing optimal care for our patients. Before we begin answering questions, we want to give you a little bit of insight about the state of CRC care and some of the reasons why activities such as this Performance Improvement (PI) initiative are really so important.

We notice an increasing acceptance that improving cancer care will require healthcare professionals, us, to measure and monitor indicators of quality with the goal of identifying areas where current practice falls below established standards, and where, thus, opportunities for improvement are clearly present. So to this end, PI is an AMA-approved CME format in which physicians work on improving our individual performance by completing stages of data collection and self assessment, as well as implementing an improvement plan into our practice. Basically, we are evaluating ourselves and then trying to figure out how we're going to change our practice. Our PI activity focuses on three general areas of care for CRC patients, namely supportive care and patient safety, the application of evidence-based surveillance, and the application of evidence-based treatment. Although there are a number of initiatives for improving the quality of care for cancer patients, to our knowledge this activity is the only PI initiative that is focused solely on the care of patients with CRC and is designed for us as oncology specialists. However, a number of quality measures that have been developed for this activity are derived from similar programs, and we'll briefly highlight how some of our early data from our activity compare to those initiatives. To do that, I'd like to turn the phone over to Dr. Cartwright.

DR. THOMAS CARTWRIGHT: Okay, thank you. As many of you may know, the 2000 National Initiative on Cancer Quality Care, which was funded by American Society of Clinical Oncology (ASCO), found that in newly diagnosed CRC, the patient had about a 1 in 5 chance of not receiving an element of care consistent with best practices. Then almost 5 years later, ASCO had a pilot program, called the Quality Oncology Practice Initiative, in which they found similar results—about 78% of patients received recommended care, and significant differences in many of the core measures were seen among practices. Perhaps one of the most notable

variances was in assessing pain in patients with CRC before death. Pain was documented in anywhere from 15% to 93% of evaluated practices, a fairly wide variation. In our initial review of the first 245 patient charts evaluated in this program, only about 52% of patients had been assessed for pain at every visit. National guidelines also recommend that all patients with cancer be screened for psychological distress as part of routine care. However, in the initial part of this program, emotional well-being had been documented in only about 53% of patient charts, which shows another example of variation

As many of you may know, a number of publications have discussed the importance of adequate lymph node sampling and how this affects staging; this has formed the basis for many quality improvement programs. In our initial data set, the mean number of lymph nodes evaluated is 15, which is above the lower limit of 12. However, in 6% of the charts, the number of lymph nodes evaluated was not documented; in another 12% of charts, a number of evaluated lymph nodes were not including in staging considerations. On the other hand, when we look at treatment decisions for patients with Stage II or III, our data set shows that 97% of the time, adjuvant chemotherapy was discussed with Stage II patients and recommended in 96% of Stage III patients, which is pretty good. Guideline-recommended regimens were administered in 99% of patients that received adjuvant chemotherapy, which is another area where the numbers look pretty good. An area where they don't look so good is in the metastatic setting, in which an example is *KRAS*. We all know the importance of testing for *KRAS* before a patient is given an EGFR inhibitor. In fact, the labels for both panitumumab and cetuximab have been changed to include *KRAS* testing, but in our initial phase of the study, only 58% of patient charts had *KRAS* documented, and 63% of patients receiving treatment with either cetuximab or panitumumab had documented wild-type *KRAS* status.

So before we go to the question session, Dr. Marshall is going to review the steps of participation in our PI activity.

DR. MARSHALL: Thanks very much. As we just reviewed, we clearly have some learning to do here. I frankly saw a patient just this past week who had been receiving second-line therapy without *KRAS* ever having been tested, so we know this is still going on out there. In this PI activity, there is a three-step process that participating healthcare



professionals can use to really evaluate ourselves. The first step is to review your own performance, or our own performance, with a retrospective chart audit. With a limited number of patients, compare your current practice to national standards and also aggregate results from other healthcare professionals. So how are you doing against other oncologists? How are you doing against other physicians? Following this self evaluation, we are all asked to design an improvement strategy for areas where we believe that we can improve upon our practice. So okay, these are your weaknesses. How are we going to work on those to improve them?

Unique to our PI activity is a certified CME implementation guide that includes a discussion of the evidence around each quality measure, including why you should care about these measures and some practical tools designed to help participants improve your practice.

The final step is another self evaluation of practice patterns following the implementation of the improvement plan. How did you do? Have you changed your behavior? The data collected through this PI activity can also be used to complete American Board of Internal Medicine Self-directed Practice Improvement module (which we all have to do, at least I have to do again coming up soon) and satisfy the practice performance improvement requirement for maintenance of certification.

So at this point let me send it back to our moderator, and we will now open to some questions that folks have sent in.

MS. FRITZ: Thank you, Doctor. At this time we will begin the question and answer session. To ask a question, please press 0 followed by a 1 on your touch tone phone. Questions will be answered in the order they are received. Again, if you have a question please press 0 followed by a 1 now. Please pause to assess whether we've received live questions in the queue.

While we pause, Med-IQ received several questions in advance for this teleconference. At this time, Sara Miller, Clinical Content Manager, will share a question that was submitted by one of your colleagues.

SARA MILLER: Thank you, Olivia. Dr. Cartwright, we have a colleague who would like to know: When is neoadjuvant chemoradiation indicated for CRC patients?

DR. CARTWRIGHT: Well, typically neoadjuvant chemoradiation is used for rectal cancer, not colon cancer. There is reasonable evidence that giving chemoradiation neoadjuvantly to rectal cancer patients is better tolerated and down-stages the patient so fewer patients needing it require a colostomy. Now it is sometimes difficult to stage patients with rectal cancer. Not everybody has the availability of endoscopic ultrasound, and so we don't want to overtreat patients. The patients with a Stage T1, very early rectal cancer, will not need chemoradiation, but the typical patients with T2 or T3 if there's a positive node receive adjuvant or neoadjuvant chemo and radiation. There are data showing chemotherapy given with radiation is more effective than radiation alone, but chemotherapy has a radiation-sensitizing effect and a therapeutic effect in itself. So the preference does vary around the country and probably around the world, but at least in the United States, the standard seems to be that at-risk patients receive neoadjuvant chemo and radiation before having surgery typical for rectal cancer.

MS. MILLER: Thank you, Dr. Cartwright. Dr. Marshall, another participant would like to know: What are the most important points of differences regarding CRC treatment planning in younger patients, especially those younger than 25, compared with older patients? And he's particularly interested in the choice of chemotherapy drugs and timing.

DR. MARSHALL: This is a great question because we have in essence bundled all of colon cancer into one big umbrella and said whether you're old or young, you have the same colon cancer. We are slowly learning that, in fact, these might be different cancers. And so let's look at, for example, the very young; they have, in fact, an inherited syndrome, and the most common one that's out there is microsatellite instability (MSI) or HNPCC. We're learning that the 20% or so of colon cancers that have this MSI genetics might be responding differently, really not as well, to chemotherapy particularly in the adjuvant setting compared to those with MSS or the other 80%. So we do need to look out for that. We also bring bias to the table with the idea that our younger patients deserve, if you will, more "aggressive" chemotherapy, so we do tend to pile on the younger patient a little bit more. And it's not clear to me that that's really the right answer. I've seen recent records of a physician who sort of insisted on maintaining adjuvant therapy dose intensity using growth factors and

the like in colon cancer, and I'm not sure we have the data that say we have to push patients to the wall with dose intensity in the adjuvant setting for colon cancer.

On the other end of the spectrum is the opposite case. These are older patients, and so we tend to be gentler. There's newer evidence, and it's controversial, that maybe the very old patient doesn't benefit from oxaliplatin in the adjuvant setting. And there are some data going back and forth that we can discuss on that, but certainly our enthusiasm for pushing that 75- or 80-year-old patient in the adjuvant setting is reduced some because of their age and because of avoidance of toxicity. I think what we're really learning over time is that molecularly these actually might be different cancers. Not just being gentler with older patients and more aggressive with younger patients, but there actually might be a difference fundamentally, and we should begin to understand those better as we keep going.

MS. FRITZ: Thank you. And so we will go next to a pre-submitted question.

MS. MILLER: Okay. Thank you, Olivia. Dr. Cartwright, we have a participant who would like to hear a little bit more about familial risks for CRC.

DR. CARTWRIGHT: Well, most colon cancer is sporadic, meaning there isn't at least an identifiable familial risk factor. The most common cause of hereditary colon cancer is familial polyposis, again probably causing fewer than 1% or 2% of colon cancer cases. These patients have hundreds of colon polyps and typically develop colon cancer at a very young age. Another common syndrome is Lynch Syndrome or heredity nonpolyposis colon cancer, which is a little more common. These patients are also at a very high risk of colon cancer. There are genetic tests; we can actually screen patients and family members for this. This is typically brought to attention when we see a patient who either has colon cancer at a very young age (typically younger than 40, but certainly somebody in their 20s would make somebody think of a hereditary syndrome), or a patient with multiple family members with the condition.

So although it's relatively uncommon for patients to have one of these syndromes, it's very important to know because if we identify this, then we need to test other family members, then those family members need to be screened at

an early age to prevent them from developing colon cancer. I recently saw a patient, a young woman, who had metastatic colon cancer and had familial polyposis; her father had the same thing and, for some reason, she sort of fell through the cracks and wasn't screened. So that's a patient with advanced colon cancer that could have been prevented.

MS. FRITZ: Thank you, Doctor. And again as a reminder to our participants, if you would like to ask a question, please press 0 followed by a 1 on your touch tone phone. While we wait for any responses to compile, I will turn it back to Sara Miller for a previously submitted question.

MS. MILLER: Dr. Marshall, we have an e-mail question here, and this participant asks: What percentage of patients diagnosed with early stages of colon cancer undergo laparoscopic procedures, and what are the complications of those procedures?

DR. MARSHALL: Well, it's interesting how laparoscopic colectomy has become the sort of standard now out there, and it's been a very quick and steep learning curve for the colorectal surgeons and the general surgeons to do laparoscopic colectomies. I think our patients now have an expectation that they can do this, and it's not just for early stage. I'm assuming that, for the caller, doing colectomies may mean between metastatic and Stage I, II, or III, but in the right hands, laparoscopic colectomies have been shown to be very effective and are associated with shorter hospital stays and quicker recovery time. One of my early concerns about these is that we would have inadequate lymph nodes dissections. I think early on we might have seen some of that particularly in those who were not really focused on lymph nodes dissections, but I think we've even kind of swung back well on that.

I'm not a surgeon. They don't even let me cut the turkey at Thanksgiving at my house, so in terms of the choice of what kind of surgical approach is taken, I really defer to the surgeon on that. The complication rates on laparoscopic colectomy, I believe, are either the same or lower than those seen with open colectomies. And our worry, of course, is whether a proper cancer operation was done in both cases. Once you're reassured in that front, I'm certainly comfortable with patients having laparoscopic colectomy.

MS. FRITZ: Thank you for your response. And we currently do have a live question in the queue. And this question comes from

Union Town, Pennsylvania. Please go ahead with your question, Doctor.

FEMALE VOICE: Hi. I would like to know from Dr. Marshall, what's the data behind the need to proceed with a full APR after complete pathologic response on rectal cancer after chemoradiation, especially on T3 lesions?

DR. MARSHALL: You don't know about your pathologic complete response until you've done the APR, so it's a very good question. Endoscopically you might not see anything with chemoradiation after the procedure is done; you do a colonoscopy, and it may be a no-evidence-of-disease state. And there is, right? About a 20% to 25% pathologic complete response (pCR). One of the hardest things to tell a patient is "okay, you need a surgery that's going to leave you with a permanent ostomy or, depending on the location of the tumor, has the risk of leaving you with a permanent ostomy." But what you're hoping for is that, in the end, you didn't need the operation because you have a pathologic complete response, which, of course, has a very good prognosis.

So I think it's a great point. Can we put the surgeons and/or the radiation oncologists out of business with our chemoradiation approaches? Memorial Sloan Kettering just published a study at ASCO this year where they just gave chemo neoadjuvantly and had a very high response rate. So it's a hard discussion. If you're advising a patient, the right answer, or the book answer, is "go have the surgery." If you're deciding not to because you're willing to take the risk, the patient needs to understand that local control can be a very miserable thing and with a pCR rate of only 20% or so, the majority of patients will have residual cancer. So it's a difficult discussion, and individual decisions are made differently by different patients. Sometimes the risk is worth it; other times it's not.

MS. FRITZ: Thank you for your question. And at this time, Sara, if you wouldn't mind continuing with a pre-submitted question?

MS. MILLER: Sure. Dr. Cartwright, can you discuss the potential use of single-agent bevacizumab and the maintenance treatment of metastatic CRC?

DR. CARTWRIGHT: Well, we're starting to hear a lot about maintenance therapy and not just in colon cancer; as

everyone probably knows, maintenance pemetrexed has been approved in lung cancer. There are some data with maintenance erlotinib, too. I think probably the person asking the question is referring to one of the oral presentations at ASCO just earlier this month on the MACRO trial, where patients received first-line XELOX (capecitabine + oxaliplatin) plus bevacizumab for 6 cycles, then were randomized to receive either XELOX plus bevacizumab or single-agent bevacizumab as maintenance therapy. The reason this question was asked, obviously, is can people only tolerate so much chemotherapy with XELOX or FOLFOX before the neurological toxicity builds up? In this study, giving maintenance bevacizumab did not appear to compromise overall survival and probably didn't affect progression-free survival either. Now the doctor that discussed this trial afterwards said you couldn't be absolutely sure there wasn't a shortening of progression-free survival, but if it did exist, it was a matter of just a few weeks. And the patient who was randomized to the arm that received maintenance bevacizumab had much less toxicity and better quality of life.

There are other data, similar data from other studies, such as OPTIMOX 1 and 2, sort of the stop-and-go type strategy. I think with the evidence we have, it's probably not a good idea to stop everything in a patient with metastatic disease, but continuing 5-FU alone or now bevacizumab alone is an option for patients. It doesn't seem to compromise survival and likely results in better quality of life and less toxicity.

MS. MILLER: Thank you, Dr. Cartwright. Dr. Marshall we have another pre-submitted question where the participant would like to know whether XELOX is an appropriate adjuvant regimen for Stage III colon cancer.

DR. MARSHALL: Yeah, I think it probably is. Now, we have to remember that one of the reasons you give capecitabine, if you will, is to try and avoid pumps, which it does. But it doesn't really, at least in our world, avoid putting ports in or some sort of central venous access because oxaliplatin is difficult to give peripherally. So in our shop, at least, we tend to put ports in these patients anyway. Then you have the issue—certainly there's a bit of randomized Phase 3 data that support giving XELOX over bolus 5-FU and leucovorin. So we have data, but then a lot of folks struggle with the dose and schedule. The dose used was a 3-week dose of oxaliplatin with a 2 on, 1 off

capecitabine, and it proved okay. It was a little bit spicy at times. And often in the United States, we make dose modifications to capecitabine, so you're always nervous in the adjuvant setting about too much in terms of dose modifications. But the short of it is, it absolutely is a valid choice. I present it to all of our patients as an option in the adjuvant setting and essentially present them as equivalent as we can know, given it is still a cross-trial comparison. But I do offer it to all patients.

MS. MILLER: Thank you. Dr. Cartwright, can you comment for another participant on how you manage a cancer case when the patient is already a chronic drug addict?

DR. CARTWRIGHT: That's a difficult situation. Patients with cancer often have pain and require pain medicine. So I typically don't manage these patients alone. Often I ask for the help of a pain management person, somebody that's specialized in pain management. If I'm managing the patient alone, I may give the patient smaller prescriptions, not large numbers of drugs or prescribe drugs like some of the narcotics that have less potential for abuse. But if the patient says they're in pain, you do have to believe them, especially if they have metastatic disease or another reason to have pain. Patients who are narcotic addicts before they develop cancer are quite a challenge to manage, and I'm not sure there's any easy solution to that other than taking a lot of time—you have to document what you're doing, and you have to be careful that the drugs you're prescribing for the patients are used appropriately and not inappropriately or diverted. So as I said, sometimes I end up managing these patients by myself, but a lot of the time, I prefer to elicit the help of a pain management specialist.

MS. MILLER: Thank you, Dr. Cartwright. I believe we have time for one final pre-submitted question. And Dr. Marshall, this participant would like to know: When do you recommend operating, and when do you treat only medically?

DR. MARSHALL: Well, I guess that refers to a patient with metastatic disease who has their primary in site and has other metastases, and we do see this more and more. Our old standard was to take that primary out and sort of ask questions later, but as our chemo got better, we started trying chemotherapy first. Low and behold, that seemed to be okay. A very important study was just published, again



at ASCO this year, called C-10; it's an NSABP study where they treated about 80 patients with primaries in place with bevacizumab-containing chemotherapy and had about a 10% rate of complications. Depending on how you look at that, that's either a high number or a low number. I think the expectation was for a much higher number of events in which the chemo had to be stopped and surgery or some other thing had to be done to intervene with the complication.

I think we have a solid data set out there that says patients with primaries in place can be given chemotherapy safely. Now on the other side, in a patient who is quite obstructed, chemo doesn't work all that quickly, and so often we need to divert these patients or have those primaries removed just to ensure the continuity of flow of the bowel. Sometimes with rapid bleeding or serious complications, we need to go ahead and operate. So there are medical situations that push us there, but in patients who have relatively asymptomatic primaries, I think one can begin with chemotherapy. Now we have a number we can quote patients, which is about 10% rate of complications from doing that.

MS. FRITZ: Thank you, Doctor. And thank you, gentlemen. This concludes today's CRC Community of Practice Teleconference provided by Med-IQ in collaboration with Oncology Today and supported by an educational grant from sanofi-aventis U.S. Three hundred specialists have enrolled in Performance Improvement Strategies in Colorectal Cancer to self assess and improve their CRC practices of care. Participants can earn up to 20 credits and points towards ABIM maintenance of certification. To join your peers or to learn more, please visit www.pi-iq.com/crc. Thank you for your time and commitment to improving CRC patient care.