Tracks 1-13

Track 1  **Case discussion:** A 55-year-old patient who presents with jaundice and a biliary tract obstruction is diagnosed with KRAS wild-type colorectal cancer (CRC) and multiple liver metastases.

Track 2  Activity and tolerability of FOLFOX/bevacizumab in metastatic CRC (mCRC)

Track 3  Treatment for patients with mCRC and an asymptomatic primary tumor

Track 4  Potential role of BRAF inhibitors in the treatment of mCRC

Track 5  Role of regorafenib as therapy for mCRC

Track 6  Counseling patients with mCRC and their families about end-of-life and hospice care

Track 7  New options for continued anti-angiogenic treatment after disease progression on first-line therapy for mCRC

Track 8  Clinical experiences with and tolerability of regorafenib in a trial as second-line versus later-line therapy

Track 9  Dosing considerations for regorafenib in mCRC

Track 10  Incidence and management of early-onset side effects with regorafenib

Track 11  Perspective on the utility of the OncoType DX® Colon Cancer assay for patients with Stage II and Stage III colon cancer

Track 12  **Case discussion:** A 41-year-old patient with locally advanced pancreatic cancer (PC) undergoes treatment with neoadjuvant FOLFOXIRI → gemcitabine with radiation therapy

Track 13  Palliative challenges in the management of metastatic PC (mPC)

Select Excerpts from the Interview

DR LOVE: What is your approach to treatment for a patient with metastatic colorectal cancer (mCRC) whose disease has progressed on first-line therapy?

DR GOLDBERG: You have to evaluate the data along with the patient and then make a decision because a single right or wrong approach does not exist. We’ve been successful in transforming metastatic colon cancer into more of a chronic disease than it was when you and I first started. And as a consequence, I want as many options as I can offer for my patients, and I want to use them in series.

I tend to administer first-line FOLFOX/bevacizumab and now tend to use FOLFIRI/bevacizumab in the second-line setting, even for patients with KRAS wild-type disease. Then I fall back to irinotecan with an EGFR inhibitor for third-line therapy. I believe that the mechanism of action of the EGFR inhibitors is so much different than that of the other agents we use earlier on that you often see satisfying and long responses.
The next question is, what about aflibercept? In my experience, the toxicity associated with this agent has been less than I expected based on the VELOUR trial results (Van Cutsem 2012). It seems to be as easy to administer as bevacizumab. I tend to consider aflibercept in the second-line setting for patients who “burn through” first-line therapy quickly and for whom I want to “reboot” and try a completely new regimen because I do believe that aflibercept is fundamentally different from bevacizumab.

Then, of course, we now have the option of regorafenib in the late-line setting. Regorafenib is a bit of a “dirty” kinase inhibitor and affects multiple important pathways in cancer cells. That may be an appealing approach in later-line therapy, with which you have a diversity of mutations that we’ve accentuated by putting pressure on the tumor with chemotherapy and targeted agents. My own experience with regorafenib in this setting is that it’s been more difficult to administer than I thought it would be. I often have to reduce the dose, particularly for older patients.

Of interest, we are conducting a Phase II study of regorafenib in combination with FOLFIRI as second-line therapy for mCRC (NCT01298570), and I’ve found it much easier to administer in an earlier line of therapy. That may be in part because we are accruing patients who are both younger and healthier. Also, these patients are earlier on in their exposure to chemotherapy agents.

› DR LOVE: Much debate is going on about what the starting dose of regorafenib should be. For practical purposes, what’s the dosing range that you consider?

› DR GOLDBERG: I don’t start patients on 160 mg unless they are 40 or younger and fit. I generally start at 80 to 120 mg. For older patients or those with a number of comorbidities I will start at a half dose and escalate. For younger patients or older patients with a good performance status I’ll start at 120 mg, although I find that I am almost never able to escalate in this group.

You need to monitor patients, especially early on. The nice aspect about oral agents is that you can intervene over the phone and say, “Take less tonight and from now on.” So I believe it’s a great idea to call patients receiving regorafenib a week after they start treatment to check in with them and see how they’re faring.

› DR LOVE: What points do you emphasize to patients beginning therapy on regorafenib, and do any preemptive approaches help prevent toxicity?

› DR GOLDBERG: When I prescribe panitumumab and cetuximab to patients, I’m a big believer in using prophylactic measures to try to improve their rashes. But I haven’t found a way to improve regorafenib-associated hand-foot syndrome other than to tell the patients to use moisturizing creams, which I’m not sure makes a big difference. The fatigue is not something you can manage. I don’t think resting or not resting makes a difference. I don’t want to start patients on other drugs for muscle aches unless they have them. So I haven’t found an effective solution to preemptively ameliorate the toxicity as of yet.

Often these issues occur quickly. An analysis of data from the CORRECT study indicated that patients who were able to tough it out through the first cycle often fared better on later cycles (Grothey 2013b; [1.1]). Toxicity seems to present and peak early. In some ways this is akin to the skin toxicity observed with EGFR-targeted antibodies, with which the most vigorous skin reaction tends to be in the first month or so, and then it improves in many patients.
Track 11

DR LOVE: Would you comment on the role of the Oncotype DX Colon Cancer assay in the management of Stage II and Stage III disease?

DR GOLDBERG: It is fairly well known that the difference between an Oncotype high-risk Recurrence Score® (RS) and an Oncotype low-risk RS is somewhere between 20% and 8%. So a patient at high risk would have a 1 in 5 chance of recurrence, and a patient with a low-risk RS would have a less than 1 in 10 chance of recurrence.

I usually discuss the modest benefit from 5-FU/leucovorin chemotherapy with my patients. I don’t administer FOLFOX to patients with low-risk, Stage II disease. We perform microsatellite instability (MSI) testing on all of our patients. If their disease is MSI high, I talk them out of treatment if I can. I present the Oncotype DX Colon Cancer assay data to patients with T2 and T3N0 disease and I say, “If a 20% risk of recurrence is going to lead you to take therapy and an 8% risk of recurrence is going to lead you to not take therapy, then it’s worth ordering the test.”

If you evaluate Stage III colon cancer as an example, the patients with the worst prognosis get the most benefit from adjuvant therapy. Patients with 15 positive nodes and a T3 tumor, or even a T4 tumor, have a terrible prognosis. However, you can modify their prognosis the most with adjuvant therapy in that setting. So the higher the risk, the higher the benefit.

SELECT PUBLICATIONS

