COMMENTARY

Over-the-Counter Tx Proves Top Shelf in CRC

David J. Kerr, CBE, MD, DSc, FRCP, FMedSci | May 22, 2015

Hello. I'm David Kerr, professor of cancer medicine at University of Oxford.

It's that time of year again— a run-up to ASCO. It's a fantastic meeting: 30,000 oncologists from around the world gathering to hear what is usually regarded as the latest, best breaking news from the world of cancerology—an excellent meeting.

As always with Medscape, we try to look for a couple of highlights that each of us in our own fields think is worthwhile. Being honest, in the world of colorectal cancer there's not a huge amount of very exciting news, nothing that will be immediately practice-changing. Nevertheless, there are some interesting studies, a couple of which I've picked out, and all of these are presented at the oral colorectal cancer session.

The first thing that caught my eye was the study of SIRFLOX.[1] This is a randomized phase 3 trial in which combination chemotherapy with FOLFOX6 plus a monoclonal antibody (bevacizumab) was compared with the same chemotherapy plus or minus selective internal radiation therapy (SIRT). These are yttrium-90 resin microspheres that are given through the hepatic artery to offer internal radiation to hepatic metastatic colorectal cancer. This is a big, well-designed study, but disappointingly it didn't meet its primary endpoint, which was looking at global progression-free survival. The subanalysis suggests that progression-free survival within the liver seems to be elongated with the addition of the SIRT spheres. Sadly, overall progression-free survival doesn't seem to have changed at all. This is an interim report, so we'll have to wait to see what happens to overall survival, but this may be a case of just choosing the wrong primary endpoint. Overall survival will be the proof of the pudding.

More Data on Over-the-Counter Prevention

The second thing that caught my eye was a study looking at vitamin D status in survival of metastatic colorectal cancer patients.[2] This was a CLGB/SWOG Alliance study in which measures of 25-hydroxyvitamin D were measured in plasma. It showed that those patients with higher vitamin D levels treated in these various trials did better. It's a story that we've told repeatedly on Medscape, but there are more and more observational data accumulating suggesting that we need to pay attention to vitamin D status. Offering vitamin D supplementation seems an entirely reasonable thing to do for those of our patients who have developed advanced or metastatic disease.

The third was a study from Norway, and again, this is as if it's over-the-counter treatment of colorectal cancer. This is a big cancer registry study looking at the impact of aspirin in secondary prevention, and a huge, unselected cohort of 25,644 patients were treated for colorectal cancer.[3] Out of the 25,000 patients treated, the investigators discovered about 6000 who'd received regular aspirin after the diagnosis of colorectal cancer had been made. They looked at overall survival and colorectal cancer–specific survival, and patients who were treated with or who took aspirin at a range of different doses did better. Again, it's another message that we've been promulgating at Medscape repeatedly—and with more data accumulating—suggesting that patients with colorectal cancer should think about taking low-dose aspirin and vitamin D supplements. For those patients with advanced disease who are looking for secondary prevention, this seems a logical thing to do.

Novel Genomic Predictor of CRC Survival

The final abstract that caught my eye—and remember: I'm interested both in the biology of colorectal cancer as well as its therapeutic management—was a beautiful study from Harvard investigators, working with colleagues in Japan.[4] They did a large, prospective study with exomic sequencing looking at microsatellite instability. What they showed was that patients with microsatellite unstable disease have a higher antigenic load—a higher

presentation of antigens to the host immune system—than those with microsatellite stable disease. And they discovered that with exome sequencing, not surprisingly, they could come up with signatures that consistently correlated with the number, degree, and type of tumor-infiltrating lymphocytes, and this proved to be good for patients. Here we have tumors that are programmed to present a much greater antigenic load to the systemic immune system. The host responds by priming and preparing tumor-infiltrating lymphocytes, and clearly there's some significant degree of immune recognition going on within the tumor that confers a relatively good prognosis. So this is a rather nice study in which they combined high-level genetics and genomic sequencing with some very careful preparations to look at the degree and type of tumor-infiltrating lymphocytes, and found correlations between the two. The link between the genomics and the tumor-infiltrating lymphocytes is the very large degree of neoantigen presentation that you get in these hypermutated microsatellite unstable tumors.

It's going to be a great meeting. I should say that if you'd like to meet me—a small plug now: I've been made editor-in-chief of ASCO's new *Journal of Global Oncology*—I'll be around at the meeting. If any of you would like to pop along and say hello, I'll be at the ASCO journals booth. It would be an opportunity to meet in person. I'd look forward to that.

For the time being, Medscapers, ahoy. Thank you.

References

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