INTERVIEW

Alan P Venook, MD

Dr Venook is Professor of Clinical Medicine at the University of California in San Francisco, California.

Tracks 1-17

Track 4

DR LOVE: What is known about the combination of TACE and sorafenib for HCC?

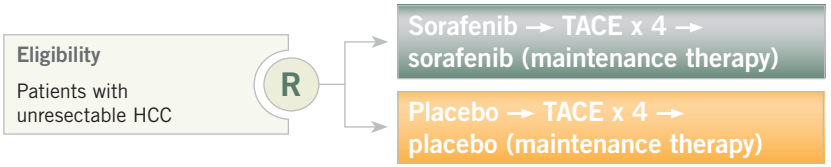
DR VENOOK: A study evaluating TACE with sorafenib in patients with advanced HCC, presented at the 2010 Gastrointestinal Cancers Symposium, showed no benefit (Okita 2010). However, sorafenib was not administered until after the embolization. Part of the issue might have been tumor revascularization because factors are proliferating after you perform embolization that would promote vessel formation, but in this study they did not use sorafenib for weeks after the embolization so it's hard to see why it would have worked.

The current ECOG-E1208 study is evaluating TACE with or without sorafenib and will attempt to address this issue. Sorafenib is administered continuously, except for the time immediately around the TACE, when there is concern about bleeding from the arterial stick (3.1).

3.1

Phase III Study of Transarterial Chemoembolization (TACE) with or without Sorafenib in Unresectable Hepatocellular Carcinoma (HCC)

Protocol ID: ECOG-E1208 **Target Accrual:** 400 (Open)



www.clinicaltrials.gov, May 2011.

Tracks 11-13

Case discussion

A 41-year-old man with a 7-cm right cecal mass and pulmonary and hepatic metastases exhibits a complete response to six cycles of FOLFIRI/bevacizumab.

DR VENOOK: This was a healthy 41-year-old with the exception of the large tumor in his right colon. The tumor occupied about half to two thirds of the lumen of the cecum, yet it was asymptomatic except for some pain. He had no bleeding or obstruction.

The relevant issue here is how to approach the asymptomatic primary. One could argue, "Why start with chemotherapy?" From my perspective, you may only get one chance to administer chemotherapy. If you perform an operation and the patient has a complication, then you may not get an opportunity to administer chemotherapy.

Some data relevant to this setting were presented at ASCO 2010 (McCahill 2010). On the Phase II NSABP-C-10 study, patients with synchronous metastatic disease and primary tumors in place received FOLFOX/bevacizumab. The study evaluated the likelihood of complications and what

percentage of patients went on to surgery. The study accrued about 90 patients and reported that 14 percent had a need for intervention — 10 patients required surgical intervention (McCahill 2010). Those data support the idea that you can administer chemotherapy in this setting, although it's a balancing act. We've all observed that the primary tumors melt away in these patients.

For this patient I requested that the far extent of the disease be tattooed because I wanted to know how far it extended into the right colon. Doing so is important because if you get a spectacular response it may make sense to resect the primary as a palliative maneuver in a patient with well-controlled metastatic disease if any tumor is left in the cecum.

DR LOVE: So what happened with this patient?

DR VENOOK: We administered FOLFIRI/bevacizumab and he had an excellent response. His symptoms disappeared in the first couple weeks and he's now received six cycles of FOLFIRI/bevacizumab. He's also had marked diminution of disease in his lung and liver.

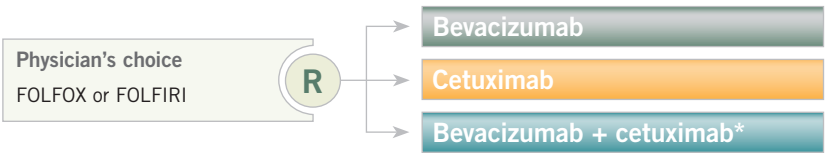
DR LOVE: Is there any interest in evaluating cases with extraordinary responses such as this one for genome sequencing?

DR VENOOK: In our CALGB-C80405 study (3.2), which is evaluating chemotherapy with bevacizumab or cetuximab, one of the correlative science studies takes the extremes — patients who fare exceptionally well or very poorly — and performs selected genome analysis. That's where we may have the best chance of finding an important genetic mutation or polymorphism. ■

3.2

CALGB-C80405 Study: Chemotherapy and Biologic Agents Alone or in Combination for the Treatment of Metastatic Colorectal Cancer

Target Accrual: 2,300 (Open)



* Arm III (bevacizumab + cetuximab) closed to accrual as of September 10, 2009

NCI Physician Data Query, May 2011.

SELECT PUBLICATIONS

McCahill LE et al. **A phase II trial of 5-fluorouracil, leucovorin, and oxaliplatin (mFOLFOX6) chemotherapy plus bevacizumab (bev) for patients (pts) with unresectable stage IV colon cancer and a synchronous asymptomatic primary tumor: Results of NSABP C-10.** *Proc ASCO* 2010;**Abstract 3527**.

Okita K et al. **Phase III study of sorafenib in patients in Japan and Korea with advanced hepatocellular carcinoma (HCC) treated after transarterial chemoembolization (TACE).** Gastrointestinal Cancers Symposium 2010;**Abstract LBA128**.