INTERVIEW

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Tracks 1-10

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Select Excerpts from the Interview

Track 1

DR LOVE: Would you discuss the data you presented at the 2011 Gastrointestinal Cancers Symposium on the use of the Onco*type* DX assay in adjuvant therapy decisions for Stage II colon cancer?

DR MEROPOL: Adjuvant therapy for Stage II colon cancer represents a challenge for all of us, and we're eager for a better method of selecting patients who will benefit the most from adjuvant therapy.

We're now in an era when a number of new platforms are under development to evaluate gene expression in colon cancer as a way to predict which tumors will relapse and which are destined never to relapse. One such platform that

is now commercially available is the Onco*type* DX colon cancer assay, which is a 12-gene expression platform that predicts risk of recurrence at three years based on a study of archived material from the European QUASAR study (Kerr 2009; [4.1]).

In our study we used the Markov model to assess outcomes associated with the use of the Onco*type* DX assay in terms of how such a tool in Stage II colon cancer would affect the use of adjuvant therapy and affect patient outcomes and costs (Meropol 2011). We asked the question, if you use a gene expression profile like Onco*type* DX to select patients for adjuvant therapy, will you come up with a different pattern of care than you would if you used the typical clinical parameters?

The Markov model cycles an imaginary patient through various health states. One pathway evaluates what the side effects are and what's gained and lost if you administer adjuvant therapy, and then another pathway evaluates the patient if you don't administer adjuvant therapy.

We aimed to evaluate whether using the Onco*type* DX assay would increase or decrease the number of quality-adjusted life years — so not only length of life but also the quality of life for the years of life remaining. We found that treatment decisions based on Onco*type* DX reduced adjuvant chemotherapy use by 17 percent, and overall in the population of patients with Stage II colon cancer in our model, an increase in quality-adjusted survival was associated with a decrease in chemotherapy use.

4.1

QUASAR/Onco*type* DX Results: Recurrence Risk in Prespecified Recurrence Risk Groups (n = 711)

Recurrence risk group	Range of Recurrence Score	Proportion of patients	Kaplan-Meier estimates of recurrence risk at 3 years*
Low	<30	43.7%	12%
Intermediate	30-40	30.7%	18%
High	≥41	25.6%	22%

* With surgery alone

Kerr D et al. *Proc ASCO* 2009;**Abstract 4000**.

Track 5

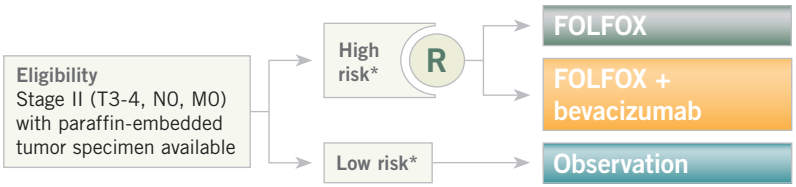
DR LOVE: What is the status of the ECOG-E5202 trial for patients with Stage II colon cancer?

DR MEROPOL: One of the objectives of this study for patients with Stage II colon cancer was to validate whether we could identify a population at low risk based on microsatellite instability and 18q loss of heterozygosity. Patients with 18q loss of heterozygosity were hypothesized to be in a higher-risk group, as

4.2

FOLFOX with or without Bevacizumab for Patients with Resected Stage II Colon Cancer at High Risk for Recurrence

Protocol ID: ECOG-E5202 **Target Accrual:** 3,610 (Closed)



* Patients who are at high risk based on microsatellite instability (MSI) and loss of heterozygosity (LOH) at chromosome 18q are randomly assigned to one of two treatment arms. Patients who are at low risk based on MSI and 18q LOH are assigned to observation.

NCI Physician Data Query, May 2011.

was the group of patients who did not have microsatellite instability or deficient mismatch repair.

Enrolled patients would have their tumors assessed for microsatellite instability and loss of 18q. Patients who were in the low-risk group were observed without adjuvant therapy and their tissue was banked for future research. The patients in the higher-risk group were randomly assigned to receive standard adjuvant therapy with FOLFOX or FOLFOX with bevacizumab (4.2).

Based on emerging data suggesting that bevacizumab does not add to the benefits of FOLFOX in the adjuvant setting (Allegra 2011), the ECOG-E5202 study was recently closed to further accrual. Because a large number of patients had already been accrued to the study, we will definitely be able to validate or refute the prognostic utility of deficient mismatch repair and 18q in the patients on this study.

Even though the sample size in the randomized arm was not sufficient to have a high power, we will be able to perform an exploratory analysis of whether bevacizumab affected outcomes in the population with Stage II disease, keeping in mind that other studies of bevacizumab in the adjuvant setting were largely of patients with Stage III disease. ■

SELECT PUBLICATIONS

Allegra CJ et al. **Phase III trial assessing bevacizumab in stages II and III carcinoma of the colon: Results of NSABP protocol C-08.** *J Clin Oncol* 2011;29(1):11-6.

Kerr D et al. **A quantitative multigene RT-PCR assay for prediction of recurrence in stage II colon cancer: Selection of the genes in four large studies and results of the independent, prospectively designed QUASAR validation study.** *Proc ASCO* 2009;**Abstract 4000**.

Meropol N et al. **Use of a multigene prognostic assay for selection of adjuvant chemotherapy in patients with stage II colon cancer: Impact on quality-adjusted life expectancy and costs.** Gastrointestinal Cancers Symposium 2011;**Abstract 491**.