INTERVIEW

Richard M Goldberg, MD

Dr Goldberg is Professor of Medicine and Physician-in-Chief at OSUCCC–James Cancer Hospital and Klotz Family Chair in Cancer Research at Ohio State University in Columbus, Ohio.

CD 2, Tracks 13-24

Track 13 Perspective on the use of the Onco*type* DX Colon Cancer assay to aid in adjuvant treatment decision-making for patients with Stage II disease

Track 14 Efficacy and tolerability of the oral multikinase inhibitor regorafenib in mCRC

Track 15 Potential use of regorafenib for patients with K-ras wild-type mCRC

Track 16 Viewpoint on the association of K-ras G13D mutation with outcome in patients with mCRC treated with cetuximab

Track 17 Use of FOLFIRINOX for select patients with metastatic pancreatic cancer (PC)

Track 18 Efficacy of regorafenib in patients with advanced GIST refractory to standard therapies

Track 19 Sequencing agents in GI neuroendocrine tumors

Track 20 **Case discussion:** A 60-year-old man with a mass in the tail of the pancreas undergoes a suboptimal pancreatectomy and splenectomy with an initial diagnosis of a neuroendocrine tumor that is revised to acinar PC during second-opinion pathology consultation

Track 21 Adjuvant treatment approach for patients with rare acinar PC

Track 22 **Case discussion:** A 44-year-old man with a poorly differentiated, high-grade neuroendocrine tumor in the cecum and liver metastasis

Track 23 **Case discussion:** A 69-year-old woman who underwent resection for a large rectal polyp with high-grade dysplasia in 2007 presents with pelvic pain and incontinence

Track 24 **Case discussion:** A 46-year-old woman with Lynch syndrome presents with upper abdominal pain and is diagnosed with invasive, moderately differentiated adenocarcinoma of the duodenum

Select Excerpts from the Interview

CD 2, Track 13

DR LOVE: Would you provide your perspective on the role, if any, of the Onco*type* DX Colon Cancer assay in the management of Stage II disease?

DR GOLDBERG: We are observing better outcomes for patients with Stage II colon cancer based on improved surgical techniques and earlier screening. So now, even for untreated patients, we're seeing a 5-year survival rate of approximately 90%.

I believe that the Onco*type* DX assay and similar tests such as ColoPrint® and others have contributed somewhat to this. The Onco*type* DX Colon Cancer assay provides a Recurrence Score based on 7 cancer-related genes that can complement tumor stage and mismatch repair status in the assessment of a patient's risk. Unlike the Onco*type* DX assay for patients with breast cancer, which is both prognostic and predictive, the colon cancer assay is only prognostic.

I occasionally order the assay in my practice. My reflex for patients with Stage II disease is to tell them that I don't believe they need chemotherapy, but I do advise them of the QUASAR data, which reported a 3.6% improvement in 5-year survival for patients with Stage II colon cancer treated with chemotherapy versus surgery alone (QUASAR Collaborative Group 2007).

If patients strongly desire chemotherapy, I ask them, "If your Recurrence Score predicts that you have a 9% recurrence risk versus a 25% recurrence risk, will that make a difference to you in whether you take treatment or not?" If they reply yes, then I order the test (Gray 2011; [4.1]).

4.1

QUASAR/Oncotype DX Results: Assessment of Recurrence Risk for Patients with Stage II Colon Cancer

Recurrence risk group	Range of Recurrence Score	Surgery alone (proportion of patients)	Kaplan-Meier estimate of of recurrence risk at 3 years with surgery alone
Low (n = 311)	<30	43.7%	12%
Intermediate (n = 218)	30-40	30.7%	18%
High (n = 182)	≥41	25.6%	22%

Methods: Study analyzed relationship between the Recurrence Score (RS) and risk of recurrence in patients treated with surgery alone and between Treatment Score (TS) and benefits of adjuvant fluoropyrimidine chemotherapy.

Conclusions: The continuous 12-gene RS has been validated in a prospective study for assessment of recurrence risk in patients with Stage II colon cancer after surgery and provides prognostic value that complements T stage and MMR. The TS was not predictive of chemotherapy benefit.

Gray RG et al. *J Clin Oncol* 2011;29(35):4611-9.

CD 2, Track 17

DR LOVE: What are your thoughts on the use of FOLFIRINOX in the systemic management of pancreatic cancer?

DR GOLDBERG: A study that was published last year investigating the use of FOLFIRINOX versus gemcitabine in pancreatic cancer demonstrated a median overall survival of approximately 1 year with FOLFIRINOX (Conroy 2011; [4.2]). The FOLFIRINOX regimen is intensive, and not every patient can tolerate it. The dose has to be adjusted for certain patients, but at least it is a step forward. Those of us who have experience with this regimen have been pleased with the tolerance and the response rate.

I administer FOLFIRINOX in practice, although the patients I see are often older, with comorbidities and a performance score of 2, so I'm not so enthusiastic. I give younger patients with metastatic disease and a performance score of 0 the option of receiving the more aggressive FOLFIRINOX regimen. I also tell patients that they could receive gemcitabine, which is easier to tolerate and has less toxicity but a modest response rate. I let the patient participate in the decision-making regarding which chemotherapy to use. ■

4.2

Efficacy of FOLFIRINOX versus Gemcitabine in a Phase II/III Study of Initial Therapy for Metastatic Pancreatic Cancer

	Gemcitabine (n = 171)	FOLFIRINOX (n = 171)	Hazard ratio	*p*-value
ORR	9.4%	31.6%	Not reported	<0.001
PFS	3.3 mo	6.4 mo	0.47	<0.001
OS	6.8 mo	11.1 mo	0.57	<0.001

Select Grade ≥3 adverse events occurring in >5% of patients

Adverse events	Gemcitabine (n = 171)	FOLFIRINOX (n = 171)	*p*-value
Neutropenia	21.0%	45.7%	<0.001
Febrile neutropenia	1.2%	5.4%	0.03
Thrombocytopenia	3.6%	9.1%	0.04
Diarrhea	1.8%	12.7%	<0.001
Sensory neuropathy	0%	9.0%	<0.001

Conclusions:

- FOLFIRINOX was associated with a survival advantage and had more toxicity compared to gemcitabine.
- FOLFIRINOX is an option for patients with metastatic pancreatic cancer and good performance status.

ORR = objective response rate; PFS = progression-free survival; OS = overall survival

Conroy T et al. *N Engl J Med* 2011;364(19):1817-25.

SELECT PUBLICATIONS

Conroy T et al. **FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer.** *N Engl J Med* 2011;364(19):1817-25.

Gray RG et al. **Validation study of a quantitative multigene reverse transcriptase-polymerase chain reaction assay for assessment of recurrence risk in patients with stage II colon cancer.** *J Clin Oncol* 2011;29(35):4611-9.

Innocenti F et al. **A genome-wide association study of overall survival in pancreatic cancer patients treated with gemcitabine in CALGB 80303.** *Clin Cancer Res* 2012;18(2):577-84.

Lorgis V et al. **Influence of localization of primary tumor on effectiveness of 5-fluorouracil/leucovorin combined with irinotecan and oxaliplatin (FOLFIRINOX) in patients with metastatic pancreatic adenocarcinoma: A retrospective study.** *Anticancer Res* 2012;32(9):4125-30.

Mahaseth H et al. **Safety and efficacy of modified FOLFIRINOX in pancreatic cancer: A retrospective experience.** *Proc ASCO* 2012;**Abstract e14614**.

Marshall JL. **Risk assessment in Stage II colorectal cancer.** *Oncology (Williston Park)* 2010;24 (1 Suppl 1):9-13.

O'Connell M et al. **Validation of the 12-gene colon cancer recurrence score (RS) in NSABP C07 as a predictor of recurrence in stage II and III colon cancer patients treated with 5FU/LV (FU) and 5FU/LV + oxaliplatin (FU + Ox).** *Proc ASCO* 2012;**Abstract 3512**.

O'Connell MJ et al. **Relationship between tumor gene expression and recurrence in four independent studies of patients with stage II/III colon cancer treated with surgery alone or surgery plus adjuvant fluorouracil plus leucovorin.** *J Clin Oncol* 2010;28(25):3937-44.

QUASAR Collaborative Group. **Adjuvant chemotherapy versus observation in patients with colorectal cancer: A randomized study.** *Lancet* 2007;370(9604):2020-29.