



INTERVIEW

David P Ryan, MD

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Tracks 1-9

- Track 1** Clinical experience with FOLFIRINOX in advanced pancreatic cancer (PC)
- Track 2** Current role of FOLFIRINOX in the adjuvant and neoadjuvant settings
- Track 3** Therapeutic options for patients with locally advanced PC
- Track 4** Adjuvant chemotherapy with or without radiation therapy in PC
- Track 5** RTOG-0848: Adjuvant gemcitabine with or without erlotinib followed by chemotherapy with or without radiation therapy for pancreatic adenocarcinoma
- Track 6** Preoperative short-course chemoradiation with proton beam therapy and capecitabine for resectable ductal adenocarcinoma of the pancreatic head
- Track 7** Second-line therapy options for patients with metastatic PC
- Track 8** Clinical relevance of EGFR and K-ras status in the treatment of PC
- Track 9** Investigating the role of early palliative care in patients with PC

Select Excerpts from the Interview

Tracks 1, 7

► **DR LOVE:** What is the most common question you receive from oncologists regarding first-line therapy for patients with advanced pancreatic cancer?

► **DR RYAN:** Oncologists want to know what our experience has been with FOLFIRINOX. I would say that you see durable responses with FOLFIRINOX that you rarely saw with gemcitabine (Conroy 2011; [2.1]). Patients experience tumor shrinkage and generally feel a lot better.

2.1

Efficacy of FOLFIRINOX versus Gemcitabine in a Phase III Study of Initial Therapy for Stage IV 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

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

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

The problem with FOLFIRINOX is that it is difficult to administer safely. Patients become dehydrated quickly as a result of the underlying nausea, pain and anorexia. They don't eat and drink as much as they should and are not in great shape physically. If you are aggressive about hydration, you can generally get patients on a dose and a schedule with this regimen that's good for them.

We administer preemptive IV fluids, and it is also important to make sure that patients are taking both ondansetron and dexamethasone to prevent nausea. With ondansetron alone patients can experience some breakthrough nausea, so it's important to also administer dexamethasone. If that approach doesn't work, we quickly move to aprepitant.

► **DR LOVE:** Do you administer FOLFIRINOX to older patients?

► **DR RYAN:** Older patients have difficulty staying hydrated and dealing with pain and constipation issues. You need to be careful when administering FOLFIRINOX in this setting. We often start older patients out with FOLFOX and add irinotecan after ascertaining that they can tolerate FOLFOX.

► **DR LOVE:** What are your thoughts on the use of erlotinib for patients with pancreatic cancer?

► **DR RYAN:** A Canadian group reported that the addition of erlotinib to gemcitabine improves survival by several weeks compared to gemcitabine alone (Moore 2007). A publication in *Cancer* from the same Canadian group evaluated the K-ras mutation status of patients on their study (de Cunha Santos 2010). Although the authors didn't report a statistically significant difference between K-ras wild-type cases and those with K-ras mutations, my own interpretation of that study is that a signal was definitely present — patients with K-ras wild-type disease had a fairly good hazard ratio if they received erlotinib compared to those who did not. I do not administer erlotinib to patients with K-ras mutation-positive disease, but for those with K-ras wild-type disease, I certainly consider it.

Tracks 4-6

► **DR LOVE:** Is there anything new and notable in adjuvant treatment of pancreatic cancer?

► **DR RYAN:** The second most common question I receive in the pancreatic cancer arena has to do with the use of radiation therapy and whether it provides sufficient benefit. There's a divide between Europe and North America.

The Europeans have moved away from using chemoradiation therapy. Results were disappointing in randomized controlled studies. An ESPAC study did not report a benefit to chemoradiation therapy administered after resection of pancreatic cancer (Neoptolemos 2004). In fact, outcomes seemed to be a little worse. It is difficult to deliver upper gastrointestinal tract chemoradiation therapy — patients don't like it and get sick, and the older the patient is, the sicker he or she becomes. Hence, in Europe they administer 6 months of gemcitabine-based chemotherapy alone.

In North America there is a lot of attention to the risk of local recurrence. Chemoradiation therapy reduces the locoregional recurrence rate. If we had better systemic therapy, we would see an improvement in survival. Hence, we still include chemoradiation in adjuvant therapy for pancreatic cancer.

An ongoing cooperative group study led by RTOG is attempting to address this divide. Patients receive adjuvant gemcitabine with or without erlotinib followed by randomization to either further gemcitabine with or without erlotinib or gemcitabine with or without erlotinib with added chemoradiation therapy (2.2).

Part of the problem in our approach in the United States is that postoperative chemoradiation therapy is difficult to administer and to tolerate. We prefer to deliver preoperative chemoradiation therapy because it is easier to tolerate. We have been experimenting on protocol with neoadjuvant capecitabine and proton beam therapy (5-times-5 fraction) (Hong 2011).

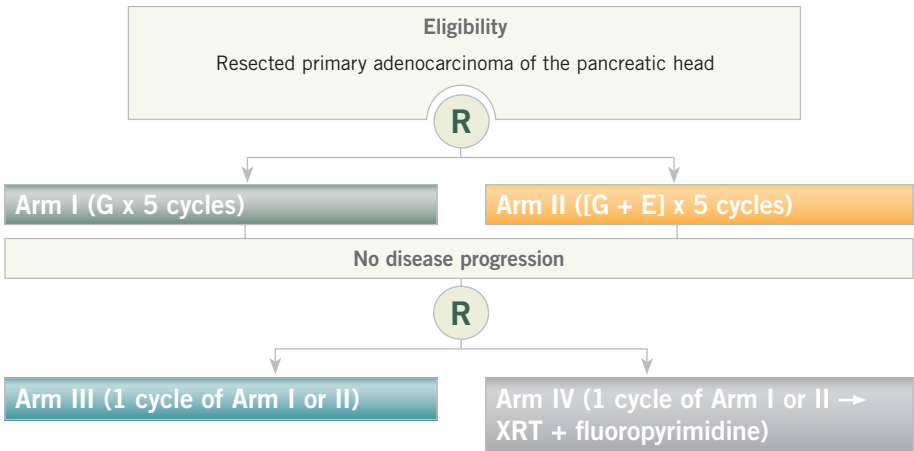
The advantage of using protons is that you can paint in the dose and avoid exposure in normal tissues, thus reducing toxicity. We use capecitabine as a radiation sensitizer for 2 weeks, patients go to surgery and after surgery we administer gemcitabine. ■

2.2

Phase III Trial of Gemcitabine (G) with or without Erlotinib (E) Followed by Chemotherapy with or without Radiation Therapy (XRT) for Patients with Resected Pancreatic Cancer

Protocol ID: RTOG-0848

Target Accrual: 950 (Open)



NCI Physician Data Query, April 2012; www.rtog.org.

SELECT PUBLICATIONS

Da Cunha Santos G et al. **Molecular predictors of outcome in a phase 3 study of gemcitabine and erlotinib therapy in patients with advanced pancreatic cancer: National Cancer Institute of Canada Clinical Trials Group Study PA.3.** *Cancer* 2010;116(24):5599-607.

Hong TS et al. **Phase I study of preoperative short-course chemoradiation with proton beam therapy and capecitabine for resectable pancreatic ductal adenocarcinoma of the head.** *Int J Radiat Oncol Biol Phys* 2011;79(1):151-7.

Moore MJ et al. **Erlotinib plus gemcitabine compared with gemcitabine alone in patients with advanced pancreatic cancer: A phase III trial of the National Cancer Institute of Canada Clinical Trials Group.** *J Clin Oncol* 2007;25(15):1960-6.

Neoptolemos JP et al. **A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer.** *N Engl J Med* 2004;350(12):1200-10.