INTERVIEW

Jean-Yves Douillard, MD, PhD

Dr Douillard is Professor of Medical Oncology and Director of Clinical and Translational Research at ICO R Gauducheau in Saint Herblain, France.

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Track 2 Immediate surgery versus perioperative systemic therapy for patients with CRC liver metastases

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Track 4

DR LOVE: The use of adjuvant therapy for Stage II colon cancer has long been controversial. Would you discuss your treatment decision-making process in that situation?

DR DOUILLARD: In low-risk Stage II disease I see no reason to administer adjuvant chemotherapy. The benefit is minimal, and if chemotherapy is administered, it is generally capecitabine or IV 5-FU. But again, the benefit is nonsignificant for overall survival and minimal for recurrence-free survival and the agents are toxic.

In high-risk Stage II disease I have no doubt that patients should receive adjuvant chemotherapy — the question is whether they should receive FOLFOX or 5-FU only.

A marker we could use is microsatellite instability (MSI). Because patients with so-called MSI-high disease generally have a better prognosis, they don't benefit from adjuvant 5-FU. They may benefit from oxaliplatin, but oxaliplatin as a single agent has almost no activity. So these cases should be discussed individually using a multidisciplinary approach. We also have to evaluate histoprognostic factors, microemboli and T4 for a high risk of recurrence. It is a difficult recommendation, and it depends on the individual patient profile.

Several gene profiles have been identified, one of which is the Onco*type* DX colon cancer assay. The technologies used for these gene profile assays vary. They are not yet standardized or routinely available, but I believe that's where the future lies.

Track 11

DR LOVE: What are your thoughts on the use of FOLFIRINOX in early and advanced-stage pancreatic cancer?

DR DOUILLARD: We have shown in France that FOLFIRINOX may almost double median survival in the metastatic setting (Conroy 2011; [4.1]), but this is not a regimen for everyone because it is toxic. If the patient has a good performance status, has not lost too much weight and is not too old, FOLFIRINOX is an option.

The key toxicity of oxaliplatin is neuropathy. Even when the treatment duration is not long, many patients experience neuropathy. We also see myelosuppression and diarrhea, so we often have to dose adapt, educate the patients and monitor them carefully.

If a patient cannot receive FOLFIRINOX we still have gemcitabine as an option, but it's clearly not satisfactory. The most interesting approach, which is now in a clinical trial, is the use of FOLFIRINOX preoperatively for patients with unresectable pancreatic tumors and no metastases. The response rate is high with tumor shrinkage, so more patients go on to surgery.

4.1

Efficacy of FOLFIRINOX versus Gemcitabine as First-Line Therapy for Metastatic Pancreatic Cancer

	FOLFIRINOX	Gemcitabine
Median overall survival	11.1 months	6.8 months
Median progression-free survival	6.4 months	3.3 months
Objective response rate	31.6%	9.4%

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

The other option for patients with resectable disease up front is adjuvant FOLFIRINOX. I have used this approach for 1 patient, but patients with resectable pancreatic cancer are rare. In the adjuvant setting I try to administer the regimen for 6 months, but often after 2 to 3 cycles dose adaptations are needed.

Track 12

DR LOVE: What is your current treatment approach to rectal cancer?

DR DOUILLARD: We have established that the sequence should be preoperative chemoradiation therapy followed by surgery after a 6-week interval and then adjuvant chemotherapy. It's important to have an idea of the effect of chemoradiation therapy on the tumor itself, which you won't see if you operate the week after the end of the radiation therapy.

The question is, however, what type of chemotherapy should be used in combination with the radiation therapy? Most of the studies I've seen that added oxaliplatin to 5-FU or capecitabine were inconclusive (Aschele 2011). The pathologic complete response rate was a bit higher in the German CAO/ARO/AIO-94 trial, although in another trial it was not significant (Roedel 2011; Roh 2011). I am not convinced that the addition of oxaliplatin to 5-FU is a breakthrough in the adjuvant treatment of colon and rectal cancer. The toxicity of oxaliplatin in the long term has to be considered. I believe the best combination remains a fluoropyrimidine with radiation therapy for 5 weeks.

DR LOVE: How do you choose between fluoropyrimidines in rectal cancer, both in the preoperative setting and as adjuvant therapy?

DR DOUILLARD: Studies have demonstrated that we can administer capecitabine instead of 5-FU and the outcome is exactly the same (Hofheinz 2011). Patients prefer that approach more in rectal cancer and colon cancer, so that is what I do. ■

SELECT PUBLICATIONS

Aschele C et al. **Primary tumor response to preoperative chemoradiation with or without oxaliplatin in locally advanced rectal cancer: Pathologic results of the STAR-01 randomized phase III trial.** *J Clin Oncol* 2011;29(20):2773-80.

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

Hofheinz R et al. **Capecitabine (cape) versus 5-fluorouracil (5-FU)-based (neo)adjuvant chemoradiotherapy (CRT) for locally advanced rectal cancer (LARC): Long-term results of a randomized, Phase III trial.** *Proc ASCO* 2011;**Abstract 3504**.

Roedel C et al. **Preoperative chemoradiotherapy and postoperative chemotherapy with 5-fluorouracil and oxaliplatin versus 5-fluorouracil alone in locally advanced rectal cancer: First results of the German CAO/ARO/AIO-04 randomized phase III trial.** *Proc ASCO* 2011;**Abstract LBA3505**.

Roh MS et al. **The impact of capecitabine and oxaliplatin in the preoperative multimodality treatment in patients with carcinoma of the rectum: NSABP R-04.** *Proc ASCO* 2011;**Abstract 3503**.