INTERVIEW

Francine Foss, MD

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Tracks 1-17

Select Excerpts from the Interview

Tracks 1-5, 9

Case discussion

A 34-year-old woman with a history of patch-plaque mycosis fungoides and erythroderma undergoes treatment with CHOP x 6 but experiences relapse within six months of completing therapy and receives romidepsin.

DR FOSS: Like many patients with cutaneous T-cell lymphoma (CTCL) who receive CHOP, she had a very good clinical response but experienced

a quick relapse. When she presented to me she had extensive plaques, areas of erythema and multiple tumors, some of which were five centimeters in diameter on her trunk and interior chest wall.

This patient illustrates an interesting point about how mycosis fungoides can evolve. Many patients who present with patches and plaques may remain free of progression for a long time. However, when the disease progresses to tumor-stage disease, you need to be concerned that it is declaring itself as a disease with a more aggressive clinical course.

It is important to rebiopsy these tumors to determine whether the histology has changed and evolved into a large cell transformation because that portends a much different prognosis for the patient. Fortunately, this patient's disease did not transform.

DR LOVE: How do you decide on the sequence of treatments to use for these patients and for this woman?

DR FOSS: This patient had previously received CHOP chemotherapy from another physician. Clinicians who are not that familiar with CTCL may view this disease as similar to other lymphomas and jump right to CHOP as a reflex reaction. So she is different from the de novo patient I would be caring for from the outset of her diagnosis. Generally speaking, for a patient with extensive patch-plaque disease, my first treatment would be a skin-based therapy along with one of the oral therapies — bexarotene or vorinostat.

Because this patient already received CHOP and experienced relapse with fairly aggressive clinical disease, a number of options are available, depending on the long-term plan for this patient.

In terms of the big picture for this patient, she's a young woman with aggressive, refractory disease. I am increasingly considering the use of allogeneic stem cell transplant in this setting, but we know that these patients need to be in remission and we need to administer effective salvage chemotherapy. If one were considering single-agent chemotherapy, liposomal doxorubicin and gemcitabine have demonstrated activity in this setting. Romidepsin, which is FDA approved for CTCL (Whittaker 2010; [3.1]), and pralatrexate, which is approved for peripheral T-cell lymphoma (PTCL), are also both options.

3.1

Final Results of a Multicenter, International Pivotal Study of Romidepsin in Refractory Cutaneous T-Cell Lymphoma

All (N = 96)		Stage IIB to IVA (n = 68)			
ORR (CR + PR)	CR	ORR (CR + PR)	CR	Median TTR	Median DOR
34%	6%	38%	7%	2 mo	15 mo

ORR = overall response rate; CR = complete response; PR = partial response; TTR = time to response; DOR = duration of response

Whittaker SJ et al. *J Clin Oncol* 2010;28(29):4485-91.

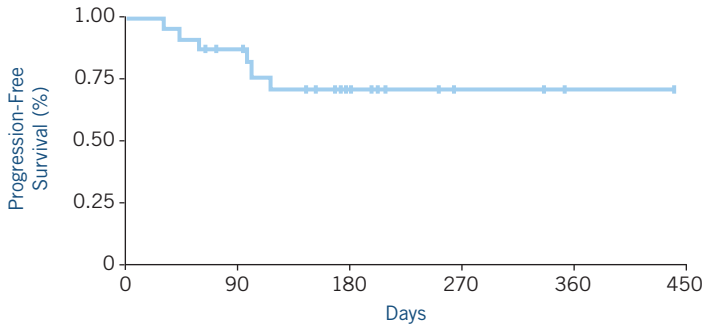
A study presented by Dr Horwitz at ASH 2010 involved more than 50 patients with relapsed or refractory CTCL, and that study showed a high response rate for pralatrexate administered at a slightly lower dose and on a different schedule than in PTCL (Horwitz 2010; [3.2]).

I decided to administer romidepsin to this patient, and she experienced a partial response for about four months before recurrence. She did not experience a response to denileukin diftitox, and we could not obtain coverage for pralatrexate. She experienced a very good partial response, if not complete response, to gemcitabine, and I am hoping to move forward with an allogeneic stem cell transplant.

A couple of clinical issues are worth considering. Once a patient is in remission, how do you keep that patient in remission? No studies address maintenance therapy, although we administer agents such as romidepsin, and even bexarotene or vorinostat, until patients experience relapse. For this patient, I decided to treat with vorinostat because it's an agent that's relatively well tolerated in this setting and I planned to administer radiation therapy to consolidate her response before the transplant.

3.2

PDX-010 Study: Progression-Free Survival with the Optimal Dose and Schedule of Pralatrexate in Relapsed or Refractory Cutaneous T-Cell Lymphoma



	n	Response rate
Response 15 mg/m^2 (3/4 weeks)	29	45%

With permission from Horwitz SM et al. *Proc ASH* 2010;**Abstract 2800**.

Tracks 9, 11

DR LOVE: Returning to the biopsy for this patient, how would your approach have changed if her disease had transformed?

DR FOSS: If the rebiopsy had shown a large cell transformation, then I probably would have been more aggressive. If you examine our clinical trials

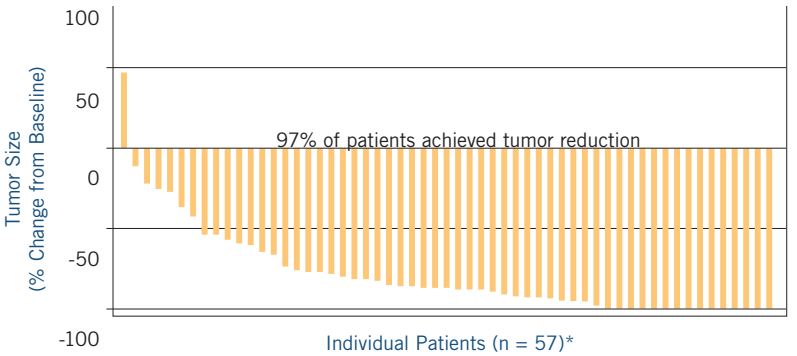
with approved agents — denileukin diftitox, bexarotene and romidepsin — we excluded patients with large cell transformation. The only study that addressed those patients was with pralatrexate. So my choice for her would probably have been pralatrexate or perhaps a more aggressive chemotherapy approach.

DR LOVE: Would you have tried to enroll her on a trial of SGN-35?

DR FOSS: SGN-35, or brentuximab vedotin, is an antibody conjugated with a toxin, and it is an active agent. Data were recently presented at ASH in ALCL with this agent that showed a high response rate in these patients who had previously treated, refractory disease (Shustov 2010; [3.3]). It was an astounding response rate in that setting. It's also well tolerated with minimal side effects. So if it were available and she had CD30-positive disease, I would have administered SGN-35, and we'd love to have clinical trials for these patients. ■

3.3

Response and Maximum Tumor Reduction in Patients with Relapsed or Refractory Systemic Anaplastic Large Cell Lymphoma Treated with Brentuximab Vedotin (SGN-35)



* 57 of 58 patients with postbaseline CT assessments

Response	Independent review facility	Investigator
Overall response rate	86%	81%
Complete remission	53%	59%
Partial remission	33%	22%

With permission from Shustov AR et al. *Proc ASH* 2010;**Abstract 961**.

SELECT PUBLICATIONS

Horwitz SM et al. **Identification of an active, well-tolerated dose of pralatrexate in patients with relapsed or refractory cutaneous T-cell lymphoma (CTCL): Final results of a multicenter dose-finding study.** *Proc ASH* 2010;**Abstract 2800**.

Shustov AR et al. **Complete remissions with brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large cell lymphoma.** *Proc ASH* 2010;**Abstract 961**.

Whittaker SJ et al. **Final results from a multicenter, international, pivotal study of romidepsin in refractory cutaneous T-cell lymphoma.** *J Clin Oncol* 2010;28(29):4485-91.