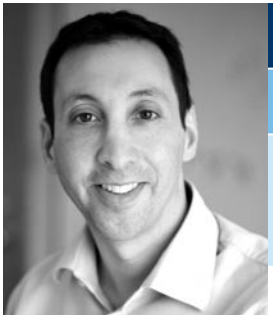

INTERVIEW

Steven M Horwitz, MD

Dr Horwitz is Assistant Attending in the Lymphoma Service, Division of Hematologic Oncology at Memorial Sloan-Kettering Cancer Center in New York, New York.

Tracks 1-14

Select Excerpts from the Interview

Tracks 3, 7

DR LOVE: Would you discuss the efficacy and safety of pralatrexate and romidepsin in T-cell lymphomas?

DR HORWITZ: I have been involved with trials evaluating the novel agents pralatrexate and romidepsin in T-cell lymphomas, and I would say that at a minimum the quality of the data that have been generated with these agents is much better than the historical data. Pralatrexate received FDA approval for relapsed or refractory peripheral T-cell lymphoma (PTCL) on the basis of

the Phase II PROPEL study, which had 109 patients who were evaluable for efficacy. Aside from these two new agents, no other study has enrolled more than 25 or 30 patients. In view of this, I believe that confidence is higher in the recent data sets.

In a single-center study initially conducted at Memorial Sloan-Kettering Cancer Center, the response rate with pralatrexate in relapsed or refractory PTCL was approximately 40 percent. When pralatrexate was investigated in the Phase II PROPEL study at more than 20 centers worldwide, the response rate by formal central review was determined to be 28 percent, with some of the responses being complete responses. The median duration of response was approximately 10 months (O'Conner 2009).

Pralatrexate is easy to administer as an intravenous push for three to five minutes. The approved dose and schedule is 30 mg/m^2 weekly for six out of seven weeks. It does not cause much nausea, and premedication with prochlorperazine may suffice.

The main side effect we noted with earlier studies was severe oral stomatitis, which limited administration. Subsequently, pralatrexate dosing was reduced and patients received presupplementation with folic acid and vitamin B12. Since these modifications, we see much less incidence of severe mucositis.

Tracks 5-6

DR LOVE: What are your thoughts on romidepsin, the other new agent for T-cell lymphomas?

DR HORWITZ: Romidepsin is a histone deacetylase inhibitor and is approved for cutaneous T-cell lymphoma (CTCL). We recently finished a 130-patient study for aggressive PTCL, similar in design to the pralatrexate PROPEL study. The central review for response rates is ongoing, and we should have the response data soon.

The National Cancer Institute experience looks good, reporting response rates of more than 30 percent across a number of different subtypes (Piekarz 2008; [2.1]). The standard dosing approved for CTCL is 14 mg/m^2, administered intravenously weekly, for three out of four weeks. The drug is administered as a four-hour infusion. In PTCL studies, the same dose and schedule are being used. The toxicities are not cumulative, so patients can continue receiving romidepsin as long as it provides a benefit.

The main issue, historically, has been a worry about QTc prolongation. If patients with known arrhythmias and those receiving concomitant medications that can cause QTc prolongation are excluded, then we do not see any changes in the QTc interval. This has been much less of a concern once people have been aware of the risk.

In the clinical studies, EKG monitoring was conducted before and after treatment. I also check electrolytes at baseline before the first cycle and make sure

that the potassium and magnesium levels are okay. If they are below normal, then I supplement them.

I also check an EKG postantiemetic and postromidepsin during the first cycle. If I don't see any QTc prolongation, then I don't conduct additional EKG monitoring. I simply make sure that the electrolytes are in the normal range before starting each cycle.

We also observe malaise with romidepsin and sometimes nausea and vomiting. High-grade fatigue, with which patients might lose weight or experience severe nausea or vomiting, is not common. For most patients the fatigue is lower grade and they experience some tiredness with a loss of appetite. The main hematologic side effect is thrombocytopenia, and occasionally we might have to hold the drug because of low platelet counts. If the drug is skipped for a week, thrombocytopenia resolves right away. ■

2.1

Phase II National Cancer Institute Multicenter Study of Romidepsin in Relapsed or Refractory Peripheral T-Cell Lymphoma (n = 43)

Overall response	Complete response	Partial response
38%	15%	23%

"This study demonstrates tolerability and durable clinical benefit...of romidepsin in pts with recurrent or refractory PTCL."

Piekarz R et al. *Proc ASH* 2008;**Abstract 1567**.

SELECT PUBLICATIONS

Coiffier B et al. **Final results from a pivotal, multicenter, international, open-label, phase 2 study of romidepsin in progressive or relapsed peripheral T-cell lymphoma (PTCL) following prior systemic therapy.** *Proc ASH* 2010;**Abstract 114**.

Goy A et al. **Pralatrexate is effective in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL) with prior ifosfamide, carboplatin, and etoposide (ICE)-based regimens.** *Proc ASH* 2010;**Abstract 1753**.

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**.

Horwitz SM et al. **Pralatrexate is active in cutaneous T-cell lymphoma (CTCL): Results of a multicenter, dose-finding trial.** *Proc ASH* 2009;**Abstract 919**.

O'Conner O et al. **PROPEL: Results of the pivotal, multicenter, phase II study of pralatrexate in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL).** *Proc ASCO* 2009;**Abstract 8561**.

Piekarz RL et al. **Phase II multi-institutional trial of the histone deacetylase inhibitor romidepsin as monotherapy for patients with cutaneous T-cell lymphoma.** *J Clin Oncol* 2009;27(32):5410-7.

Piekarz R et al. **Results of a Phase 2 NCI multicenter study of romidepsin in patients with relapsed peripheral T-cell lymphoma (PTCL).** *Proc ASH* 2008;**Abstract 1567**.

Pinter-Brown L et al. **Safety and management of pralatrexate treatment in relapsed or refractory peripheral T-cell lymphoma (PTCL).** *Proc ASH* 2009;**Abstract 1675**.

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.