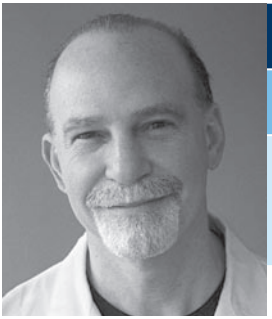

INTERVIEW

Steven T Rosen, MD

Dr Rosen is Genevieve Teuton Professor of Medicine and Director of the Robert H Lurie Comprehensive Cancer Center of Northwestern University in Chicago, Illinois.

Tracks 1-10

Track 1	Classification and spectrum of T-cell lymphomas
Track 2	Pralatrexate: A novel antifolate agent with activity in T-cell lymphomas
Track 3	HDAC inhibitors depsipeptide and vorinostat in T-cell lymphomas
Track 4	Role of denileukin diftitox in T-cell lymphomas
Track 5	Efficacy and safety of bexarotene in cutaneous T-cell lymphomas
Track 6	Common side effects of pralatrexate, depsipeptide and denileukin diftitox
Track 7	Treatment algorithm in the management of T-cell lymphomas
Track 8	**Case discussion:** A 60-year-old man with Sézary syndrome remains in complete response for four years with matched sibling miniallogeneic transplant after a relapsing-remitting course over 10 years
Track 9	**Case discussion:** A 65-year-old man with systemic cytotoxic T-cell lymphoma is in complete response for two years after receiving combination chemotherapy
Track 10	**Case discussion:** A 75-year-old man with mycosis fungoides achieves a partial response with single-agent pralatrexate after a relapsing-remitting course over nine years with multiple therapeutic regimens

Select Excerpts from the Interview

Tracks 2, 6

DR LOVE: Would you discuss what we know about the efficacy and safety of pralatrexate in T-cell lymphomas (Savage 2009; [4.1]; Shustov 2010; [4.2])?

DR ROSEN: Within the past few months, two new agents have been approved for the treatment of T-cell lymphomas. Although these agents do not have a novel mechanism of action, they do have a novel level of activity. Pralatrexate is an antifolate agent and has a higher affinity for the folate carrier compared to methotrexate. It also appears to be more potent than methotrexate in vitro.

According to data from the original trials, pralatrexate was effective in patients who were unresponsive to methotrexate and in those with only brief responses to methotrexate.

Regarding the adverse events, thrombocytopenia and mucositis have been reported with the administration of pralatrexate. The use of folic acid and vitamin B_{12} appear to reduce this complication.

4.1

Treatment Response to Pralatrexate in Patients with Peripheral T-Cell Lymphomas and No Evidence of Response to Most Recent Prior Therapy (n = 69)

Overall response	Median response duration	Median number of therapies
25%	99 days	3

Savage K et al. *Proc ASH* 2009;**Abstract 1678**.

4.2

Relationship between Response and Survival in Patients with Peripheral T-Cell Lymphoma Treated with Pralatrexate (n = 109)

Overall response*	Reduction in risk of death for responding patients	Hazard ratio	*p*-value
29%	44%	0.56	0.07

* By independent central review using International Workshop Criteria

Shustov AR et al. *Proc ASCO* 2010;**Abstract 8054**.

Tracks 3, 6

DR LOVE: What about the other new agent, romidepsin? Would you discuss the novel histone deacetylase (HDAC) inhibitors in T-cell lymphomas and the data recently presented at ASCO (Kim 2010; [4.3])?

DR ROSEN: Romidepsin — formerly called depsipeptide — is another new drug and is classified as an HDAC inhibitor. Vorinostat, an orally administered agent, is another HDAC inhibitor that was approved earlier for mycosis fungoides and Sézary syndrome. Romidepsin is administered intravenously, and associated adverse effects include fatigue, malaise, nausea and transient

4.3

Romidepsin Activity in All Three Disease Compartments (Skin, Blood and Lymph Nodes) in Patients with Cutaneous T-Cell Lymphoma

Overall response by composite endpoint[1]	≥50% skin response	≥50% reduction in Sézary cells	≥30% reduction by RECIST
33/96 (34%)	38/96 (40%)	10/13 (77%)	13/37 (35%)

[1] Composite endpoint defines complete response as total resolution of skin disease, no abnormal lymph nodes and no circulating Sézary cells. A partial response is 50 percent or greater improvement in the sum of the three assessments with at least a 30 percent reduction in skin disease.

Kim E et al. *Proc ASCO* 2010;**Abstract 8047**.

cytopenias. Some concern surrounds potential cardiac toxicity due to QT prolongation, but this has not been a major problem during the clinical trials for patients with lymphoma.

Tracks 4, 6

DR LOVE: Which other agents have been used for the treatment of T-cell lymphomas, and how do they compare to some of the newer ones?

DR ROSEN: Another agent is denileukin diftitox, a recombinant protein comprising interleukin-2 and diphtheria toxin. It affects protein synthesis using the diphtheria toxin, and approximately one third of the patients who receive this agent seem to respond.

Of note, the response rates do not differ dramatically according to the expression of CD25, which is one of the three peptides that make up the interleukin-2 receptor. Patients who express the other two peptides still experience favorable benefits from this treatment.

The major problem associated with denileukin diftitox is peripheral edema because of a vascular leak syndrome that can occur. Other problems can include transient liver enzyme abnormalities, fatigue and malaise. When steroids are administered concurrently, these symptoms are ameliorated.

Track 5

DR LOVE: What is the role of bexarotene for the treatment of T-cell lymphomas?

DR ROSEN: Bexarotene, an oral agent, is effective. It is associated with higher response rates than other agents we've discussed, although a direct comparison has not been made. Bexarotene is extremely well tolerated, but two issues must be addressed during treatment. One issue is fairly simple: Patients develop central hypothyroidism, which requires the use of levothyroxine. The second issue, hyperlipidemia, can consist of elevations in both triglyceride and cholesterol levels, and it can be significant. ■

SELECT PUBLICATIONS

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**.

Kim E et al. **Romidepsin activity in all three disease compartments (skin, blood, lymph nodes) in patients with cutaneous T-cell lymphoma (CTCL).** *Proc ASCO* 2010;**Abstract 8047**.

Piekarz R et al. **Final results of a phase 2 NCI multicenter study of romidepsin in patients with relapsed peripheral T-cell lymphoma (PTCL).** *Proc ASH* 2009;**Abstract 1657**.

Savage K et al. **Pralatrexate induces responses in patients with highly refractory peripheral T-cell lymphoma (PTCL).** *Proc ASH* 2009;**Abstract 1678**.

Shustov AR et al. **Pralatrexate in patients with relapsed/refractory peripheral T-cell lymphoma (PTCL): Relationship between response and survival.** *Proc ASCO* 2010;**Abstract 8054**.