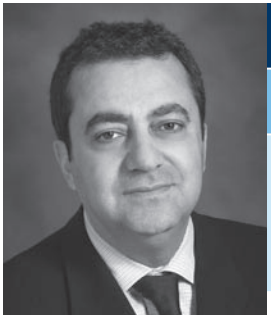

INTERVIEW

Anas Younes, MD

Dr Younes is Director of the Clinical and Translational Research Program and Professor of Medicine in the Department of Lymphoma/Myeloma at The University of Texas MD Anderson Cancer Center in Houston, Texas.

Tracks 1-16

Select Excerpts from the Interview

Tracks 1-2

DR LOVE: What are some of the new agents or therapeutic strategies in the management of Hodgkin lymphoma (HL)?

DR YOUNES: A few novel classes of drugs are being investigated in HL. Brentuximab, or SGN-35, is an antibody-drug conjugate and a leading agent under investigation, and a pivotal trial has recently been completed (NCT00848926).

In addition, administration of the mTOR inhibitor everolimus resulted in response rates of approximately 50 percent, which is remarkable for heavily pretreated disease (Johnston 2010), and the data are being followed up with a large Phase II study from the Mayo Clinic (NCT00436618).

We also have a large randomized trial evaluating ABVD with or without rituximab, which is based on Phase II data from our group (Copeland 2009). The rationale for this approach is that cancer cells can be rendered more sensitive to ABVD chemotherapy by depleting reactive B lymphocytes in the microenvironment.

Another randomized trial in early-stage HL in Europe is evaluating ABVD with either rituximab or radiation therapy. The question is, can we replace radiation therapy with a less toxic drug such as rituximab?

Tracks 4-5

DR LOVE: Would you describe the risk factors and management of tumor lysis syndrome (TLS)?

DR YOUNES: TLS is not a common syndrome, but it is potentially fatal. It is characterized by metabolic derangements from the massive and abrupt release of cellular components in the blood after the rapid lysis of cancer cells.

Until recently, we did not have effective prophylaxis for TLS. The only management strategy available was allopurinol with aggressive hydration. Allopurinol inhibits the formation of uric acid but does not affect the existing uric acid. Now a new agent, rasburicase, is available. This is a recombinant enzyme that breaks down existing uric acid.

In a Phase I/II study evaluating the safety and efficacy of rasburicase in patients at risk for developing TLS, administration of rasburicase improved uric acid levels (Pui 2001; [3.1]). More importantly, significant decreases in serum creatinine levels occurred in patients both with and without hyperuricemia, and none of the patients required dialysis or developed other signs of TLS.

A panel recently provided guidelines on the risk stratification and optimal prophylactic management of TLS (Coiffier 2008; [3.2]). Patients with Burkitt's lymphoma, acute lymphocytic leukemia or AML with high white blood cell counts are in the high-risk category, and those with diffuse large B-cell lymphoma (DLBCL) are currently considered to be in the intermediate-risk category.

3.1

Improved Serum Uric Acid Levels with the Administration of Rasburicase in Patients at High Risk for TLS

	Median uric acid level at baseline	Median uric acid level four hours postrasburicase	*p*-value
All patients (n = 131)	5.7 mg/dL	0.5 mg/dL	<0.0001
Preexisting hyperuricemia (n = 65)	9.7 mg/dL	1.0 mg/dL	0.0001
Normal baseline uric acid levels (n = 66)	4.3 mg/dL	0.5 mg/dL	0.0001

Pui CH et al. *J Clin Oncol* 2001;19(3):697-704.

However, a patient with DLBCL and high-risk features such as high LDH or large masses should be monitored carefully, and rasburicase should be administered at the sign of early TLS.

3.2 **Guidelines for Management of TLS Individualized to Risk Category**

	Low risk for TLS	Intermediate risk for TLS	High risk for TLS
Guideline	Laboratory monitoring	Hydration and allopurinol or rasburicase	Hydration and rasburicase

Coiffier B et al. *J Clin Oncol* 2008;26(16):2767-78.

Tracks 11-12

DR LOVE: Would you describe some of the controversies and novel approaches in MCL?

DR YOUNES: The issue with MCL is that all available data are either from small single-arm Phase II trials or retrospective studies. The NCCN outcomes study showed equivalent benefit with R-hyper-CVAD and R-CHOP followed by transplant (LaCasce 2009), although the Phase II studies suggested that R-hyper-CVAD is better. In the absence of randomized trials, I believe that both of these approaches are fine.

Another agent that is moving up front is bortezomib. It is currently approved for relapsed MCL and is now being combined with R-CHOP, R-EPOCH or R-hyper-CVAD in the initial treatment of this lymphoma.

Lenalidomide is another interesting agent, with a response rate of approximately 30 percent as a single agent for relapsed MCL. Ongoing trials in relapsed MCL are evaluating the lenalidomide/rituximab combination. ■

SELECT PUBLICATIONS

Coiffier B et al. **Guidelines for the management of pediatric and adult tumor lysis syndrome: An evidence-based review.** *J Clin Oncol* 2008;26(16):2767-78.

Copeland AR et al. **Rituximab plus ABVD for patients with newly diagnosed advanced stage classical Hodgkin lymphoma: Results of long follow up and comparison to institutional historical data.** *Proc ASH* 2009;**Abstract 1680**.

Johnston PB et al. **A Phase II trial of the oral mTOR inhibitor everolimus in relapsed Hodgkin lymphoma.** *Am J Hematol* 2010;85(5):320-4.

LaCasce A et al. **R-CHOP followed by high dose therapy and autologous stem cell rescue and R-hyper-CVAD have equivalent PFS and are superior to R-CHOP alone in younger patients with MCL: A comparative effectiveness analysis from the NCCN NHL outcomes database project.** *Proc ASH* 2009;**Abstract 403**.

Pui CH et al. **Recombinant urate oxidase for the prophylaxis or treatment of hyperuricemia in patients with leukemia or lymphoma.** *J Clin Oncol* 2001;19(3):697-704.