INTERVIEW

Julie M Vose, MD

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Tracks 1-22

Track 1 Novel agents — CAL-101 and the Bruton's tyrosine kinase (Btk) inhibitor PCI-32765 — under investigation in B-cell lymphomas

Track 2 Brentuximab vedotin in relapsed or refractory anaplastic large cell lymphoma (ALCL) and Hodgkin lymphoma (HL)

Track 3 Evaluating roles for lenalidomide in non-Hodgkin lymphoma (NHL)

Track 4 Activity and durability of response with lenalidomide in relapsed or refractory transformed NHL

Track 5 Effect of rituximab on long-term outcome in Grade I/II follicular lymphoma (FL)

Track 6 Duration of maintenance rituximab in FL

Track 7 **Case 1 discussion:** A 66-year-old man with blastic mantle-cell lymphoma (MCL) achieves a complete remission with R-hyper-CVAD but experiences relapse 18 months later with pancytopenia and splenomegaly

Track 8 Bendamustine, bortezomib and rituximab (BVR) for relapsed MCL

Track 9 Planned Intergroup study of bendamustine/rituximab (BR) versus BVR with rituximab with or without lenalidomide maintenance therapy for older patients with newly diagnosed MCL

Track 10 Planned Intergroup study of R-hyper-CVAD versus BR followed by autologous stem cell transplant (ASCT) for younger patients with newly diagnosed MCL

Track 11 Off-protocol treatment approach for younger patients with MCL

Track 12 **Case 2 discussion:** A 27-year-old pregnant woman with composite diffuse large B-cell lymphoma (DLBCL) and FL experiences a complete remission after treatment with R-CHOP and presents 2 years later with Grade II FL during a second pregnancy

Track 13 Radioimmunotherapy for relapsed FL

Track 14 Role of transplant in FL

Track 15 **Case 3 discussion:** An 80-year-old woman with symptomatic DLBCL who has a significant history of cardiac disease

Track 16 **Case 4 discussion:** A 55-year-old man with ALK-negative, symptomatic ALCL

Track 17 Clinical trials of brentuximab vedotin in newly diagnosed and relapsed ALCL

Track 18 Long-term outcome of patients with T-cell lymphomas treated with standard therapies

Track 19 Activity and side effects of pralatrexate and romidepsin in peripheral T-cell lymphoma (PTCL)

Track 20 Studies of brentuximab vedotin alone or in combination with chemotherapy in CD30-positive PTCL

Track 21 Front-line management of chronic lymphocytic leukemia (CLL) in younger patients

Track 22 Prophylaxis and treatment of tumor lysis syndrome in CLL

Select Excerpts from the Interview

Track 3

DR LOVE: What new systemic therapy strategies are under investigation for patients with non-Hodgkin lymphoma (NHL)?

DR VOSE: An important area of study includes the expanded use of existing agents such as lenalidomide, which appears to have favorable activity in some types of NHL. Lenalidomide is administered orally and has a good toxicity profile. In both mantle-cell lymphoma (MCL) and diffuse large B-cell lymphoma (DLBCL), it appears to have good activity. In some studies, lenalidomide is being evaluated as maintenance therapy, which is another area that seems promising.

DR LOVE: Would you talk about the paper published by your group earlier this year evaluating single-agent lenalidomide for patients with transformed NHL?

DR VOSE: Patients with transformed lymphoma had fairly good, durable responses to lenalidomide (Czuczman 2011). Transformed lymphoma is difficult to treat, and we're always looking for new agents or new combinations to use in this setting. Because lenalidomide has relatively low toxicity, I believe it's a good option for these patients, and it may be of use in combination with other agents.

Track 5

DR LOVE: Would you discuss your study that evaluated survival over the past 3 decades for patients with Grade I or II follicular lymphoma (FL) treated with rituximab?

DR VOSE: After evaluating a number of different patients at our center treated over the past several decades, it appeared that rituximab was associated with continued improvement in outcomes over time with the greatest effect in those patients who received rituximab as initial treatment rather than as salvage therapy (Bociek 2011; [1.1]). The effects were dependent on the different grades of FL.

For symptomatic patients who require treatment, evidence exists that rituximab either alone or in combination is beneficial and improves progression-free survival (PFS) and, in some studies, overall survival (OS).

However, in patients whose disease is asymptomatic, controversy persists with regard to whether improving PFS makes a difference in outcome. At this time, no studies indicate that rituximab improves OS for asymptomatic patients, but it definitely improves the time that patients are in remission.

DR LOVE: What are your thoughts on the use of rituximab maintenance in FL?

DR VOSE: Based on the PRIMA data (Salles 2011; [1.2]), we administer rituximab maintenance after rituximab/chemotherapy using the same schedule the PRIMA study used.

We normally do not treat beyond 2 years because we have no supportive data at this time. Additionally, a small number of patients on rituximab maintenance develop adverse effects, such as infections or low immunoglobulin levels. Although it doesn't occur that often, it does happen to some patients and they develop repeated sinopulmonary infections.

1.1

Effect of Rituximab (R) on Survival in Patients with Grade 1 or 2 Follicular Lymphoma Treated over the Past 3 Decades*

	No R	Initial R	Salvage R	*p*-value
Five-year probability of survival	72% Reference	89% HR = 0.33	90% HR = 0.60	<0.001

HR = hazard ratio

Conclusions: In this analysis, patients with Grade 1 or 2 follicular lymphoma in the Nebraska Lymphoma Study Group database who received initial or salvage R experienced prolonged survival compared to those who never received R. This effect was independent of FLIPI score, and the effect was greatest for patients who received R starting with their initial therapy.

* Retrospective analysis of patients in the Nebraska Lymphoma Study Group database who received therapy between June 1981 and January 2008

Bociek G et al. *Proc ASCO* 2011;**Abstract e18509**.

1.2

Rituximab (R) Maintenance for Patients with Follicular Lymphoma Responding to Immunochemotherapy: Survival and Adverse Events (AEs) in the PRIMA Study at 36 Months Median Follow-Up

	R maintenance	Observation	Hazard ratio (HR) or risk ratio (RR)	*p*-value
Three-year PFS (n = 505, 513)	74.9%	57.6%	0.55 (HR)	<0.0001
Grade 3 or 4 AEs (n = 501, 508)	24%	17%	1.46 (RR)	0.0026
Grade 2 to 4 infections	39%	24%	1.62 (RR)	<0.0001
Treatment discontinued because of AE	4%	2%	2.41 (RR)	0.029

PFS = progression-free survival

Salles G et al. *Lancet* 2011;377(9759):42-51.

Track 21

DR LOVE: What is your usual approach to first-line treatment of chronic lymphocytic leukemia (CLL)?

DR VOSE: For up-front therapy with an asymptomatic patient, we use a watch-and-wait approach. In general, we have been administering fludarabine/cyclophosphamide/rituximab (FCR) to a younger patient who has cytopenias or is otherwise symptomatic, although bendamustine/rituximab (BR) is now being used more often because of the decreased toxicity profile. For younger patients with relapsed disease, we consider an allogeneic transplant, especially for patients with high-risk cytogenetics.

We are also currently enrolling patients in the CALGB-10404 study — which is a randomized Phase II trial — that is evaluating the addition of cyclophosphamide and/or lenalidomide to fludarabine/rituximab (FR) in CLL (1.3).

DR LOVE: What has been your experience with tumor lysis syndrome in patients with CLL — particularly those with a high white blood cell count — and how do you approach it clinically?

DR VOSE: Tumor lysis syndrome is often easily managed, so we generally don't have to discontinue treatment. Patients with a high white blood cell count and those with large, bulky disease or a large tumor burden are definitely at higher risk, so we carefully monitor these patients.

Unless a patient with CLL has transformed disease, I would not necessarily administer rasburicase. However, in other types of aggressive lymphomas — Burkitt's lymphoma or lymphoblastic lymphoma, which have a high proliferation rate — we administer rasburicase to patients with a high risk of tumor lysis, and we have had excellent experiences with it. ■

1.3

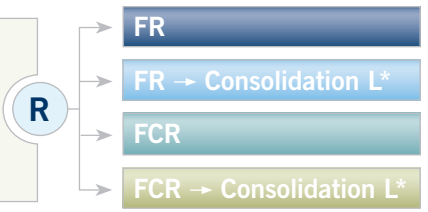
Fludarabine (F) and Rituximab (R) with or without Lenalidomide (L) and/or Cyclophosphamide (C) for Patients with Symptomatic, Previously Untreated Chronic Lymphocytic Leukemia (CLL)

Protocol IDs: CALGB-10404; ECOG-10404; NCIC-CTG-C10404; SWOG-C10404

Target Accrual: 405 (Open)

Eligibility

- ≥18 years old with untreated B-cell CLL
- Symptomatic
- PS 0 to 2
- Intermediate or high risk (Rai stage)



* Consolidation therapy for patients with complete or partial response or stable disease after induction therapy

www.clinicaltrials.gov. Identifier NCT00602459.

SELECT PUBLICATION

Czuczman MS et al. **The differential effect of lenalidomide monotherapy in patients with relapsed or refractory transformed non-Hodgkin lymphoma of distinct histological origin.** *Br J Haematol* 2011;154(4):477-81.