INTERVIEW

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Tracks 1-17

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Track 16 Perspective on the Phase III LYM-3002 trial results: Bortezomib, rituximab, cyclophosphamide, doxorubicin and prednisone (VR-CAP) versus R-CHOP for newly diagnosed, transplant-ineligible MCL

Track 17 Approach to CD30 testing in T-cell and diffuse large B-cell lymphomas and the use of brentuximab vedotin

Select Excerpts from the Interview

Tracks 1-2

DR LOVE: Would you discuss the Phase III GADOLIN trial evaluating the combination of bendamustine and the type 2 anti-CD20 monoclonal antibody obinutuzumab for patients with rituximab-refractory indolent non-Hodgkin lymphoma (NHL)?

DR SALLES: This trial randomly assigned 413 patients with rituximab-refractory disease to single-agent bendamustine or bendamustine with obinutuzumab followed by obinutuzumab maintenance for 2 years. The median PFS on the bendamustine arm was approximately 15 months and was not reached on the bendamustine/obinutuzumab arm. These results are striking, with a hazard ratio of 0.55 (Sehn 2015; [4.1]). This

4.1

GADOLIN: Results of a Phase III Study of Bendamustine (B) with or without Obinutuzumab (O) in Rituximab-Refractory Indolent Non-Hodgkin Lymphoma

Efficacy	B + O	B	HR, *p*-value
Overall response rate (n = 188, 189) Complete response Partial response	69.2% 11.2% 58%	63% 12.2% 50.8%	NR
Median PFS (n = 194, 202)	Not reached	14.9 mo	0.55, 0.0001

Select Grade 3 or 4 adverse events	B + O (n = 194)	B (n = 198)
Infusion-related reactions	10.8%	5.6%
Neutropenia	33%	26.3%
Thrombocytopenia	10.8%	16.2%
Anemia	7.7%	10.1%

HR = hazard ratio; NR = not reported; PFS = progression-free survival

Sehn LH et al. *Proc ASCO* 2015;**Abstract LBA8502**.

suggests that the addition of obinutuzumab to bendamustine in patients with rituximab-refractory disease is beneficial. I believe that these results will be practice changing.

Infusion-related reactions were the only side effect in the GADOLIN trial that were significantly more common on the combination arm. Hematological toxicities were comparable. Infusion-related reactions in older patients can be a problem. They can be managed with steroids and antihistamines.

DR LOVE: Do you believe that obinutuzumab has greater efficacy than rituximab in FL?

DR SALLES: The question regarding which agent is more effective cannot be answered from the GADOLIN study. A head-to-head comparison of obinutuzumab versus rituximab as single agents in indolent NHL demonstrated some benefit in response rates with obinutuzumab but no benefit in PFS (Sehn 2011). Ongoing Phase III trials that are currently underway comparing obinutuzumab to rituximab will provide a more definitive answer to this question (NCT01332968; NCT01287741).

Tracks 5, 7-9

DR LOVE: In what situations, if any, do you use rituximab alone or in combination with lenalidomide as up-front therapy for patients with FL?

DR SALLES: I use single-agent rituximab treatment for some patients with low tumor burden but who still have minor symptoms and are not comfortable with the watch-and-wait approach.

The R^2 regimen (lenalidomide/rituximab) was evaluated in patients with untreated indolent NHL by Nathan Fowler and colleagues. Those results were recently published in *The Lancet Oncology* and showed a high response rate. The regimen is associated with some toxicity. Approximately 30% to 40% of patients experienced Grade 3 or 4 neutropenia. Side effects such as fatigue, muscle pains and thrombosis were also reported (Fowler 2014; [4.2]). I would not use R^2 in the first-line setting until longer follow-up data are presented. The Phase III RELEVANCE trial comparing R^2 to rituximab with chemotherapy in untreated FL has completed accrual (NCT01476787).

4.2

Phase II Trial: Activity and Safety of Lenalidomide/ Rituximab for Untreated Indolent Lymphomas

	All patients		By lymphoma type		
Efficacy	ITT (n = 110)	Eval (n = 103)	FL (n = 46)	MZL (n = 27)	SLL (n = 30)
ORR	85%	90%	98%	89%	80%

Select Grade 3 and 4 adverse events included neutropenia (35%), rash (7%), fatigue (5%) and thrombocytopenia (4%).

ITT = intent-to-treat population; eval = evaluable patients; FL = follicular lymphoma; MZL = marginal-zone lymphoma; SLL = small lymphocytic lymphoma; ORR = overall response rate

Fowler NH et al. *Lancet Oncol* 2014;15(12):1311-8.

DR LOVE: What is your view on the role of idelalisib in the treatment algorithm for FL?

DR SALLES: Currently idelalisib is indicated for patients with relapsed FL who have received at least 2 prior systemic therapies. We presented the results of a Phase II study at ASCO 2015 on the efficacy and safety of idelalisib in patients with relapsed/refractory FL. The data demonstrated that the patients who experience response, especially those who achieve complete response, have a long duration of response (Salles 2015).

DR LOVE: What are your thoughts on the efficacy of ibrutinib in FL?

DR SALLES: At ASH 2014, preliminary results from a Phase II study of single-agent ibrutinib in patients with relapsed/refractory FL were presented. The response rate with ibrutinib was 30%, which is less than that with idelalisib in the same setting. The PFS is less than a year, which is not that different from what is observed with idelalisib (Bartlett 2014). So I believe this drug is not as effective in this setting but may be useful for select patients.

DR LOVE: What is known about the activity of venetoclax in FL?

DR SALLES: Venetoclax is an inhibitor of Bcl-2, a protein that is overexpressed in FL, so we do have a rationale to investigate this agent. However, we currently have limited data regarding the efficacy of venetoclax in FL. The response rates that have been reported are in the range of 30% to 40%. Clinical trials are underway evaluating venetoclax in combination with rituximab, BR or R-CHOP. We need to see more definitive data with longer follow-up before we can establish if venetoclax will be useful for patients with FL. ■

SELECT PUBLICATIONS

Bartlett NL et al. **Ibrutinib monotherapy in relapsed/refractory follicular lymphoma (FL): Preliminary results of a Phase 2 consortium (P2C) trial.** *Proc ASH* 2014;**Abstract 800**.

Fowler NH et al. **Safety and activity of lenalidomide and rituximab in untreated indolent lymphoma: An open-label, phase 2 trial.** *Lancet Oncol* 2014;15(12):1311-8.

Salles GA et al. **Idelalisib efficacy and safety in follicular lymphoma patients from a phase 2 study.** *Proc ASCO* 2015;**Abstract 8529**.

Sehn LH et al. **Randomized Phase II trial comparing GA101 (obinutuzumab) with rituximab in patients with relapsed CD20+ indolent B-cell non Hodgkin lymphoma: Preliminary analysis of the GAUSS study.** *Proc ASH* 2011;**Abstract 269**.