INTERVIEW

Craig Moskowitz, MD

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Tracks 1-16

Select Excerpts from the Interview

Track 4

DR LOVE: In what settings do you administer brentuximab vedotin for Hodgkin lymphoma (HL) in your own practice?

DR MOSKOWITZ: I use it as the label directs. I administer brentuximab vedotin for patients with HL after failure of autologous stem cell transplant, but I also use it for patients who are ineligible for transplant. This agent can be administered on first relapse. Some clinicians believe they need to administer multiagent chemotherapy to these patients, but brentuximab vedotin is approved for patients who are in first relapse

and ineligible for transplant. It is my belief that brentuximab vedotin also will be approved within the next year as part of salvage treatment for HL.

We recently reported data from a Phase II trial of PET-adapted sequential therapy with brentuximab vedotin and augmented ICE for patients with relapsed/refractory HL. Only about a third of patients achieved a PET-negative state with brentuximab vedotin alone, but the sequential treatment has been remarkable — approximately 85% of patients were in remission at the time of transplant with little toxicity (Moskowitz 2013).

Tracks 10, 13

DR LOVE: The novel B-cell receptor inhibitors ibrutinib and idelalisib are being studied in chronic lymphocytic leukemia (CLL), but what has been presented with these agents recently in indolent non-Hodgkin lymphoma (NHL)?

DR MOSKOWITZ: Idelalisib seems to be an active agent in follicular lymphoma (FL) based on data presented at ASCO 2013, and I am convinced that it will be approved in FL (Leonard 2013; [1.1]). Idelalisib causes liver function test abnormalities, which has been a bit of a problem on study because the drug must be held if patients experience Grade 3 AST or ALT abnormalities. I've observed few side effects with ibrutinib, although it can cause some diarrhea.

DR LOVE: A number of reports have come out recently evaluating these 2 agents in combination with various regimens. What's your global take on this approach?

DR MOSKOWITZ: You can imagine that the addition of a novel agent to rituximab would not be all that great for patients with heavily pretreated, rituximab-refractory NHL, but it's critical to see those results to make sure that additive toxicity doesn't occur because these agents will be moved up in the armamentarium and combined with an anti-CD20 antibody (Younes 2013; [1.2]).

With regard to diffuse large B-cell lymphoma (DLBCL), it is interesting that ibrutinib has selective activity in the activated B-cell (ABC) subtype. A Phase I/II study we participated in reported a 41% response rate to single-agent ibrutinib in patients with the ABC subtype of DLBCL but little to no activity in any of the other subtypes (deVos 2013). A large Phase III study of R-CHOP with or without ibrutinib for patients with the ABC subtype of DLBCL has been initiated (NCT01855750).

1.1 **Phase I Study of Idelalisib with Rituximab (R) and/or Bendamustine (B) in Previously Treated Indolent Non-Hodgkin Lymphoma**

	Idelalisib + R (n = 32)	Idelalisib + B (n = 33)	Idelalisib + BR (n = 14)	Idelalisib + all combinations (n = 79)
Overall response rate	72%	85%	71%	78%

For all cohorts, select Grade 3 or higher adverse events included pneumonia (15%), diarrhea (8%), rash (8%), fatigue (4%) and pyrexia (3%). Idelalisib was generally well tolerated in combination therapy for a period of 2.5 years.

Leonard J et al. *Proc ASCO* 2013;**Abstract 8500**.

1.2

Phase Ib Study of Ibrutinib with R-CHOP for Patients with Treatment-Naïve, CD20-Positive B-Cell Non-Hodgkin Lymphoma

	Ibrutinib + R-CHOP (n = 15)
Overall response rate	100%

Dose expansion study: 280 mg (n = 6), 420 mg (n = 4), 560 mg (n = 5) in patients with diffuse large B-cell lymphoma (n = 7), follicular lymphoma (n = 3) and mantle-cell lymphoma (n = 5)

Younes A et al. *Proc ASCO* 2013;**Abstract 8502**.

Track 11

DR LOVE: What are your thoughts on the new data being reported on the efficacy of the anti-CD20 antibody obinutuzumab in CLL?

DR MOSKOWITZ: Stage I results from the Phase III CLL11 study were presented at ASCO 2013. The study evaluated chlorambucil alone versus chlorambucil with either rituximab or obinutuzumab. Both anti-CD20 antibody-containing arms were superior to chlorambucil alone, and that arm was closed (Goede 2013; [1.3]). The investigators are now expanding the remaining 2 cohorts of patients to ascertain which of the remaining treatments is superior. If the obinutuzumab arm is superior, that could lead to approval of this agent in CLL. (Editor's note: Subsequent to this interview additional important findings from this study were reported in a press release [1.3]). ■

1.3

Stage I Results from the Phase III CLL11 Trial of Obinutuzumab (GA101) with Chlorambucil (Clb) or Rituximab (R) with Clb versus Clb Alone in Previously Untreated Chronic Lymphocytic Leukemia

	Stage Ia		Stage Ib	
Efficacy[1]	GA101 + Clb	Clb	R + Clb	Clb
Overall response rate (n = 212, 106, 217, 110)	75.5%	30.2%	65.9%	30.0%
Median progression-free survival (n = 238, 118, 233, 118)	23.0 mo	10.9 mo	15.7 mo	10.8 mo
	HR = 0.14; $p < 0.0001$		HR = 0.32; $p < 0.0001$	

Press release (July 24, 2013): At a preplanned interim analysis, an independent data monitoring committee determined that the study met its primary endpoint, showing that GA101 with chlorambucil helped people live significantly longer without their disease worsening (progression-free survival) compared to rituximab with chlorambucil. Final data from the CLL11 study will be submitted to the American Society of Hematology's 55th Annual Meeting in December 2013.[2]

[1] Goede V et al. *Proc ASCO* 2013;**Abstract 7004**; [2] Available at: **http://www.roche.com/media/media_releases/med-cor-2013-07-24.htm**.

SELECT PUBLICATIONS

DeVos S et al. **The Bruton's tyrosine kinase (BTK) inhibitor, ibrutinib (PCI-32765), has preferential activity in the activated B cell-like (ABC) subtype of relapsed/refractory (R/R) DLBCL: Interim Phase 2 results.** *Proc EHA* 2013;**Abstract S1180**.

Moskowitz AJ et al. **PET-adapted sequential therapy with brentuximab vedotin and augmented-ICE induces FDG-PET normalization in 92% of patients with relapsed and refractory Hodgkin lymphoma.** *Proc ICML* 2013;**Abstract 141**.