



INTERVIEW

Myron S Czuczman, MD

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Tracks 1-13

- Track 1** Clinical strategies with brentuximab vedotin in Hodgkin lymphoma
- Track 2** **Case discussion:** A man in his late sixties who underwent triple coronary bypass surgery is diagnosed with ALK-negative anaplastic large cell lymphoma
- Track 3** **Case discussion:** A 70-year-old woman with transformation of follicular lymphoma (FL) to diffuse large B-cell lymphoma experiences relapse 6 months after ASCT and responds to lenalidomide on a study
- Track 4** Duration of lenalidomide for relapsed, aggressive lymphomas
- Track 5** Role of lenalidomide in relapsed or refractory non-Hodgkin lymphoma
- Track 6** Selection of initial therapy for Grade I/II (bendamustine/rituximab [BR]) and Grade III (R-CHOP) FL
- Track 7** Bendamustine/rituximab (BR) in FL
- Track 8** Perspective on the PRIMA trial results with maintenance rituximab in patients with high tumor burden FL responding to immunochemotherapy
- Track 9** Approach to induction and maintenance therapy for patients with Grade I/II FL
- Track 10** **Case discussion:** A fragile 85-year-old woman with multiple comorbidities presents with diffuse polyposis and gastrointestinal bleeding, is diagnosed with mantle-cell lymphoma (MCL) with extensive lymphadenopathy and achieves a complete response with BR
- Track 11** Maintenance rituximab in elderly patients with MCL
- Track 12** Front-line treatment approach for younger patients with MCL
- Track 13** SWOG-S1106: A randomized Phase II study of R-hyper-CVAD or BR followed by ASCT for older patients with MCL

Select Excerpts from the Interview

Track 1

► **DR LOVE:** Would you comment on the antibody-drug conjugate brentuximab vedotin in Hodgkin lymphoma?

► **DR CZUCZMAN:** Brentuximab vedotin was recently approved by the FDA for patients with Hodgkin lymphoma who relapsed or experienced disease progres-

sion after ASCT. Brentuximab vedotin is a monoclonal antibody that binds CD30. When brentuximab vedotin binds a CD30-positive tumor cell it delivers the antimicrotubule agent monomethyl auristatin E inside the tumor cells.

Clinical trials are evaluating whether we can remove bleomycin from this setting. ABVD (doxorubicin/bleomycin/vinblastine/dacarbazine) is curative, but the lung toxicity is underestimated. The idea was to use AVD and add brentuximab vedotin, but it's similar to vinblastine so we need to determine whether this is optimal.

We want to avoid severe PN from combining 2 agents in the same family — the goal is less toxicity, not more. A theme in the future will be more frequent incorporation of these agents that are active in the refractory setting (3.1) in the up-front setting.

3.1

Response and Maximum Tumor Reduction with Brentuximab Vedotin (SGN-35) in Relapsed or Refractory Hodgkin Lymphoma (HL) and Anaplastic Large Cell Lymphoma (ALCL)*

	HL ¹ (n = 102)	ALCL ² (n = 58)
Overall response rate	75%	86%
Complete remission	34%	53%
Maximum tumor reduction (n = 96, 57)	94%	97%

* By independent review facility

¹ Chen R et al. *Proc ASCO* 2011; **Abstract 8031**.

² Shustov AR et al. *Proc ASH* 2010; **Abstract 961**.

Tracks 6-9

► **DR LOVE:** What is your clinical decision-making algorithm for up-front treatment of follicular lymphoma (FL) in elderly patients?

► **DR CZUCZMAN:** I generally use a watch-and-wait approach for older patients with comorbidities or those with limited disease. For an older patient in good shape, I try to minimize toxicity and go with bendamustine/rituximab (BR) unless other issues dictate more aggressive therapy.

I believe patients with Stage I/II disease should receive involved-field radiation therapy, but for patients with a fair amount of disease I'd probably administer BR. For patients with Grade I/II FL with low or low-intermediate FLIPI scores and no bad prognostic factors who are not eligible for a clinical trial, I also administer BR, and they exhibit favorable responses (Rummel 2010; [3.2]).

Many physicians are administering BR to patients with Grade I/II FL, but for patients with bulky disease, B symptoms or high-grade FLIPI scores I consider R-CHOP. For Grade III FL, anthracycline-based therapy should still be considered standard.

Efficacy Data from the Phase III Study Comparing Bendamustine/Rituximab (BR) to R-CHOP in Front-Line Indolent Lymphomas

	Overall response	Complete response	Progression-free survival	Median time to next treatment
BR (n = 260)	92.7%	39.6%	54.9 months	Not reached
R-CHOP (n = 253)	91.3%	30.0%	34.8 months	46.7 months
p-value	—	0.0262	0.00012	0.0281

Rummel MJ et al. *Proc ASCO* 2010. ASCO/ASH Joint Session.

► **DR LOVE:** What are your thoughts on the use of rituximab maintenance in indolent lymphoma?

► **DR CZUCZMAN:** It's controversial in that not all oncologists have embraced 2-year rituximab maintenance for all patients (Salles 2011).

For a patient at high risk, such as an elderly patient with fewer options, I administer rituximab maintenance if I'm concerned about early relapse, but it shouldn't be an automatic reaction for all patients.

► **DR LOVE:** What about rituximab maintenance after BR?

► **DR CZUCZMAN:** Most of the patients on the PRIMA study received R-CHOP, although some received R-CVP or R-FCM. We don't have data on BR with or without 2 years of rituximab maintenance.

A trial reportedly ongoing in Germany is administering BR and randomly assigning patients to 2 years of rituximab maintenance or nothing, and another trial in low-grade lymphoma will use "R squared" — rituximab and lenalidomide — or rituximab/chemotherapy. The patients who receive R squared will go on to R squared maintenance, and the patients who receive rituximab/chemotherapy will go on to rituximab maintenance.

The question is whether all patients need maintenance, however, and what the long-term effects are in terms of the tumor cell. My preference would be to use something different from what was initially used for induction, such as a novel noncross-resistant approach, to try to eradicate residual cells.

Track 13

► **DR LOVE:** What are your thoughts on the SWOG trial of R-hyper-CVAD or BR prior to ASCT in mantle-cell lymphoma (MCL) (3.3)?

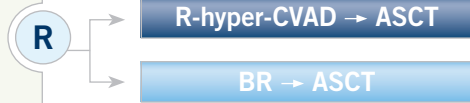
► **DR CZUCZMAN:** It's an important study that goes against the premise of "more is better." It's astounding that so many patients are receiving R-hyper-CVAD — we're pushing the envelope with significant toxicity. Before bendamustine, some patients received fludarabine/rituximab and obtained complete responses too.

SWOG-S1106: A Randomized, Phase II Trial of R-Hyper-CVAD versus Bendamustine/Rituximab (BR) in Previously Untreated Mantle-Cell Lymphoma

Target Accrual: 180 (Open)

Eligibility

- Previously untreated Stage III, Stage IV or bulky Stage II mantle-cell lymphoma
- Age ≤65
- No central nervous system involvement
- Eligible for autologous stem cell transplant (ASCT)



Primary endpoint: 2-year progression-free survival

Secondary endpoints: Overall survival, objective response rate, safety

www.clinicaltrials.gov. Accessed December 5, 2011.

Do we have to use intensive therapy? Can we administer less toxic therapy up front? I'm anxious to see if we can obtain equivocal or better results or if we need to witness a lot of toxicity to achieve our goals. ■

SELECT PUBLICATIONS

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Younes A et al. **Brentuximab vedotin (SGN-35) for relapsed CD30-positive lymphomas.** *N Engl J Med 2010*;363(10):1812-21.