INTERVIEW

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Tracks 1-13

Track 1 Approved indications and ongoing evaluation of brentuximab vedotin-based regimens in Hodgkin lymphoma (HL)

Track 2 CheckMate 205: An ongoing Phase II study of the anti-PD-1 agent nivolumab for patients with classical HL after failure of autologous stem cell transplant

Track 3 Management of brentuximab vedotin-associated peripheral neuropathy

Track 4 Incidence of brentuximab vedotin-associated pancreatitis

Track 5 Ongoing trials evaluating brentuximab vedotin in HL

Track 6 Management of early-stage HL with combined-modality treatment versus a nonradiation therapy-containing approach

Track 7 Novel agents and pathways under investigation in HL

Track 8 Differential management of T-cell lymphoma (TCL) subtypes

Track 9 ECHELON-2: A Phase III trial of brentuximab vedotin in combination with CHP versus CHOP as front-line therapy for CD30-positive mature TCL

Track 10 Correlation between CD30 positivity and benefit from brentuximab vedotin

Track 11 Rationale for combining romidepsin with the novel Aurora A kinase inhibitor alisertib for relapsed/refractory aggressive B-cell and T-cell lymphomas

Track 12 Sequencing of romidepsin, pralatrexate and belinostat in patients with TCL

Track 13 Activity of lenalidomide alone or in combination regimens in diffuse large B-cell lymphoma

Select Excerpts from the Interview

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DR LOVE: What are your thoughts on where we are and where we are heading with brentuximab vedotin in Hodgkin lymphoma (HL)?

DR FANALE: Brentuximab vedotin was approved a few years ago for relapsed classical HL in the third-line setting for patients who had further disease relapse after an autologous stem cell transplant. It was then evaluated in combination with doxorubicin/bleomycin/vinblastine/dacarbazine (ABVD) in the front line for advanced HL, but we had to drop bleomycin from the regimen because of pulmonary toxicity. The early PET scans from that study showed a high negativity rate with both ABVD/brentuximab and AVD/brentuximab (Younes 2013).

We have performed a retrospective study analyzing progression-free survival as a secondary endpoint of this trial, and the data are promising. We hope to present those findings at ASH 2014. Our institution is also a participating center for the Phase III trial comparing AVD/brentuximab vedotin to ABVD for classical HL.

DR LOVE: What has been your experience with brentuximab vedotin-associated PN?

DR FANALE: I haven't ever seen it become a problem to the point at which I've needed to stop treatment. When I've seen issues with neuropathy, it's generally been in someone who already had some baseline PN. Those patients seem to have a higher chance of developing Grade 2 or 3 PN. I will generally hold treatment, if necessary, and then I will deescalate the dose. I'll take them from 1.8 to 1.2 mg/kg, still at every 3 weeks. I've had an occasional patient for whom I spread it out to every 5 weeks or 6 weeks, but I've never needed to actually stop treatment because of PN.

DR LOVE: Have any of your patients receiving brentuximab vedotin experienced pancreatitis?

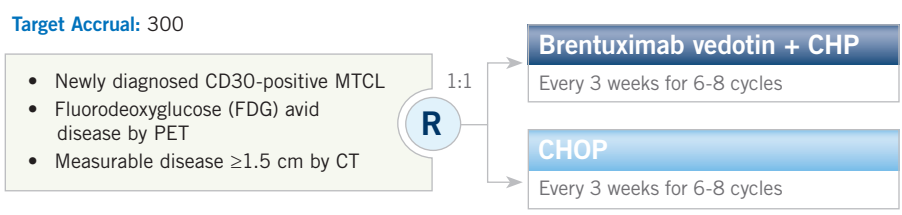
DR FANALE: Reports have been made of small numbers of patients developing pancreatitis (Gandhi 2013), but I've never seen any cases or had any patients experience issues with pancreatitis or even amylase lipase elevation.

DR LOVE: Would you also discuss the ECHELON-2 trial comparing brentuximab vedotin combined with CHP to CHOP chemotherapy for T-cell lymphoma (TCL)?

DR FANALE: ECHELON-2 is an ongoing front-line trial for patients with newly diagnosed TCL and lymph node involvement (4.1). Patients must have a level of CD30 expression on the surface of their cancer cells of 10% or more by IHC. Other upcoming trials will evaluate CHOP with belinostat and, internationally, CHOP with romidepsin.

4.1

ECHELON-2: An Ongoing Phase III Trial of Brentuximab Vedotin/CHP versus CHOP Chemotherapy in the Front-Line Treatment of CD30-Positive Mature T-Cell Lymphoma (MTCL)



Primary endpoint: Progression-free survival by independent review

CHP = cyclophosphamide/doxorubicin/prednisone

O'Connor OA et al. *Proc ASCO* 2013;**Abstract TPS8611**.

Tracks 11-12

DR LOVE: Would you discuss how you manage relapsed/refractory TCL?

DR FANALE: Right now we are focusing on single agents under evaluation or combinations of drugs that have already been approved as single agents. Romidepsin is approved for cutaneous TCL (CTCL) and peripheral TCL (PTCL), and I am involved in a trial that is administering romidepsin in combination with the oral Aurora A kinase inhibitor alisertib (NCT01897012). The thought behind that is that we know romidepsin generally yields response rates of approximately 30% (Coiffier 2012).

Initial data on alisertib from a Phase II trial for patients with PTCL indicated an overall response rate of approximately 50% (Friedberg 2014). The hope is that by administering the combination we can drive up the response rate. Typically, if I see a patient who has already received CHOP, ICE and ASCT, I consider this for the next line.

DR LOVE: How else has alisertib, which is orally bioavailable and also seems to be clinically active in aggressive B-cell lymphomas (Friedberg 2014), been studied, and how, if at all, do you see its role in the future?

DR FANALE: Alisertib is being compared to standard options, such as romidepsin or gemcitabine-based therapy, for patients with relapsed/refractory disease. It's an attractive agent from a patient perspective because it's oral. I am interested in seeing the final results of the large registration trial and whether alisertib can now follow those agents that have already been approved, like romidepsin, pralatrexate and, most recently, belinostat and brentuximab vedotin for patients with anaplastic large cell lymphoma.

DR LOVE: What is your approach to sequencing romidepsin, pralatrexate and belinostat for patients with TCL?

DR FANALE: Response rates with romidepsin, pralatrexate and belinostat are reasonably equivalent (Petrich 2013). Typically, for patients who have undergone ASCT, received 2 lines of therapy and do not meet the eligibility for or prefer not to participate in a trial, I consider romidepsin, pralatrexate or belinostat. Belinostat stands apart from romidepsin in that it results in a lower rate of significant thrombocytopenia (O'Connor 2013).

Another difference is in dosing. Romidepsin has a long infusion time, and it's administered once a week for 3 weeks. The infusion time for belinostat is significantly shorter, but it's administered for 5 days in a row. That choice is somewhat personal.

I also use pralatrexate, which is an effective agent, but the main issue to keep in mind is mucositis, especially if a patient is already debilitated from the disease itself. I can generally manage it by dose reducing or spreading out the doses in a CTCL-based schema, and some studies are evaluating leucovorin, which would be administered with methotrexate to try to decrease the mucositis. I don't know what the final word will be, but that would make it more palatable. ■

SELECT PUBLICATIONS

Coiffier B et al. **Therapeutic options in relapsed or refractory peripheral T-cell lymphoma.** *Cancer Treat Rev* 2014;40(9):1080-8.

Coiffier B et al. **Results from a pivotal, open-label, Phase II study of romidepsin in relapsed or refractory peripheral T-cell lymphoma after prior systemic therapy.** *J Clin Oncol* 2012;30(6):631-6.

Friedberg JW et al. **Phase II study of alisertib, a selective Aurora A kinase inhibitor, in relapsed and refractory aggressive B- and T-cell non-Hodgkin lymphomas.** *J Clin Oncol* 2014;32(1):44-50.

Gandhi M et al. **Pancreatitis in patients treated with brentuximab vedotin: A previously unrecognized serious adverse event.** *Proc ASH* 2013;**Abstract 4380**.

O'Connor OA et al. **Belinostat, a novel pan-histone deacetylase inhibitor (HDACi), in relapsed or refractory peripheral T-cell lymphoma (R/R PTCL): Results from the BELIEF trial.** *Proc ASCO* 2013;**Abstract 8507**.

Petrich AM, Rosen ST. **Peripheral T-cell lymphoma: New therapeutic strategies.** *Oncology (Williston Park)* 2013;27(9):878-84.

Younes A et al. **Brentuximab vedotin combined with ABVD or AVD for patients with newly diagnosed Hodgkin's lymphoma: A phase 1, open-label, dose-escalation study.** *Lancet Oncol* 2013;14(13):1348-56.