Managing Hodgkin Lymphoma Expert Interview Series

A Perspective on the Role CD30 Plays in Treating Hodgkin Lymphoma

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Editor's Note:
The treatment of patients with Hodgkin lymphoma (HL) is one of the major success stories in oncology. Currently between 70–90% of treatment-naïve patients are cured of their malignancy depending on clinical stage and risk factors.[1] In patients with refractory or relapsed disease, high-dose chemotherapy (HDCT) followed by autologous hematopoietic stem cell transplant (HSCT) is the standard of care, and can lead to a cure in ~50% of patients.[2] However, current combined modality treatment regimens for first diagnosed HL patients can induce severe, life-threatening treatment-related side effects, which include secondary cancers and cardiovascular disease. Despite success in both treatment-naïve patients and patients with refractory or relapsed disease, new treatment options are needed. On behalf of *ManagingHodgkinLymphoma.com* (MHLC), George Davatelis, PhD, spoke with Craig Moskowitz, MD, professor of medicine at Weill Medical College of Cornell University, and clinical director of the Hematologic Oncology Memorial Sloan-Kettering Cancer Center in New York City, to get his perspective on the role CD30 plays in treating Hodgkin lymphoma.

MHLC: *CD30 has emerged as an important molecule in the field of targeted therapy because its expression is nearly restricted to specific diseases such as Hodgkin lymphoma and anaplastic large cell lymphomas (ALCL), and CD30 expression is considered essential to differential diagnosis for these malignancies. Can you give us a brief overview on CD30?*

Dr. Craig Moskowitz: CD30 is expressed on a wide variety of lymphoma subtypes. We have it in our diagnostic panel at Sloan Kettering, so all new cases of suspected lymphoma are stained for CD30, and the general consensus is that CD30 is integral in helping to subcategorize lymphoma. One cannot make the diagnosis of Hodgkin's lymphoma (HL) without the tumor being CD30 positive.

Many cases of primary mediastinal large B-cell lymphoma are also positive for CD30, as well as a host of T-cell lymphomas. In addition, a minority of diffuse large B-cell

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lymphoma (DLBCL) samples are also CD30 positive. Our group sees it as a standard marker for our lymphoma workup. In two specific diseases, HL and ALCL, the disease cannot be diagnosed without CD30 staining.

MHLC: *You did mention some other malignancies are CD30-positive as well. Can you elaborate a little bit more?*

Dr. Craig Moskowitz: As I've stated, HL and T-cell ALCL by definition require CD30-positive staining.

A number of peripheral T-cell lymphomas, cutaneous T-cell lymphomas, and DLBCLs are also CD30-positive. In addition, these have varied expression of CD30.

MHLC: *One of the most difficult tasks for obtaining correct results for CD30 comes from the biopsy sample itself, whether the sample size is too small or necrotic tissue is present. What problem do you see in obtaining correct results for CD30?*

Dr. Craig Moskowitz: A biopsy sample in patients with HL consists of necrotic tissue, Reed-Sternberg cells, and mixed inflammatory cells. If anything, CD30 staining helps us to find the Reed-Sternberg cells in the sample.

MHLC: *Brentuximab vedotin shows positive activity and it is fairly well tolerated from the toxicity profile. There have been a couple of phase II trials which led the FDA to grant accelerated approval and the treatment for Hodgkin's after failure of stem cell transplant or after failure for two multiagent chemotherapeutic regimens. Can you give us an idea of how it works and how it is being used at Sloan-Kettering and specifically in your practice?*

Dr. Craig Moskowitz: I have been studying brentuximab vedotin (BV) since 2009. Our group has been involved in the original phase I and phase II studies. I wrote and am the principal investigator of the AETHERA[3] study, which is in press in *The Lancet*. In addition, we are participating in the ECHELON-1 and ECHELON-2 studies.[4,5] We have our own internal study that includes BV and AVD in early stage HL. We recently published a salvage therapy study using sequential BV and ICE in *Lancet Oncology*. It is my opinion that within 5 years all patients with HL will receive BV as part of therapeutic options.

There are some general rules of thumb with BV when administered in the relapsed setting. First, it is well tolerated. The major side effect is neuropathy. It can cause a rash especially in patients who are not heavily pretreated. Concerning efficacy, nearly all patients who get a complete response will do so after the first restaging, commonly after two or three treatments. I have never seen a patient convert from partial to complete response with BV.

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If the patient does have a complete response, I recommend continuing the treatment. If the patient has a partial response, I recommend considering the patient for an allogeneic transplant.

MHLC: *You mentioned involvement in an early stage study giving brentuximab vedotin (BV) and AVD (Adriamycin, vinblastine and dacarbazine) followed by involved field radiotherapy. Can you give us a little hint as to how that study is going?*

Dr. Craig Moskowitz: The primary endpoint of the study is pulmonary toxicity. The reason for that is there is limited data when giving BV sequentially with radiation therapy, a known treatment that can cause pulmonary toxicity. We are concerned because BV cannot be combined concomitantly with bleomycin or gemcitabine, two drugs that cause pulmonary dysfunction. Thus far in our study there has been no pulmonary toxicity.

MHLC: *That sounds very promising. You also mentioned earlier the ECHELON trials. Can you give us a little insight into those studies?*

Dr. Craig Moskowitz: The ECHELON-1 is for HL and ECHELON-2 is for ALCL. There is no doubt in my mind that BV will become standard of care for patients when combined with CHOP-like in ALCL. The ECHELON-1 study on the other hand is being studied in patient populations of advanced HL where the cure rate is already 75%. In my opinion, the study arm [BV-AVD] will need to be at least 10% better if it will become standard of care.

MHLC: *We do not have the equivalent of the NICE that Great Britain has as far as really making decisions on approving a drug based on the cost.*

Dr. Craig Moskowitz: No, but in reality though, there is no doubt that BV-AVD is more toxic than ABVD. It has to be given with growth factors. As I stated above, 10% improvement is the bar that is needed by the FDA to approve BV-AVD in HL.

MHLC: *Doctors in Europe may be a little reluctant to introducing this in the earlier setting because of several parameters, including cost. Do you think this would change if cost were taken out of the equation?*

Dr. Craig Moskowitz: I think cost is a major issue; but, in general oncologists practice based upon random assignment trials, if it is not positive, they are not going to change the treatment.

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1. Illidge T XVII. Radiotherapy in early stage Hodgkin lymphoma. *Hematol Oncol*. 2013;31 Suppl 1:92-95.
2. von Tresckow B, Diehl V. An update on emerging drugs for Hodgkin lymphoma. *Expert Opin Emerg Drugs*. 2014;19(2):215-224.
3. Moskowitz CH, Nadamanee A, Masszi T, et al. The Aethera trial: results of a randomized, double-blind, placebo-controlled phase 3 study of brentuximab vedotin in the treatment of patients at risk of progression following autologous stem cell transplant for Hodgkin lymphoma. Presented at: 2014 ASH Annual Meeting; December 6-9, 2014; San Francisco, CA. Abstract 673.
4. *ClinicalTrials.gov.* Phase 3 Frontline Therapy Trial in Patients With Advanced Classical Hodgkin Lymphoma. *https://clinicaltrials.gov/ct2/show/NCT01712490?term=echelon&rank=11*
5. *ClinicalTrials.gov*. ECHELON-2: A Comparison of Brentuximab Vedotin and CHP With Standard-of-care CHOP in the Treatment of Patients With CD30-positive Mature T-cell Lymphomas. *https://clinicaltrials.gov/ct2/show/NCT01777152?term=echelon&rank=4*

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