Case report of brentuximab vedotin utilization in a young woman with multiply relapsed Hodgkin lymphoma

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The CD30 targeted antibody drug conjugate brentuximab vedotin (BV) represents a relatively recent and novel mechanism of drug delivery and presents an exciting new option for treatment of relapsed and refractory disease. We present the case of a 31-year-old woman with multiply relapsed Hodgkin lymphoma (HL), successfully undergoing treatment with BV.

Our patient initially presented with axillary discomfort aggravated by exercise in May 2011. Later that year she developed uncomfortable right lymphadenopathy, shortness of breath, pruritus and night sweats. Nodular sclerosing HL was diagnosed by axillary node biopsy (Figure 1). Her disease was non-bulky stage IIB with involvement of more than 3 nodal sites and elevated erythrocyte sedimentation rate (ESR). She received 6 cycles of doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD), requiring a 50% vinblastine dose reduction for neuropathy after cycle 3B. Interim restaging positron emission tomography (PET) showed a partial remission; however, end-of-treatment imaging showed a complete remission (CR).

In November 2012 she developed a lump along her manubrium, which was followed clinically until April 2013, when PET/computed tomography (CT) imaging showed diffuse hypermetabolic lymphadenopathy. Treatment at that time included intensive salvage chemotherapy with cyclophosphamide, etoposide and cisplatin, followed by high-dose melphalan and autologous stem cell transplantation (ASCT) in July 2013. Prior to ASCT, the patient experienced a reversible neurologic deficit due to a cerebrovascular accident, which was likely related to a patent foramen ovale and central venous catheter-related left upper extremity thrombosis. She only achieved a partial remission (PR) to intensive salvage chemotherapy, and progressed shortly after ASCT. Mantle field radiotherapy was then administered in September 2013.

Unfortunately, our patient went on to develop a second relapse in the manubrium in May 2014 that was initially followed without intervention. She became increasingly symptomatic, with profound fatigue, pain and constitutional symptoms, leading to the initiation of BV in January 2015. Subsequent PET/CT in March and August 2015 demonstrated CR (Figure 2). Complications have been limited to mild nausea following cycle 2 that was effectively managed with antiemetics, mild peripheral neuropathy following cycle 3 that has not appreciably worsened after 12 BV doses, and mild fatigue. She is planned to receive a total of 16 BV doses, and then is contemplating allogeneic hematopoietic stem cell transplantation (HSCT).

DISCUSSION
BV efficacy was first established in relapsed and refractory CD30-positive lymphomas. Building on a previous phase 1 trial, Younes et al1 evaluated 102 patients with persistent or relapsed HL after ASCT who received BV every 3 weeks to a maximum of 16 cycles.2 Overall response rate (ORR) was 75%, with 34% CR. Median progression-free survival (PFS) was 5.6 months, although those in CR enjoyed a median duration of response of 20.5 months. Peripheral sensory neuropathy was the most common side effect, seen in 42% of patients, followed by nausea and fatigue. In these patients, the average time to relapse after ASCT was 6.7 months, suggesting this study is generalizable to our patient, who had aggressive disease that progressed quickly post transplant. More recently, results of the AETHERA trial suggest a role for 16 doses of BV as consolidation therapy post ASCT for HL patients with early time to progression of <1 year post ABVD, or extranodal disease at relapse from ABVD. This...
trial demonstrated significantly increased median PFS, from 24.1 months with placebo to 42.9 months with BV, however no improvement in overall survival, potentially due to high crossover to BV and greater use of salvage allogeneic HSCT in the placebo arm.3

Due to its efficacy in treating relapsed/refractory HL, trials are now underway to evaluate BV as part of upfront therapy. Initial phase 1 trials of BV in combination with ABVD or AVD have demonstrated CR rates of approximately 95% of patients, however unacceptable pulmonary toxicity was seen when combining BV with ABVD.2 The role of BV with AVD and with modified BEACOPP (BRECADD: brentuximab, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) is currently being evaluated in large phase 3 trials.

Concurrently, BV has been investigated in a phase 2 trial for relapsed/refractory anaplastic large cell lymphoma demonstrating ORR of 86% and CR of 57% with median duration of response of 12.6 months.4 BV is also being investigated for other lymphoma subtypes that can express CD30 such as cutaneous T cell lymphoma and lymphomatoid granulomatosis,5 peripheral T cell lymphoma with or without conventional chemotherapy6, and CD30+ diffuse large B cell lymphoma where an ORR of 44% and CR rate of 17% have been reported7.

Disclosure: Dr. G. Davies has no conflicts to declare. Dr. D. Stewart has received honoraria from Seattle Genetics for ad hoc advisory boards.

References