Trial Watch

HODGKIN'S LYMPHOMA PROGRESS

Improvements in chemotherapy and radiotherapy have increased durable remission rates for Hodgkin's lymphoma, especially when diagnosed early, but patients who are diagnosed with advanced disease and those with relapsed or refractory disease have a poorer prognosis. The results of two trials suggest ways in which the treatment of these patients might be improved.

The first trial aimed to improve efficacy, while reducing toxicity, of chemotherapy for advanced stage Hodgkin's lymphoma. The ABVD regimen (doxorubicin, bleomycin, vinblastine and dacarbazine) is widely used, and although an alternative regimen (escalated BEACOPP (bleomycin, etoposide doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisone)) can improve disease control, it increases toxicities and has not yet been shown to improve overall survival. Engert *et al.* report results of a Phase III open-label trial of 2,182 patients that examined whether a reduced number of escalated BEACOPP cycles (from eight to six) or a reduced BEACOPP dose (baseline BEACOPP) given more frequently (every 14 days versus every 21 days) could reduce toxicity while retaining efficacy. Patients receiving six escalated BEACOPP cycles had significantly higher freedom from treatment failure (the primary end point of the trial; 89.3% versus 84.4%) and improved overall survival at 5 years (95.3% versus 91.9%) compared with those who received eight escalated BEACOPP cycles. Six escalated BEACOPP cycles also led to fewer toxicities, including half as many secondary neoplasias (17 (2.4%) versus 33 (4.7%)). Baseline BEACOPP given more frequently had fewer advantages, so a higher dose may be necessary for improved efficacy.

The second trial examined the efficacy of an antibody–drug conjugate (ADC) in patients with relapsed or refractory Hodgkin's lymphoma following high-dose chemotherapy and autologous stem cell transplantation (auto-SCT), for whom no standard of care is available. In this open-label Phase II trial, Younes *et al.* treated 102 patients with brentuximab vedotin, an ADC that delivers the antimicrotubule agent monomethyl auristatin E to cells expressing CD30 (a member of the tumour necrosis factor superfamily that is expressed by malignant Reed–Sternberg cells in Hodgkin's lymphoma). In this patient population with a poor prognosis (median time to relapse after auto-SCT was 6.7 months), brentuximab vedotin resulted in an objective response rate of 75%, with complete remission achieved in 34% of patients, as determined by an independent review facility. After a median follow-up of 18.5 months (range 1.8–23.5 months), 31 patients (30.4%) remained alive without documented disease progression. This is notable given that patients who relapse within 1 year have a median survival of ~1.2 years. Toxicities were manageable. These results support the evaluation of brentuximab vedotin in Phase III trials, and in patients with earlier stage Hodgkin's lymphoma.

ORIGINAL RESEARCH PAPERS Engert, A. *et al.* Reduced-intensity chemotherapy and PET-guided radiotherapy in patients with advanced stage Hodgkin's lymphoma (HD15 trial): a randomised, open-label, phase 3 non-inferiority trial. *Lancet* 3 Apr 2012 (doi:10.1016/S0140-6736(11)61940-5) | Younes, A. *et al.* Results of a pivotal Phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin's lymphoma. *J. Clin. Oncol.* 26 Mar 2012 (doi:10.1200/JCO.2011.38.0410)