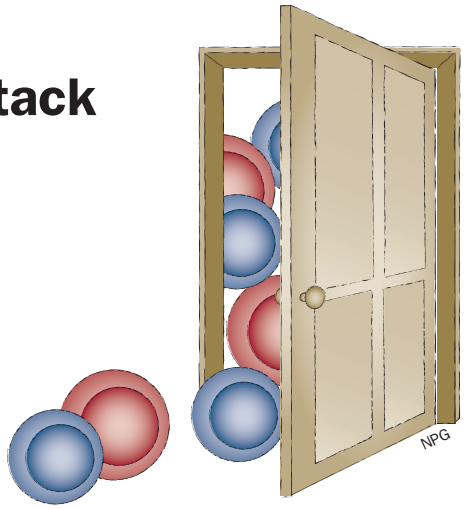
Nature Reviews Clinical Oncology **12**, 65 (2015); published online 23 December 2014; doi:10.1038/nrclinonc.2014.227

HAEMATOLOGICAL CANCER

PD-1 blockade: opening the door to attack



Tumour cells that express programmed cell death 1 (PD-1) ligands on their surface can interact with PD-1 receptors expressed on T cells, preventing T-cell activation and immune responses. The ligands for PD-1 (PD-L1 and PD-L2) are commonly overexpressed in Hodgkin lymphoma due to genetic alterations or Epstein–Barr virus infection. Previous studies have shown that antibodies that block PD-1 can result in some impressive and durable clinical responses, which led to a phase I expansion cohort of an ongoing trial to test these agents in patients with Hodgkin lymphoma.

Stephen Ansell, who co-led the phase I study, elaborates: "Hodgkin lymphoma is biologically unique in that the malignant cells are in the minority in the tumour microenvironment and a rich infiltrate of non-malignant immune cells predominates. Blocking PD-1 to activate the T-cell response was a logical therapeutic approach." His team assessed the PD-1 blocking antibody nivolumab in 23 patients with relapsed or refractory Hodgkin lymphoma, a setting in which few therapeutic options exist. All patients were heavily pretreated, with 87% treated with at least three previous regimens. In total, 78% of patients had previously undergone autologous stem-cell transplantation and 78% had previously received the anti-CD30 immunotherapy brentuximab vedotin.

Drug-related adverse events were reported in 78% of patients, the most common being rash and decreased platelet count. Grade 3 adverse events were reported in 5 patients (22%), which was similar to results of trials of nivolumab in patients with solid tumours.

An objective response was reported in 87% of patients, with complete response noted in four patients and partial response in 16 patients. Of the four patients with a complete response, three had not received brentuximab vedotin. The progression-free survival rate at 24 weeks was 86%. Median overall survival had not been reached.

"This is an extremely high response rate in a difficult-to-treat patient population. Nivolumab was reasonably well tolerated with a side-effect profile that seems similar to that seen in previous studies of patients with other malignancies," explains Ansell. Thus, nivolumab-mediated PD-1 blockade represents a promising targeted treatment for patients with Hodgkin lymphoma.

Lisa Hutchinson

Original article Ansell, S. M. *et al.* PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma. *N. Engl. J. Med*. doi:10.1056/NEJMoa1411087