immune effector cells and evade the immune response. Nivolumab is a member of the new class of immunotherapies, so called "checkpoint" inhibitors, with tremendous activity in solid tumours as well as Hodgkins lymphoma.[1]

Case Report: Here we describe the outcome of a 25 yo woman diagnosed with Hodgkin's lymphoma (HL, classical nodular) in 2009 after presenting with neck lymphadenopathy. She was treated but relapsed in October of 2010 and received salvage chemotherapy followed by autologous stem cell transplantation.

In November 2011, she relapsed again and achieved partial remission after multiple rounds of therapies including brentuximab vedotin. In October 2013, she underwent an allogeneic stem cell transplant (ASCT) with fludarabine and busulfan conditioning from a matched unrelated donor. Her transplant course was complicated by mild chronic GVHD presenting as nausea, vomiting and joint pains. She also developed an atypical "chronic" GVHD manifested as intermittent hemibody sensory loss, tingling, and weakness with periodic confusions which could only be controlled by low dose daily prednisone.

At day+590 post ASCT, she relapsed classical nodular sclerosing HL. At a second institution, she began Nivolumab at 3mg/Kg intravenously. Fourteen days after her first dose, she developed grade III transaminitis and was placed on prednisone 2mg/kg for 7 day but 24 days after the Nivolumab dose, she presented to our ER with RUQ abdominal pain, pruritis, jaundice and grade IV transaminitis with bilirubin of 10 which subsequently peaked to 31 (Figure 1). A workup for infectious etiology (EBV, hepatitis, CMV, Adenovirus and HHV6) was negative. An abdominal ultrasound was negative for VOD/SOS. A liver biopsy was consistent with aGVHD as evidenced by loss of interlobular bile ducts, mild centrilobular perivenular fibrosis, increased intrasinusoidal kupffer cells, and hepatocyte injury (Figure 2). She also developed severe low TSH/free T4 levels suggestive of central hypothyroidism. She was restarted on steroids at 2mg/kg but after 2 weeks, developed hepatorenal syndrome and hypotension. Hemodislysis/Plasmaphoresis followed by extracorporeal photophoresis was initiated but unfortunately her condition rapidly deteriorated. She ultimately succumbed to hypotension with disseminated intravascular coagulation and multi-organ failure.

Conclusion: To our knowledge this is the first case of documented acute GVHD induced by an anti-PD1 antibody following ASCT. The use of immune checkpoint inhibitors after ASCT should be examined carefully.

References

Ansell SM, Lesokhin AM, Borrello I, Halwani A et al. PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma. N Engl J. Med. 2015; 372(4):311-319.

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Azacytidine Enhances Regulatory T-Cells In Vivo and Prevents Experimental Xenogeneic Graft-Versus-Host Disease

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Background: The demethylating agent 5-azacytidine (AZA) has proven its efficacy as treatment for myelodysplastic syndrome and acute myeloid leukemia. In addition, AZA can demethylate *FOXP3* intron 1 (*FOXP3i1*) leading to the generation of regulatory T cells (Tregs).

Objective: We investigated the impact of AZA on xenogeneic graft-versus-host disease (xGVHD) in a humanized murine model of transplantation, and described the impact of the drug on human T cells *in vivo*.

Methods: In order to induce xGVHD, human peripheral blood mononuclear cells ($_{hu}$PBMC) were administered intravenously in NOD-scid IL-2Rγ^{null} (NSG) mice.

Results: AZA successfully improved both survival ($p<0.0001$) and xGVHD scores ($p<0.0001$). Further, AZA significantly decreased human T-cell proliferation as well as INF-γ and TNF-α serum levels, and reduced the expression of GRANZYME B and PERFORIN 1 by cytotoxic T cells. In addition, AZA administration significantly increased the function, proliferation and frequency of Tregs through demethylation of *FOXP3i1* and higher secretion of IL-2 by conventional T cells due to *IL2* gene promoter site 1 demethylation. Interestingly, among AZA-treated mice surviving the acute phase of xGVHD, there was an inverse correlation between the presence of Tregs and signs of chronic GVHD. Finally, Tregs harvested from the spleen of AZA-treated mice were suppressive and stable over time since they persisted at high frequency in secondary transplant experiments.

Conclusion: These findings emphasize a potential role for AZA as prevention or treatment of GVHD.

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Pulse Cyclophosphamide for Steroid-Refractory Chronic Graft-Versus-Host Disease

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Background: Chronic graft-versus-host disease (cGVHD) is the most common cause of morbidity and mortality after allogeneic stem cell transplant (alloSCT) for hematologic malignancies. While 50% of patients respond to

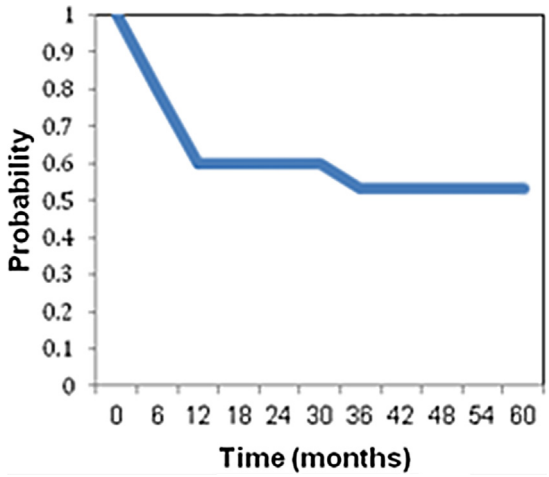

Figure 1. Overall survival.