Checkpoint kinase inhibition

Checkpoint kinase inhibition has been studied as a way of enhancing the effectiveness of DNA-damaging agents. More recently, histone deacetylase inhibitors have shown efficacy in several cancers, including non-Hodgkin lymphoma. To evaluate the effectiveness of this combination for the treatment of lymphoma, we examined the combination of AR42, a histone deacetylase inhibitor, and Checkpoint kinase 2 inhibitor II in vitro and in vivo. The combination resulted in up to 10-fold increase in potency in 5 Burkitt's lymphoma cell lines when compared to either drug alone. Both drugs inhibited tumor progression in xenograft models, but the combination was more effective than either agent alone resulting in regression of established tumors. No toxicity was observed. These results suggest that the combination of histone deacetylase inhibition and checkpoint kinase inhibition represent an effective and non-toxic treatment option that should be further explored in pre-clinical and clinical studies [1)].

1)
Kong Y, Barisone GA, Sidhu RS, O'donnell RT, Tuscano JM. Efficacy of Combined Histone Deacetylase and Checkpoint Kinase Inhibition in a Preclinical Model of Human Burkitt Lymphoma. Mol Med. 2015 Aug 24. doi: 10.2119/molmed.2015.00032. [Epub ahead of print] PubMed PMID: 26322845.