Immune checkpoint inhibitor in lymphoma

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Lymphoma is a clonal disorder of lymphocytes that can typically infiltrate the sites of disease, including the secondary lymphoid organs, bone marrow and extranodal sites. In addition to the presence of malignant lymphocytes, many immune cells are also observed within the tumor microenvironment. Recent works have documented the cellular and molecular mechanism underlying the suppressed anti-tumor immune response in the lymphoma microenvironment and have developed the therapeutic strategies to overcome such impairment in eradicating tumor cells. In fact, trials of monoclonal antibody drugs blocking immune checkpoint receptors that downregulate T cell function have achieved noteworthy clinical benefit in several types of malignant lymphoma.

Of note, anti-programmed death-1 (PD-1) antibody monotherapy has been effective and safe in patients with relapsed/refractory Hodgkin lymphoma, with more than two third of patients experiencing an objective response of impressive duration. The responsiveness to the treatment is associated with expression of programmed death ligand 1 (PD-L1) on tumor cells resulting from genetic alteration if the *PD-L1/PD-L2* locus on chromosome 9p24.1. As immune checkpoint inhibitors have been actively studied also in the treatment of non-Hodgkin lymphoma, the clinical benefit has been reported in several subtypes, including primary mediastinal large B-cell lymphoma. However, response rates reported from the study of immune checkpoint inhibitor monotherapy in hematologic malignancies are not satisfactory. In addition to the clinical data of the overall treatment outcome and safety in the prospective clinical trials, therefore, the current studies of immune checkpoint inhibitors are also focusing on the biomarkers that predict who will get benefit from the treatment. Also, to maximize the efficacy outcome of immune checkpoint inhibitor, combination approaches have been also actively studied by adding cytotoxic agents or other immune checkpoint modulating agents.

In this presentation, the recent results reported from the clinical trials in the treatment of lymphoid malignancies will be briefly introduced. Current status of efforts to improve the clinical outcomes of immune checkpoint modulation will be also discussed in terms of biomarker development and combination approaches.