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Immune modulation as a treatment strategy in angioimmunoblastic T-cell lymphoma

Angioimmunoblastic T-cell lymphoma (AITL) is a rare and complex lymphoproliferative disorder. The lack of standard and effective treatments to date poses significant challenges for physicians treating patients with AITL. There is little consensus on the optimal chemotherapy regimen in either the frontline treatment or relapsed setting. In several series the median survival of AITL patients has been estimated to be between 11 and 30 months, with only 30% of patients surviving more than 2 years.

Significant progress has been made in the understanding of AITL since its recognition as a clonal T-cell disorder with associated deregulation of B-cells and endothelial cells within a unique malignant microenvironment. Recently, the follicular helper T-cell has been implicated as the cell of origin along with B-cell deregulation and over expression of angiogenic factors such as VEGF and other signaling pathways in a unique immunomodulatory loop. Emerging preclinical data suggest other molecular targets such as c-Maf, NF-κB, and Syk may also play a role in immunomodulation. The vast majority of AITL cases contain EBV-harboring cells and several lines of evidence support a possible pathogenic role for EBV within AITL including the frequently associated clonal proliferations of B cells and the development of concomitant aggressive B-cell lymphomas. These recent developments in the understanding of the pathogenesis of AITL at a cellular and molecular level all have therapeutic implications and strategies attempting to exploit this immunomodulatory loop are ongoing. Agents such as Cyclosporine, Rituximab, Bevacizumab, among others, potentially disrupt this loop and have shown encouraging results in early clinical trials. The ongoing experience with their use in AITL will be discussed.