

B Cell Targeted Therapies: Are they all the Same?

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Recent data derived from animal studies and clinical studies in humans provide evidence supporting a central role of B cells in the immunopathogenesis of autoimmune diseases including rheumatoid arthritis, systemic lupus erythematosus and multiple sclerosis. The recent development of biologic agents that can deplete B cells or block their function provide evidence that targeting B cells may be an effective treatment for autoimmunity. However, there are distinct differences between the current B-cell targeted therapies with respect to their mode of action and the specificity of the B cells that they target. Animal studies have provided compelling insights into how these B cell therapies differ and provide initial evidence supporting the potential different outcomes for their use in treatment of human disease.

Atacicept is a novel B-cell targeted therapy that binds to and neutralizes homotrimeric and heterotrimeric forms of two potent B cell survival factors, BLyS (B Lymphocyte Stimulator), and APRIL (A-PRoliferation Inducing Ligand) that mediate B cell effector function, differentiation, and survival. Although BLyS seems to play a dominant role in enabling B cell development past the immature B cell stage, both BLyS and APRIL play important roles in promoting immunoglobulin class-switching, enhanced antigen presentation to T cells, and the differentiation and survival of antibody-secreting plasma cells. Therefore, atacicept represents a novel B cell therapy by virtue of its unique ability to target both BLyS and APRIL. Other emerging B cell targeted therapies neutralize only BLyS, or target B cells expressing CD20 or BAFF-receptor. Animal studies have revealed important mechanistic differences between these B cell directed agents, with possible implications for clinical outcomes in human trials.

References

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