

Long-term exposure to monoclonal anti-TNF is associated with an increased risk of lymphoma in BAFF-transgenic mice

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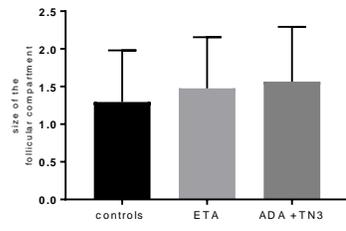
Abstract

The impact of treatment on the risk of lymphoma in patients with rheumatoid arthritis (RA) is unclear. Here, we aimed to assess if the risk of lymphoma differs according to the type of Tumor Necrosis factor inhibitor (TNFi), comparing monoclonal anti-TNF antibodies (Ab) to the soluble TNF receptor. We used BAFF-transgenic (Tg) mice as a model of autoimmunity-associated lymphoma. Six-month aged BAFF-Tg mice were treated with TNFi for 12 months. Histological examination of the spleen, assessment of the cellular composition of the spleen by flow cytometry and assessment of B cell clonality were performed at sacrifice. Crude mortality and incidence of lymphoma were significantly higher in mice treated with monoclonal anti-TNF Ab compared to both controls and mice treated with the soluble TNF receptor, even at high dose. Flow cytometry analysis revealed decreased splenic macrophage infiltration in mice treated with monoclonal anti-TNF Ab. Overall, this study demonstrates, for the first time, that a very prolonged treatment with monoclonal anti-TNF Ab increase the risk of lymphoma in B cell-driven autoimmunity. This data suggests a closer monitoring for lymphoma development in patients suffering from B cell-driven autoimmune disease with long-term exposure to monoclonal anti-TNF Ab.

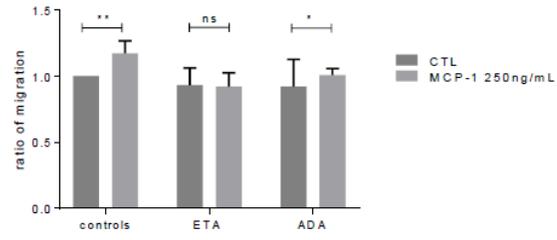
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BAFF-Tg_AntiTNF_CEI_VDef.pdf available at <https://authorea.com/users/383464/articles/499352-long-term-exposure-to-monoclonal-anti-tnf-is-associated-with-an-increased-risk-of-lymphoma-in-baff-transgenic-mice>

Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3

