A157 EPRATUZUMAB AFFECTS B CELLS TRAFFICKING IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Epratuzumab, a humanised anti-CD22 monoclonal antibody, is under investigation as a therapeutic antibody in non-Hodgkin's lymphoma and systemic lupus erythematosus (SLE), but its mechanism of action on B cells remains elusive. Treatment of SLE patients with epratuzumab leads to a reduction of circulating $CD27^{negative}$ B cells, although epratuzumab is weakly cytotoxic to B cells in vitro. Therefore, potential effects of epratuzumab on adhesion molecule expression and the migration of B cells have been evaluated.

Methods Epratuzumab binding specificity and the surface expression of adhesion molecules (CD62L, β7 integrin and β1 integrin) after culture with epratuzumab was studied on B cell subsets of SLE patients by flow cytometry. In addition, in vitro transwell migration assays were performed to analyse the effects of epratuzumab on migration towards different chemokines such as CXCL12, CXCL13 or to CXCR3 ligands, and to assess the functional consequences of altered adhesion molecule expression.

Results Epratuzumab binding was considerably higher on B cells relative to other cell types assessed. No binding of epratuzumab was observed on T cells, while weak non-specific binding of epratuzumab on monocytes was noted. On B cells, binding of epratuzumab was particularly enhanced on $CD27^{negative}$ B cells compared to $CD27^{positive}$ B cells, primarily related to a higher expression of CD22 on $CD27^{negative}$ B cells. Moreover, epratuzumab binding led to a decrease in the cell surface expression of CD62L and β7 integrin, while the expression of β1 integrin was enhanced. The effects on the pattern of adhesion molecule expression observed with epratuzumab were principally confined to a fraction of the $CD27^{negative}$ B cell subpopulation and were associated with enhanced spontaneous migration of B cells. Furthermore, epratuzumab also enhanced the migration of $CD27^{negative}$ B cells towards the chemokine CXCL12.

Conclusions The current data suggest that epratuzumab has effects on the expression of the adhesion molecules CD62L, β7 integrin and β1 integrin as well as on migration towards CXCL12, primarily of $CD27^{negative}$ B cells. Therefore, induced changes in migration appear to be part of the mechanism of action of epratuzumab and are consistent with the observation that $CD27^{negative}$ B cells are preferentially removed from the peripheral blood under treatment.