Plasma cell but not CD20-mediated B-cell depletion protects from bleomycin-induced lung fibrosis

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Shareable abstract (@ERSpublications)
Bortezomib-mediated depletion of plasma cells but not anti-CD20-mediated B-cell depletion inhibited bleomycin-induced lung fibrosis, suggesting that plasma cells are a therapeutic target for fibrotic lung disease such as IPF. https://bit.ly/3Nv4w5P

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Abstract

Idiopathic pulmonary fibrosis (IPF) is an interstitial lung disease associated with chronic inflammation and tissue remodelling leading to fibrosis, reduced pulmonary function, respiratory failure and death. Bleomycin (Blm)-induced lung fibrosis in mice replicates several clinical features of human IPF, including prominent lymphoid aggregates of predominantly B-cells that accumulate in the lung adjacent to areas of active fibrosis. We have shown previously a requirement for B-cells in the development of Blm-induced lung fibrosis in mice. To determine the therapeutic potential of inhibiting B-cell function in pulmonary fibrosis, we examined the effects of anti-CD20 B-cell ablation therapy to selectively remove mature B-cells from the immune system and inhibit Blm-induced lung fibrosis. Anti-CD20 B-cell ablation did not reduce fibrosis in this model; however, immune phenotyping of peripheral blood and lung resident cells revealed that anti-CD20-treated mice retained a high frequency of $CD19^+$ $CD138^+$ plasma cells. Interestingly, high levels of $CD138^+$ cells were also identified in the lung tissue of patients with IPF, consistent with the mouse model. Treatment of mice with bortezomib, which depletes plasma cells, reduced the level of Blm-induced lung fibrosis, implicating plasma cells as important effector cells in the development and progression of pulmonary fibrosis.

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