CCL24 modulates fibrosis development in Primary Sclerosing Cholangitis. Correlation of human serum CCL24 levels with fibrosis markers and data from the MDR2/- mouse model

Introduction
Primary sclerosing cholangitis (PSC) is a progressive cholestatic disease involving liver inflammation and fibrosis, with no effective medical treatment. CCL24, a chemokine that was shown to be involved in the development of liver inflammation and fibrosis is robustly expressed in liver biopsies of PSC patients. Blocking CCL24, was shown to attenuate liver fibroblast activation and reduce liver fibrosis in both NASH and PSC models.

Aim
• To assess the effect of CCL24 blockage in the Mdr2/- mouse PSC model
• To study the correlation between CCL24 and fibrotic biomarkers in PSC patients serum samples

Method
• The effect of blocking CCL24, using the neutralizing monoclonal antibody CM-101 (D8), was evaluated in the Mdr2/- PSC mouse model

Conclusions
• CCL24 levels in PSC patients serum positively correlates with TIMP-1 and ELF score
• In the Mdr2/- PSC mouse model treatment with CM-101, blocking CCL24, reduces cholestasis and hepatic fibrosis
• CCL24 was found to play a key role in PSC liver related pathologies. CM-101, a neutralizing CCL24 mAb, is currently being tested in a Phase Ila clinical trial as a potential treatment for PSC

References

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Results
In Mdr2/- mouse model blocking CCL24 using the mAb CM-101 (D8) ameliorated cholestatic injury and liver damage indicated by reduced serum ALP and bile acid levels

Expression of the fibrotic marker TIMP-1 was significantly reduced following 6 weeks of CM-101 (D8) treatment

In human PSC serum samples CCL24 correlated with the fibrotic markers ELF and TIMP-1, suggesting an association between CCL24 and PSC-related fibrosis

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