Ex-vivo translational assay of hepatic stellate cells using patient-derived serum characterizes the anti-fibrotic activity of CM-101

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Introduction

CCL24, a chemokine that regulates inflammatory and fibrotic activities, was found to be highly expressed in livers of patients with liver fibrosis including those with primary sclerosing cholangitis (PSC)¹ and metabolic dysfunction-associated steatohepatitis (MASH)². Treatment with CM-101, a first-in-class humanized antibody targeting CCL24, has impacted consequential biomarkers of liver fibrosis in patients with MASH (NCT05824156) and in multiple PSC preclinical models³,⁴.

Aim

This study aimed to better characterize CM-101’s anti-fibrotic activity in patients using an ex-vivo hepatic stellate cells (HSC) activation model.

Methods

- Activation of HSC [human LX2 cell line]: Cells were activated by 24-hour incubation with either recombinant proteins or sera from MASH patients (NCT05824156) before or after 16 weeks of exposure to either placebo (vehicle) or CM-101 (5 mg/kg subcutaneous every 3 weeks). Activators were added on top of 10% FCS in the media. Quantification of the fibrotic marker αSMA (smooth muscle actin) was assessed by flow-cytometry.
- The secretome of CCL24-stimulated LX2 was examined by RayBio L-507 protein array.
- Serum proteomic analysis: Sera of PSC patients (Royal Free Hospital bio-bank and baseline sera of patients enrolled in the SPRING study, NCT04595825) and healthy controls (NCT06025851) were analyzed using Olink proximity extension assay.

Results

CM-101 treated patients display reduced serum-based HSC activation

![Image](image1.png)

Conclusions

- A serum-based ex-vivo HSC activation assay can help in characterizing anti-fibrotic drug effects.
- A serum-based assay derived from MASH patients treated with CM-101 restored HSC activation.
- A protein signature generated from CCL24-activated HSC predicted PSC disease and its severity.
- These findings support CM-101’s mode of action in liver fibrosis.
- CM-101 is currently being tested in a phase 2 study in PSC patients.

References