Targeting CCL24 in primary sclerosing cholangitis with CM-101: rationale and study design

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Background
Primary sclerosing cholangitis (PSC) is a rare, chronic cholestatic liver disease characterized by progressive inflammation, fibrosis, and destruction of the intrahepatic and extra-hepatic bile ducts. Animal models of PSC have shown that cytokines and chemokines may be important pathogenetic mediators of liver inflammation and fibrosis.

CCL24 (eotaxin-2) is a chemokine that promotes cell trafficking and regulates inflammatory and fibrotic activities through the CCR3 receptor

CCL24 plays a key role in PSC pathogenesis

CM-101, a humanized IgG1 anti-human CCL24 monoclonal antibody, has been shown in pre-clinical models to significantly reduce migration and activation of immune cells and fibroblasts, including hepatic stellate cells

CM-101 Reduces Liver Fibrosis by >80% in TAA Model

Methods
We are currently conducting a Phase 2a, randomized, double-blind, placebo-controlled, multiple-dose, international study to understand the role of CCL24 in the pathogenesis of PSC, the effects of blockade of CCL24 with CM-101, and to evaluate the safety and tolerability of CM-101 in adult patients with PSC. (NCT04595825).

Overall Study Design

6-Week Screening

15-Week Double-Blinded Treatment Period

33-Week Open Label Treatment Period

12-Week Follow-up

N = 68 patients

Placebo IV Q3W (n=18)

CM-101 10mg/kg IV Q3W (n=25)

CM-101 20mg/kg IV Q3W (n=25)

Jon Clarke, đúng, a randomized, double-blind, placebo-controlled, multiple-dose, international study to understand the role of CCL24 in the pathogenesis of PSC, the effects of blockade of CCL24 with CM-101, and evaluate the safety and tolerability of CM-101 in adult patients with PSC. (NCT04595825).

Pre-Clinical Data of CM-101 Targeting CCL24

CM-101 Reduces Liver Injury and Fibrosis in PSC model

Results
- This trial is ongoing.
- The Data Monitoring Committee met in May 2023 and had no safety concerns.

Conclusions
- Results of this trial are expected in the latter half of 2024 and will further elucidate the role of CCL24 in inflammatory and fibrotic disease pathology, and the clinical impact of CM-101 in reducing the over expression of CCL24 in PSC. This will guide future development of CM-101 in PSC.

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References