# INTERNATIONAL SUMMIT ON HEPATOLOGY AND NEPHROLOGY RESEARCH

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## Targeting the CCL24 Pathway with nebokitug in Primary Sclerosing Cholangitis: Safety and Biological Activity from a Phase 2 Study

**Abstract:**

**Introduction:** Nebokitug (CM-101) is an anti-CCL24 monoclonal antibody with anti-inflammatory and anti-fibrotic activities. This phase 2 study aimed to assess the safety, tolerability, and biological activity of nebokitug in patients with primary sclerosing cholangitis (PSC).

**Methods:** SPRING is a randomized, double-blind (DB), placebo-controlled trial with an open-label extension phase. Patients with large-duct PSC and ALP >1.5× ULN were randomized to receive intravenous nebokitug (10 mg/kg or 20 mg/kg) or placebo every 3 weeks for 15 weeks (five doses total). Following the DB period, eligible participants could enter a 33-week open-label treatment phase and a subsequent 15-week follow-up. The primary endpoint was safety and tolerability. Secondary endpoints included changes from baseline to week 15 in liver stiffness measurement (LSM), enhanced liver fibrosis (ELF) score, liver biochemistry, and pharmacokinetic (PK)/pharmacodynamic (PD) parameters. Biological activity and responder analyses were conducted in a prespecified subgroup with baseline LSM >8.7 kPa.

**Results:** Seventy-six patients received at least one dose (placebo n=20; nebokitug n=56). Sixty-six patients (placebo n=16; nebokitug 10 mg/kg n=22; 20 mg/kg n=28) completed the DB period, received all five doses, and had baseline and at least one post-baseline measurement for ALP and ELF. Baseline characteristics were comparable: mean age 52 years (range 23–75), 74% male, 71% with IBD, and 72% on UDCA. Treatment-emergent adverse events (TEAEs) were similar between groups (nebokitug: 82%; placebo: 75%). Most frequent TEAEs included fatigue, headache, and pruritus. Serious TEAEs occurred in three patients (1 placebo, 2 nebokitug), none of which were treatment related. PK analysis demonstrated dose-proportional increases in nebokitug levels and target engagement. Patients treated with nebokitug 20 mg/kg showed consistent reductions in liver biochemistries compared to nebokitug 10 mg/kg and placebo. Biomarkers including PRO-C3, IL-6, IL-8, and TGFβ improved in a dose-dependent manner, especially among patients with baseline LSM >8.7 kPa. In this subgroup, patients receiving nebokitug 10 mg/kg and 20 mg/kg had mean LSM reductions of 1.5 and 1.4 kPa, respectively, compared to a 3.0 kPa increase in placebo (p=0.01 for both groups). Majority of nebokitug 20mg/kg treated patients in this subgroup had ELF scores that did not increase > 0.19, a threshold predictive of worse clinical outcomes.

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Conclusions:

Nebokitug was well tolerated and demonstrated a safety profile comparable to placebo. After 15 weeks of treatment, nebokitug showed anti-fibrotic, anti-inflammatory, and anti-cholestatic biological effects in PSC patients. These phase 2 data support the progression of nebokitug to more advanced clinical trials in PSC.

**Biography:**

Chief executive Officer, Chief Scientific Officer and Co-founder at Chemomab Therapeutics

Adi Mor founded Chemomab at 2011 and has been leading Chemomab as its CEO and CSO from early discovery stage and into Phase 2/3 clinical trials. She has extensive knowledge and experience in immunology focusing on autoimmune and inflammatory-fibrotic diseases and broad experience in designing, promoting and patenting a novel class of monoclonal antibodies to treat inflammatory and fibrotic diseases. Dr. Mor is a senior executive with a track record of strong cross functional leadership with deep understanding of drug development, business development, corporate strategy and clinical operations. Dr. Mor earned her PhD in immunology from Tel Aviv University in the Department of Neurobiochemistry and is the lead author of numerous scientific journal publications in immunology and inflammatory disorders