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Oral Presentations

LO1: A PHASE 2, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED DOSE-FINDING STUDY OF THE EFFICACY AND SAFETY OF NAMODENOSON (CF102), AN A3 ADENOSINE RECEPTOR (A3AR) AGONIST, IN TREATING NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND NON-ALCOHOLIC STEATOHEPATITIS (NASH)

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Background: Namodenoson, an A_3AR agonist, demonstrated improved liver function and pathology in a NASH preclinical model. **Methods:** This phase 2 randomized double-blind placebo-controlled dose-finding study investigated orally administered namodenoson in patients (pts) with NAFLD and serum ALT levels ≥60 U/L (including a subset with NASH). Pts were randomized (1:1:1) to receive namodenoson 25 mg BID, 12.5 mg BID, or placebo for 12 wks and were followed up until wk 16. Endpoints included efficacy parameters, safety profile, and study of relevant biomarkers. **Results:** The analysis included 60 pts. ALT levels decreased consistently during the study with namodenoson treatment in a dose-dependent manner (wk 12 mean change from baseline [CFB]:-14.6, -8.7, and -4.2 U/L in the 25 mg, 12.5 mg, and placebo groups, respectively; p=0.066 for 25 mg vs placebo); 37%, 24%, and 10% of pts in the 25 mg, 12.5 mg, and placebo groups, respectively, achieved ALT normalization at 16 wks (p=0.038 for 25 mg vs placebo). AST levels also decreased throughout the study in a dose-dependent manner (wk 12 mean CFB:-8.4, -5.9, and -0.8 U/L in the 25 mg, 12.5 mg, and placebo groups, respectively; p=0.03 for 25 mg vs placebo). In addition, a significant improvement in adiponectin was noted (wk 12 mean CFB: 266, 559, and -137 ng/mL for 25 mg, 12.5 mg, and placebo, respectively; p=0.03 for 12.5 mg vs placebo). At wk 12, a significant decrease in liver fat volume (determined by MRI-PDFF) was observed with namodenoson (mean CFB: -159, -31, and -74 cm^3 for 25 mg, 12.5 mg, and placebo, respectively; p=0.03 for 25 mg vs placebo). In addition, a significant decrease in Fib4-scores was noted with namodenoson (wk 12 mean CFB: -0.28,-0.09, and -0.03 for 25 mg, 12.5 mg, and placebo, respectively; p=0.011 for 25 mg vs placebo) suggesting an inhibitory effect of namodenoson on fibrosis progression. A consistent dose-dependent decrease in body weight was recorded in all study groups over time (wk 12 mean loss from BL: 2.1, 1.6, and 0.5 kg in the 25 mg, 12.5 mg, and placebo groups, respectively). A_3AR expression levels were stable over time in all study groups. Namodenoson was well-tolerated at both doses with no drug-emergent severe adverse events and no hepatotoxicity. **Conclusion:** A_3AR is a valid target whose levels remain stable after chronic treatment. Namodenoson at 25 mg BID is safe and more effective than 12.5 mg BID.