NGM313, a Novel Once-Monthly Activator of βKlotho-FGFR1c, Significantly Reduces Hepatic Steatosis and Key Biomarkers of Non-Alcoholic Steatohepatitis: Results of a Randomized, Active-Controlled Clamp Study in Obese Insulin-Resistant Patients with NAFLD

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BACKGROUND AND AIMS

NGM313 is an once-monthly, humanized, monoclonal antibody directed to βKlotho and modulates activity of the βKlotho-FGFR1c receptor complex. It has the potential to decrease liver fat content in patients with NAFLD. This study was designed to evaluate the efficacy, safety, and tolerability of NGM313 240 mg as a single dose compared to Pioglitazone (PIO) 45 mg daily PO, in insulin-resistant patients with NAFLD.

METHODS

A randomized, double-blind, placebo-controlled, active-clamp study of NGM313 240 mg (single dose) vs. PIO 45 mg daily PO in 108 NAFLD subjects from Day 0 to Day 28. Included patients aged 21 to 70 years, with at least 50% hepatic fat content and metabolic syndrome, and with FPG ≥ 100. The primary objective was to evaluate the safety and tolerability of NGM313 240 mg as a single dose compared to PIO 45 mg daily PO in insulin-resistant patients with NAFLD.

RESULTS

Baseline Patient Characteristics

Inclusion criteria included males and females 16-45 years of age, fasting glucose ≤125 mg/dL, fasting insulin ≤20 μU/mL, BMI ≥ 35 kg/m², waist circumference ≥40 inches in males and ≥36 inches in females, NAFLD with 10% liver fat content as measured by magnetic resonance imaging proton density fat fraction (MRI-PDFF).

Liver Fat Content

Liver fat content was measured by MRI-PDFF at Day 1, Day 23 and Day 36. A single dose of NGM313 240 mg resulted in a reduction in absolute liver fat content of 6.3%, and relative reduction of 37%, at Day 36. NGM313 appeared to exert greater effects on steatosis reduction than daily PIO.

Lipids

A single dose of NGM313 produced a favorable lipid profile in patients with NAFLD:

- Δ Triglycerides (46%) - Δ LDL-C (54%) - Δ HDL-C (20%)

Safety

All AEs were mild in severity.

CONCLUSION

NGM313 was safe and well tolerated in obese, insulin-resistant, non-diabetic subjects with NAFLD.