**Pemvidutide significantly decreased serum lipids including inflammatory lipid sub-species at Week 12.**

**Introduction**
- Approximately 70% of people with either obesity or MASH have dysregulated serum lipid profiles, with high levels of lipids and toxic lipid species associated with increased cardiovascular risk.
- Dyslipidemia can result in increased hepatic and systemic inflammation, exacerbating comorbidities such as cardiovascular disease and insulin resistance.
- Pemvidutide is a balanced glucagon-like peptide 1 (GLP-1)/glucagon dual receptor agonist in clinical development for the treatment of MASH and obesity.
- Pemvidutide achieved up to 15.6% weight loss in a 48-week clinical trial of subjects with obesity.

**Aim**
- To analyze the change in lipidomic profile of subjects with overweight/obesity (NCT04561245) or overweight/obesity and MASLD (NCT05006885) following pemvidutide treatment.

**Methods**
- Subjects with overweight/obesity or overweight/obesity and MASLD were treated with pemvidutide (1.2 mg, 1.8 mg, 2.4 mg) or placebo administered subcutaneously weekly for 12 weeks.
- Plasma samples from study completers were analyzed by ultra-high performance liquid chromatography–mass spectrometry (UHPLC-MS) or nuclear magnetic resonance (NMR) at baseline, Week 6, and Week 12.

**Results**
- Pemvidutide achieved significant reductions from baseline across multiple glycerol- and phospholipid sub-species associated with MASH, including triglycerides, lyso-phosphatidylinositols (Lyso-PI) and lyso-phosphatidylethanolamines (Lyso-PE).
- Pemvidutide treatment resulted in significant reductions in atherosclerotic sphingolipids including ceramides.
- Pemvidutide improved bile acid dysregulation, yielding reductions in glycol- and tauro-conjugated bile acids.

**Conclusions**
- Pemvidutide administered weekly resulted in significant improvements in plasma lipidomic profiles, including reductions in triglycerides and MASH-associated glycerol- and phospholipid species at 12 weeks of treatment.
- Decreases in cardio-inflammatory Lyso-PI and Lyso-PC sub-species may reduce cardiovascular disease.
- Lyso-PE decreases may reduce fat accumulation in MASH patient livers (Yamamoto et al. 2022).
- Elevated glycol- and tauro-conjugated bile acids are associated with fibrosis and increased MASLD activity, suggesting that pemvidutide improves these histological factors (Kalhan et al. 2011).
- These findings support pemvidutide’s potential benefit on MASH-associated co-morbidities, including atherosclerosis and metabolic syndrome.
- These data support the evaluation of pemvidutide in an ongoing biopsy-confirmed, 24-week Phase 2b MASH trial (IMPACT: NCT05989711).

**References**
- Yamamoto, Y et al. Nutrients 2022 PMC839386.
- Kalhan, S et al. Metabolism 2011 PMC2950914.

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