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Pegozafermin Added to Background GLP-1 Therapy Led to Greater Improvement in Non-invasive Markers of Liver Fat, Injury and Fibrosis as well as Glycemic Control in NASH Patients with F2/F3 Fibrosis at 24 weeks: A Posthoc Analysis from ENLIVEN

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Abstract

Background: Non-alcoholic steatohepatitis (NASH) is characterized by excess hepatic fat accumulation, inflammation, and cellular injury, with or without the presence of fibrosis. Pegozafermin (PGZ), a long-acting fibroblast growth factor 21 (FGF21) analog, was evaluated in NASH patients with proven F2/F3 fibrosis (ENLIVEN trial) for efficacy/safety. This study demonstrated the benefit of PGZ in both hepatic and extra-hepatic parameters, including histologic improvements. Glucagon-like peptide-1 receptor agonists (GLP-1 therapy), approved for T2DM and obesity, decrease hepatic steatosis and inflammation and are currently being investigated as a treatment for NASH. A subset of ENLIVEN patients were on stable background GLP-1 therapy.

Aim: To investigate the efficacy/safety of PGZ when added to existing background GLP-1 therapy.

Methods: This posthoc analysis of the ENLIVEN trial included 37 full analysis population patients (F2 or F3 and NAS ≥4) who received GLP-1 therapy for a minimum of 6 months prior to enrollment. Twenty-five received PGZ (30 mg QW or 44 mg Q2W); 12 received placebo. Changes in liver steatosis, fibrosis and inflammatory markers, metabolic effects, safety and tolerability were evaluated.

Results: Addition of PGZ to background GLP-1 therapy led to greater improvement in markers of liver fat (MRI-PDFF), liver injury (ALT), fibrosis (ELF score, VCTE, ProC3) and glycemic control (HbA1c, TG, adiponectin) compared to GLP-1 therapy alone (PBO group). Combination therapy retained acceptable safety and tolerability with no treatment-related discontinuations.

Conclusion: This exploratory analysis demonstrates PGZ has the potential to offer additive benefit to NASH patients on GLP-1 therapy. More data are needed to confirm these findings.

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