2nd GLOBAL LIVER HEALTH FORUM

ESSENTIAL PHOSPHOLIPIDS (EPLs) – EFFICACY ACROSS THE SPECTRUM OF NAFLD ORIGINS

Prof. Evgenii Sas

Saint Petersburg State Pediatric Medical University and S. M. Kirov Military Medical Academy, Russia

SANOFI

Resources

ESSENTIAL PHOSPHOLIPIDS (EPLs) – EFFICACY ACROSS THE SPECTRUM OF NAFLD ORIGINS

Current treatment landscape

Currently, there are no therapeutics that are considered standard of care for the treatment of NAFLD; all medications recommended in this therapeutic area target the comorbid diseases associated with NAFLD, such as T2DM or CVD. These include metformin, DPP-4 inhibitors and GLP-1 agonists. Other drug classes including hepatoprotective agents, such as EPL, may improve clinical outcomes for patients with NAFLD and could form an important part of the treatment landscape.[1]

What are EPLs?

Phospholipids are key components of all cellular and sub-cellular membranes. They are responsible for or assist a range of important cellular functions, such as the activation of phospholipid-dependent enzymes and increasing metabolic activity and detoxification of the liver. EPLs also have anti-inflammatory and antioxidant properties, contributing to their hepatoprotective effects. EPLs are being investigated for the treatment of a spectrum of liver diseases, such as, cirrhosis, alcoholic steatohepatitis, NAFLD, drug-induced liver injury and viral hepatitis.[2]

EPLs in patients with T2DM and NASH

Professor Sas presents results of a prospective, single-blind clinical trial of EPLs in patients with T2DM and NASH. In this study, 215 patients with well-controlled T2DM receiving metformin were randomized to receive EPL 1368 mg* daily or metformin for 6 months from 1998 to 2012.[3]

In patients who received EPL treatment, reductions from baseline in liver enzymes including ALT, AST and γ-GT were significantly larger compared with patients receiving metformin. Significant reductions in HbA1c were also seen in 96% of patients receiving EPL treatment after 6 months of treatment.[3]

Signs of steatosis were also decreased in patients receiving EPLs. After 6 months of treatment, hepatic echo-texture results were significantly improved in patients, and sonographic signs of steatosis were significantly decreased in patients who received EPL treatment versus those who received standard of care. In patients who developed hepatic fibrosis, the development occurred at a slower rate in patients who were treated with EPLs versus those who were not.[3]

EPLs in patients with ALD

The hepatoprotective properties of EPLs may also have a beneficial effect in patients with ALD. In a prospective, single-blind clinical trail, 86 patients with ALD were randomized to receive basic treatment (diet + abstinence from alcohol + physical regimen) in combination with EPL 1368 mg daily or vitamin E 400 mg daily for 6 months. At the end of treatment, 87.5% of patients who received EPL treatment had improvements in their hepatic echo-texture by ultrasound. A significant increase in steatosis occurred in patients receiving vitamin E, whereas a decrease in steatosis was observed in the EPL group ($p<0.05$). Levels of liver enzymes, insulin levels and insulin resistance scores decreased from baseline in patients receiving EPLs.[4]

EPLs and MetS

Professor Sas then presents the results of a meta-analysis of RCTs of EPLs in combination with antidiabetic treatments compared with antidiabetic treatments alone. Regimens containing EPLs resulted in significantly greater reductions of ALT ($p<0.003$), triglycerides ($p<0.001$) and cholesterol ($p<0.001$) compared with antidiabetic treatments alone. EPL-based regimens also resulted in substantial clinical improvements from baseline in 58% of patients.[5]

EPLs in combination with antibiotics and prebiotics

Finally, Professor Sas presents the results of a study investigating daily EPLs (1368 mg) in combination with a daily antibiotic (800 mg) and a prebiotic for 2 years in patients with NAFLD. The results showed that this combination regimen reduced the rate of fibrosis progression and resulted in significant reductions in liver steatosis ($p<0.02$) and disease activity ($p<0.03$) from baseline in patients with NAFLD.[6]

References

1. Dajani A, et al. Saudi J Gastroenterol 2016;22:91–105
2. Gundermann KJ, et al. Pharmacol Rep 2011;63:643–59
3. Sas E, et al. J Hepatol 2013;58:S549
4. Sas E, et al. J Hepatol 2011;54:S506
5. Dajani A, et al. World J Clin Cases 2020;8(21):5235–49
6. Grinevich V, et al. Poster presented at Obesity 2012

*1368 mg in China is equal to 1300 mg in other countries due to differences in methods used to measure the active pharmaceutical ingredient

ALD, alcoholic liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CVD, cardiovascular disease; DPP-4, dipeptidyl peptidase-4; EPL, essential phospholipid; GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; RCT, randomized controlled trial; T2DM, type 2 diabetes mellitus; r-GT, gamma glutamyl transferase

Learning objectives:

- Understand the current treatment landscape for NAFLD and its associated comorbidities
- Understand the role of EPLs in promoting liver health
- Become familiar with the clinical data supporting the use of EPLs in patients with diseases affecting the liver, including NAFLD in patients with T2DM and MetS, as well as in ALD

Main takeaways:

- There is currently no standard of care pharmacotherapy for the treatment of NAFLD
- Although currently approved therapeutic approaches rely on treating comorbidities, drug classes such as hepatoprotective agents given in addition to standard of care may improve NAFLD-associated clinical outcomes
- EPLs assist a number of hepatic functions, such as enhancing metabolism and detoxification in the liver
- Clinical data show that EPL treatment in patients with T2DM and NASH resulted in reduced levels of liver enzymes and improved steatosis findings from baseline
- EPL treatment may also improve liver enzyme levels in patients with ALD and in patients with MetS, and improve hepatic echo-texture results in patients with ALD

ALD, alcoholic liver disease; EPL, essential phospholipids; MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; T2DM, type 2 diabetes mellitus

MAT-GLB-2103106
Date of approval: XXX