



Press release First Late Breaking News Session: Bempedoic acid + ezetimibe

EMBARGOED until Monday 27th May, 2019 15:45 CET

**87th Annual Congress of the European Atherosclerosis Society (EAS)
May 26-29th 2019, Maastricht, The Netherlands**

Phase 3 data for fixed combination bempedoic acid-ezetimibe in high risk patients not at LDL cholesterol goal

Maastricht, 27 May, 2019 – An oral once-daily fixed combination of bempedoic acid plus ezetimibe, two treatments with complementary action, provides effective low-density lipoprotein (LDL) cholesterol lowering in high risk patients not at goal.

Statins are the cornerstone of therapy to lower LDL cholesterol.¹ Yet even on maximally tolerated statin treatment some patients fail to attain LDL cholesterol goal. In addition, patients unable to tolerate statin therapy need further options to attain LDL cholesterol goal. Ezetimibe, a cholesterol absorption inhibitor, is routinely recommended by guidelines as an add-on treatment to statin therapy, or as an alternative to a statin, but further LDL cholesterol lowering may be needed in high risk patients.

Bempedoic acid is a first-in-class non-statin agent that inhibits ATP Citrate Lyase, an enzyme at a step preceding 3-hydroxy-3-methylglutaryl-coenzyme A reductase, the enzyme that is inhibited by statins. As a result, bempedoic acid reduces cholesterol biosynthesis and lowers LDL cholesterol by up-regulating the LDL receptor.² Like statins, bempedoic acid also reduces high sensitivity C-reactive protein, a key marker of inflammation associated with cardiovascular disease. There are now extensive data that bempedoic acid is effective in lowering LDL cholesterol and well tolerated when administered with background statin therapy, or as monotherapy in patients who are unable to tolerate statins.^{3,4}

Given that bempedoic acid and ezetimibe are orally administered agents with complementary mechanisms of action, it makes sense to combine these two agents. This rationale is also supported by phase 2 data showing that adding bempedoic acid to ezetimibe led to further LDL cholesterol lowering.⁴ The use of a fixed combination of bempedoic acid and ezetimibe offers a convenient approach for patients at high cardiovascular risk who do not attain LDL cholesterol goal with conventional therapy.

This double-blind study enrolled patients at high risk of cardiovascular events such as heart attack or stroke who were not at guideline-recommended LDL cholesterol goal despite

maximally tolerated statin therapy. Patients who were unable to tolerate a statin were also included. Patients were eligible if they had clinical cardiovascular disease and/or heterozygous familial hypercholesterolaemia (inherited high cholesterol) and LDL cholesterol levels 2.6 mmol/L (100 mg/dL) or higher, or if they had no clinical cardiovascular disease but multiple risk factors and LDL cholesterol levels of 3.4 mmol/L (130 mg/dL) or higher. Patients were randomly allocated to once-daily treatment with bempedoic acid 180 mg, ezetimibe 10 mg, the fixed combination, or placebo for 12 weeks.

The study enrolled 301 evaluable patients, 65 per cent of whom were on a statin. At the end of 12 weeks, the fixed combination of bempedoic acid plus ezetimibe reduced LDL cholesterol by 36.2 per cent (least squares mean value), which was significantly greater than with ezetimibe alone (23.2 per cent) or bempedoic acid alone (17.2 per cent). There was an increase of 1.8 per cent on placebo, thus the fixed combination of bempedoic acid plus ezetimibe had a 38 per cent reduction of LDL cholesterol compared to placebo. The fixed combination of bempedoic acid plus ezetimibe also reduced non-high-density lipoprotein cholesterol, a secondary lipid target, and high sensitivity C-reactive protein to a greater extent than the individual components.

The fixed combination was well tolerated.

Lead author Professor Christie Ballantyne (Baylor College of Medicine, Houston, Texas, USA) commented: 'The results of this study show that a fixed combination of bempedoic acid and ezetimibe, two oral lipid lowering agents with complementary mechanisms of action, has the potential to meet the needs of high risk patients who are unable to attain LDL cholesterol goal with currently available therapies. The fixed combination is also a convenient once daily option for patients.'

LATE BREAKING NEWS: Late Breaking News: Pharmacology of Dyslipidemia

Monday 27th May, 15:45-17:15, Marten Hofker Hall

Ballantyne C, Laufs U, Ray KK, Leiter LA, Bays HE, Goldberg AC, Stroes ESG, MacDougal D, Zhao X, Catapano AL. Efficacy and safety of bempedoic acid + ezetimibe fixed-dose combination in patients at high CVD risk and with elevated LDL-C receiving maximally tolerated statin therapy. Abstract EAS19-1133.

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Notes for editors

Funding

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References

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2. Saeed A, Ballantyne CM. Bempedoic acid (ETC-1002): a current review. *Cardiol Clin* 2018;36:257-64.
3. Ray KK, Bays HE, Catapano AL, Lalwani ND, Bloedon LT, Sterling LR, Robinson PL, Ballantyne CM; CLEAR Harmony Trial. Safety and efficacy of bempedoic acid to reduce LDL cholesterol. *N Engl J Med* 2019;380:1022-32.
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5. Ballantyne CM, Banach M, Mancini GBJ, Lepor NE, Hanselman JC, Zhao X, Leiter LA. Efficacy and safety of bempedoic acid added to ezetimibe in statin-intolerant patients with hypercholesterolemia: A randomized, placebo-controlled study. *Atherosclerosis*;277:195-203.

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