LYCOSTATIN™

In many cases one of the main limitations of statin therapy is to achieve the optimal reduction of plasma low-density lipoproteins (LDL). The main reason behind this is a set up of the maximum dose, exceeding of which may increase the possibility of development of toxic side effects. About 90% of LDL is synthetised in the liver. If statin molecules were concentrated in this organ, and not randomly distributed by the main circulation around different organs, then the therapeutic efficacy of the drug would be increased within its established safe dose-range.

Although elevated LDL is an established risk factor in the development of atherosclerosis and cardiovascular diseases (CVD), inflammatory oxidative damage (IOD) is another independent factor, which can cause formation of toxic forms of these particles, ox-LDL, and further increase their pro-atherogenic properties.

To address these two issues, Lycotec has developed Simvastatin Lycosome, LYCOSTATIN, which not only facilitates delivery of statin molecules to the liver, but also inhibits IOD and conversion of LDL into their oxidised pathogenic form.

Lycostatin

This is a combinatory product where molecules of Simvastatin are clustered together with *trans*-lycopene, without creating any new chemical entities. The liver contains one of the highest levels of carotenoid receptors, hence lycopene in this LYCOSTATIN complex serves as the delivery vector to this organ. In addition, lycopene molecules are one of strongest hydrophobic inhibitors of IOD. Therefore, this complex provides a synergetic combination of two functionalities: liver-targeted, hence more efficient suppression of cholesterol biosynthesis and inhibition of ox-LDL formation.

Clinical Trial – Phase IIa

To validate the efficacy of LYCOSTATIN, a proof-of-concept trial was undertaken. It was an examiner-blinded, randomised, controlled study on 24 patients with hyperlipidaemia, with serum LDL level > 150 mg/dL, positive on markers of IOD and presence of ox-LDL. These patients were divided into 3 groups, who received daily either 20 mg of Simvastatin, or 7 mg of *trans*-lycopene, or LYCOSTATIN, a complex of the two previous molecules in the same dose. The duration of the trial was 4 weeks.

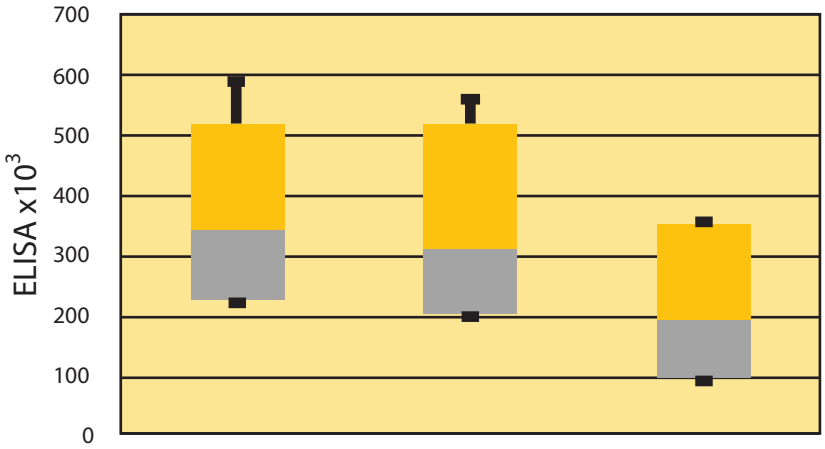
LDL reduction

It was demonstrated that by the end of the trial in the group which received Simvastatin the reduction of LDL was by 23.5 mg/dL, but in the LYCOSTATIN group it was significantly lower, by 38.5 mg/dL, $p < 0.05$. There were no changes of this parameter in the group which received Lycopene alone.

ox-LDL and IOD inhibition

In was also observed that the level of ox-LDL was reduced by a comparable level of 24-26% in the Lycopene and Simvastatin groups, but in those who took LYCOSTATIN the reduction was by 60%, figure 1.

Figure 1. Serum level of ox-LDL by the end of 4 weeks administration of *trans*-Lycopene (left column), Simvastatin (central column) or LYCOSTATIN (right column)



Ivan M Petyaev - Improvement of hepatic bioavailability as a new step for the future of statin. Arch Med Sci (2015) 11, 2: 406–410

Ivan M. Petyaev, Pavel Y. Dovgalevsky, Natalia E. Chalyk, Victor Klochkov, Nigel H. Kyle - Reduction of cholesterol and markers of oxidation in serum of hypercholestrolemic patients treated with lycosome formulation of simvastatin. Int J of Res Med Sci (2016) 4(2):349-355.

Simvastatin vs. LYCOSTATIN

In a separate randomised clinical study, on 12 patients similar to those in the previous trial, we determined that the efficacy in the reduction of the serum LDL concentration by 20 mg of Simvastatin in the LYCOSTATIN complex was between 60 and 80 mg of free Simvastatin.

Therefore, these results indicate that LYCOSATIN has a significantly lower therapeutic dose than free statin molecules. Hence it provides a broader range of interventional safe doses for more aggressive LDL lowering therapy. In addition LYCOSTATIN has a second beneficial mode of action to inhibit formation of pro-atherogenic ox-LDL and inflammatory oxidative damage in patients with hyperlipidaemia.

Next Step

The main objective of Lycotec is to find funding and/or a partner to take LYCOSTATIN to the next level of clinical development, Phase II, to further evaluate its LDL-lowering and anti-inflammatory activity, not only in patients with hyperlipidaemia alone, but with CVD too.

Regulatory

Simvastatin is already approved as a drug up to 80 mg per day. *trans*-Lycopene is safe for humans and does not require FDA or other countries' regulatory body approval for oral administration in its therapeutic dose-range.

For more information and enquiries please contact: info@lycotec.com

Granta Park, McClintock Building, Great Abington, Cambridge CB21 6GP
Phone: +44 (0)1223 651411
www.lycotec.com