

New developments in diabetes drugs

A new generation of drugs to inhibit the onset of diabetes is in the pipeline at the major pharmaceutical companies and is one of the big talking points in the drug development world. Here, Steve Ohlsen, a biochemist with long experience of the industry, surveys the scene. Steve now runs of Point of Care Services Ltd, the UK distributor of Cholestech's LDX Analyzer system.

Diabetes is set to become a dominant, if not *the* dominant, theme in healthcare. The disease has already reached epidemic proportions in the USA, and the problem seems to be further exacerbated by racial differences between the Caucasian population and migrant populations from Africa, India and Asia. Those who have re-located into European and the USA and adopted their lifestyles are particularly vulnerable.

Obesity and the consequent metabolic syndrome are the twin evils leading to a number of long-term conditions, including cardiovascular disease, musculoskeletal conditions and diabetes itself, which in turn lead to organ failure and a boosted susceptibility to further cardiovascular conditions. The diabetes challenge is to break this cycle through either weight loss or better glycaemic control.

Current anti-diabetic drugs are inadequate on a number of fronts, not least since most cause weight gain. There is clearly room for drugs which do not cause weight gain, or, better still, reduce weight, improve glycaemic control, as measured by HbA1c levels. And emerging to meet this need are three important new classes of drug: GLP-1, DPP-IV and Riminobant.

GLP-1 (glucagon-like peptide) stimulates insulin secretion, slows down gastric emptying and increases feeling of fullness or satiety, thereby lowering food intake. The effect of increasing GLP-1 levels should be to improve the control of blood glucose levels. GLP-1 is set to be the first major advance in the treatment of Type 2 diabetes since the glitazones in the early 1990s. The most advanced product in this group is exenatide, which has recently been approved as Byetta and is being marketed by the developer, Amylin Pharmaceuticals, and its partner Eli Lilly.

The **DPP-IV** inhibitors are a class of small molecule that boost the level of naturally-occurring GLP-1, and are seen to have enormous potential in the treatment of Type 2 diabetes. DPP-IV inhibitors have been in development for a number of years and the most promising product, vildagliptin from Novartis, is now at the end of phase III clinical trials. Further behind in clinical development are products from Merck (sitagliptin) Bristol Myers Squibb (saxagliptin) and Glaxo Smithkline.

Riminobant is the first in a novel class of drugs that selectively block the cannabinoid-1 receptor – part of the newly-discovered endocannabinoid system, which contributes to the regulation of energy balance, food intake, and lipid and glucose metabolism. Rimonabant can help reduce body weight, waist circumference, glycated haemoglobin (HbA1c) and cardiovascular risk factors. Sanofi Aventis is the leader in this important sector, developing riminobant under the name Acomplia.

So, I believe we are on the cusp of clinical and commercial change in the diabetes pharmaceutical market, which in turn will have a great impact on the diagnostic parameters, such as HbA1c, used to benchmark drug effectiveness.