

the American Heart Association (Skyler JS, Bergenstal R, Bonow RO, Buse J, Deedwania P, et al, 2009).

Liraglutide is a once-daily analogue of human glucagonlike peptide-1 (GLP-1), and the molecule shares 97% of the amino acid sequence of native GLP-1. The efficacy and safety of liraglutide treatment has been compared with those of standard treatments across the continuum of care in type 2 diabetes in a comprehensive phase 3a trial programme Liraglutide Effect and Action in Diabetes (LEAD) trial programme (Marre M, Shaw J, Brandle M et al. 2009) (Nauck MA, Frid A, Hermansen K et al. , 2009) (Garber A, Henry R, Ratner R et al. ,2009) (Zinman B, Gerich J, Buse J et al. ,2009) (Russell-Jones D, Vaag A, Schmitz O et al. ,2009) (Buse J, Rosenstock J, Sesti G et al. , 2009).

## **1.2 Hypercholesterolemia and atorvastatin**

Hypercholesterolemia is a key feature of the metabolic syndrome in humans and a risk factor for the development of cardiovascular diseases, such as myocardial infarction. Statins are widely used in the treatment of hypercholesterolemia. By competitive inhibition of 3-hydroxy-3-methylglutarylcoenzyme A reductase (HMGCR), the rate-limiting enzyme in cholesterol synthesis, statins enhance the intracellular depletion of cholesterol and stimulate the expression of the low-density lipoprotein (LDL) receptor thereby increasing the LDL uptake (Horton *et al.*, 2002; Poli, 2007).

Atorvastatin has been prescribed for many years and is considered as one of the most potent agents within the statin drug class, in terms of the LDL cholesterol-lowering effect (Poli, 2007). However, the therapeutic response at a given dose is highly variable between individuals (Pedro-Botet *et al.*, 2001), and the correlation between its plasma concentrations and response to atorvastatin is poor (Lennernäs, 2003). One reason may be the extensive first-pass