



Glucagon-like-Peptide 1 Analogues

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The diabetes epidemic presents a global burden as a debilitating and costly disease associated with severe complications. Therefore, successful diabetes therapy should prevent micro- and macrovascular complications which improves life expectancy and quality of life.

Landmark studies - The Diabetes Control and Complications Trial (DCCT)¹ and United Kingdom Prospective Diabetes Study (UKPDS)² have established that lowering glycaemia (measured as HbA_{1c}) reduces microvascular complications in type 1 as well as type 2 diabetes. The benefits of lower glycaemia have been further supported by recent evidence of a 'glycaemic metabolic memory'. More than 10 years after the study, patients with tighter glycaemic control during the study developed less micro- and macrovascular complications.^{3,4}

In reality, despite a clear need to control glycaemia as tight and as early in the disease process as possible, high levels of HbA_{1c}, especially in type 2 diabetes patients is still prevalent.

Effective therapy measures include lifestyle changes to reduce overweight, increase physical activity, and the use of glucose lowering treatments. However, existing treatment options brings concerns on risk of hypoglycaemia and weight gain. They also fail to address progressive decline in beta cells and cardiovascular risk factors.

There is available evidence which indicates that unlike current anti-diabetic treatments, incretin based therapy offers effective glycaemic and weight control to patients with type 2 diabetes. The therapy does not increase the risk of hypoglycaemia. In this regard, this novel therapy offers a promising new option for the treatment of type 2 diabetes.

This supplement aims to provide information on incretin-based therapies, and focuses on the GLP-1 receptor agonist, liraglutide, approved in Europe and recently in US and India.

In the first article, Ramachandran A et al summarises the prevalence of diabetes and the state of diabetes care in India. There is an urgent need to improve diabetes care in India and new therapeutic options which controls glycaemia, reduces risk of weight gain and hypoglycaemia.

The second article summarises the discovery and development of incretin therapy. Bhansali A et al explore the rationale behind incretin therapy from the early discovery of incretin effect to current pharmacological components. The two classes of incretin therapy - the GLP-1 receptor agonists and DPP-4 inhibitors are reviewed in terms of molecular structure and clinical data. One of the incretin therapies is the GLP-1 receptor agonists, liraglutide, and the development of liraglutide molecule and its pharmacokinetic properties are reviewed in

the third article by Mohan V et al. Results from pre-clinical and clinical trials with liraglutide are presented. Essentially, the encouraging results from phase 2 trials led to confirmatory phase 3 trials. Sethi BK et al then reviews the results from the large phase 3 LEAD (Liraglutide Effect and Ation in Diabetes) clinical programme. The efficacy and safety of liraglutide both as mono- or combination therapy with various anti-diabetic drugs were evaluated in the LEAD programme and covered the entire continuum of disease progression in patients with type 2 diabetes. Relevant clinical assessments such as HbA_{1c}, FPG, PPG, body weight, systolic blood pressure and patients' safety are reviewed. Furthermore, a composite endpoint reflecting a broad measure of diabetes control including HbA_{1c} < 7.0%, no weight gain and no hypoglycaemia is assessed. There have been preliminary but promising results of the effect of liraglutide on cardiovascular risks and beta cell function, besides typical glycaemic control from anti-diabetic agents. This is an exciting prospect for patients and their physicians as cardiovascular risks and declined beta-cell function is a common concern. In the fifth article, Bhattacharyya A et al explores the effect of liraglutide and weighs if liraglutide may meet some of the unmet needs in diabetes care.

Finally, Tandon N et al provides their point of view on liraglutide in clinical practice. A case study of a patient who was treated with liraglutide in a LEAD study is presented to illustrate the effect of liraglutide in real-life.

In summary, we hope that the articles in this supplement will give readers a good appreciation of the physiologic and clinical evidence supporting the role of incretins in diabetes treatment. New treatment options, such as the incretin-based therapies, may meet some of the unmet needs in glucose control.

References

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