

Introduction

According to the Centers for Disease Control and Prevention, 25.6 million Americans age 20 and older currently have diabetes. An estimated 79 million Americans age 20 and older have prediabetes.¹ If current trends continue, 1 in 3 adults in the United States are predicted to have diabetes in 2050.² As the prevalence of diabetes increases, the cost burden related to diabetes will also increase, intensified by disease progression and diabetes-related complications, particularly in patients with type 2 diabetes mellitus (T2DM).

There is a clear call-to-arms for practitioners to actively manage T2DM, and the number of available treatment options reflects this need. Currently, there are many classes of drugs indicated for glycemic control in patients with T2DM, with differing mechanisms of action. With such a variety of different treatment options available, there is a need to clarify the best treatment options for individual patients, as well as possibly reduce treatment costs and improve the overall quality of public health. Comparative effectiveness research (CER) is a relatively new strategy in drug development and healthcare designed to help meet this need. The article by Ahmann,³ the first in this supplement, reviews available CER and its application to T2DM therapies.

One of the newest areas of innovation for the treatment of T2DM involves agents that impact the incretin system, which include the glucagon-like peptide-1 (GLP-1) receptor agonists (eg, exenatide, liraglutide) and the dipeptidyl peptidase-4 (DPP-4) inhibitors (eg, sitagliptin, saxagliptin). Although these drugs affect the same physiologic pathway, each has unique functions and characteristics that have the potential to impact their use in clinical practice.

One important difference between the GLP-1 receptor agonists and the DPP-4 inhibitors is their mechanism of action. DPP-4 inhibitors protect endogenous GLP-1 from degradation by DPP-4, thereby achieving a physiologic level of GLP-1. In contrast, GLP-1 receptor agonists act directly on the GLP-1 receptor, achieving a pharmacologic

level of GLP-1 activity.^{4,6} These different mechanisms yield different effects on diabetes and weight loss.⁶ This and additional differences between GLP-1 receptor antagonists and DPP-4 inhibitors will be discussed in detail in the article by Calabrese,⁷ the second in this supplement.

The first once-daily GLP-1 receptor agonist, liraglutide, was evaluated for safety and efficacy in the Liraglutide Effect and Action in Diabetes (LEAD) studies, which were large, randomized multicenter phase 3 trials in adults with T2DM.⁸⁻¹³ Liraglutide was also evaluated in a head-to-head comparison with sitagliptin.¹⁴ The article by Bode,¹⁵ the last in this supplement, describes in detail the clinical evidence supporting liraglutide and its role in the treatment of T2DM.

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