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Introducing a novel therapy for type 2 diabetes to primary care

Stephen A. Brunton

Touro University California, Vallejo, CA, USA

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Type 2 diabetes (T2D) is a chronic, complex condition that covers a broad spectrum of patients. Uncontrolled blood glucose levels can result in macro- and microvascular complications such as cardiovascular disease and chronic kidney disease (CKD) [1], further adding to the complexity and burden of T2D. At the forefront of care for the vast majority of these patients are the physicians, physician assistants, and nurse practitioners who work in the primary care setting [2]. As primary care clinicians are typically the first point of contact in the healthcare system for a patient with T2D, they are best placed to inform, educate, and develop the treatment plan. Any treatment plan must also integrate how to manage comorbidities or other medical issues the patient may have.

The importance of the primary care setting is in part driven by the elderly, with around 20% of the T2D population aged ≥ 65 years [3]. Furthermore, with the already high prevalence of T2D in the US, which is globally forecasted to rise even further in the coming years [4], the primary care setting will remain an integral part of T2D management. Therefore, it is important for those working in primary care to stay well informed of the latest guidelines and developments for effective and timely treatment, and to understand the benefits versus risks of the available therapies across the full spectrum of T2D patient populations.

Different guidelines and treatment algorithms are available to help with decision-making when it comes to choosing the right therapy for the right patient and at the right time [5–9]. This is important since T2D treatment should be tailored to the patient's individual needs for optimal disease control [10]. Despite the many proven effective therapies and comprehensive guidelines available to help navigate the treatment decision-making process, it is estimated that around half of patients do not reach the standard glycemic target of glycated hemoglobin (HbA_{1c}) $< 7\%$ [11]. Moreover, only $\sim 20\%$ of patients have been historically reported to simultaneously achieve all three treatment goals for HbA_{1c} ($< 7\%$), blood pressure ($< 140/90$ mmHg), and cholesterol/lipids (low-density lipoprotein [LDL] < 100 mg/dL) (collectively termed the ABCs) [12]. Reasons for the apparent discrepancy between the availability of effective treatment options and inadequate control of disease could be due to clinical inertia [13] or suboptimal adherence to medication, which can arise from a variety of

factors including lack of patient-directed education, treatment complexity, and misconceptions surrounding treatment [14]. The articles within this supplement are intended to provide primary care clinicians involved in the care of patients with T2D with the necessary information when tailoring treatment to their patients' individual needs.

Glucagon-like peptide-1 receptor agonist (GLP-1RA) therapy is highly effective in reducing both hyperglycemia and body weight [15–17], but until recently, this class of antihyperglycemic agents has only been available for subcutaneous administration. Oral semaglutide is the first GLP-1RA available for oral administration [18], potentially overcoming some limitations encountered with other therapies, such as injectable GLP-1RAs. In the first article in this supplement, Dr Wysham and myself describe the clinical experience of GLP-1RAs to date and why there was a need to develop an oral alternative of this highly effective drug class. Within this article, the development and evaluation of oral semaglutide is described.

Metformin is recommended as first-line therapy for most patients with T2D but, since T2D is a progressive disease, further therapies may also be required. These include oral antihyperglycemic agents such as sulfonylureas, sodium-glucose co-transporter-2 inhibitors (SGLT2is), dipeptidyl peptidase-4 inhibitors, and thiazolidinediones [7]. Other second-line therapy options include GLP-1RAs or basal insulins [7–9]. In addition, patients with certain comorbidities, such as cardiovascular disease (CVD) or indicators of high cardiovascular risk, CKD, and heart failure, may benefit from a GLP-1RA or SGLT2i with proven cardiovascular or renal benefits early in the treatment algorithm [8]. In the second article, Dr Lavernia and Dr Blonde review studies establishing the efficacy and safety of oral semaglutide versus placebo and versus the oral antihyperglycemic agents empagliflozin and sitagliptin.

For some patients and clinicians alike, there may be a reluctance to initiate an injectable therapy [19], which can result in delayed treatment intensification [20] and lead to longer periods of time with uncontrolled glycemic levels [19,20]. Therefore, the third article by Wright and Aroda later in this supplement considers oral semaglutide in the setting whereby an injectable GLP-1RA or insulin would traditionally have been recommended.

Since people with T2D may have comorbidities such as CVD and CKD, both of which are associated with increased rates of morbidity [21] and mortality [22,23] compared with patients without T2D, it is important to understand the potential effects of a therapy in these special populations. In the fourth article, Drs Mosenzon, Miller, and Warren examine the efficacy and tolerability profile of oral semaglutide in patients with such comorbidities, and in elderly patients.

As oral semaglutide has only recently been approved in the US [18], primary care clinicians involved in treating T2D might be unfamiliar with its potential clinical effects, patient populations likely to benefit, safety profile, dosing requirements, and concomitant use with other drugs. In our final article, Dr Mosenzon, Dr Wright, and myself summarize all the information from the preceding articles in the context of clinical practice, providing answers to key questions primary care practitioners may face, using illustrative patient cases.

GLP-1RA therapy in an oral form represents an important therapeutic advancement, providing primary care clinicians with an additional treatment option for their patients. These articles provide key information and recommendations for the management of T2D in different patient populations, with a focus on oral semaglutide in these patients. It is our intention that this supplement will enable those at the forefront of T2D management to make informed decisions regarding appropriate treatment strategies and help counsel patients through their treatment journey.

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References

- Dal Canto E, Ceriello A, Rydén L, et al. Diabetes as a cardiovascular risk factor: an overview of global trends of macro and micro vascular complications. *Eur J Prev Cardiol.* 2019;26(2_suppl):25–32.
- Davidson JA. The increasing role of primary care physicians in caring for patients with type 2 diabetes mellitus. *Mayo Clin Proc.* 2010;85(12 Suppl):S3–S4.
- National Institute of Diabetes and Digestive and Kidney Diseases. Diabetes in America. 3rd ed. 2018. Chapter 3 [cited 2020 May 25]. Available from: <https://www.niddk.nih.gov/about-niddk/strategic-plans-reports/diabetes-in-america-3rd-edition>
- Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019;157:107843.
- American Diabetes Association. 4. Comprehensive medical evaluation and assessment of comorbidities: Standards of Medical Care in Diabetes 2020. *Diabetes Care.* 2020;43(Suppl 1):S37–S47.
- American Diabetes Association. 12. Older adults: Standards of Medical Care in Diabetes 2020. *Diabetes Care.* 2020;43(Suppl 1):S152–S162.
- American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes 2020. *Diabetes Care.* 2020;43(Suppl 1):S98–S110.
- Garber AJ, Handelsman Y, Grunberger G, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm - 2020 executive summary. *Endocr Pract.* 2020;26:107–139.
- Buse JB, Wexler DJ, Tsapas A, et al. 2019 update to: Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care.* 2020;43:487–493.
- American Diabetes Association. 1. Improving care and promoting health in populations: Standards of Medical Care in Diabetes 2020. *Diabetes Care.* 2020;43(Suppl 1):S7–S12.
- Carls G, Huynh J, Tuttle E, et al. Achievement of glycated hemoglobin goals in the US remains unchanged through 2014. *Diabetes Ther.* 2017;8(4):863–873.
- Cowie CC. Diabetes diagnosis and control: missed opportunities to improve health: the 2018 Kelly West Award lecture. *Diabetes Care.* 2019;42(6):994–1004.
- Khunti S, Khunti K, Seidu S. Therapeutic inertia in type 2 diabetes: prevalence, causes, consequences and methods to overcome inertia. *Ther Adv Endocrinol Metab.* 2019;10:2042018819844694.
- Nelson LA, Wallston KA, Kripalani S, et al. Assessing barriers to diabetes medication adherence using the Information-Motivation-Behavioral skills model. *Diabetes Res Clin Pract.* 2018;142:374–384.
- Aroda VR. A review of GLP-1 receptor agonists: evolution and advancement, through the lens of randomised controlled trials. *Diabetes Obes Metab.* 2018;20(Suppl 1):22–33.
- Chatterjee S, Davies MJ, Khunti K. What have we learnt from “real world” data, observational studies and meta-analyses. *Diabetes Obes Metab.* 2018;20(Suppl 1):47–58.
- Levin PA, Nguyen H, Wittbrodt ET, et al. Glucagon-like peptide-1 receptor agonists: a systematic review of comparative effectiveness research. *Diabetes Metab Syndr Obes.* 2017;10:123–139.
- Rybelsus[®] (semaglutide) prescribing information [updated Jan 2020; cited 2020 May 25]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213182s000,213051s001lbl.pdf
- Santos Cavaioia T, Kiriakov Y, Reid T. Primary care management of patients with type 2 diabetes: overcoming inertia and advancing therapy with the use of injectables. *Clin Ther.* 2019;41:352–367.
- Schmieder RE, Tschöpe D, Koch C, et al. Individualised treatment targets in patients with type-2 diabetes and hypertension. *Cardiovasc Diabetol.* 2018;17(1):18.
- Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the sustainable development goals. *Bull World Health Organ.* 2018;96(6):414–422D.
- Gregg EW, Cheng YJ, Srinivasan M, et al. Trends in cause-specific mortality among adults with and without diagnosed diabetes in the USA: an epidemiological analysis of linked national survey and vital statistics data. *Lancet.* 2018;391(10138):2430–2440.
- Taylor KS, Heneghan CJ, Farmer AJ, et al. All-cause and cardiovascular mortality in middle-aged people with type 2 diabetes compared with people without diabetes in a large U.K. primary care database. *Diabetes Care.* 2013;36(8):2366–2371.