



EXPLORING CLINICAL UTILITY OF INNOVATOR R-DNA ORAL SEMAGLUTIDE: A CASE SERIES OF DIVERSE PATIENT PROFILES

Diabetology

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a heterogeneous, progressive condition requiring treatment strategies tailored to glycaemic status, body weight, comorbidities, treatment preferences, and adherence-related factors. Innovator r-DNA oral semaglutide, the first orally administered glucagon-like peptide-1 receptor agonist, provides a non-injectable treatment option for adults requiring further glycaemic and metabolic improvement. **Case series:** This case series describes five adults with T2DM treated with innovator r-DNA oral semaglutide in five clinically distinct settings: early in the diabetes journey with suboptimal glycaemic control; T2DM with chronic kidney disease (CKD) receiving oral semaglutide as an add-on to an SGLT2 inhibitor; established cardiovascular disease (CVD) with replacement of a DPP-4 inhibitor; T2DM with and fatty liver; and unfavourable body composition. Oral semaglutide was initiated at 3 mg once daily and titrated according to tolerability and clinical response. Reported weight reduction ranged from 6.5 to 8.5 kg. In the CKD case, eGFR increased from 48 to 54 mL/min/1.73 m² and UACR decreased from 185 to 105 mg/g. In the CVD case, replacing a DPP-4 inhibitor with oral semaglutide was followed by improvements in HbA1c, body weight, waist circumference, and blood pressure. The patient with T2DM and fatty liver achieved improved glycaemic control and improvement in AST levels. In the body-composition case, fat mass decreased from 34.4 to 25.7 kg, accompanied by a small reduction in skeletal muscle mass from 24.8 to 24.1 kg. Mild, transient nausea was reported during treatment initiation or titration. No severe hypoglycaemia or treatment discontinuation was recorded. **Conclusion:** The cases illustrate the potential role of innovator r-DNA oral semaglutide as part of an individualised treatment strategy for adults with T2DM. Oral semaglutide was associated with clinically relevant improvements in glycaemic control and body weight across diverse patient profiles, with additional favourable changes in selected metabolic, renal, cardiovascular, and body-composition parameters.

KEYWORDS

Type 2 Diabetes Mellitus; Oral Semaglutide; GLP-1 Receptor Agonist; Glycaemic Control; Weight Reduction; Chronic Kidney Disease; Cardiovascular Disease; Adherence; Body Composition.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a progressive and heterogeneous metabolic disorder characterised by persistent hyperglycaemia and frequently accompanied by obesity, hypertension, dyslipidaemia, chronic kidney disease (CKD), and cardiovascular disease. Achieving and maintaining adequate glycaemic control can be challenging because treatment selection must consider glucose-lowering efficacy, effects on body weight, risk of hypoglycaemia, associated comorbidities, treatment burden, and patient preferences. Current standards therefore recommend an individualised, patient-centred approach to pharmacotherapy based on the clinical and metabolic characteristics of each patient. [1,2]

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) improve glycaemic control through glucose-dependent stimulation of insulin secretion, suppression of inappropriate glucagon secretion, delayed gastric emptying, and reduction in appetite. In addition to lowering glycated haemoglobin (HbA1c), these agents are associated with clinically meaningful weight reduction and may provide cardiovascular and kidney-related benefits in appropriately selected patients with T2DM. [3–5] However, the injectable route of administration of most GLP-1 RAs may be a barrier for patients with needle anxiety, frequent travel requirements, concerns regarding injection technique, or a strong preference for oral therapy.

Innovator r-DNA oral semaglutide is the first GLP-1 RA developed for oral administration. It is co-formulated with the absorption enhancer sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (SNAC, 300 mg), which facilitates the gastric absorption of semaglutide. [3,6] The efficacy and safety of oral semaglutide have been evaluated across the PIONEER clinical trial programme in patients with different durations of T2DM, background glucose-lowering therapies, and comorbidity profiles. These studies demonstrated improvements in glycaemic

control and body weight compared with placebo and several commonly used glucose-lowering therapies. [4,7,8] More recently, the SOUL cardiovascular outcomes trial demonstrated a 14% reduction in major adverse cardiovascular events among high-risk adults with T2DM receiving oral semaglutide compared with placebo, with a 27% reduction reported in the Asia subgroup [5]. Real-world evidence from India has also described the use of oral semaglutide across diverse patient profiles in routine clinical practice [9].

Although randomised controlled trials provide robust evidence regarding treatment efficacy and safety, case-based clinical observations can illustrate how a therapy may be incorporated into individualised treatment plans in routine practice. This case series presents five adults with T2DM treated with innovator r-DNA oral semaglutide in distinct clinical settings: early in the diabetes journey, CKD with oral semaglutide added to an SGLT2 inhibitor, established CVD with replacement of a DPP-4 inhibitor, T2DM with fatty liver, and unfavourable body composition. The objective is to describe the clinical rationale for treatment initiation, the treatment course, and observed changes in glycaemic, weight-related, renal, cardiovascular, and body-composition parameters during follow-up, while recognising the descriptive and uncontrolled nature of these observations.

Case-series methodology

This is a descriptive case series of five adults with type 2 diabetes who were prescribed innovator r-DNA oral semaglutide as part of routine outpatient care at a multispecialty clinic, between January 2025 and January 2026. Cases were purposively selected from the clinic's patient panel to illustrate five distinct clinical contexts in which oral semaglutide is commonly considered: early in the diabetes journey with suboptimal glycaemic control, chronic kidney disease, established cardiovascular disease, T2DM with fatty liver, and unfavourable body composition.

Clinical, laboratory, and anthropometric data were recorded at baseline and at scheduled follow-up from the medical record. Case 1 reflects an interim review at 6 months, conducted before the standard 12-month follow-up used for Cases 2–5; its findings are therefore not directly comparable in duration with the other cases. Missing values are marked as not reported rather than estimated or imputed. The complete adverse-event profile for each patient has been recorded, and body-composition measurements in Case 5 were obtained by bioelectrical impedance analysis using a segmental multi-frequency body composition analyser, with the same device and fasting/hydration conditions used at baseline and follow-up. Case selection and data verification are summarised further under Limitations.

Table 1. Summary of the five cases

Case (profile)	Age/sex · duration of T2DM · BMI	Key comorbidity	HbA1c: baseline → f/u	Weight: baseline → f/u	Other notable change	Adverse events
1. Early in the T2DM journey with suboptimal glycaemic control	62 y M · 2 y · 27.2	Hypertension, dyslipidaemia	8.9% → 7.2% (6 mo)	NR → -6.5 kg (Δ)*	—	Mild transient nausea
2. T2DM + chronic kidney disease as an add-on to SGLT2i	58 y F · 12 y · 29.8	CKD G3aA2, hypertension	8.5% → 6.9% (12 mo)	78 → 71.5 kg	eGFR 48 → 54 mL/min/1.73 m ² ; UACR 185 → 105 mg/g	Mild early nausea
3. T2DM + cardiovascular disease and switch from a DPP-4 inhibitor	59 y M · 10 y · 33.4	CAD, prior MI, hypertension	8.7% → 6.8% (12 mo)	92 → 83.5 kg	BP 138/84 → 128/78; waist -8 cm	Transient mild nausea
4. T2DM and fatty liver	52 y M · 8 y · 24.4	Fatty liver	9.2% → 7.1% (12 mo)	81 → 79.5 kg	AST decrease from 64 to 48 U/L reported	Mild nausea on titration
5. T2DM + unfavourable body composition	49 y F · 6 y · 31.8	Obesity, hypertension	8.3% → 6.8% (12 mo)	82 → 73.5 kg	Fat mass 34.4 → 25.7 kg; muscle mass 24.8 → 24.1 kg (-0.7 kg); waist -10 cm	Mild transient nausea

Abbreviations: BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; F, female; f/u, follow-up; G3aA2, CKD category with mildly to moderately decreased eGFR and moderately increased albuminuria; HbA1c, glycated haemoglobin; M, male; MI, myocardial infarction; mo, months; NR, not reported; T2DM, type 2 diabetes mellitus; UACR, urine albumin-to-creatinine ratio; y, years; Δ, change from baseline.

No severe hypoglycaemia and no treatment discontinuation occurred in any case. For Case 1: baseline weight was not recorded (NR), so only the reported 6-month change (-6.5 kg) is shown; this is a change value, not an absolute follow-up weight. Narrative detail for each case follows below.

Case 1. Early in the type 2 diabetes journey: suboptimal glycaemic control

A 62-year-old man with a 2-year history of T2DM, hypertension, dyslipidaemia, and a body mass index (BMI) of 27.2 kg/m² presented with progressively worsening glycaemic control with HbA1c of 8.9%, fatigue, postprandial hyperglycaemia, and an approximately 5-kg weight gain over the preceding 3 years. His medications included telmisartan 40 mg once daily and rosuvastatin 10 mg once daily. Given the relatively early stage of his diabetes journey and the need for greater glycaemic efficacy and weight reduction, early treatment intensification with innovator r-DNA oral semaglutide and metformin was considered.

Oral semaglutide was initiated at 3 mg once daily for 30 days, followed by escalation to 7 mg and subsequently 14 mg once daily. At 6 months, HbA1c decreased from 8.9% to 7.2%, with a reported weight reduction of 6.5 kg; the baseline absolute weight was not available. The patient also reported improved satiety and energy levels. Mild nausea occurred during the first 2 weeks and resolved without treatment discontinuation. No severe hypoglycaemia was reported.

Case 2. Type 2 diabetes with chronic kidney disease: oral semaglutide as an add-on to SGLT2 inhibitor therapy

A 58-year-old woman with a 12-year history of T2DM, CKD G3aA2, hypertension, dyslipidaemia, and a BMI of 29.8 kg/m² presented with persistent hyperglycaemia, fatigue, reduced exercise tolerance, and occasional pedal oedema. At baseline, her estimated glomerular filtration rate (eGFR) was 48 mL/min/1.73 m² and urine albumin-to-creatinine ratio (UACR) was 185 mg/g. Given the presence of CKD with albuminuria, hypertension, dyslipidaemia, overweight, and long-standing T2DM, she was considered to have a high cardiovascular-risk profile despite no documented established ASCVD. Her medications included metformin 500 mg twice daily, empagliflozin 10 mg once daily, telmisartan 40 mg once daily, and atorvastatin 20 mg once daily. Innovator r-DNA oral semaglutide was considered as an add-on to ongoing SGLT2 inhibitor therapy, together with lifestyle modification, to improve glycaemic control and weight while contributing to a broader cardiorenal and cardiovascular risk-reduction strategy.

Oral semaglutide was initiated at 3 mg once daily and titrated to 7 mg once daily, while empagliflozin and telmisartan were continued. At 12 months, HbA1c decreased from 8.5% to 6.9%, body weight decreased from 78 to 71.5 kg, and BMI decreased from 29.8 kg/m² to approximately 27.3 kg/m². The patient also reported improved exercise tolerance compared with baseline. The eGFR increased from 48 to 54 mL/min/1.73 m², while UACR decreased from 185 to 105 mg/g. Mild early nausea was reported, with no severe hypoglycaemia or treatment interruption. Oral semaglutide, used in addition to the continued SGLT2 inhibitor and lifestyle modification, was associated with improved glycaemic control, weight and BMI reduction, better exercise tolerance, and a favourable renal trajectory.

Case 3. Type 2 diabetes with established cardiovascular disease: switch from a DPP-4 inhibitor

A 59-year-old man with a 10-year history of T2DM, established coronary artery disease, previous myocardial infarction, hypertension, dyslipidaemia, obesity, and a BMI of 33.4 kg/m² presented with suboptimal glycaemic control, progressive weight gain, and reduced exercise tolerance. His medications included metformin 1000 mg twice daily, sitagliptin 100 mg once daily, empagliflozin 25 mg once daily, aspirin 75 mg once daily, rosuvastatin 20 mg once daily, telmisartan 40 mg once daily, and metoprolol 25 mg once daily. Frequent travel made injectable therapy less acceptable to him. Given his established ASCVD, obesity, and persistent hyperglycaemia, sitagliptin was discontinued and directly replaced with innovator r-DNA oral semaglutide to provide greater glycaemic and weight-lowering efficacy together with demonstrated cardiovascular benefit.

Oral semaglutide was initiated at 3 mg once daily and gradually escalated to 7 mg and subsequently to 14 mg once daily over 6 months. The patient tolerated the treatment well, with only mild nausea reported during dose escalation, which was managed with lifestyle modification and dietary counselling. Cardiovascular medications were continued, and dietary and physical-activity counselling was reinforced. At 12 months after replacement of sitagliptin with oral semaglutide, HbA1c decreased from 8.7% to 6.8%, body weight decreased from 92 to 83.5 kg, blood pressure decreased from 138/84 to 128/78 mmHg, and waist circumference decreased by 8 cm. Transient

mild nausea occurred during titration. No severe hypoglycaemia or cardiovascular hospitalisation was reported during follow-up.

Case 4. T2DM with fatty liver

A 52-year-old man with an 8-year history of T2DM, hypertension, a BMI of 24.4 kg/m², and documented fatty liver presented with inadequate glycaemic control with HbA1c of 9.2%. His medications included metformin 1000 mg twice daily and amlodipine 5 mg once daily. In the context of T2DM and fatty liver, an oral therapy capable of improving glycaemic control while supporting weight reduction was preferred.

Innovator r-DNA oral semaglutide was initiated at 3 mg once daily and titrated to 7 mg once daily, while metformin was continued. The patient received dietary counselling focused on calorie quality, portion control, and increased physical activity, together with counselling on correct fasting-state administration of oral semaglutide.

At 12 months, HbA1c decreased from 9.2% to 7.1%. Mild nausea during titration resolved without treatment discontinuation. AST decreased from 64 to 48 U/L reported. No repeat imaging was reported; therefore, the case demonstrates improvement in glycaemic control and improvement of AST level in a patient with coexisting fatty liver.

Case 5. Type 2 diabetes with unfavourable body composition

A 49-year-old woman with a 6-year history of T2DM, obesity, hypertension, and a BMI of 31.8 kg/m² had stable body weight during the preceding year but showed excess adiposity and suboptimal muscle mass on body-composition assessment. Her medications included metformin 1000 mg twice daily, dapagliflozin 10 mg once daily, and telmisartan 40 mg once daily. She wished to achieve better glycaemic control, meaningful weight loss, and improvement in obesity-related comorbidities without injectable therapy. Baseline body-composition assessment was therefore performed to characterise adiposity and muscle mass and to objectively evaluate changes during follow-up.

Innovator r-DNA oral semaglutide was initiated at 3 mg once daily and titrated to 7 mg and 14 mg once daily over 4 months. Metformin and dapagliflozin were continued, together with moderate-intensity exercise and protein-focused dietary counselling. Body composition was assessed using the same segmental multifrequency bioelectrical impedance analyser under comparable fasting and hydration conditions at baseline and follow-up.

At 12 months, HbA1c decreased from 8.3% to 6.8%, and body weight decreased from 82 to 73.5 kg. Fat mass decreased from 34.4 to 25.7 kg, waist circumference decreased by 10 cm, and skeletal muscle mass showed a small decrease from 24.8 to 24.1 kg. Mild transient nausea was reported.

Across the five cases, mild nausea was the most frequently documented adverse event. No severe hypoglycaemia or treatment discontinuation was reported.

DISCUSSION

This case series describes innovator r-DNA oral semaglutide use across five clinically distinct profiles of adults with type 2 diabetes mellitus (T2DM): early in the diabetes journey with suboptimal glycaemic control, chronic kidney disease (CKD), established cardiovascular disease with replacement of a dipeptidyl peptidase-4 (DPP-4) inhibitor, T2DM with fatty liver, and unfavourable body composition. During 6–12 months of follow-up, HbA1c decreased by 1.5–2.1 percentage points to 6.8%–7.2%, while reported weight reduction ranged from 6.5 to 8.5 kg. Notably, oral semaglutide has also demonstrated substantial efficacy when used early in the diabetes treatment journey. In a post-hoc analysis of PIONEER 1, patients who initiated oral semaglutide within ≤1 year of T2DM diagnosis achieved greater reductions in HbA1c and body weight with the 14-mg dose than placebo (−1.6% vs −0.4% for HbA1c and −4.3 vs −1.6 kg for body weight at 26 weeks); 45% of these patients achieved an HbA1c <6.0%. These findings support consideration of oral semaglutide early in the course of T2DM rather than reserving it only for later treatment intensification. Consistent with this, the prescribing information supports oral semaglutide as an adjunct to diet and exercise to improve glycaemic control in adults with T2DM, including use as monotherapy in patients inadequately controlled with diet and exercise. [10,11]

Selected improvements were also observed in renal, cardiovascular, and body-composition parameters. However, these uncontrolled observations occurred within multifactorial treatment strategies and cannot establish causality.

Glycaemic control and body-weight reduction

The improvements in HbA1c and body weight were broadly consistent with the clinical trial evidence for oral semaglutide. In PIONEER 1, oral semaglutide 14 mg reduced HbA1c by approximately 1.4 percentage points at 26 weeks, compared with 0.3 percentage points with placebo. [7] Across the PIONEER programme, the 14-mg dose generally produced HbA1c reductions of approximately 1.0–1.4 percentage points, together with clinically relevant weight reduction. [3,6] In PIONEER 2, oral semaglutide achieved greater HbA1c reduction than empagliflozin at 26 weeks, with greater weight reduction evident during longer follow-up. [8] In a post-hoc analysis of the PIONEER 1–8 programme, oral semaglutide was associated with a greater likelihood of achieving clinically relevant improvements in multiple risk factors, including ≥1 percentage-point reduction in HbA1c, ≥5% reduction in body weight, ≥5 mmHg reduction in systolic blood pressure, and ≥0.5 mmol/L reduction in LDL-C compared with placebo or active comparators. [12] Across the PIONEER programme, favourable changes were also observed in lipid parameters, while HDL-C was generally maintained. In exploratory analyses of PIONEER 1, 2 and 5, oral semaglutide additionally reduced systemic inflammation as assessed by hsCRP; compared with placebo, hsCRP was 24% lower with oral semaglutide 14 mg in PIONEER 1, while a 30% reduction versus empagliflozin was observed in PIONEER 2. [13] In the PIONEER subgroup analysis and PIONEER REAL India study, Indian adults with type 2 diabetes treated with oral semaglutide achieved a dramatic HbA1c reduction of up to 2.6% in high-baseline groups and an average body weight loss approaching 7.5%, demonstrating powerful real-world metabolic benefits respectively. [9,14]

Some patients preferred oral therapy because of frequent travel or reluctance to initiate injectable treatment. Oral semaglutide may be considered as an early treatment option and can also facilitate treatment intensification in appropriate patients. Case 1 illustrates oral semaglutide introduced relatively early in the diabetes journey when additional glycaemic efficacy and weight reduction were desired while maintaining an oral treatment approach. This positioning is distinct from using oral semaglutide only after prolonged treatment failure and highlights the potential for earlier individualised intensification in appropriately selected patients.

Oral semaglutide in chronic kidney disease

In the patient with CKD G3aA2, HbA1c decreased from 8.5% to 6.9%, body weight decreased by 6.5 kg, estimated glomerular filtration rate increased from 48 to 54 mL/min/1.73 m², and urine albumin-to-creatinine ratio decreased from 185 to 105 mg/g over 12 months.

PIONEER 5 demonstrated that oral semaglutide improved HbA1c and body weight in patients with T2DM and moderate renal impairment, with a safety profile consistent with the GLP-1 receptor agonist class. [4] More recently, a prespecified kidney analysis of the SOUL trial showed that oral semaglutide significantly slowed annual eGFR decline compared with placebo in the overall population (−1.67 vs −2.06 mL/min/1.73 m²/year; estimated treatment difference 0.40; 95% CI 0.27–0.53; P<0.0001). Among participants with baseline eGFR <60 mL/min/1.73 m², the difference was numerically greater (−1.04 vs −1.59 mL/min/1.73 m²/year; estimated treatment difference 0.55; 95% CI 0.31–0.80; P<0.0001). [15] In the present case, innovator r-DNA oral semaglutide was positioned as an add-on to ongoing SGLT2 inhibitor therapy for renal protection.

Cardiovascular-risk profile

The patient with established coronary artery disease and previous myocardial infarction experienced improvements in HbA1c, body weight, waist circumference, and blood pressure over 12 months after sitagliptin was replaced with innovator r-DNA oral semaglutide. Beyond glycaemic and weight reduction, oral semaglutide has demonstrated favourable effects across several cardiometabolic risk factors. In a post-hoc analysis of the PIONEER 1–8 programme, oral semaglutide was associated with a greater likelihood of achieving clinically relevant improvements in multiple risk factors, including ≥1 percentage-point reduction in HbA1c, ≥5% reduction in body weight, ≥5 mmHg reduction in systolic blood pressure, and ≥0.5 mmol/L

reduction in LDL-C compared with placebo or active comparators.[12] Across the PIONEER programme, favourable changes were also observed in lipid parameters, while HDL-C was generally maintained. In exploratory analyses of PIONEER 1, 2 and 5, oral semaglutide additionally reduced systemic inflammation as assessed by hsCRP; compared with placebo, hsCRP was 24% lower with oral semaglutide 14 mg in PIONEER 1, while a 30% reduction versus empagliflozin was observed in PIONEER 2. [13]

These cardiometabolic effects are complemented by cardiovascular outcome data from the SOUL trial. Among 9,650 adults with T2DM and established ASCVD, CKD, or both, oral semaglutide reduced 3-point MACE—cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke—by 14% versus placebo (12.0% vs 13.8%; HR 0.86, 95% CI 0.77–0.96) over a mean follow-up of 47.5 months. [5] Consistent with these findings, the current U.S. prescribing information indicates oral semaglutide for reduction of MACE in adults with T2DM who are at high risk for these events, without restricting the indication only to those with established ASCVD. [11,16] Thus, replacing sitagliptin with innovator r-DNA oral semaglutide in this patient provided an opportunity for greater glycaemic and weight control together with use of an oral GLP-1 receptor agonist with an approved cardiovascular risk-reduction indication, alongside continued SGLT2 inhibitor, statin, antiplatelet, antihypertensive therapy, and lifestyle modification.

T2DM with fatty liver

In the patient with T2DM and fatty liver, HbA1c decreased from 9.2% to 7.1%, accompanied by a 6.5-kg weight reduction. AST decreased from 64 to 48 U/L. In a study by Santhosh R et al., initiation of oral semaglutide therapy resulted in a significant attenuation of the median FIB-4 score over 6 months, declining from a baseline of 1.81 to 1.16 ($p < 0.001$) alongside marked reductions in hepatic transaminases and glycaemic indices. [17]

Changes in body composition

In the patient with unfavourable body composition, weight decreased from 82 to 73.5 kg and fat mass from 34.4 to 25.7 kg. Skeletal muscle mass decreased slightly from 24.8 to 24.1 kg, indicating that complete muscle-mass preservation was not achieved. This pattern is consistent with emerging evidence suggesting that the majority of semaglutide-associated weight loss is attributable to fat loss, with comparatively smaller reductions in lean tissue. In the STEP UP body-composition substudy, approximately 84.5% of the weight lost was derived from adipose tissue and 15.5% from lean tissue, with significant reductions in total and visceral adipose tissue and no significant between-group reduction in muscle volume [18]. Similarly, the SEMALEAN study showed a 12.7% reduction in body weight and an 18.9% reduction in total fat mass at 12 months, while lean mass decreased initially by approximately 3 kg and subsequently stabilised; importantly, handgrip strength improved by 4.5 kg and the prevalence of sarcopenic obesity decreased from 49% to 33%. [19] These findings suggest that semaglutide-induced weight loss is 80–90% driven by adipose-tissue reduction, with relative preservation of lean mass and muscle function, although appropriate protein intake and resistance exercise remain important during substantial weight loss. [20]

A prospective real-world study using bioelectrical impedance analysis reported reductions in weight and fat mass with relative preservation of fat-free and skeletal muscle mass during oral semaglutide treatment. [21] Although the same device and fasting conditions were used at both assessments in the present case, bioelectrical impedance remains sensitive to hydration and measurement variability.

Tolerability and safety

Mild, transient nausea occurred during treatment initiation or dose escalation in all five cases. No severe hypoglycaemia or treatment discontinuation was recorded. This is consistent with the PIONEER programme, in which nausea was the most commonly reported gastrointestinal adverse event and, when experienced, was predominantly mild to moderate in severity and transient in nature, particularly during treatment initiation and dose escalation. [7,22]

GI adverse-event mitigation: Gastrointestinal symptoms associated with GLP-1 receptor agonists can often be minimised through anticipatory counselling, gradual dose escalation, and dietary modification. Patients should be advised to eat smaller meals, eat slowly, stop eating when comfortably full, avoid high-fat or spicy

foods, maintain adequate hydration, and avoid overeating. If symptoms occur during dose escalation, delaying further dose escalation or temporarily maintaining the current dose may improve tolerability; persistent or severe symptoms warrant clinical reassessment and, where appropriate, dose adjustment or symptomatic treatment. [23,24]

Relevance to routine clinical practice

These cases reflect five practical situations in which innovator r-DNA oral semaglutide may be considered: early treatment intensification in the diabetes journey; add-on therapy to an SGLT2 inhibitor in CKD; replacement of a DPP-4 inhibitor in a patient with established CVD; treatment of T2DM with fatty liver; and management of an unfavourable body-composition profile. Evidence from Indian adults with T2DM demonstrated substantial glycaemic and weight benefits of oral semaglutide, with HbA1c reductions of up to 2.6 percentage points among patients with higher baseline HbA1c and mean weight loss approaching 7.5 kg. [9,14]

Treatment selection in this series was influenced not only by HbA1c, but also by body weight, cardiovascular and kidney comorbidities, travel requirements, adherence behaviour, route-of-administration preference, failure of other oral glucose-lowering agents and body composition. This is consistent with the contemporary emphasis on individualised T2DM management.

Strengths and limitations

A strength of this series is the inclusion of five deliberately differentiated clinical profiles and outcomes extending beyond glycaemic control, including renal, cardiovascular, fatty-liver-associated metabolic, and body-composition observations. However, the series included only five purposively selected patients and had no comparator group, limiting generalisability and introducing selection bias. Follow-up was also unequal: Case 1 was assessed at 6 months, while Cases 2–5 were followed for 12 months. Concomitant pharmacotherapy, lifestyle counselling, exercise interventions, and structured follow-up prevent attribution of outcomes to oral semaglutide alone.

Some outcomes, including subjective well-being, were patient-reported. Renal and body-composition outcomes were based on limited measurements and may have been influenced by biological or measurement variability. In Case 4, no liver-specific follow-up measurement or repeat imaging was available, so no inference regarding change in fatty liver can be made.

CONCLUSION

The cases illustrate distinct potential clinical positions for innovator r-DNA oral semaglutide: early in the diabetes journey, as an add-on to SGLT2 inhibitor therapy in CKD, as a replacement for a DPP-4 inhibitor in established CVD, in T2DM with fatty liver, and in patients with unfavourable body composition. Across these cases, oral semaglutide was associated with improvements in glycaemic control and body weight, with additional changes in selected renal, cardiovascular, and body-composition parameters.

Declarations

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