

# Exploring the Multifaceted Role of GLP-1 RAs



# Transforming Cardiovascular-Kidney-Metabolic (CKM) Health

ARE YOU UP TO DATE WITH GLP-1 RECEPTOR AGONISTS (RAS) FOR CKM?

#### CASE CHALLENGE

A 54-year-old Asian woman who had a myocardial infarction a year ago asks about medications for weight loss. She has an HbA1c of 6.0%, hypertension, a BMI of 25 mg/kg<sup>2\*</sup>, and an eGFR of 68 mL/min.

\*The World Health Organization (WHO) recommends lower BMI thresholds for Asian populations,  $\geq 23 \text{ kg/m}^2$  for overweight and  $\geq 27.5 \text{ kg/m}^2$  for obesity, due to higher cardiometabolic risk at lower BMI levels.

# Would you consider a GLP-1 RA for her?

## **QUICK FACTS**

- 1 in 3 U.S. adults has ≥ 3 CKM risk factors
- GLP-1 RAs are now recommended for some patients with chronic kidney disease (CKD), atherosclerotic cardiovascular disease (ASCVD), or obesity regardless of diabetes status

Watch CME Outfitters' 6-episode webcast series on CKM health and GLP-1 RAs to learn more! Complete all 6 activities and claim your badge as a Patient-First Diabetes Management Champion!

#### CARDIOVASCULAR SYSTEM

- Reduction in Major Adverse Cardiovascular Events (MACE): 14% in T2D (dulaglutide, liraglutide, semaglutide); 20% in obesity without T2D (semaglutide, tirzepatide\*)
- Stroke Prevention: 17% reduction in stroke risk
- Heart Failure: Improved symptoms and exercise tolerance in HFpEF (semaglutide\*)
- Blood Pressure: Modest but meaningful reduction (dulaglutide\*, liraglutide\*, semaglutide\*)

#### **KIDNEYS**

- Reduction of Kidney Disease Events in T2D+ CKD Compared with Standard Care
  - 22% reduction with liraglutide\*
  - 24% reduction with semaglutide
  - 42% reduction with tirzepatide\*

## **METABOLIC EFFECTS**

#### Reduction in HbA1c in T2D

- 0.8-1.8% with GLP-1 RAs (dulaglutide, exenatide, liraglutide, semaglutide)
- 2.0-2.4% with GLP-1 RAs/GIP (tirzepatide)

## Weight management (obesity/overweight)

- Liraglutide
- Semaglutide
- Tirzepatide (additional indication for OSA)

## Metabolic dysfunction-associated steatohepatitis (MASH)

- "Until the FDA approves GLP-1 RAs for MASH, [any of] these drugs should be considered the
  preferred treatments for T2D and/or obesity in individuals with MASH." ~2025 Global Consensus
  Recommendations for Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) and
  Steatohepatitis
- Liraglutide, semaglutide, and tirzepatide have positive data in MASH

BMI = body mass index; eGFR = estimated glomerular filtration rate; T2D = type 2 diabetes; HFpEF = heart failure with preserved ejection fraction; GIP = gastric inhibitory polypeptide; OSA = obstructive sleep apnea.

# Want your questions answered? Ask the experts!

Scan or click the QR code to submit a question for a chance to have it answered during a live webinar.





<sup>\*</sup>Not FDA-approved for this indication

#### REFERENCES

- American Diabetes Association Professional Practice Committee. Pharmacologic approaches to glycemic treatment: standards of care in diabetes—2025. Diabetes Care. 2025;48(Suppl 1):S158-S178.
- Armstrong MJ, Gaunt P, Aithal GP, et al. Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a
  multicentre, double-blind, randomised, placebo-controlled phase 2 study. Lancet. 2016;387(10019):679-690.
- Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a doubleblind, randomised placebo-controlled trial. Lancet. 2019;394(10193):121-130.
- 4. Heerspink HJL, et al. Effects of tirzepatide versus insulin glargine on kidney outcomes in type 2 diabetes in the SURPASS-4 trial: post-hoc analysis of an open-label, randomised, phase 3 trial. *Lancet Diabetes*. Endocrinol 2022; 10:774–785.
- Holman RR, Bethel MA, Mentz RJ, et al. Effects of once-weekly exenatide on cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2017;377(13):1228-1239.
- 6. Husain M, Birkenfeld AL, Donsmark M, et al. Oral semaglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med*. 2019;381(9):841-851.
- Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. Kidney Int. 2022;102(5S):S1-S127.
- Kosiborod MN, Abildstrøm SZ, Borlaug BA, et al. Semaglutide in patients with heart failure with preserved ejection fraction and obesity. N Engl J Med. 2023;389(12):1069-1084.
- Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. N Engl J Med. 2023;389(24):2221-2232.
- 10. Mann JFE, Ørsted DD, Brown-Frandsen K, et al. Liraglutide and renal outcomes in type 2 diabetes. *N Engl J Med*. 2017;377(9): 839-848.
- 11. Marso SP, Bain SC, Consoli A, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2016;375(19):1834-1844.
- 12. Newsome PN, Buchholz K, Cusi K, et al. A placebo-controlled trial of subcutaneous semaglutide in nonalcoholic steatohepatitis. N Engl J Med. 2021;384(12):1113-1124.
- 13. Perkovic V, Tuttle KR, Rossing P, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. *N Engl J Med*. 2024;391(2):109-121.
- 14. Rosenstock J, Wysham C, Frías JP, et al. Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial. *Lancet*. 2021;398(10295):143-155.
- Sattar N, Lee MMY, Kristensen SL, et al. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomised trials. Lancet Diabetes Endocrinol. 2021;9(10):653-662.
- Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med. 2021;384(11):989-1002.
- 17. Younossi ZM, Zelber-Sagi S, Lazarus JV, et al. Global consensus recommendations for metabolic dysfunction-associated steatotic liver disease and steatohepatitis. *Gastroenterology*. 2025:1-16.

