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GLP-1/GIP Agonists for Obesity in CKD

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Tirzepatide is a once-weekly dual GIP/GLP-1 receptor agonist that has become one of the most effective pharmacological options for obesity treatment. In general obesity populations, tirzepatide produces substantial and sustained weight loss, with additional benefits on waist circumference, blood pressure, glycaemic status, lipids, and obesity-related cardiometabolic risk. Therefore, tirzepatide should be understood not only as a weight-loss drug, but also as a therapy that can improve the broader cardiovascular–kidney–metabolic risk profile associated with obesity. For patients with chronic kidney disease, the clinical question is whether these benefits can translate into kidney protection. Current evidence is promising but still incomplete. In post-hoc analyses of SURMOUNT-1 and SURMOUNT-2, tirzepatide reduced albuminuria in adults with overweight or obesity, with or without type 2 diabetes, and the effect was greater in those with baseline albuminuria. In SURMOUNT-1, favourable changes were also observed in cystatin C-based and combined creatinine–cystatin C eGFR. However, these trials were not specifically designed as CKD-enriched kidney outcome studies. The most directly relevant ongoing study is TREASURE-CKD, which enrolls adults with overweight or obesity and CKD, with or without type 2 diabetes. This study evaluates kidney oxygenation by MRI, measured GFR, eGFR, and UACR, and may clarify whether tirzepatide has kidney-specific effects beyond weight loss and metabolic improvement. Additional supportive evidence comes from SUMMIT, in obesity-related HFpEF, where CKD subgroup analyses showed favourable clinical outcomes and highlighted the importance of cystatin C-based kidney-function assessment during major weight loss. SURPASS-4 and SURPASS-CVOT also support kidney-protective potential, but these were studies in type 2 diabetes and should be presented as diabetes-specific supportive evidence rather than direct evidence for non-diabetic CKD. When using tirzepatide or other anti-obesity medications in CKD, several issues require special

attention. First, the treatment goal should include not only body-weight reduction, but also UACR, eGFR slope, blood pressure, cardiovascular risk, physical function, and quality of life. Second, gastrointestinal adverse events can cause reduced intake, dehydration, and acute kidney injury, particularly during dose escalation or in patients taking diuretics, RAAS blockers, or SGLT2 inhibitors. Third, rapid weight loss may reduce muscle mass; therefore, resistance exercise and individualized nutritional support are essential. Fourth, creatinine-based eGFR may be misleading during major weight loss, so cystatin C or combined eGFR equations may be useful. In summary, tirzepatide is highly effective for obesity and promising for CKD-associated cardiometabolic risk. However, definitive renal outcome evidence in obese CKD patients regardless of diabetes status awaits dedicated CKD trials such as TREASURE-CKD.

Keywords: Tirzepatide, Obesity, CKD