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Incretin-Based Therapies: Add on as Needed or Fourth Pillar for Managing Diabetic Kidney Disease?

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Diabetic kidney disease (DKD) remains a leading cause of kidney failure worldwide despite glucose-lowering, blood pressure control, and renin–angiotensin system inhibition. The sodium–glucose cotransporter-2 (SGLT2) inhibitors and non-steroidal mineralocorticoid receptor antagonists offer additional renal benefits independent of glycaemic and blood pressure control. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) and dual incretin agonists have also shown broad metabolic, cardiovascular, and renal benefits. However, their place within contemporary DKD management remains uncertain. Should incretin therapies be reserved as add-on agents for glycaemic optimisation, significant weight loss, or for patients with residual significant albuminuria after all other agents have been used? Or should they be considered a foundational “fourth pillar” of kidney protection, to be used early in combination in high-risk individuals with DKD? This presentation examines the evolving evidence supporting incretin-based therapies in DKD, including potential mechanistic pathways, such as regression of diabetes, weight loss, and post-prandial dysmetabolism. Clinical trial data demonstrating reductions in albuminuria, slowing of estimated glomerular filtration rate decline will be reviewed, alongside emerging evidence from dedicated renal outcome studies. The presentation will also address practical considerations, including patient selection, combination therapy with other agents, tolerability, cost-effectiveness, and ease of implementation in routine clinical care in patients with moderate to severe renal impairment. As the therapeutic landscape of DKD rapidly evolves, incretin-based therapies likely represent more than an alternative to insulin. Defining whether they function best as selective add-on therapies or should be an essential component of integrated cardiorenal protection for all patients with DKD has important implications for future treatment paradigms and guideline

development.

Keywords: GLP-1 receptor agonist, Diabetic kidney disease, albuminuria, weight loss, post-prandial dysmetabolism