GLP-1 RECEPTOR AGONISTS IN NEPHROLOGY PRACTICE

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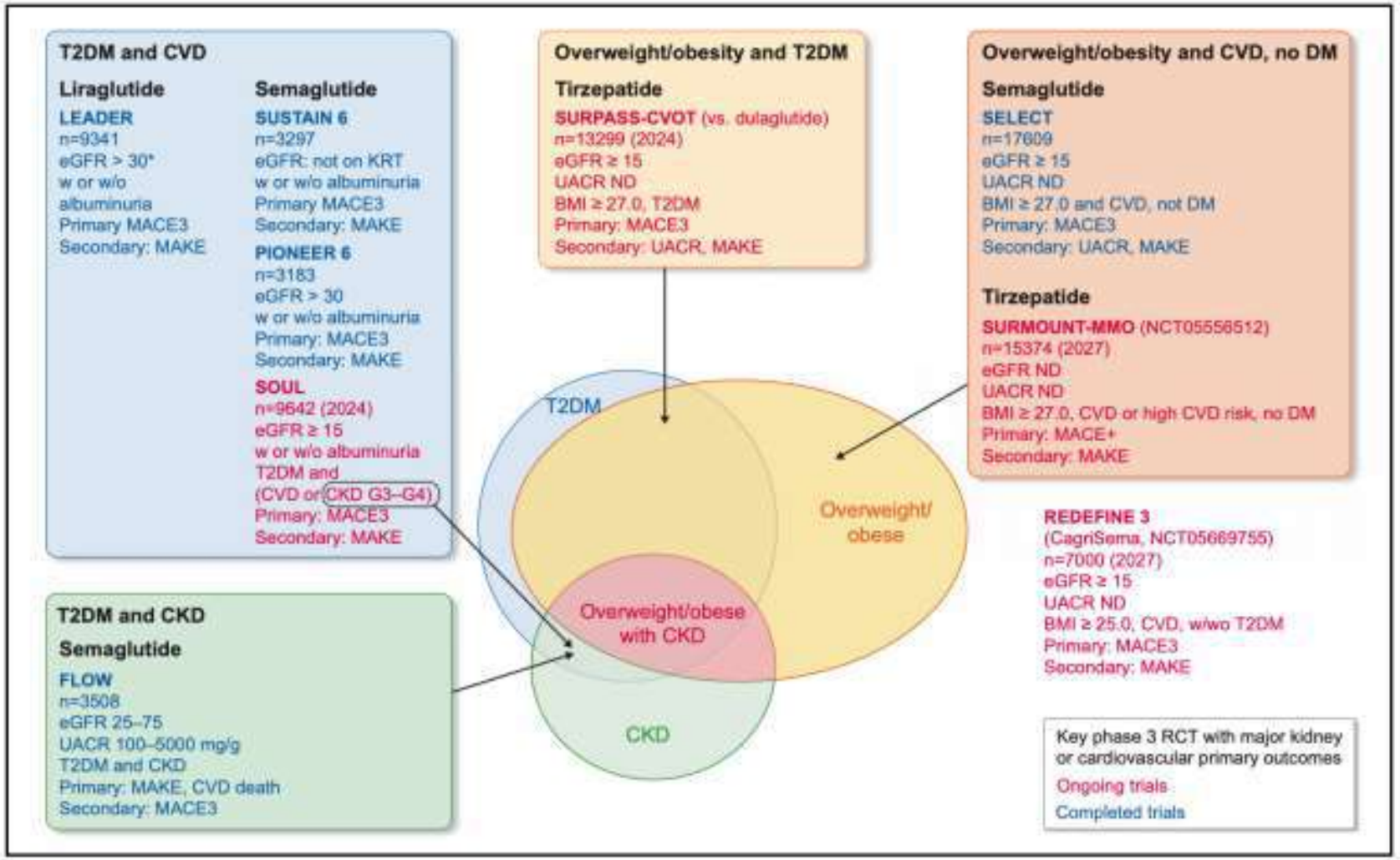
GLP-1 Receptor Agonists — Overview

- Incretin-based therapy acting via **GLP-1 receptor stimulation**
- Proven **cardio-renal-metabolic benefits** beyond glycaemic control
- Agents: **Liraglutide, Semaglutide, Dulaglutide, Exenatide, Lixisenatide, Tirzepatide**
- Major outcome trials: **LEADER, SUSTAIN-6, REWIND, FLOW (2024), SURPASS series (Tirzepatide)**
- Now emerging as **4th pillar in diabetic kidney disease (DKD)** management

Trials in GLP 1 analogues



Mechanism of Action

- ↑ **Glucose-dependent insulin secretion**
- ↓ **Glucagon secretion**
- **Delayed gastric emptying** → improved post-prandial control
- **Promotes satiety** → weight loss
- **Renal effects**:
  - ↓ Intraglomerular pressure
  - ↓ Albuminuria
  - Anti-inflammatory and anti-oxidative actions

Dosing & Titration

Agent	Dose Schedule	Renal Consideration
Liraglutide	0.6 → 1.8 mg SC daily	Use with caution in CKD
Dulaglutide	0.75 → 1.5 mg SC weekly	Use with caution
Semaglutide (inj.)	0.25 → 1 mg SC weekly	
Oral Semaglutide	3 → 14 mg daily	Safe in mild–mod CKD
Exenatide	5–10 µg SC BID	**Avoid if eGFR < 30**
Lixisenatide	10–20 µg SC daily	**Avoid if eGFR < 30**
Tirzepatide	2.5 → 15 mg SC weekly (increase every 4 wks)	No dose change needed in CKD

Practical points:

- Not first-line for hyperglycaemia.
- Do **not combine with DPP-4 inhibitors**.
- **Slow titration** in patients with diabetic retinopathy (monitor within 6 months).

Contraindications

- Personal/family history of **medullary thyroid carcinoma**
- **MEN 2A/2B** syndromes
- Prior **pancreatitis**
- **Severe gastrointestinal disease** (gastroparesis, obstruction)
- **Renal impairment**:
- **Exenatide, Lixisenatide** contraindicated if **eGFR < 30 ml/min**
- **Liraglutide, Dulaglutide, Semaglutide, Tirzepatide** – use with caution

Adverse Effects & Use in Transplant

- **Adverse Effects**
  - Nausea, vomiting, diarrhea, constipation
  - Tachycardia, mild injection-site reactions
  - Usually transient; improve with gradual up-titration
- **Use in Transplant Recipients**
  - Useful in **post-transplant diabetes and obesity**
  - May lower **insulin requirement** and **body weight**
  - No known direct nephrotoxicity
  - **Monitor tacrolimus/cyclosporine levels** if GI absorption issues occur

Take-Home Message

- **GLP-1 RAs and Tirzepatide** target multiple pathways: glycaemic, renal, cardiovascular, metabolic
- **4th pillar of DKD management** alongside RAAS blockade, SGLT2 inhibitors, and MRAs
- **Adverse effects manageable** with slow titration and patient education
- **Cost and access** remain major limitations for routine nephrology practice