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FLOW Study Results

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Over the past years, several new treatment options became available for the management of diabetic nephropathy. However, there is still a significant residual risk of evolution to end-stage kidney disease and death due to cardiovascular disease in this patient population.

The FLOW study is the first dedicated kidney outcome trial with GLP-1RA to evaluate kidney and cardiovascular outcome as well as mortality with once weekly semaglutide in patients with type 2 diabetes and chronic kidney disease. FLOW is a randomised, double-blind, parallel-group, multinational, phase 3b trial that included a total of 3533 participants with a median follow-up of 3.4 years. Patients were randomized to once weekly SC semaglutide 1 mg on top of standard of care or to placebo. Key eligible criteria were patients above 18 years of age, suffering from type 2 diabetes, with Hb1ac < 10%, on RAAS blockade, with eGFR between ≥ 50 and ≤75 ml/min/1.73m^2 and UACR > 300 and < 5000 mg/g or eGFR ≥ 25 and < 50 ml/min/1.73m^2 and UACR > 100 and < 500 mg/g.

The primary endpoint of the study was a composite of major kidney events consisting of:

- Onset of persistent ≥ 50% reduction of eGFR compared with baseline
- Kidney failure
  - Onset of persistent eGFR < 15 ml/min/1.73m^2
  - Initiation of chronic kidney disease replacement therapy (dialysis of transplantation)
- Kidney death
- CV death

FLOW enrolled a diverse group of patients with CKD and diabetes, that had a substantial CV burden at baseline (42% had a history of prior MI, stroke or heart failure). 95% were on RAAS-inhibitors but only a minority were on SGLT-2 inhibitors (16%). When looking at the primary endpoint of the study, 23.2% of the placebo group experienced the primary endpoint compared to 18.7% in the treatment group (HR of 0.76 (95% CI 0.66 – 0.88), p=0.0003). The absolute difference in primary outcome at week 154 was 4.9%, with **a number needed to treat of 20.** No difference was noticed in the effect of semaglutide in the subgroup analysis, concluding that patients on SGLT2-inhibition would also benefit from add-on GLA-1RA treatment. Moreover, all-cause mortality was reduced with 20% in patients treated with semaglutide.

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