Oral presentation 53

Efficacy and safety of semaglutide 1.0 mg once weekly vs. liraglutide 1.2 mg once daily as add-on to 1–3 oral glucose-lowering drugs in subjects with type 2 diabetes (SUSTAIN 10)

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Background and aims: Semaglutide and liraglutide are glucagon-like peptide-1 analogues for the treatment of type 2 diabetes (T2D). SUSTAIN 10 compared the efficacy and safety of the anticipated most frequent semaglutide dose (1.0 mg) vs. the most frequently prescribed liraglutide dose in Europe (1.2 mg).

Materials and methods: In this phase 3b, open-label trial, 577 adults with T2D (HbA_{1c} 7.0–11.0%) on 1–3 oral glucose-lowering drugs (metformin, sulphonylurea, sodium-glucose cotransporter-2 inhibitors) were randomised 1:1 to semaglutide 1.0 mg once weekly or liraglutide 1.2 mg once daily, both administered subcutaneously. Primary and confirmatory secondary endpoints were change in HbA_{1c} and body weight, respectively, from baseline to week 30. Supportive secondary efficacy endpoints included other glycaemic and weight parameters. Treatment satisfaction (change from baseline in Diabetes Treatment Satisfaction Questionnaire status version [DTSQs] scores) was also assessed.

Results: Mean HbA_{1c} (baseline 8.2%) decreased by 1.7%-point with semaglutide vs. 1.0%-point with liraglutide (estimated treatment difference [ETD] –0.69%-point; 95% CI –0.82 to –0.56; $p<0.0001$; **Table**); 80.4% vs. 45.9% of subjects achieved HbA_{1c} <7.0% (odds ratio [OR] 5.98; $p<0.0001$) and 58.5% vs. 24.8% achieved HbA_{1c} ≤6.5% (OR 4.84; $p<0.0001$). Mean body weight (baseline 96.9 kg) decreased by 5.8 kg with semaglutide vs. 1.9 kg with liraglutide (ETD –3.83 kg; 95% CI –4.57 to –3.09; $p<0.0001$); 55.9% vs. 17.7% of subjects achieved weight loss ≥5% (OR 5.89; $p<0.0001$) and 19.1% vs. 4.4% achieved weight loss ≥10% (OR 4.99; $p<0.0001$). HbA_{1c} <7.0% without severe or blood glucose-confirmed symptomatic hypoglycaemia and no weight gain was achieved by 75.6% of subjects on semaglutide and 36.8% on liraglutide (OR 6.07; $p<0.0001$). The DTSQs summary score improved in both treatment arms (ETD 0.63; $p=0.0814$). Overall, 70.6% and 66.2% of exposed subjects reported treatment-emergent adverse events (TEAEs) with semaglutide and liraglutide, respectively; 5.9% and 7.7% reported serious TEAEs. No fatal TEAEs were reported. The most frequently reported TEAEs with semaglutide (43.9%) and liraglutide (38.3%) were gastrointestinal (GI) disorders. The proportion of subjects with TEAEs leading to premature treatment discontinuation was 11.4% with semaglutide and 6.6% with liraglutide; 7.6% and 3.8% discontinued due to GI AEs.

Conclusion: Semaglutide 1.0 mg was superior to liraglutide 1.2 mg in reducing HbA_{1c} and body weight. Safety profiles were generally similar, except for a higher proportion of subjects with GI TEAEs with semaglutide.

Table. Key primary and secondary outcomes from the SUSTAIN 10 trial

	Overall baseline, mean	Change from baseline at week 30, mean		ETD [95% CI]
		Semaglutide 1.0 mg n=290	Liraglutide 1.2 mg n=287	
HbA_{1c}, %	8.2	–1.7	–1.0	–0.69* [–0.82; –0.56]
Body weight, kg	96.9	–5.8	–1.9	–3.83* [–4.57; –3.09]
FPG, mmol/L	9.9	–2.7	–1.4	–1.24* [–1.54; –0.93]
7-point SMBG: mean, mmol/L	10.3	–3.0	–2.1	–0.89* [–1.15; –0.64]
Postprandial increment of 7-point SMBG, mmol/L	2.3	–0.9	–0.4	–0.53* [–0.77; –0.28]
		Proportion of responders at week 30 (%)		
		Semaglutide 1.0 mg n=290	Liraglutide 1.2 mg n=287	OR [95% CI]
HbA_{1c} <7.0%		80.4	45.9	5.98* [3.83; 9.32]
HbA_{1c} ≤6.5%		58.5	24.8	4.84* [3.21; 7.30]
Weight loss ≥5%		55.9	17.7	5.89* [3.93; 8.81]
Weight loss ≥10%		19.1	4.4	4.99* [2.57; 9.68]
HbA_{1c} <7.0% without severe or BG-confirmed symptomatic hypoglycaemia and no weight gain		75.6	36.8	6.07* [4.02; 9.15]

*p<0.0001. BG, blood glucose; CI, confidence interval; ETD, estimated treatment difference; FPG, fasting plasma glucose; OR, odds ratio; SMBG, self-measured blood glucose.

Clinical Trial Registration Number: NCT03191396