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Effect of liraglutide on cardiovascular outcomes in patients with or without prior heart failure history in LEADER

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Background and aims: Some type 2 diabetes (T2D) therapies are associated with an increased risk of heart failure (HF). In the LEADER trial, liraglutide significantly reduced the risk of major adverse cardiovascular (CV) events (MACE) by 13% vs placebo (PBO) when added to standard of care in people with T2D and high CV risk. Here, we report post hoc analyses conducted to assess the risk of CV events, including HF hospitalisation, in LEADER participants with or without a history of New York Heart Association (NYHA) class I-III HF.

Materials and methods: In LEADER, 9340 patients with T2D and high CV risk were randomised 1:1 to add liraglutide or PBO to standard of care, and followed for 3.5-5 years. Chronic NYHA IV HF was an exclusion criterion.

Results: At baseline, 18% of patients in both treatment arms had a history of HF (NYHA I-III); 14% had a history of NYHA II-III HF. Overall, fewer patients were hospitalised for HF with liraglutide vs PBO during the trial (HR [95% CI]: 0.87 [0.73-1.05], p=0.14; Table). There was no interaction between treatment and history of NYHA I-III HF for the risk of the primary CV endpoint, an expanded CV endpoint or HF hospitalisation (Table).

Conclusion: No increased risk of MACE or hospitalisation due to HF was observed in patients either with or without a history of HF in the LEADER trial. The point estimates were in favour of liraglutide for MACE and expanded MACE, in patients both with and without a history of HF.

Table: Risk of CV events with liraglutide or placebo by NYHA I–III HF status at baseline

	Number of patients with an event (%)		HR (CI)	*p*-value
	Liraglutide	Placebo		
Primary composite MACE: first occurrence of CV death, non-fatal myocardial infarction, or non-fatal stroke				
Overall	608/4668 (13.0)	694/4672 (14.9)	0.87 (0.78–0.97)	0.01
Baseline NYHA I–III HF status Without With	 466/3833 (12.2) 142/835 (17.0)	 524/3840 (13.6) 170/832 (20.4)	 0.88 (0.78–1.00) 0.81 (0.65–1.02)	0.53
Expanded composite MACE: CV death, non-fatal myocardial infarction, non-fatal stroke, coronary revascularisation, or hospitalisation for unstable angina pectoris or HF				
Overall	948/4668 (20.3)	1062/4672 (22.7)	0.88 (0.81–0.96)	0.005
Baseline NYHA I–III HF status Without With	 704/3833 (18.4) 244/835 (29.2)	 786/3840 (20.5) 276/832 (33.2)	 0.89 (0.80–0.98) 0.86 (0.72–1.02)	0.72
Hospitalisation for HF				
Overall	218/4668 (4.7)	248/4672 (5.3)	0.87 (0.73–1.05)	0.14
Baseline NYHA I–III HF status Without With	 110/3833 (2.9) 108/835 (12.9)	 140/3840 (3.6) 108/832 (13.0)	 0.78 (0.61–1.00) 0.98 (0.75–1.28)	0.22
HRs and *p*-values estimated using Cox proportional hazards model with treatment as a factor. For subgroups with or without NYHA I–III HF at baseline, *p*-values are for interaction between treatment and subgroup.				

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