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Synopsis of the original article *'Semaglutide (SUSTAIN and PIONEER) reduces cardiovascular events in type 2 diabetes across varying cardiovascular risk'*

Husain M, et al. Diabetes Obes Metab. 2020;22(3):442-451

Synopsis created and reviewed by Novo Nordisk

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Study design: Post hoc analysis

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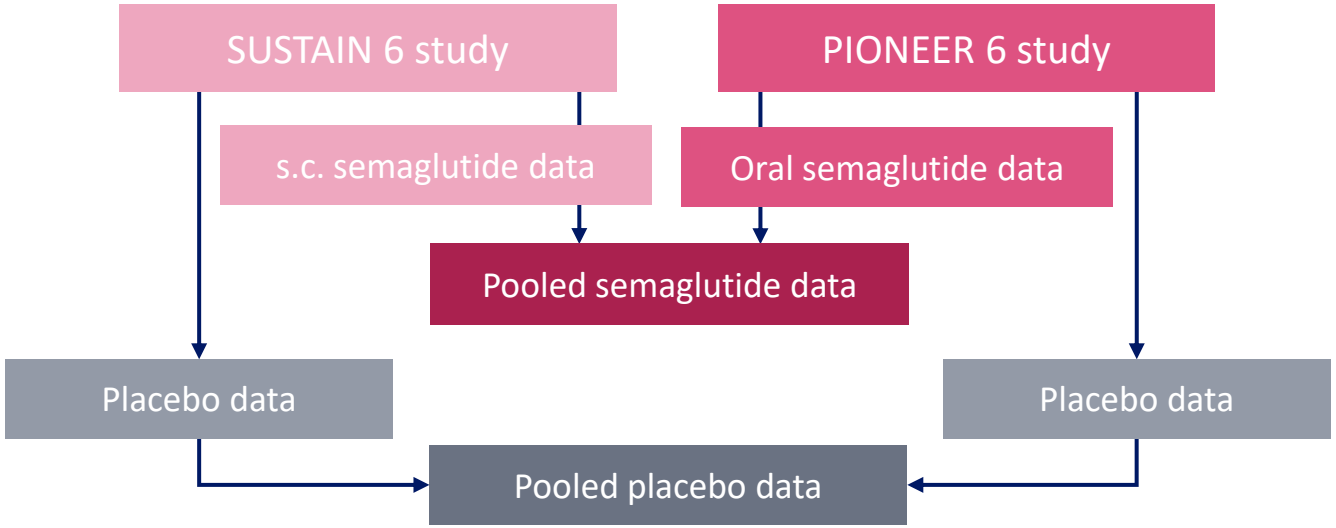
Study objective

To investigate the effects of semaglutide vs comparators on MACE* and hospitalisation for HF in the SUSTAIN and PIONEER studies across subgroups of varying CV risk



MACE were analysed in patients with and without:

- Established CV disease and/or CKD
- Prior MI or stroke
- Prior HF

Pooled patient-level data were analysed to assess the effect of semaglutide and comparators on MACE and HF

MACE was also assessed in the SUSTAIN and PIONEER glycaemic efficacy studies

*MACE: CV death, nonfatal MI and nonfatal stroke.
CKD, chronic kidney disease; CV, cardiovascular; HF, heart failure; MACE, major adverse cardiovascular events; MI, myocardial infarction; s.c., subcutaneous.

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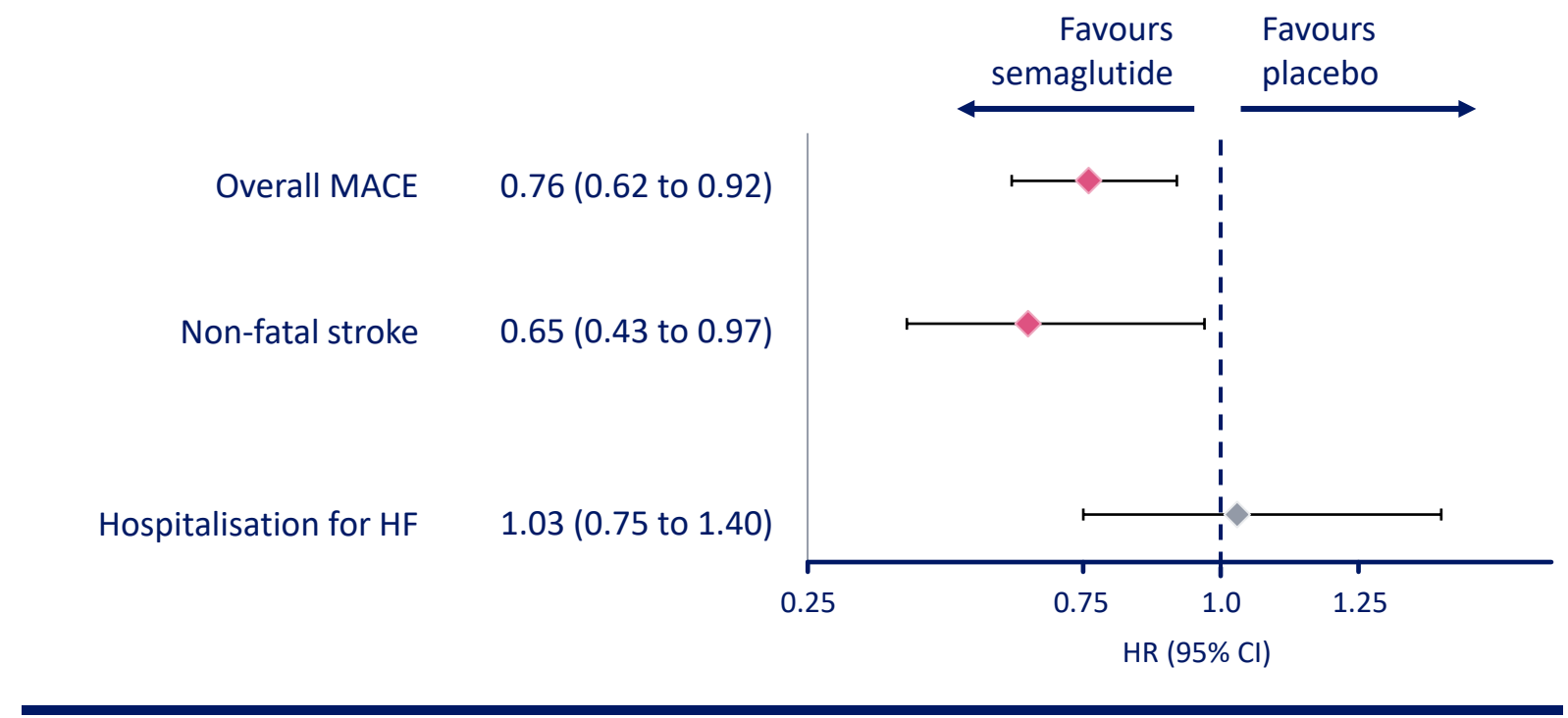
Semaglutide reduced MACE vs placebo in SUSTAIN 6 and PIONEER 6 combined



The reduced risk of MACE in the pooled semaglutide group was mainly driven by the effect on non-fatal stroke

In all subgroups, the HRs for MACE were <1.0, except for those with prior HF: HR 1.06 (95% CI 0.72 to 1.57)

P-values for interaction of subgroup on treatment effect were >0.05, except for HF (0.046)

In the combined glycaemic efficacy trials, the effect of semaglutide vs comparators on MACE was: HR 0.85 (95% CI 0.55 to 1.33)

CI, confidence interval; HF, heart failure; HR, hazard ratios; MACE, major adverse cardiovascular events.

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Conclusions

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Compared with placebo, semaglutide resulted in:

- A reduced risk of MACE
- Consistent effects on MACE across varying CV risk groups
- No effect of semaglutide on MACE was observed in patients with prior HF

CV, cardiovascular; HF, heart failure; MACE, major adverse cardiovascular events.

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Supplementary references: SUSTAIN

- Sorli C, Harashima SI, Tsoukas GM, et al. Efficacy and safety of once-weekly semaglutide monotherapy versus placebo in patients with type 2 diabetes (SUSTAIN 1): a double-blind, randomised, placebo-controlled, parallel-group, multinational, multicentre phase 3a trial. Lancet Diabetes Endocrinol. 2017;5:251-260.
- Ahrén B, Masmiquel L, Kumar H, et al. Efficacy and safety of once-weekly semaglutide versus once-daily sitagliptin as an add-on to metformin, thiazolidinediones, or both, in patients with type 2 diabetes (SUSTAIN 2): a 56-week, double-blind, phase 3a, randomised trial. Lancet Diabetes Endocrinol. 2017;5:341-354.
- Ahmann AJ, Capehorn M, Charpentier G, et al. Efficacy and safety of once-weekly semaglutide versus exenatide ER in subjects with type 2 diabetes (SUSTAIN 3): a 56-week, open-label, randomized clinical trial. Diabetes Care. 2018;41:258-266.
- Aroda VR, Bain SC, Cariou B, et al. Efficacy and safety of once-weekly semaglutide versus once-daily insulin glargine as add-on to metformin (with or without sulfonylureas) in insulin-naive patients with type 2 diabetes (SUSTAIN 4): a randomised, open-label, parallel-group, multicentre, multinational, phase 3a trial. Lancet Diabetes Endocrinol. 2017;5:355-366.
- Rodbard HW, Lingvay I, Reed J, et al. Semaglutide added to basal insulin in type 2 diabetes (SUSTAIN 5): a randomized, controlled trial. J Clin Endocrinol Metab. 2018;103:2291-2301.
- Marso SP, Bain SC, Consoli A, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2016;375:1834-1844.
- Seino Y, Terauchi Y, Osonoi T, et al. Safety and efficacy of semaglutide once weekly vs sitagliptin once daily, both as monotherapy in Japanese people with type 2 diabetes. Diabetes Obes Metab. 2018;20:378-388.
- Kaku K, Yamada Y, Watada H, et al. Safety and efficacy of once-weekly semaglutide versus additional oral antidiabetic drugs, in Japanese subjects with inadequately controlled T2D: a randomised trial. Diabetes Obes Metab. 2018;20:1202-1212.

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Supplementary references: PIONEER

- Aroda VR, Rosenstock J, Terauchi Y, et al. PIONEER 1: randomized clinical trial comparing the efficacy and safety of oral semaglutide monotherapy with placebo in patients with type 2 diabetes. Diabetes Care. 2019;42:1724-1732.
- Rodbard HW, Rosenstock J, Canani LH, et al. Oral semaglutide vs empagliflozin in patients with type 2 diabetes uncontrolled on metformin: the PIONEER 2 Trial. Diabetes Care. 2019;42:2272-2281.
- Rosenstock J, Allison D, Birkenfeld AL, et al. Effect of additional oral semaglutide vs sitagliptin on glycated hemoglobin in adults with type 2 diabetes uncontrolled with metformin alone or with sulfonylurea: the PIONEER 3 randomized clinical trial. JAMA. 2019;321:1466-1480.
- Pratley R, Amod A, Hoff ST, et al. Oral semaglutide versus subcutaneous liraglutide and placebo in type 2 diabetes (PIONEER 4): a randomised, double-blind, phase 3a trial. Lancet. 2019;394:39-50.
- Mosenzon O, Blicher TM, Rosenlund S, et al. Efficacy and safety of oral semaglutide in patients with type 2 diabetes and moderate renal impairment (PIONEER 5): a placebo-controlled, randomised, phase 3a trial. Lancet Diabetes Endocrinol. 2019;7:515-527.
- Husain M, Birkenfeld AL, Donsmark M, et al. Oral semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2019;381:841-851.
- Pieber TR, Bode B, Mertens A, et al. Efficacy and safety of oral semaglutide with flexible dose adjustment versus sitagliptin in type 2 diabetes (PIONEER 7): a multicentre, open-label, randomised, phase 3a trial. Lancet Diabetes Endocrinol. 2019;7:528-539.
- Zinman B, Aroda VR, Buse JB, et al. Efficacy, safety and tolerability of oral semaglutide versus placebo added to insulin ± metformin in patients with type 2 diabetes: the PIONEER 8 Trial. Diabetes Care. 2019;42:2262-2271.
- Yamada Y, Katagiri H, Hamamoto Y, et al. Efficacy and safety of oral semaglutide monotherapy vs placebo or liraglutide in Japanese T2D patients: PIONEER 9 trial. Paper presented at: Asian Association for the Study of Diabetes, February 7–9, 2019; Osaka, Japan.
- Yabe D, Nakamura J, Kaneto H, et al. Safety and efficacy of oral semaglutide vs dulaglutide in Japanese T2D patient: the PIONEER 10 trial. Paper presented at: Asian Association for the Study of Diabetes, February 7–9, 2019; Osaka, Japan.

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