Patients (pts) with T2D uncontrolled on metformin ± SGLT-2i were randomized to oral semaglutide (sema) 14 mg once daily (N=285), liraglutide (lira) 1.8 mg (N=284) or placebo (pbo, N=142) in a phase 3a, 52-week (wk), double-blind, double-dummy trial (NCT02863419). Endpoints: Change (baseline to Wk 26) in HbA1c (primary) and body weight (BW, confirmatory secondary). Two estimands addressed two efficacy-related questions: Treatment policy (regardless of trial product discontinuation or rescue medication) and trial product (on trial product without rescue medication) in all randomized pts. Treatment policy estimand: Oral sema was non-inferior (margin 0.4%) to lira and superior to pbo in reducing HbA1c, and superior to both in reducing BW at Wk 26 (Table). Differences in both HbA1c and BW were significant at Wk 52. Trial product estimand: Oral sema gave significant reductions in HbA1c and BW vs. lira and pbo at Wks 26 and 52. Oral sema had comparable tolerability to lira; 11% (oral sema) vs. 9% (lira) and 4% (pbo) prematurely discontinued trial product due to adverse events (primarily gastrointestinal; 5% [oral sema] vs. 3% [lira] discontinued due to nausea). In conclusion, oral sema was well tolerated in pts with T2D on metformin ± SGLT-2i, was non-inferior vs. lira and superior vs. pbo in reducing HbA1c, and was superior in reducing BW vs. both lira and pbo. The reduction in HbA1c was significantly better vs. lira when evaluated by the trial product estimand.