

The Lancet publishes results from the ACHIEVE-3 trial comparing A1c reductions for orforglipron versus oral semaglutide in T2D – February 26, 2026

Orforglipron 36 mg demonstrated A1c reductions of 1.91% from a baseline of 8.3% (vs. 1.5% reduction with oral semaglutide 14 mg) in the treatment policy estimand

The Lancet just [published](#) by Dr. Julio Rosenstock (UT Southwestern) et al., results from the phase 3 [ACHIEVE-3](#) trial (n=1,698) of Lilly's oral GLP-1 RA orforglipron in the first head-to-head comparison against Novo Nordisk's oral semaglutide. All primary non-inferiority comparisons were met, with both orforglipron doses showing subsequent superiority in A1c reductions compared to both semaglutide doses.

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Orforglipron conferred greater A1c reduction and weight loss than oral semaglutide

Results showed a clear advantage for A1c reduction at 52 weeks for both the 12 mg and 36 mg doses of orforglipron. Participants with T2D who were already taking metformin achieved A1c reductions from a baseline of 8.3% to final levels of 6.4% and 6.1% with orforglipron 12 mg and 36 mg, respectively, compared with 7.2% and 6.8% with oral semaglutide 7 mg and 14 mg, respectively, as per the efficacy estimate. A1c targets of <6.5% were achieved by 77% and 51% with orforglipron 36 mg and oral semaglutide 14 mg, respectively (efficacy estimand).

Notably, orforglipron 12 mg and 36 mg resulted in mean percentage body weight changes by week 52 of -6.1% and -8.2%, respectively, compared with semaglutide 7 mg and 14 mg, which showed reductions of -3.9% and -5.3%, as per the treatment policy estimand. Whereas the efficacy estimand revealed bodyweight changes of -6.7% and -9.2% with orforglipron 12mg and 36mg, respectively, vs. -3.7% and -5.3% with semaglutide 7 mg and 14 mg, respectively.

Gastrointestinal adverse events were more common among people taking orforglipron

GI adverse events were more common with orforglipron, at 59% and 58% on 12 mg and 36 mg doses, respectively, compared with 37% and 45% on semaglutide 7 mg and 14 mg. Discontinuation rates due to adverse events were 8.7% and 9.7% for orforglipron 12 mg and 36 mg vs. 4.5% and 4.9% for oral semaglutide 7 mg and 14 mg, respectively.

-- by Kayla Mathieu, Nour Khachemoune, Monica Oxenreiter, and Kelly Close