

3082-LB

The selective amylin analog, eloralintide, enhanced weight-loss efficacy when combined with tirzepatide in diet-induced obese rats.

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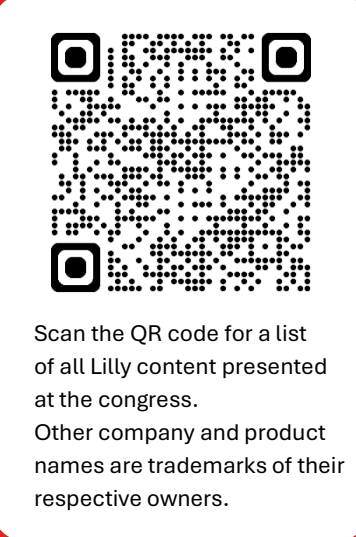
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OBJECTIVE

- To evaluate eloralintide (LY3841136), a long-acting selective amylin agonist, in combination with tirzepatide, a GIP and GLP-1 receptor agonist, for the treatment of obesity in diet-induced obese rats.

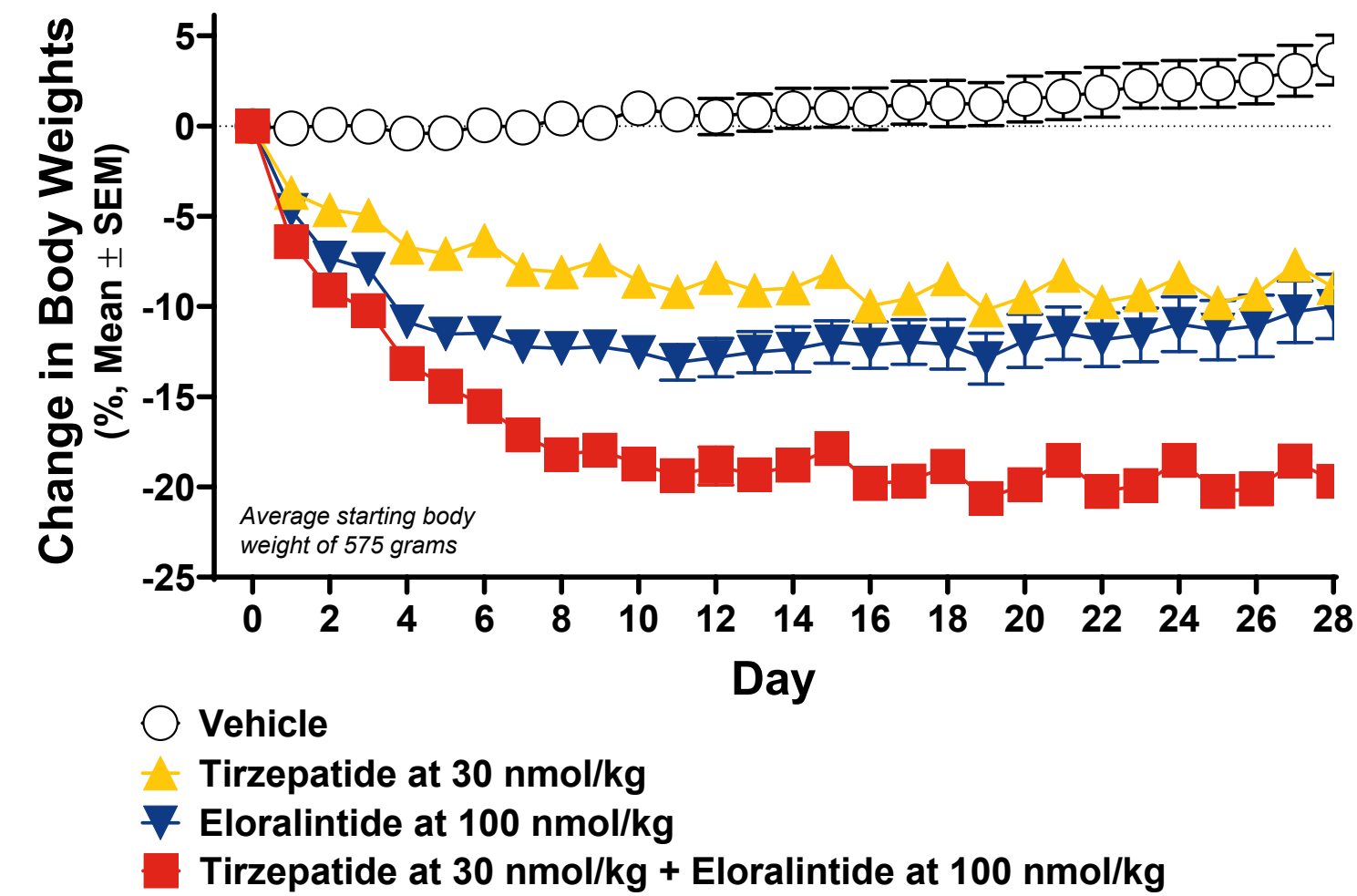
CONCLUSION

- Combinations of eloralintide and tirzepatide, either as co-administration or adjunctive treatment, led to additive weight loss effects in DIO rats.
- These observations support clinical investigation of eloralintide as an obesity therapeutic in combination with tirzepatide.



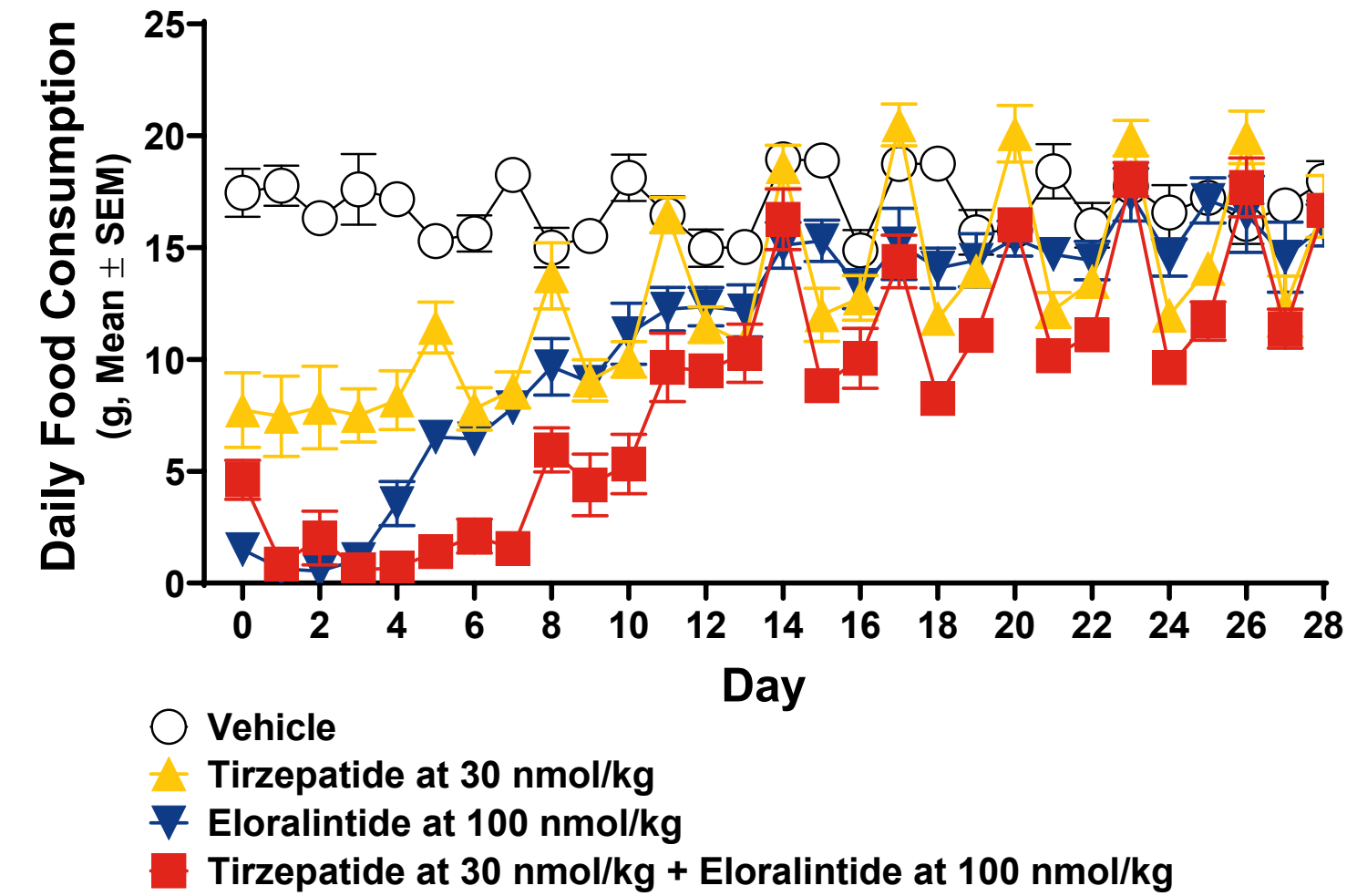
CO-ADMINISTRATION – BODY WEIGHT CHANGES

Simultaneous treatment of eloralintide and tirzepatide enhanced body weight loss in diet-induced obese rats.



CO-ADMINISTRATION – DAILY FOOD INTAKE

Simultaneous treatment of eloralintide and tirzepatide enhanced daily food intake reductions in diet-induced obese rats.



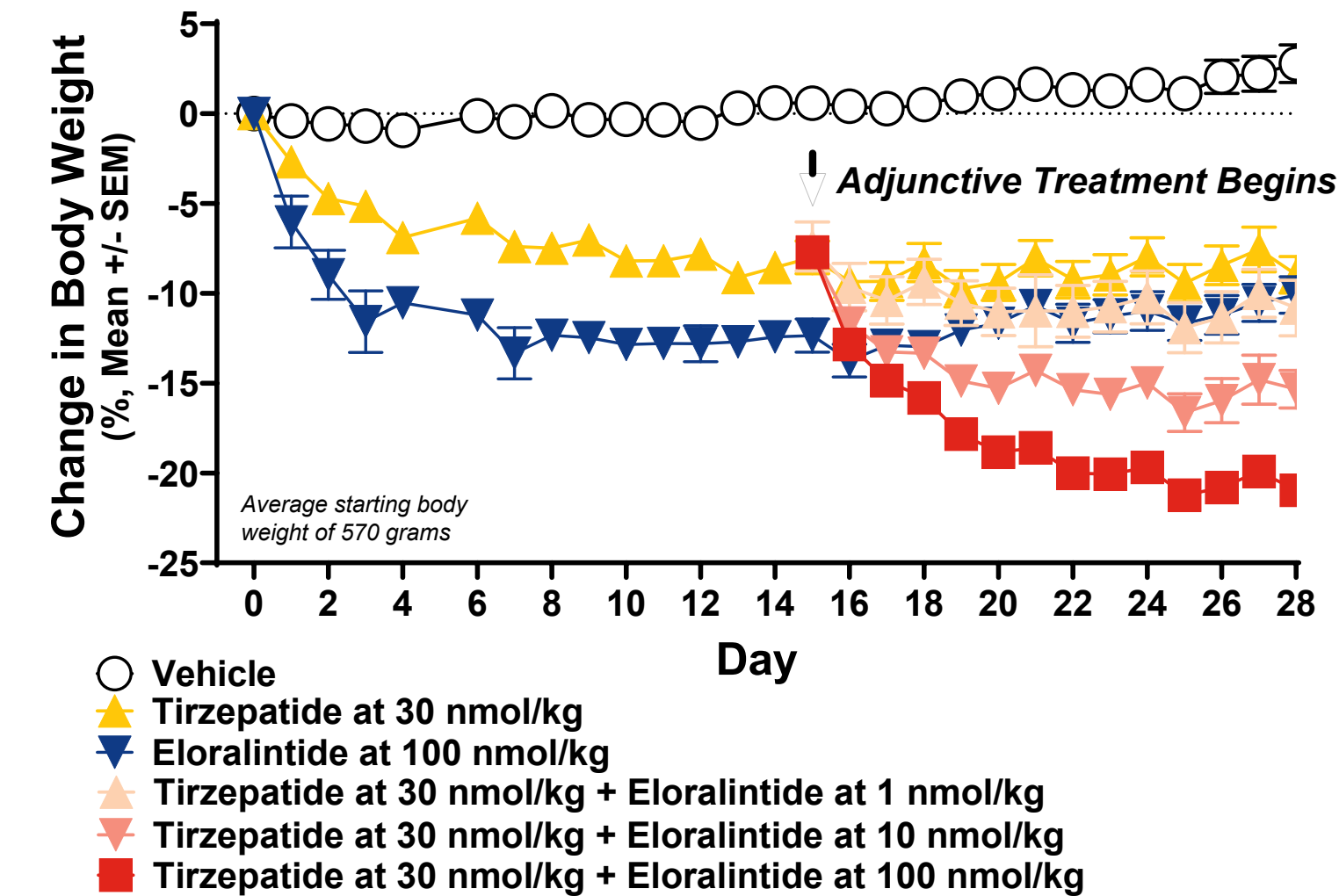
CO-ADMINISTRATION – % CHANGES AT 4 WEEKS

Simultaneous treatment of eloralintide and tirzepatide resulted in additive effects on changes on body weight and fat mass.

Treatment	% Change from Baseline	
	Body Weight	Fat Mass
Vehicle	3.66 (1.38)	13.51 (2.98)
Tirzepatide at 30 nmol/kg	-8.96 (0.59)	-32.87 (4.45)
Eloralintide at 100 nmol/kg	-10.00 (1.78)	-46.35 (5.66)
Tirzepatide at 30 nmol/kg + Eloralintide at 100 nmol/kg	-19.68 (0.49)	-65.90 (3.50)

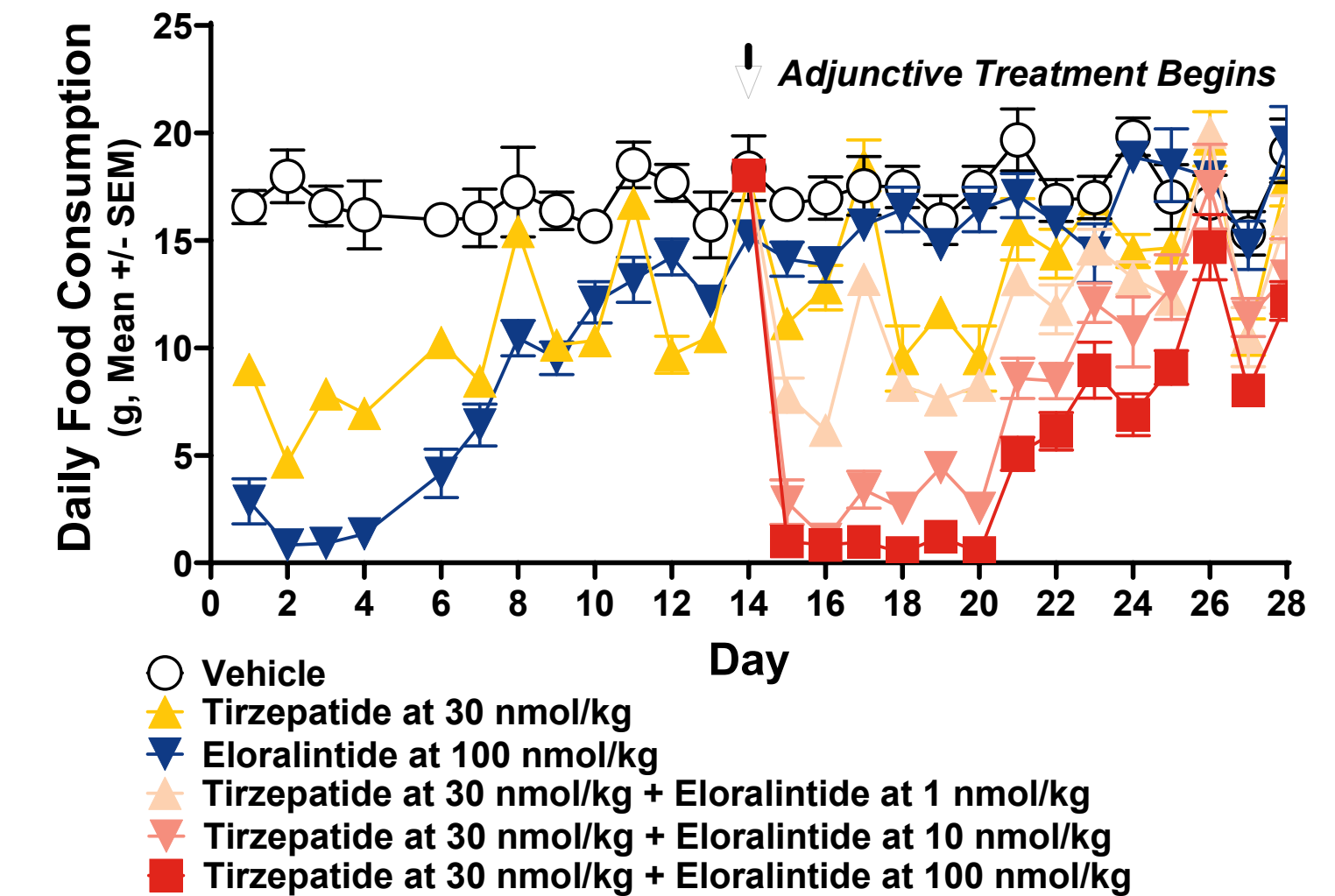
ADJUNCTIVE – BODY WEIGHT CHANGES

Add-on treatment of eloralintide to tirzepatide dose-dependently enhanced body weight loss in diet-induced obese rats.



ADJUNCTIVE – DAILY FOOD INTAKE

Add-on treatment treatment of eloralintide and tirzepatide enhanced daily food intake reductions in diet-induced obese rats.



ADJUNCTIVE – % CHANGES AT 4 WEEKS

Add-on treatment of eloralintide to ongoing tirzepatide resulted in additive effects on changes on body weight and fat mass.

Treatment	% Change from Baseline	
	Body Weight	Fat Mass
Vehicle	2.78 (1.06)	18.55 (5.49)
Tirzepatide at 30 nmol/kg	-8.97 (1.03)	-25.79 (3.56)
Eloralintide at 100 nmol/kg	-10.10 (1.01)	-35.02 (2.92)
Tirzepatide at 30 nmol/kg + Eloralintide at 1 nmol/kg	-10.82 (1.55)	-41.97 (2.84)
Tirzepatide at 30 nmol/kg + Eloralintide at 10 nmol/kg	-15.34 (1.04)	-55.65 (6.09)
Tirzepatide at 30 nmol/kg + Eloralintide at 100 nmol/kg	-20.96 (0.74)	-55.95 (4.40)

RESULTS

- Co-administration of tirzepatide at 30 nmol/kg and eloralintide at 100 nmol/kg for 4 weeks in DIO rats resulted in additive effects (-20%) on changes in body weight compared to eloralintide (-10%) or tirzepatide (-9%) alone.
- For adjunctive treatment, two weeks of tirzepatide at 30 nmol/kg, followed by the addition of eloralintide at 100 nmol/kg for 2 additional weeks, resulted in additive body weight lowering (-21%) compared to eloralintide (-10%) or tirzepatide alone (-9%).
- Lower adjunctive combinations of eloralintide (1 & 10 nmol/kg) led to enhanced weight loss (-11% or -15%) versus tirzepatide alone.
- This enhanced weight loss was mediated, at least in part, by further and prolonged reductions in daily food intake and reflected in greater changes in fat mass at 4 weeks of treatment.

MATERIALS AND METHODS

- Co-administration studies: Male Long Evans DIO rats were subcutaneously dosed every 3 days (Q3D) with vehicle, tirzepatide at 30 nmol/kg, eloralintide at 100 nmol/kg, or separate injections of tirzepatide and eloralintide for 4 weeks.
- Adjunctive studies: DIO rats were dosed Q3D for 2 weeks with tirzepatide at 30 nmol/kg, followed by addition of 1, 10, or 100 nmol/kg Q3D of eloralintide to ongoing tirzepatide for 2 further weeks.
- Body weights and food intake were measured daily. Fat mass measured at baseline and 4 weeks using QNMR.