



Potent weight loss effects of Amylin analog ZP8396 in combination with tirzepatide in DIO rats

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INTRODUCTION

- ZP8396 is a novel amylin analog designed for once weekly dosing that has demonstrated the potential to reduce body weight both in human studies and animal models.
- Semaglutide (GLP-1R agonist) and tirzepatide (GIPR and GLP-1R dual agonist) have shown great potential as pharmacotherapy to reduce body weight.
- Combination therapy consisting of peptide hormone therapies with complementary modes of action may provide even greater weight loss than that achieved with either semaglutide or tirzepatide alone without compromising safety and tolerability.

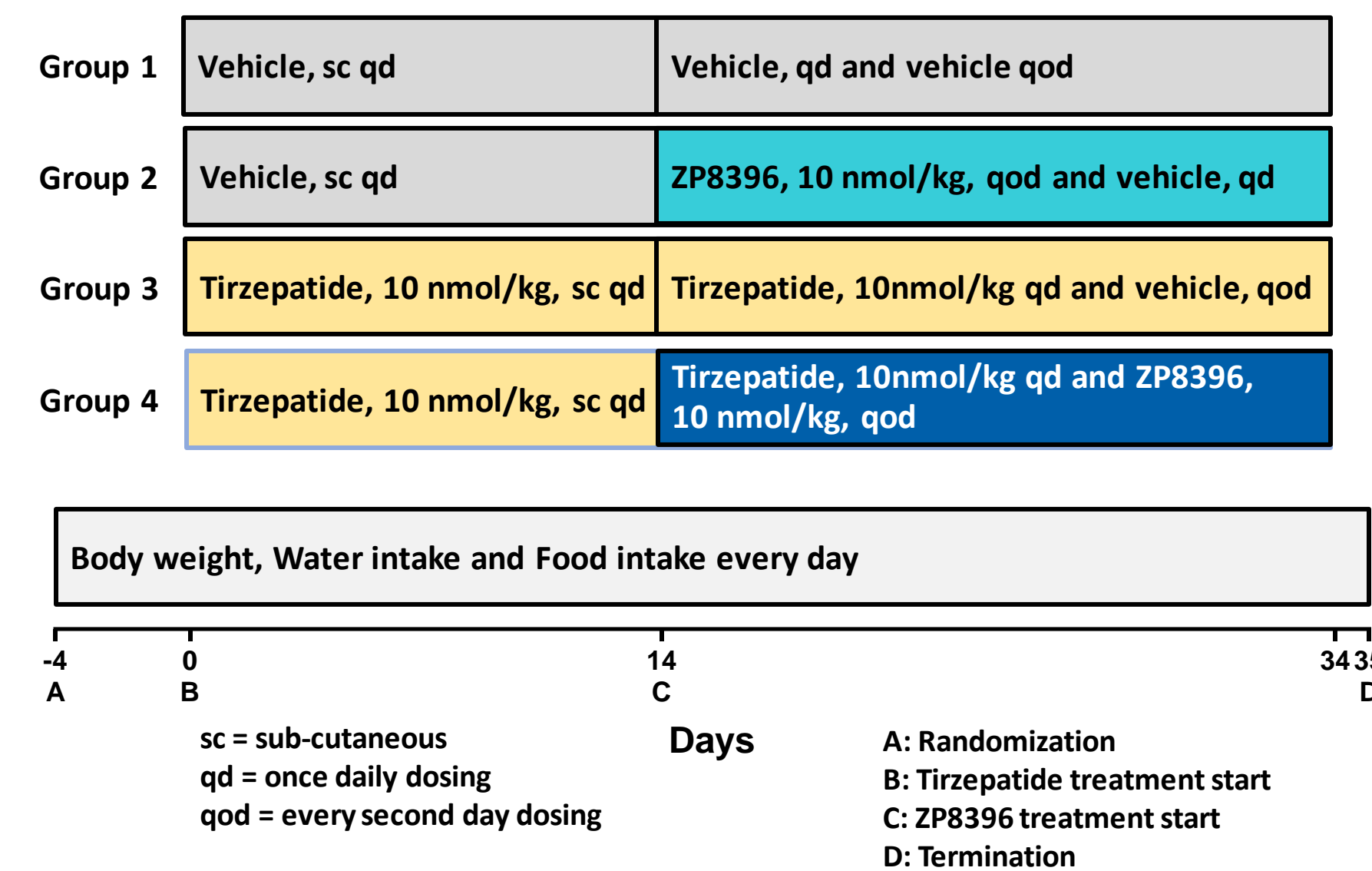
STUDY OBJECTIVE

In this study we investigate the combined weight loss effects of ZP8396 and tirzepatide in diet-induced obese (DIO) rats.

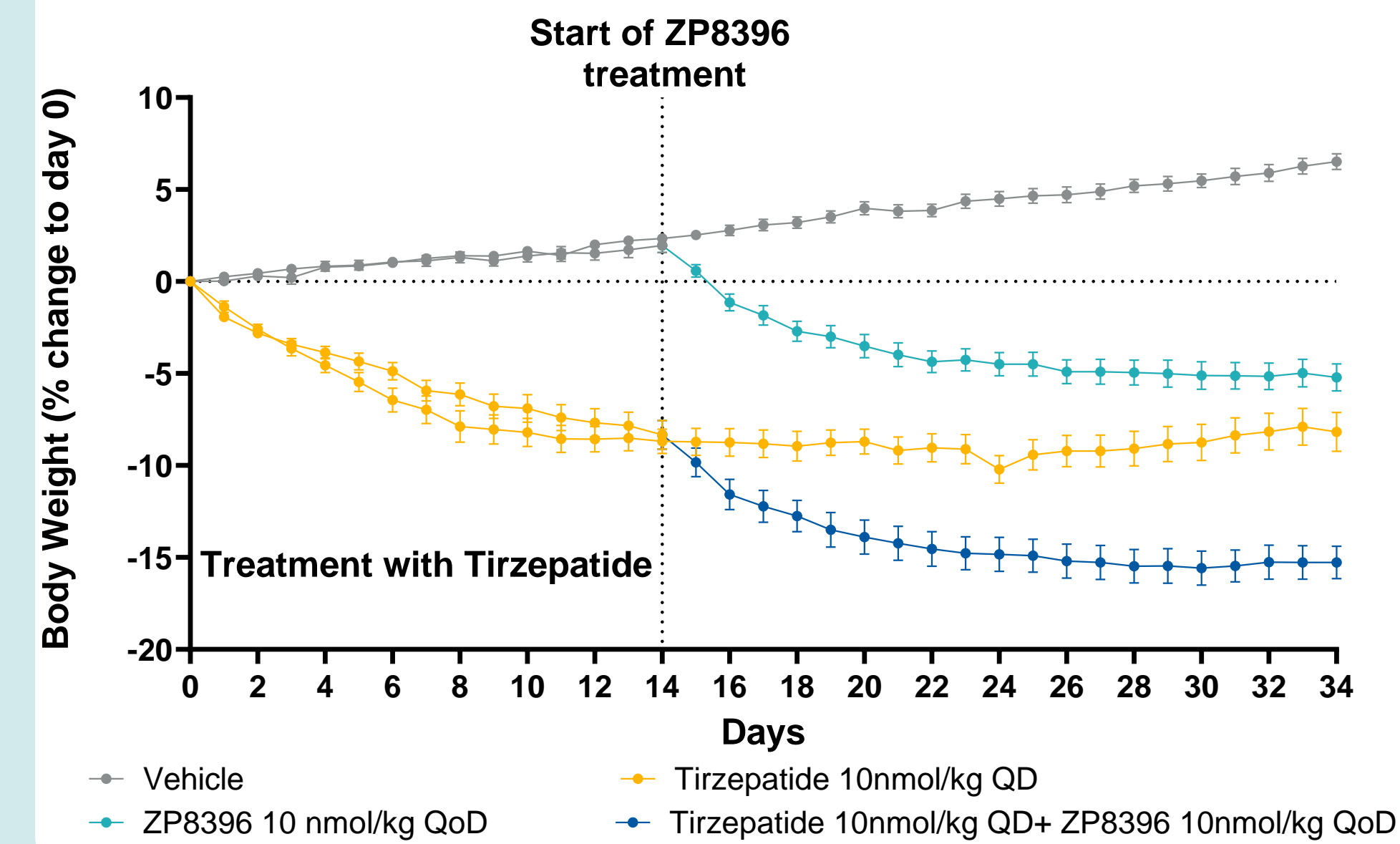
METHODS

- DIO rats were treated for 14 days with either vehicle or tirzepatide 10 nmol/kg by once daily subcutaneous injection.
- From day 14 to 34, vehicle-treated rats continued either on vehicle or were switched to ZP8396 10 nmol/kg, every 2nd day by subcutaneous injection.
- Likewise, tirzepatide-treated rats continued either on tirzepatide or were switched to tirzepatide plus ZP8396. The weight loss effects were assessed by measurement of body weight and food intake.

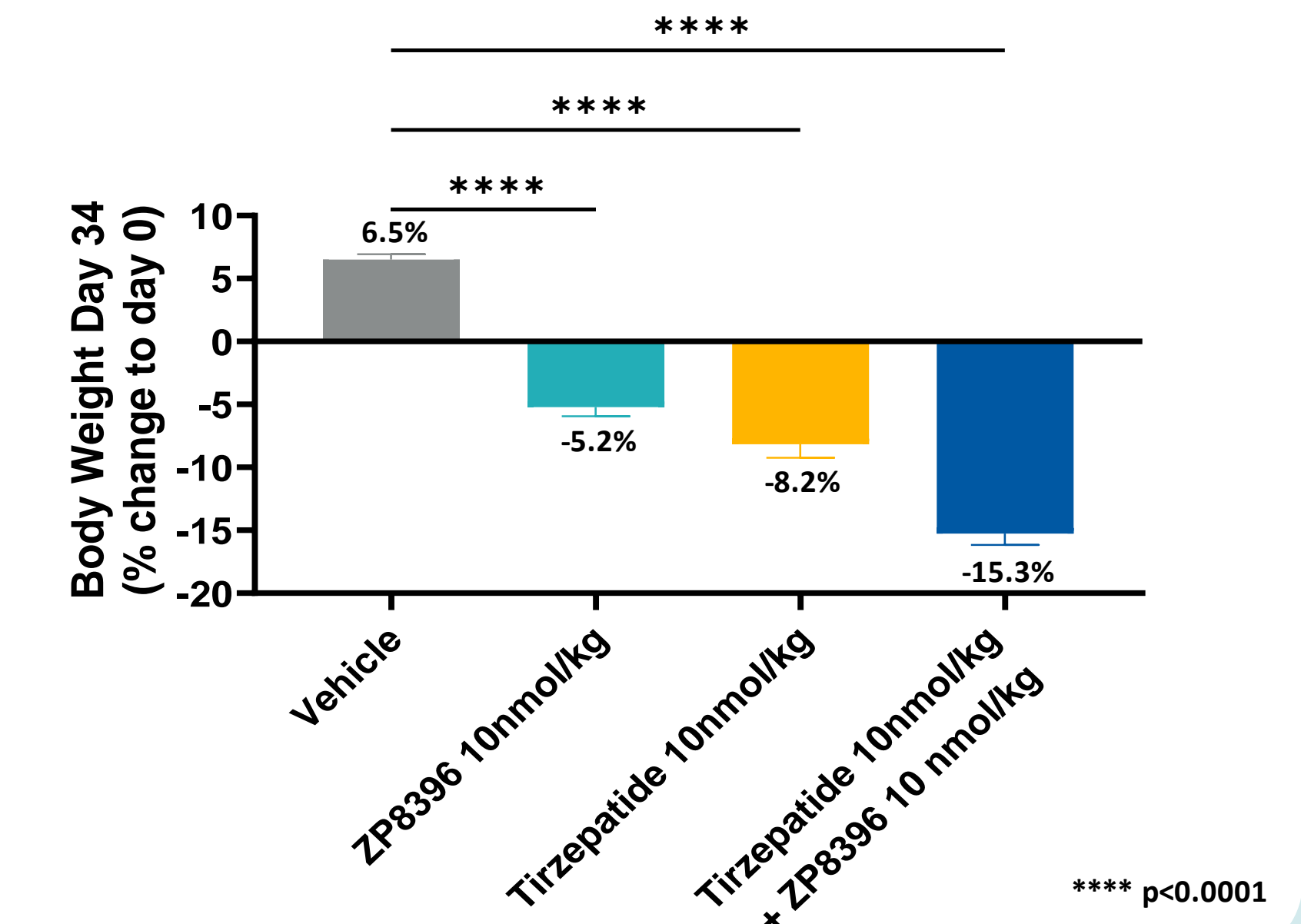
STUDY DESIGN



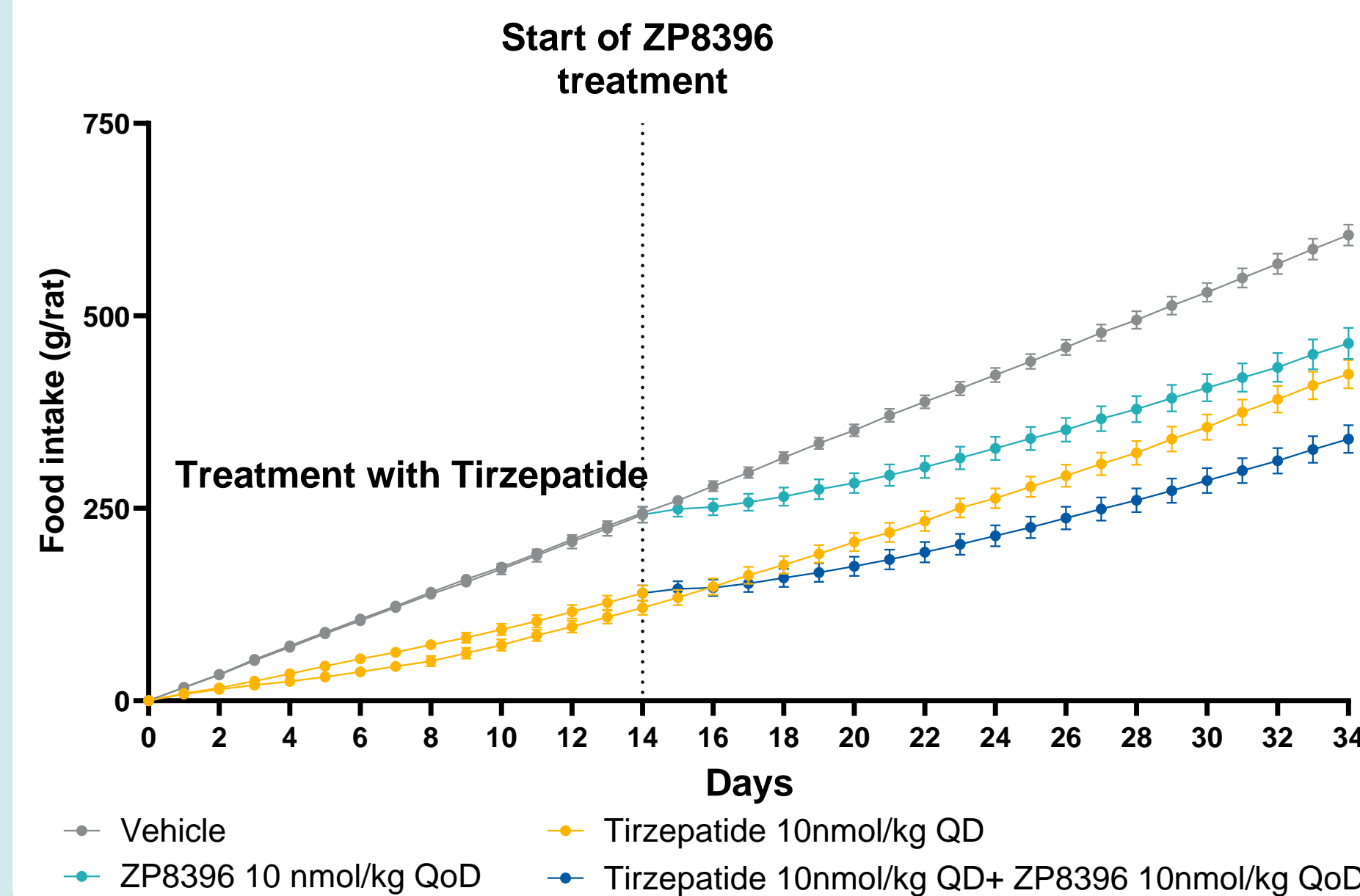
BODY WEIGHT CHANGE



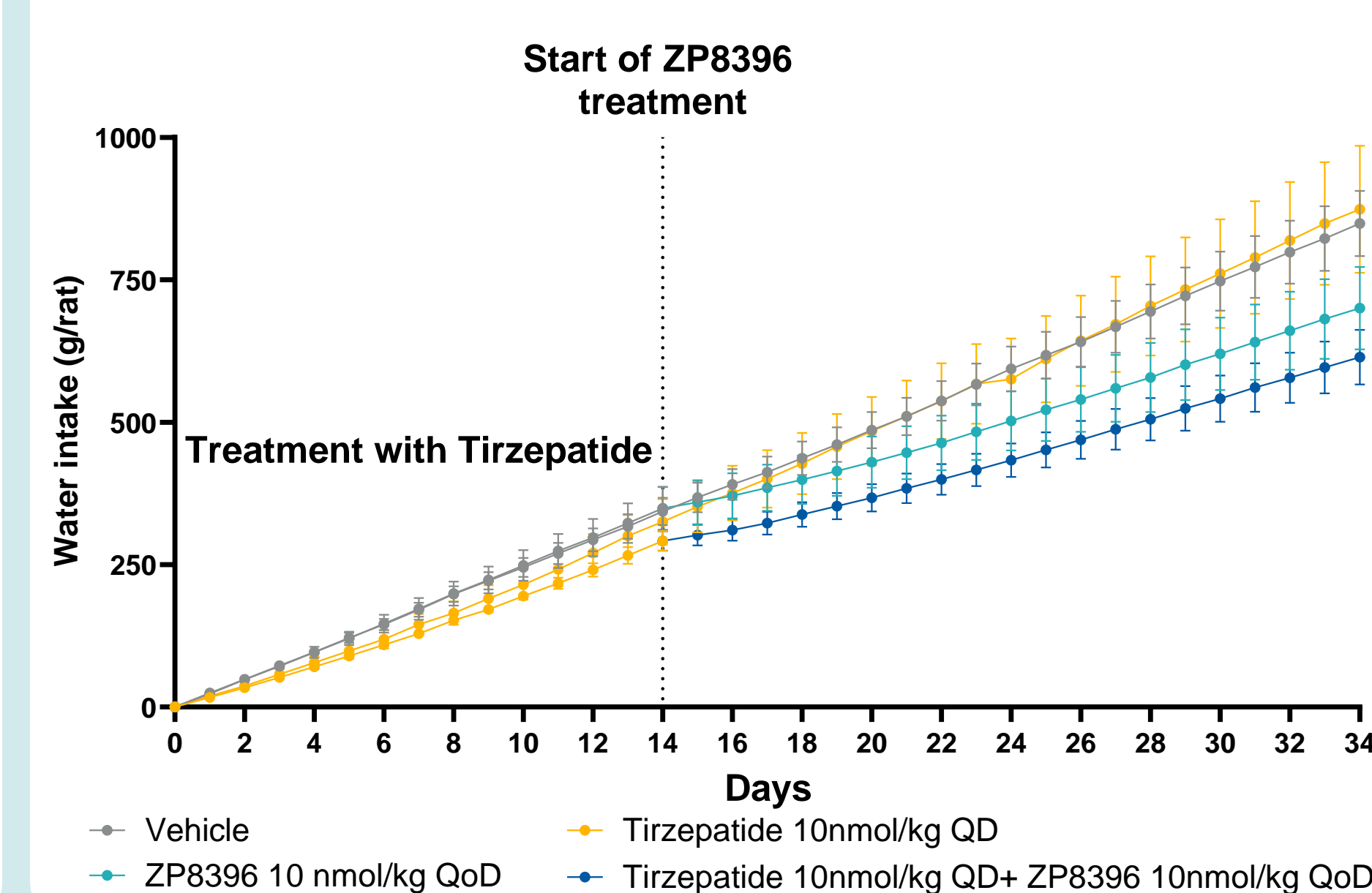
BODY WEIGHT CHANGE DAY 34



FOOD INTAKE



WATER INTAKE



RESULTS

Combined treatment with ZP8396 and tirzepatide achieved a significant, sustained, and greater reduction in cumulative food intake and body weight reduction compared to vehicle- and each mono-treated group. Exposure was determined for ZP8396 and tirzepatide, and was similar for each compound between comparative groups (data not shown).

CONCLUSIONS

- In conclusion, combining ZP8396 and tirzepatide in DIO rats resulted in significantly greater body weight loss compared to either monotherapy alone.
- Combining the amylin analog ZP8396 and tirzepatide offers the potential for even greater weight reduction in people living with overweight and obesity.