Can Anti-Obesity-Drug-Induced Terminal Body Weight Loss be Predicted from Initial Caloric Intake Reduction, Independent of Obesity Drug Class?

Craig Fancourt*, Maria Trujillo, Ryan Vargo, Sandra A.G. Visser

Merck & Co., Inc., Kenilworth, NJ USA

Objectives: Determine the predictability of anti-obesity-drug/placebo-induced late caloric reduction or body weight (BW) loss from early caloric reduction or BW loss, for comparator modeling and clinical trial design.

Methods: A dynamic BW model was driven by a caloric intake exponential rebound sub-model [1] with parameters: \( p_{\text{early}} \) and \( p_{\text{late}} \) (initial and final caloric intake reduction), and \( \tau \) (time-constant from \( p_{\text{early}} \) to \( p_{\text{late}} \)). The model predicts terminal DBW=\( p_{\text{late}}/e \), where \( e \approx 22 \) kcal/kg/day is the change in energy expenditure per DBW. Parameters from model fits to BW timecourse data for 14 drugs/placebo in 28 trial-arms [1], and per-protocol-completer data from a multiple-dose Liraglutide/Orlistat/Placebo 52 wk trial [2], were separately fit to two linear models of \( p_{\text{late}} \) vs. \( p_{\text{early}} \). Using the dynamic models, DBW was predicted at weeks 4, 12, 24, and data from [1] and [2] were separately fit to linear models of DBW at 12 and 24 vs. 4 wk, and compared to a linear regression meta-analyses [3] of DBW at the same fixed timepoints for 10 drugs/placebo in 110 trial-arms.

Results: The linear fit of \( p_{\text{late}} \) vs. \( p_{\text{early}} \) from [1] was good (Figure), and agreed with the fit from [2] (not shown). No other covariates were significant, including study duration, drug vs. placebo, age, initial BW or BMI, and percent female or T2DM. The linear fit of dynamic model predicted DBW at both 12 and 24 vs. 4 wk was good, and agreed with fits to data from [2] and [3] (not shown).

Conclusions: Anti-obesity-drug/placebo model-derived early caloric reduction or BW loss is predictive of late caloric reduction or BW loss independent of drug vs. placebo, and agrees with a multiple-dose liraglutide study. This suggests the relationship may also be independent of drug class, but instead driven by the physiological reaction to caloric reduction or BW loss.