Evaluating Glucose and Insulin as Predictors of Weight Loss in GLOW: A Novel Statistical Approach

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INTRODUCTION

- Identifying effective predictors of weight loss will further enable individualized approaches to weight management.
- Previous studies have demonstrated that patients with impaired baseline fasting glucose lose more weight than those with normal glycemia when exposed to diets higher in vegetables, fruits, and wholegrains.[1]
- Gelesis100 (Plenity®) is constructed from modified cellulose cross-linked with citric acid, creating a non-systemic, superabsorbent hydrogel with elasticity similar to ingested vegetables and fruits **(Figure 1)**.[2]
- Gelesis100 promotes weight loss primarily through increasing volume and elastic response of ingested foods in the stomach and small intestine.

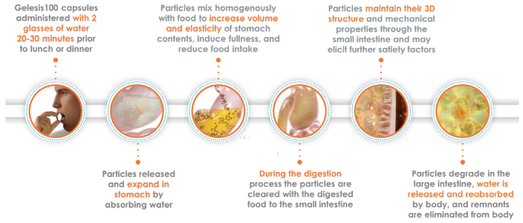
OBJECTIVE

The purpose of this post-hoc analysis was to evaluate the usefulness of pre-treatment fasting plasma glucose (FPG) and fasting plasma insulin (FPI) as biomarker predictors of weight change in subjects from the Gelesis Loss Of Weight (GLOW) study.

METHODS

- The GLOW study assessed the effects of Gelesis100 in subjects with a BMI of 27-40 kg/m^2.
- Subjects were randomized to Gelesis100 or placebo taken with 500 mL of water before lunch and dinner while on a hypocaloric diet (-300 kcal/day) for 24 weeks.
- Body weight was measured throughout and FPG and FPI were measured prior to randomization. Insulin resistance (HOMA-IR) was calculated using FPG and FPI.
- Subjects with an FPG of 70-126 mg/dL were included in this post-hoc analysis.
- Weight was described by linear mixed models.
- Individualized predictions were estimated as contrasts of intercepts and slopes of pre-treatment biomarkers (FPG or FPI).

Figure 1. Gelesis100 hydrogel in the gastrointestinal tract



RESULTS

- 436 subjects were randomized in the GLOW study, of which 425 met the FPG inclusion criteria for this post-hoc analysis.
- In the GLOW study, the mean (± SD) body weight losses from baseline to the end of treatment were 6.4 ± 5.8% and 4.4 ± 5.5% (P = 0.0007), in the Gelesis100 and placebo arms, respectively. There was no difference in the incidence and severity of adverse events (AEs) between the Gelesis100 and placebo group other than an increase in overall gastrointestinal AEs.
- For each 1 mg/dL increase in FPG, subjects on Gelesis100 experienced a greater weight change of –0.14 kg (95%CI –0.19 - –0.08, P=0.001) compared to –0.04 kg (95%CI –0.09 - 0.01, P=0.11) for those on placebo (mean difference: 0.10 kg; 0.02-0.17, P=0.011) **(Figure 2 & 3)**.
- Weight loss amount (in kg) for Gelesis100 was estimated using the formula [Weight Change (Gelesis100) = 7.0 – 0.14 x FPG].

Figure 2. Weight change per unit FPG for Gelesis100 vs. Placebo.

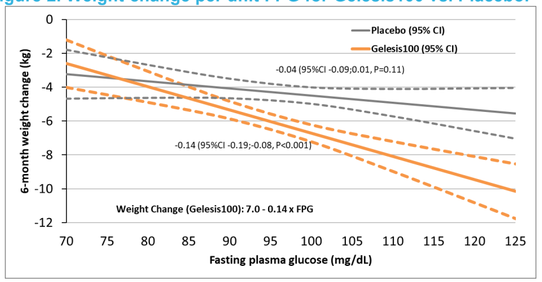
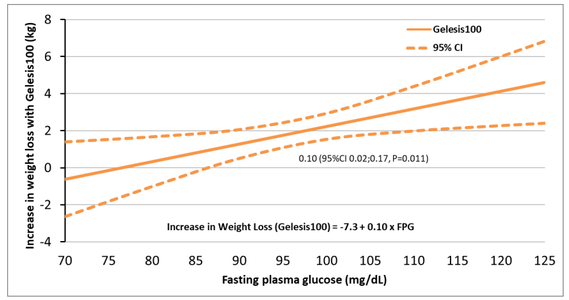
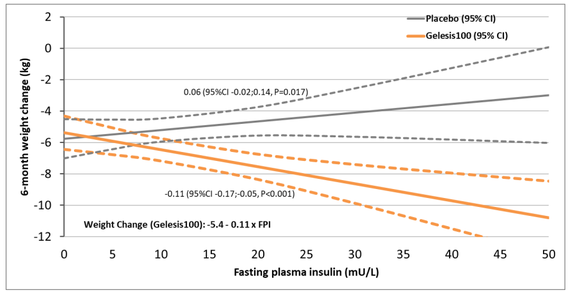


Figure 3. Increase in weight loss per unit FPG for Gelesis100.



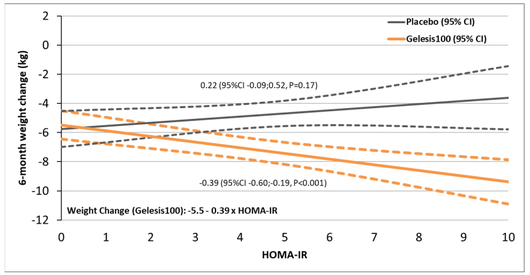
- In subjects who lost ≥5% body weight by study end, the mean between-group difference in weight loss for each 1 mg/dL increase in FPG was 0.16 kg (95%CI 0.07-0.25, P<0.001).
- Weight change per unit increase in FPG on Gelesis100 was pronounced in subjects that were using metformin (n=29) (mean difference: 0.25 kg per 1mg/dL; 0.06-0.43, P=0.011).
- In subjects with elevated FPG (95-126mg/dL; n=187), each unit increase in FPI (mIU/l) predicted a greater weight loss of 0.16 kg (95%CI 0.06 – 0.26, P<0.001) for Gelesis100 compared to placebo **(Figure 4).**

Figure 4. Weight change per unit FPI for Gelesis100 vs. Placebo.



- Similarly, each unit increase in HOMA-IR predicted a greater weight loss of 0.61kg (95%CI 0.24 – 0.98, P<0.001) for Gelesis100 **(Figure 5)**.

Figure 5. Weight change per unit HOMA-IR for Gelesis100 vs. Placebo.



- Interestingly, in contrast to FPG, FPI and HOMA-IR, baseline HbA1c was not an effective predictor of weight loss (P>0.05).

CONCLUSIONS

- Baseline fasting plasma glucose can be a predictor of weight loss for Gelesis100 treatment.
- Fasting plasma insulin could add an additional level of prediction for individuals with elevated FPG.
- Clinicians should consider these factors when individualizing treatment for patients with overweight or obesity.

REFERENCES

1. Hjorth MF, Ritz C, Blaak EE, et al. AM J Clin Nutr 2017;106:499-505. 2. Demitri C, Zohar Y, Heshmati HM, et al. 2017; Porto, Portugal. Abstract P938.

DISCLOSURES

MFH, CR, and **AA** have received funding/grant support from Gelesis, and **AA** owns Gelesis stock options as a scientific advisor. **DB** is employed by Gelesis and owns Gelesis stock options.

GELESIS