Plenity® Treatment In The Gelesis Loss of Weight (GLOW) Study Was Associated With Improvement In Liver Health, As Measured By The NAFLD Fibrosis Score

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INTRODUCTION

- Nonalcoholic fatty liver disease (NAFLD) prevalence is >50% in people with obesity, and weight loss remains the cornerstone treatment of this disease. [1]
- Plenity® is a non-systemic orally administered, superabsorbent hydrogel (OSH) bioengineered from modified cellulose cross-linked with citric acid to create elastic properties similar to ingested vegetables and fruits **(Figure 1)**. [2]
- OSH promote weight loss primarily through increasing volume and elastic response of ingested foods in the stomach and small intestine.
- The Gelesis Loss of Weight (GLOW) study investigated the efficacy and safety of Plenity®, an OSH previously shown to elicit meaningful weight loss compared to placebo. [3]

OBJECTIVE

This exploratory analysis examined the impact of OSH treatment on liver health as measured by the NAFLD fibrosis score[4] (NFS; **Figure 2**), which predicts the presence of significant fibrosis using common clinical and laboratory values.

METHODS

- The GLOW study assessed the effects of OSH treatment in subjects with a BMI of 27-40 kg/m^2.
- 317/436 with complete pre-post data were included in this analysis.
- The NFS was calculated, and scores were categorized as either higher (combining intermediate and high; i.e. score ≥ -1.45) or lower (score < -1.45) probability of liver fibrosis. Outliers were removed from the analysis (2 OSH, 1 placebo).
- The absolute and categorical scores were calculated at baseline and 6 months for:
  1. The entire cohort
  2. Subjects with prediabetes or T2 diabetes at baseline
  3. Subjects who lost ≥ 10% weight
- Paired sample t-test was used for within subject treatment responses, ANCOVA was used for all other parameters.

Figure 1. OSH in the gastrointestinal tract

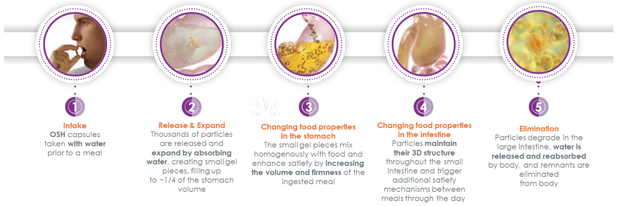
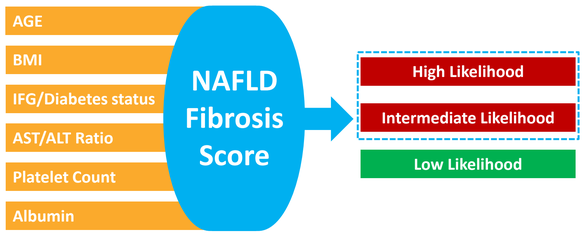


Figure 2. The NAFLD fibrosis score (NFS)[4]. For this analysis, high and intermediate likelihood of fibrosis was combined.

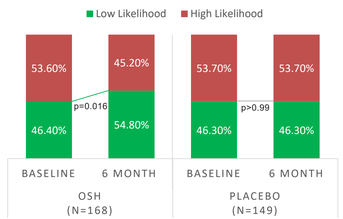


Equation: -1.675 + 0.037 × age + 0.094 × BMI (kg/m^2) + 1.13 × IFG/diabetes (yes = 1, no = 0) + 0.99 × AST/ALT ratio - 0.013 × platelet count (×10^9/L) - 0.66 × albumin (g/dL)

RESULTS

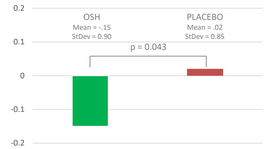
- At baseline, 90/168 (53.6%) subjects in the OSH and 80/149 (53.7%) in the placebo had NFS in the higher probability for fibrosis category (p=0.98; **Figure 3**). More subjects in the OSH group were in the lower probability risk category (p=0.016) at the end of treatment, while no difference was observed in placebo (p>0.99).

Figure 3. Fatty liver risk categorization amongst subjects with complete data at baseline and 6 months.



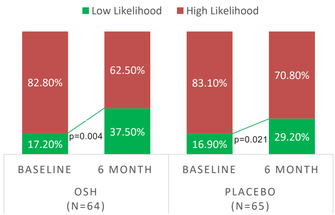
- When absolute scores were compared between baseline and 6 months, there was a statistically significant reduction in NFS within OSH (-0.15 ± 0.90; p=0.030), but not the placebo (0.02 ± 0.85; p=0.824). The difference between groups was statistically significant (**Figure 4;** ANCOVA; p=0.043).

Figure 4. Comparison of the change in absolute NFS between baseline and 6 months in the OSH and placebo groups.



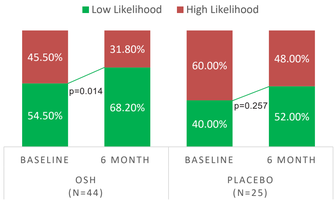
- In the subgroup with prediabetes or T2 diabetes (n=64 OSH; n=65 placebo), absolute NFS was lower in both groups (OSH -0.53 ± 0.88, p<0.0001; placebo -0.34 ± 1.04, p=0.0097). Similarly, more subjects in the OSH group (p=0.004) and placebo (p=0.021) were in the lower risk NFS category at end of treatment (**Figure 5**).

Figure 5. Fatty liver risk categorization amongst subjects with prediabetes or type 2 diabetes.



- Amongst subjects who lost at least 10% weight (n=44 in OSH, n=25 in placebo), the absolute mean change in NFS was greater for OSH (OSH -0.37 ± 0.80, p=0.004; placebo -0.34 ± 0.98, p=0.096), and more subjects were in lower NFS category in OSH at end of treatment (p=0.014) but not placebo (p=0.257; **Figure 6**).

Figure 6. Fatty liver risk categorization amongst subjects who lost at least 10% of their body weight during treatment.



- The most common GI-related AEs in the OSH arm were abdominal distension, diarrhea, infrequent bowel movements, flatulence, abdominal pain, and constipation **(Table 1).**

Table 1. Subjects with the most common AEs in the safety population.

Parameter	OSH (n = 223)	Placebo (n = 211)	P value
Any AE probably or possibly related, n (%)	88 (39.5)	64 (30.3)	0.0557
Eye disorders, n (%)	0 (0.0)	1 (0.5)	0.4862
GI Disorders, n (%)	84 (37.7)	58 (27.5)	0.0248
General disorders and administration site conditions, n (%)	1 (0.4)	1 (0.5)	1.0000
Infections and infestations, n (%)	2 (0.9)	1 (0.5)	1.0000
Investigations, n (%)	3 (1.3)	3 (1.4)	1.0000
Metabolism and nutrition disorders, n (%)	0 (0.0)	4 (1.9)	0.0551
Musculoskeletal and connective tissue disorders, n (%)	2 (0.9)	0 (0.0)	0.4992
Nervous system disorders, n (%)	4 (1.8)	2 (0.9)	0.6860
Renal and urinary disorders, n (%)	1 (0.4)	0 (0.0)	1.0000
Reproductive system and breast disorders, n (%)	0 (0.0)	1 (0.5)	0.4862
Respiratory, thoracic, and mediastinal disorders, n (%)	1 (0.4)	1 (0.5)	1.0000
Skin and subcutaneous tissue disorders, n (%)	1 (0.4)	3 (1.4)	0.3599

NS: non-significant.

CONCLUSIONS

- Liver health should be considered in the treatment of obesity, as over half of the subjects in GLOW, of which 68% had pre-obesity or Class I obesity[3], had NFS of moderate or high at baseline (Fig. 1).
- OSH-induced weight loss was associated with a statistically significant reduction in NFS score compared to placebo in this exploratory analysis.
- Reduction in the NFS were seen in the total cohort of patients, amongst patients with prediabetes or T2 diabetes, and amongst patients who lost at least 10% weight or greater during the study duration.

REFERENCES

1. Brunner KT. *et al.* 2019. Curr Obes Rep. 8(3):220-8.
2. Zohar Y, Heshmati HM, et al. 2017; Porto, Portugal. Abstract P938.
3. Greenway FL. *et al.* 2019. Obesity. 27(2):205-16.
4. Angulo P. *et al.* 2007. Hepatology. 45(4):846-54.

DISCLOSURES

CS: Consultant (Novo Nordisk, Ethicon Endosurgery, Covidien) Speaker Bureau (Novo Nordisk), Research Grant (Ethicon Endosurgery). **FG:** Advisory Board Participant (Jenny Craig and Pfizer), Consultant (Basic Research, GNC, NovMeta Pharma, Stock/Options (Plensat, Slim Health Nutrition, Ketogenic Health Systems, Rejuvenate Bio, UR Labs) . **EC, BJ** and **HL** are employed by Gelesis and own Gelesis stock options.

GELESIS