EP4.14 Safety and tolerability of Gelesis200 in the management of overweight and obesity in people with prediabetes or type 2 diabetes: comprehensive analysis of the LIGHT-UP study

Pawel Bogdanski[1], Frank Lyons Greenway[2], Sam Stanley Miller[3], Erika Matejkova[4], Barry Mclean[5], Witold Zmuda[6], Malgorzata Arciszewska[7], Anders Mikael Sjödin[8], Judith Salz[9], Anna Bochenek Mularczyk[10], Lorena Lewy Alterbaum[11], Peter Weissman[12], William Benjamin Smth[13], Michael Bain Butcher[14], Mihaly Dudas[15], Livio Luzi[16], Harry Leider[17], Yishai Zohar[17], Alessandro Sannino[17], Henry Wilson Calderon[17], Lorien E Urban[17], Hassan Massoud Heshmati[17]

[1]Poznan University of Medical Sciences, Poznan, Poland
[2]Pennington Biomedical Research Center, Baton Rouge, LA, USA
[3]SAM Clinical Research Center, San Antonio, TX, USA
[4]Health & Care, sro, Prague, Czech Republic
[5]Central Alabama Research, Birmingham, AL, USA
[6]Medicome Sp z o o, Oswiecim, Poland
[7]NZOZ Specjalistyczny Osrodek Internistyczno - Diabetologiczny, Bialystok, Poland
[8]University of Copenhagen, Frederiksberg C, Denmark
[9]Wake Research - Clinical Research Center of Nevada, LLC, Las Vegas, NV, USA
[10]Centrum Badawcze Wspolczesnej Terapii, Warszawa, Poland
[11]ALL Medical Research, LLC, Cooper City, FL, USA
[12]Baptist Diabetes Associates, P.A., Miami, FL, USA
[13]Volunteer Research Group and New Orleans Center for Clinical Research, Knoxville, TN, USA
[14]Sterling Research Group, Ltd, Cincinnati, OH, USA
[15]Bekes Megyei Kozponti Korhaz Pandy Kalman Tagkorhaz, Gyula, Hungary
[16]University of Milan, Milan, Italy
[17]Gelesis, Inc, Boston, MA, USA

OBJECTIVES

Anti-obesity medications are prescribed in less than 2% of people with overweight or obesity in the US mainly due to concerns about the safety or tolerability of existing medications. There is a need for alternative treatments that can induce clinically relevant weight loss, with no increased safety risk, especially in people with type 2 diabetes (T2D) since they typically face increased challenges losing weight and have higher risk of comorbidities.

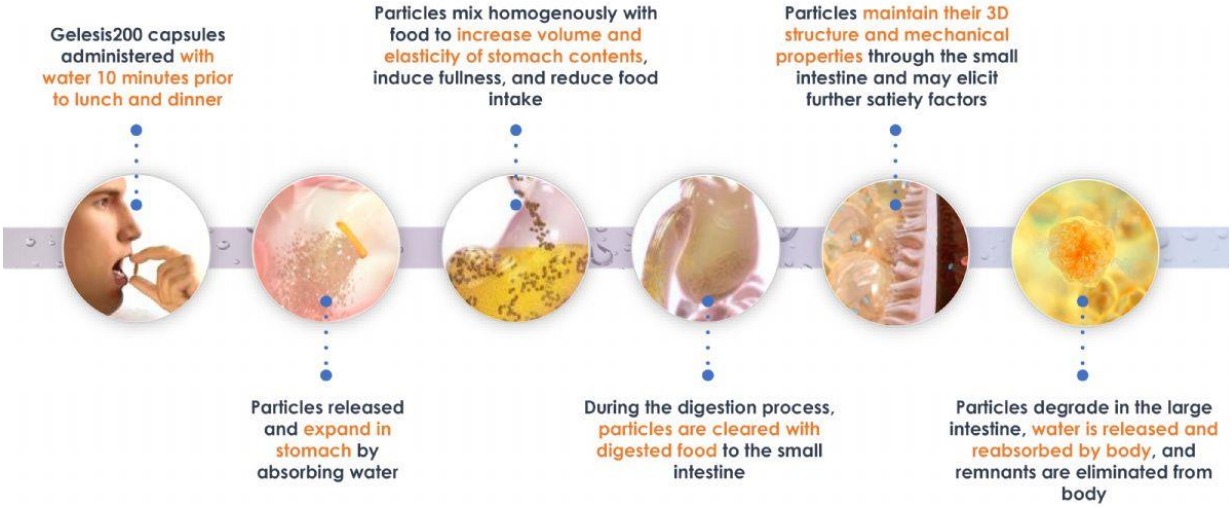
MATERIALS-METHODS

LIGHT-UP (NCT03058029), a multicenter, double-blind, randomized, placebo-controlled study, assessed the effects of Gelesis200, a non-systemic, investigational superabsorbent hydrogel, in people with a body mass index (BMI) between 27 and 40 kg/m2, with prediabetes (PD) or T2D (untreated or treated) over 25 weeks.

Participants were randomized to 2.10 g of Gelesis200 or placebo in capsules taken with water 10 minutes before lunch and dinner while given advice to support a 300 kcal/day energy-deficit diet with moderate-intensity physical activity (Figure 1).

This report provides a comprehensive analysis of the safety and tolerability data of the LIGHT-UP study. The assessments were made by recording treatment-emergent adverse events (TEAEs) and serious TEAEs, and monitoring results from physical examination, vital signs, and fasting laboratory tests, including hematology, blood chemistry, and serum vitamins.

Figure 1



Gelesis200 hydrogel in the gastrointestinal tract.

RESULTS

The intention-to-treat population included 254 adults (males 40.2%, females 59.8%, mean age 49.6 years, mean BMI 34.7 kg/m2, PD 50.8%, untreated T2D 4.3%, treated T2D 44.9%) from 36 investigational sites in Europe and North America (Table 1).

Gelesis200 demonstrated a significant superiority over placebo in terms of weight loss.

The overall incidence and severity of TEAEs was similar between the 2 arms (62.7% vs. 62.2%, with Gelesis200 vs. placebo, respectively) and 95% of all TEAEs in the Gelesis200 arm were mild or moderate in intensity (Tables 2 and 3). The only difference was observed for the system organ class of gastrointestinal disorders where the incidence of constipation was higher with Gelesis200 vs. placebo (14.3% vs. 3.9%) but with no severe cases (Table 4). The incidence of gastrointestinal-related TEAEs over time with Gelesis200 is reported in Figure 2. The incidence of study treatment discontinuation due to TEAEs was 1.6% in both arms. Serious TEAEs were observed in 4.0% and 1.6% of participants on Gelesis200 and placebo, respectively, with no deaths (Table 2). All serious TEAEs were considered unrelated to the investigational product.

No relevant differences in physical examination, vital signs, hematology, blood chemistry (including serum sodium, potassium, calcium, and magnesium), and serum vitamins (vitamins A, B1, B2, B6, B9, B12, D, and E) were observed between the 2 arms.

Table 1

Parameter	Gelesis200 (n = 127)	Placebo (n = 127)	*P* value
Female, n (%)	76 (59.8)	76 (59.8)	NS
Postmenopausal, n (%)	28 (22.0)	30 (23.6)	NS
Age (years)*	50.1 ± 10.7	49.1 ± 10.8	NS
BW (kg)*	100.7 ± 15.5	101.0 ± 17.4	NS
BMI (kg/m^2)*	34.8 ± 3.4	34.6 ± 3.4	NS
Overweight, n (%)	13 (10.2)	13 (10.2)	NS
Obese, n (%)	114 (89.8)	114 (89.8)	NS
WC (cm)*	114.3 ± 11.4	113.1 ± 12.4	NS
Current smokers, n (%)	23 (18.1)	19 (15.0)	NS
Dyslipidemia, n (%)	59 (46.5)	62 (48.8)	NS
Hypertension, n (%)	29 (22.8)	30 (23.6)	NS
PD, n (%)	63 (49.6)	66 (52.0)	NS
Untreated T2D, n (%)	6 (4.7)	5 (3.9)	NS
Treated T2D, n (%)	58 (45.7)	56 (44.1)	NS

N: Number of subjects; BW: Body weight; BMI: Body mass index; WC: Waist circumference; PD: Prediabetes; T2D: Type 2 diabetes; NS: Non-significant; *Mean ± SD.

Baseline characteristics of the intention-to-treat population.

Table 2

Parameter	Gelesis200 (n = 126)	Placebo (n = 127)	*P* value
Any TEAEs, n (%)	79 (62.7)	79 (62.2)	NS
Mild TEAEs, n (%)	28 (22.2)	29 (22.8)	-
Moderate TEAEs, n (%)	47 (37.3)	48. (37.8)	-
Severe TEAEs, n (%)	4 (3.2)	2 (1.6)	-
Any serious TEAEs, n (%)	5 (4.0)	2 (1.6)	NS
Withdrawal due to TEAEs, n (%)	2 (1.6)	2 (1.6)	NS

TEAE: Treatment-emergent adverse event; N: Number of subjects; NS: Non-significant.

Overall characteristics of the TEAEs in the safety population.

Table 3

Parameter	Gelesis200 (n = 126)	Placebo (n = 127)	*P* value
Infections and infestations, n (%)	37 (29.4)	35 (27.6)	NS
Gastrointestinal disorders, n (%)	36 (28.6)	30 (23.6)	NS
Musculoskeletal and connective tissue disorders, n (%)	16 (12.7)	14 (11.0)	NS
Nervous system disorders, n (%)	15 (11.9)	7 (5.5)	NS
Injury, poisoning and procedural complications, n (%)	8 (6.3)	8 (6.3)	NS
Vascular disorders, n (%)	8 (6.3)	4 (3.1)	NS
Investigations, n (%)	6 (4.8)	6 (4.7)	NS
Respiratory, thoracic and mediastinal disorders, n (%)	4 (3.2)	6 (4.7)	NS

TEAE: Treatment-emergent adverse event; N: Number of subjects; NS: Non-significant.

Most common TEAEs by system organ class in the safety population.

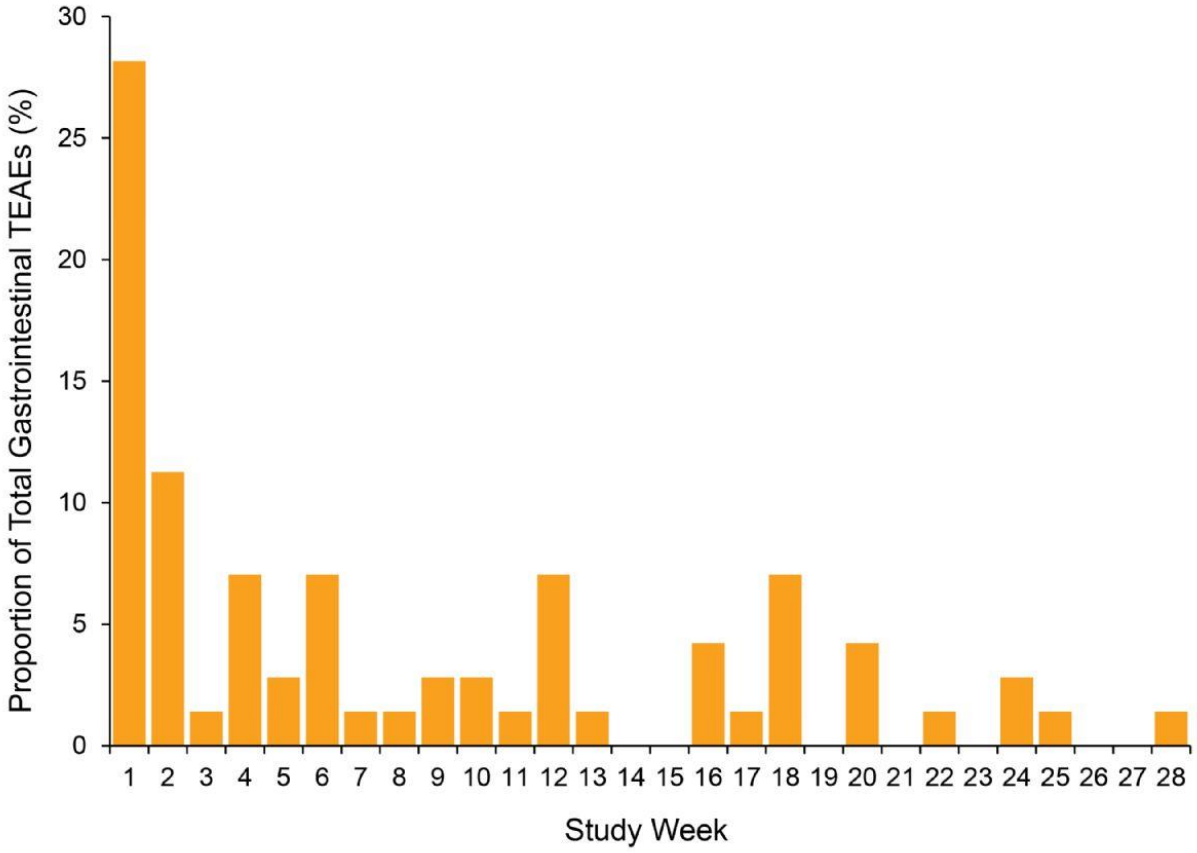
Table 4

Parameter	Gelesis200 (n = 126)	Placebo (n = 127)	*P* value
Constipation, n (%)	18 (14.3)	5 (3.9)	0.0044
Diarrhea, n (%)	10 (7.9)	7 (5.5)	NS
Flatulence, n (%)	9 (7.1)	5 (3.9)	NS
Abdominal distension, n (%)	6 (4.8)	6 (4.7)	NS
Nausea, n (%)	3 (2.4)	6 (4.7)	NS
Vomiting, n (%)	3 (2.4)	3 (2.4)	NS
Abdominal pain, n (%)	2 (1.6)	4 (3.1)	NS

TEAE: Treatment-emergent adverse event; N: Number of subjects; NS: Non-significant.

Most common gastrointestinal TEAEs in the safety population.

Figure 2



Incidence of gastrointestinal-related TEAEs over time in Gelesis200 arm.

CONCLUSIONS

In the LIGHT-UP study, Gelesis200 demonstrated similar safety and tolerability compared to placebo in people with PD or T2D with overweight or obesity.