GELESIS Superabsorbent Hydrogel Prevents Hepatic Steatosis and Insulin Resistance in High Fat Diet–Induced NAFLD Pre-Clinical Model

A. Silvestri, MSc¹; A. Sannino, PhD²; M. Vitale, PhD¹; J. Mouries, PhD¹; I. Spadoni, PhD¹; C. Demitri, PhD²; E. Chiquette, PharmD²; M. Rescigno, PhD¹

Humanitas Clinical and Research Center – IRCCS, via Manzoni 56, 20089 Rozzano (Mi) – Italy; GELESIS Inc, 501 Boylston, Boston, MA, USA

BACKGROUND

- Nonalcoholic fatty liver disease (NAFLD) is an emerging epidemic paralleling obesity and diabetes, without safe and effective clinical therapeutic options.
- Obesity, insulin resistance, and disrupted gut homeostasis are major contributors to the pathophysiology of NAFLD and its progression to nonalcoholic steatohepatitis (NASH).
- GELESIS novel hydrogel platform technology is based on crosslinked, modified cellulose admixed with
  - Gelesis100, the first in this platform technology, demonstrated, in clinical studies, weight loss and improvement in insulin sensitivity
  - Gel-B, with double the viscoelasticity of Gelesis100, was designed to restore gut barrier integrity based on previous preclinical work.

OBJECTIVES

Our aim was to evaluate whether Gel-B can prevent hepatic steatosis by
- Restoring gut barrier function, reducing insulin resistance, affecting gut dysbiosis, and inducing weight loss, all mechanisms involved in NAFLD/NASH.

EXPERIMENTAL DESIGN

- C57BL/6J wild-type male mice were fed with either an isocaloric low-fat diet (LFD; 10% fat, 70% CHO) or high-fat diet (HFD; 45% fat, 36% CHO) for 18 weeks.
- In parallel, 2 groups of mice were fed with HFD that was enhanced with 10% fat, 70% CHO.
- Changes in body weight, glucose/insulin tolerance, glucagon-like peptide 1 (GLP-1), and epididymal adipose tissue (EAT) were measured.
- Oil red O staining was performed to evaluate triglyceride accumulation in the liver.
- Expression of zonula occludens-1 (ZO-1) and circulating levels of bacteria-derived lipopolysaccharides (LPS) were used to assess gut barrier function.
- Feces were collected and total genomic DNA was extracted and sequenced.

RESULTS

Figure 1. Gel-B reduced body weight gain and EAT enlargement

Body weight variation curves and epididymal adipose tissue (EAT) weight at sacrifice displayed in percentage of body weight

Figure 2. Gel-B prevented triglyceride accumulation in liver

Figure 3. Gel-B prevented insulin-resistance development

Figure 4. Gel-B administration increased GLP-1 serum levels

Figure 5. Gel-B administration modified gut microbiota composition

Figure 6. Gel-B improved gut barrier function

DISCLOSURES