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(54) **TREATMENT OF SHORT BOWEL SYNDROME PATIENTS WITH COLON-IN-CONTINUITY**

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(52) **U.S. Cl.**

CPC ***A61K 38/26*** (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

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(57) **ABSTRACT**

Intestinal absorption is enhanced in short bowel syndrome patients presenting with colon-in-continuity by treatment with a GLP-2 receptor agonist, such as teduglutide.

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Figure 1.

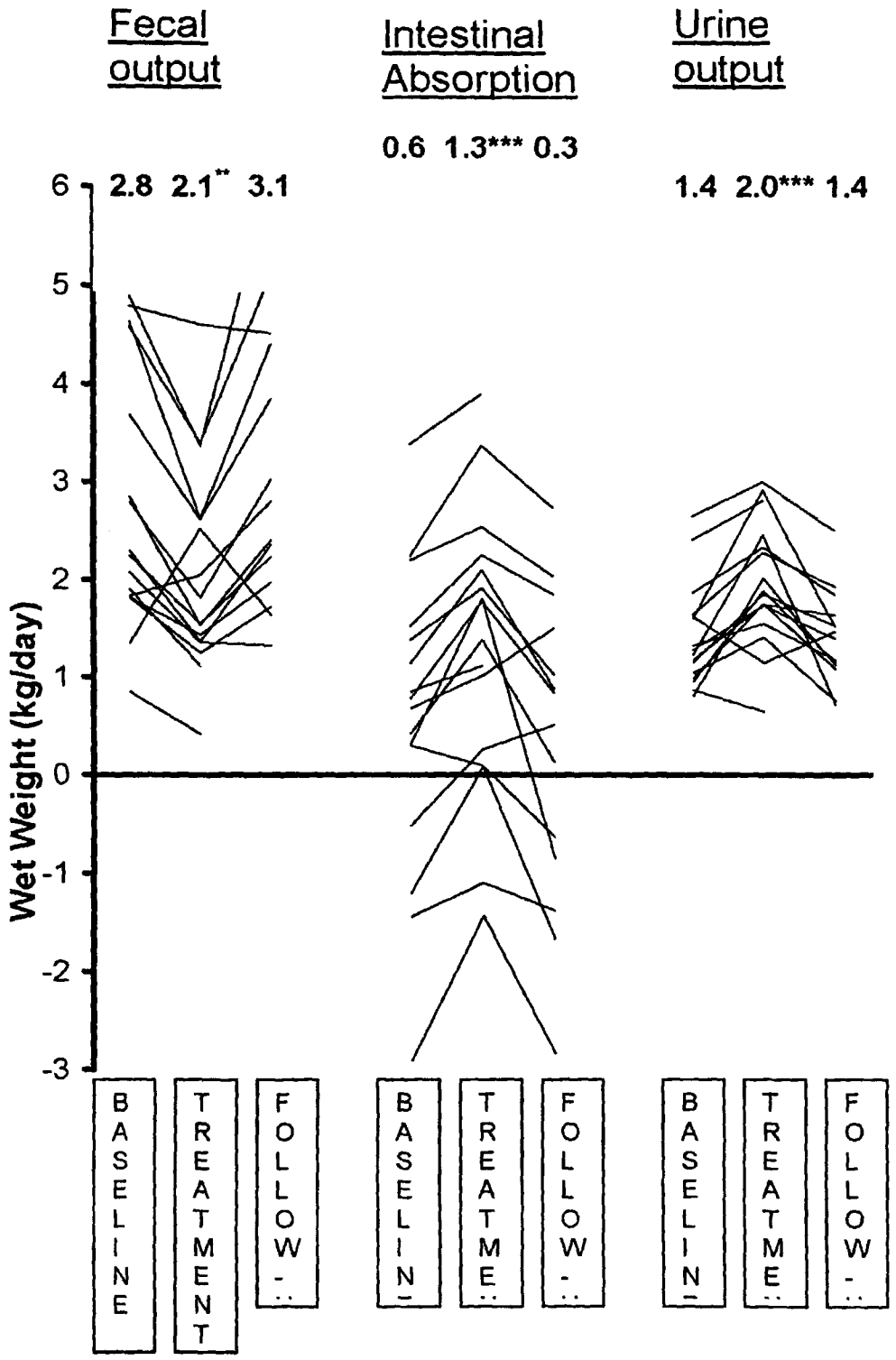
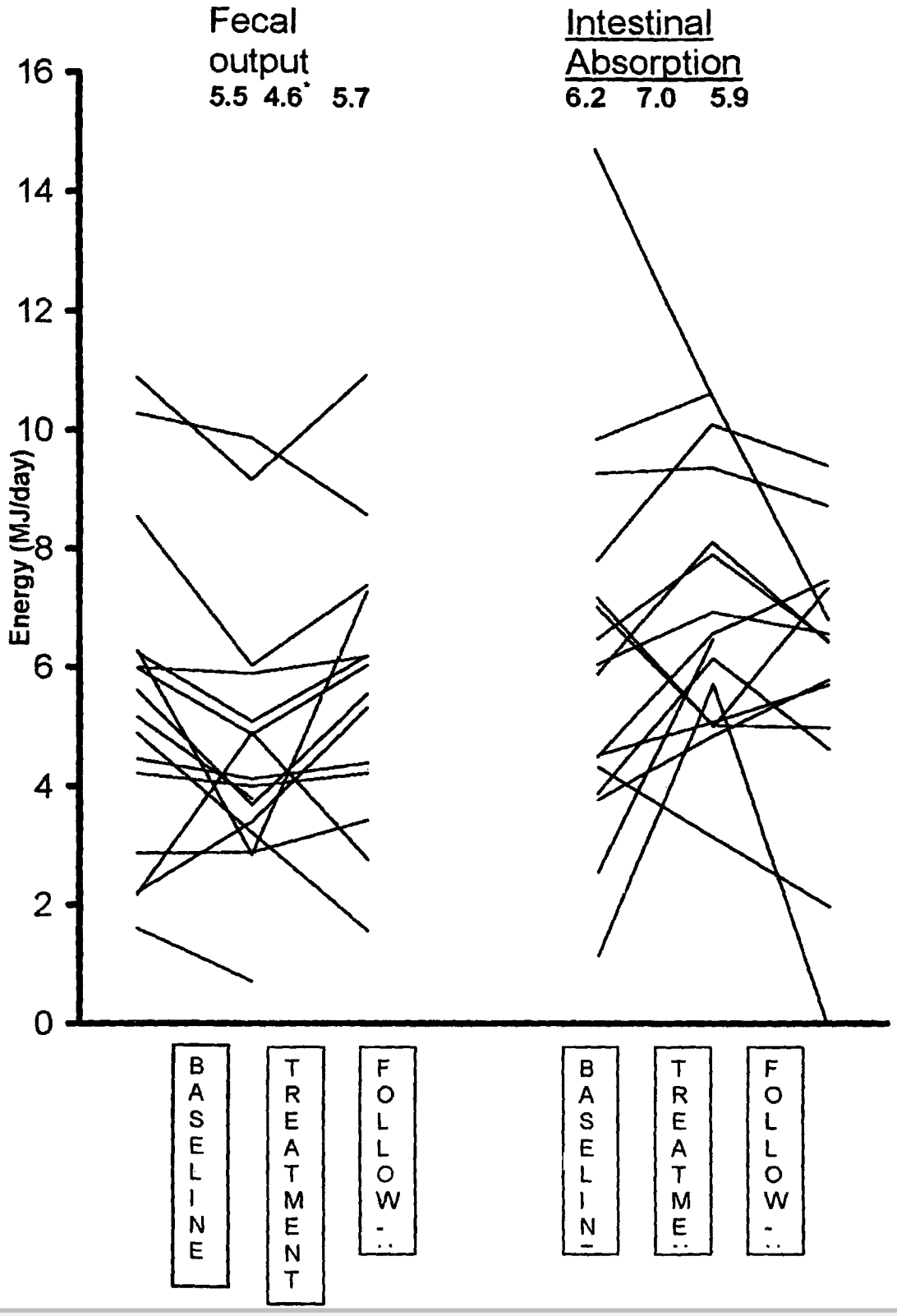


Figure 2.



TREATMENT OF SHORT BOWEL SYNDROME PATIENTS WITH COLON-IN-CONTINUITY

FIELD OF THE INVENTION

This invention relates to products and methods useful medically to treat patients presenting with short bowel syndrome. More particularly, the invention relates to glucagon-like peptide 2 (GLP-2) and other GLP-2 receptor agonists effective to improve intestinal function particularly in patients presenting with short bowel syndrome with colon-in-continuity.

BACKGROUND TO THE INVENTION

The estimated prevalence of short bowel syndrome (SBS) patients with non-malignant disease requiring home parenteral nutrition (HPN) is at least 40 per million of the U.S. population. SBS usually results from surgical resection of some or most of the small intestine for conditions such as Crohn's disease, mesenteric infarction, volvulus, trauma, congenital anomalies, and multiple strictures due to adhesions or radiation. Surgical resection may also include resection of all or part of the colon. SBS patients suffer from malabsorption that may lead to malnutrition, dehydration and weight loss. Some patients can maintain their protein and energy balance through hyperphagia; more rarely they can sustain fluid and electrolyte requirements to become independent from parenteral fluid.

Although long-term parenteral nutrition (PN) is life saving in patients with intestinal failure, it is expensive, impairs quality of life and is associated with serious complications such as catheter sepsis, venous occlusions and liver failure. Treatments that amplify absolute intestinal absorption, and eliminate or minimize the need for PN have great potential significance to SBS patients.

The endogenous meal-stimulated hormone, glucagon-like peptide-2 (GLP-2), raises considerable interest for SBS patients. GLP-2 functions to slow gastric emptying, reduce gastric secretions, increase intestinal blood-flow and stimulate growth of the small and large intestine. In animal studies, GLP-2 administration induces mucosal epithelial proliferation in the stomach and small and large intestine by stimulation of crypt cell proliferation and inhibition of enterocyte apoptosis.

SBS patients with end-jejunostomy and no colon have low basal GLP-2 levels and limited meal-stimulated GLP-2 secretion due to removal of GLP-2 secreting L-cells, which are located primarily in the terminal ileum and colon. This GLP-2 deficiency results in a minimal adaptive response following resection and could explain the gastric hypersecretion, rapid intestinal transit and lack of intestinal adaptation observed in these SBS patients.

Jeppesen et al. (Gastroenterology 2001; 120:806-815) have described positive benefit in an open-label study using pharmacologic doses of native GLP-2 in SBS jejunostomy patients. There was significant improvement in intestinal wet weight absorption and a more modest improvement in energy absorption that led to an increase in body weight, lean body mass and a rise in urinary creatinine excretion.

In contrast, SBS patients with colon-in-continuity have elevated basal endogenous GLP-2 levels resulting in an adap-

benefit of pharmacologic doses of GLP-2 receptor agonists in these patients is not obvious and has not been studied.

SUMMARY OF THE INVENTION

It has now been determined that intestinal absorption is enhanced in SBS patients presenting with colon-in-continuity when those patients are treated with a GLP-2 receptor agonist.

Thus, in one aspect, the present invention provides a method for enhancing intestinal absorption in a patient with short bowel syndrome, comprising the steps of selecting for treatment a short, bowel syndrome patient presenting with at least about 25% colon in continuity with remnant small intestine, and treating said patient with a GLP-2 receptor agonist to enhance intestinal absorption by said patient.

In a related aspect, the present invention provides for the use of a GLP-2 receptor agonist in the preparation of a medicament for enhancing intestinal absorption in short bowel syndrome patients presenting with at least about 25% colon in continuity with remnant small intestine.

In a preferred embodiment, the GLP-2 receptor agonist is [Gly2]hGLP-2, known as teduglutide.

BRIEF REFERENCE TO THE DRAWINGS

Embodiments of the invention are now described with reference to the accompanying drawings in which:

FIG. **1** illustrates results measured in terms of fecal wet weight, intestinal wet weight absorption and urine weight in the individual patients at Baseline (Days—3 to 0), during treatment (Days 18 to 21), and at follow-up (Days 39 to 42).

FIG. **2** illustrates results measured in terms of fecal energy excretion and intestinal absorption in the individual patients at Baseline (Days—3 to 0), during treatment (Days 18 to 21), and at follow-up (Days 39 to 42).

DETAILED DESCRIPTION

The positive effect of GLP-2 receptor agonists on intestinal absorption in SBS patients that retain at least some, e.g., >25%, of their colon is particularly surprising. These patients have essentially retained GLP-2 producing tissue and, indeed, show elevated basal levels of the endogenous GLP-2 that can be as high as meal stimulated levels in normal, healthy individuals and that, in normal individual, is responsible for maintenance of the intestinal lining required for intestinal absorption. There is nevertheless significant clinical benefit for these patients, manifest principally as enhanced intestinal absorption as indicated by increased absolute wet weight absorption, when they are treated in accordance with the present method.

More particularly, patient candidates for the present treatment are those presenting with SBS resulting from small intestine resection which may be secondary to Crohn's disease, vascular ischemic disease, malrotation or volvulus, trauma, congenital anomalies, or multiple strictures due to adhesions or radiation and who require parenteral nutrition to meet their needs. As patients presenting with short bowel syndrome, such patients typically retain, following resection, a length of small intestine that is within the range from at least about 25 cm and at most about 200 cm., e.g., from about 50-150 cm. Such SBS patients include those patients present-

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