***SUPPLEMENTAL DIGITAL CONTENT 1 (SDC1)***

**SUPPLEMENTAL METHODS**

**GES and WMC Methodology Details**

Medications that suppressed acid production were discontinued prior to testing including proton pump inhibitors for 7 days, histamine-2 receptor antagonists for 3 days, and antacids for 1 day. All prokinetics (metoclopramide, erythromycin, domperidone, pyridostigmine), anticholinergic antispasmodics, opiates, cannabinoids, and laxatives were discontinued at least 3 days before testing and were held for 4-7 days after swallowing the WMC. After overnight fasting, subjects presented to the study center for testing. The WMC (SmartPill, Medtronic, Yokneam, Israel) was calibrated and activated prior to testing.

The WMC measures 26 mm x 13 mm and transmits data to a data receiver. WMC sensors measure intraluminal pH (every 5 seconds for the first 24 hours, every 10 seconds from 24-48 hours, and every 2.5 minutes after 48 hours; accurate to +0.5 pH units), pressure from 0-350 mmHg (every 0.5 seconds for the first 24 hours, every second afterwards; accurate to +5 mmHg <100 mmHg and +10% >100 mmHg), and temperature from 25-49oC (every 20 seconds for the first 24 hours, every 40 seconds afterwards; accurate to +1oC)(5).

An egg substitute meal (120 gm egg substitute [Egg Beaters, Conagra Brands, Chicago, IL], 2 bread slices, 30 gm strawberry jam, and 70 mL water—255 kcal, 72% carbohydrate, 24% protein, 2% fat) was consumed over 20 minutes. Anterior and posterior scintigraphic images from the stomach were taken in the 140 keV 99mTc peak with a 20% window (140 keV+10%) immediately after meal completion and 1, 2, and 4 hours after eating. After consuming the radiolabelled meal, the WMC (SmartPill®, Medtronic, Minneapolis, MN) was swallowed with 50 mL water (5). Data receivers were worn for 5 days or until capsules passed in the stool. Subjects refrained from caloric intake for 8 hours after WMC ingestion then consumed 250 mL liquid nutrients (Ensure, Abbott Laboratories, Abbott Park, IL) followed by another hour of fasting before resuming their customary diets.

Abnormal GES and WMC transits were determined using standard analyses (5, 21, 22, 23). Delayed GES gastric emptying was >10% 4 hour retention; rapid emptying was <38% 1 hour retention (2, 3). WMC gastric emptying times (GET) were calculated from ingestion to duodenal passage, defined by persistent >2 pH unit increases to pH>4. Delayed GET was >5 hours; rapid GET was <1:45 hours (21). Abrupt, prolonged >1 hour pH decreases characterized ileocecal junction transit. Small bowel transit times (SBTT) were calculated from pyloric to ileocecal junction passage. Delayed SBTT was >6 hours; rapid SBTT was <2:15 hours (21). Anal evacuation was detected by 0.025oC/second temperature decreases. Colon transit times (CTT) were calculated from ileocecal junction to anal passage. Delayed CTT was >58:45 hours (21).

**Management Decision Protocol Details**

GES findings and WMC digital files were supplied to data managers with the sponsor and then to a central reader within 3 days. Specific medication categories that were queried included prokinetics, antiemetics, neuromodulators (such as tricyclic agents, serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, anitdepressants with more complex pharmacology like mirtazapine and olanzapine, gabapentin, pregabalin, buspirone), laxatives, and transit retardants (such as antidiarrheals, anticholinergic antispasmodics, opiates). Categories of new testing ordered included endoscopy and imaging tests (such as esophagogastroduodenoscopy, colonoscopy, computed tomography, ultrasound, barium contrast radiography), motility tests (such as esophageal, antroduodenal or anorectal manometry, radioopaque marker colon transit studies, dynamic radiography like defecography, gallbladder scintigraphy), and miscellaneous other tests (such as blood studies, lab testing, esophageal pH monitoring, duodenal cultures, nutritional assessments, physical therapy evaluations). As recommendations for test ordering were being compared for GES vs. WMC results, management decisions in which site investigators ordered additional GES testing on the basis of WMC findings or ordered additional WMC testing on the basis of GES findings were not included in these analyses.

In particular, changes recommending new treatments in prokinetics, antiemetics, neuromodulators, laxatives, and transit retardants were compared to gastric emptying profiles including delayed vs. normal GES, delayed vs. normal WMC GET, normal GES vs. normal GET, normal GES vs. normal WMC transit in all 3 gut regions, and delayed GES vs. delayed GET. Changes recommending similar new treatments were also compared to extragastric WMC transit measures including delayed vs. normal SBTT, isolated SBTT delays vs. normal SBTT, delayed vs. normal CTT, isolated CTT delays vs. normal CTT, and isolated transit delays in 1 region vs. generalized transit delays in 2 or more regions. The third subgroup for which new treatments were compared related to rapid transit including rapid vs. normal GES, rapid vs. normal GET, and rapid SBTT vs. normal SBTT.

Changes recommending additional diagnostic tests including endoscopy/imaging, motility testing, and miscellaneous other tests were related to similar gastric and extragastric transit comparisons as for recommended treatment changes. Further comparisons of additional testing recommendations involving advocating multiple (2 or more) motility tests were conducted to define if numbers of tests ordered were influenced by transit findings.