The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

**GSK Medicine:** GSK962040/camicinal

**Study No**: MOT114479

**Title :** A Randomized, Double-Blind, Placebo-Controlled Multicenter Phase II Study to Evaluate the Safety and Efficacy and Dose Response of 28 Days of Once-Daily Dosing of the Oral Motilin Receptor Agonist GSK962040, in Type I and II Diabetic Male and Female Subjects with Gastroparesis

**Rationale:** Gastroparesis is a common complication for patients with diabetes; often resulting in symptoms (post-prandial fullness, nausea, vomiting, abdominal pain) that effect their quality of life. The purpose of this study was to assess the ability of GSK962040 (camicinal) to enhance gastric emptying and improve symptoms of gastroparesis. Additionally, the safety, tolerability, and pharmacokinetics of camicinal was assessed after 28 days of once-daily dosing in Type 1 and Type 2 diabetes mellitus (DM) subjects with gastroparesis.

**Phase:** 2

**Study Period:** 3 May 2011 – 26 Feb 2013

**Study Design:** MOT114479 was a multi-center, randomized, double-blind, placebo controlled study that consisted of a screening/baseline period of up to 45 days, a 28-day treatment period, a post treatment safety follow-up visit and a 14-day post-treatment assessment of symptoms.

**Centres:** 22 sites in Australia (1), Belgium (2), Canada (4), Sweden (1), UK (5), and US (9).

**Indication:** Diabetic gastroparesis

**Treatment:** Subjects were assigned to one of the treatments (10 mg, 50 mg, 125 mg or placebo), in a ratio of 1:1:1:1, in accordance with the randomization schedule generated prior to the start of the study.

**Objectives:** The primary objective was:

- To investigate the pharmacodynamic effect of 28 days of repeated doses of camicinal on gastric emptying of an isotope-labelled test meal, as measured by the 13C-oral breath test (OBT) in DM subjects with gastroparesis.

**Primary Outcome (Endpoints)/Efficacy :** The primary endpoint of the study was gastric half emptying time (GE t½) as measured by the 13C-Oral Breath Test:

**Secondary Outcome (Endpoints)/Efficacy :**

The secondary endpoints of the study included:

- safety and tolerability of camicinal,
- population pharmacokinetic parameters (Cmax, Tmax, and AUC(0-24)),
- change in upper gastrointestinal (GI) symptoms as assessed by Gastroparesis Cardinal Symptom Index- Daily Diary (GCSI–DD; e.g., postprandial fullness, early satiety, nausea, vomiting),
- total gastric emptying time, small bowel transit time, colonic transit time, and total bowel transit time as determined by Wireless Motility Capsule (WMC), and
- bowel movement consistency, frequency and time to first movement.

**Statistical Methods:**

All analyses presented herein were performed on the 'All Subjects Population', which includes all subjects who received at least one dose of study medication. The proposed original sample size of at least N=12 per dose level and placebo was statistically powered (95% power, alpha=0.05) to detect a linear relationship between the primary endpoint GE t1/2 and dose. This was based on the change from placebo observed in study MOT111809 and deemed a relevant change of 98.75 mins (with an assumed between subject SD of 58.7 mins) at the 125 mg dose for GE t1/2. The study was not sized to determine significance in the secondary endpoints (e.g., symptom changes).

Pharmacodynamic Analyses:

Primary outcome:

The dose-response relationship was assessed by estimating the slope of gastric emptying t1/2 against dose [hypothesis testing was not used]. The slope and 95% confidence intervals were estimated using a linear mixed model, including terms for intercept (random), diabetes type and the interaction between dose (as a continuous variable) and visit (either day 1 or day 28). The baseline data for each subject was included in the model with dose=0 to give additional information for the intercept random effect.

Gastric emptying t1/2 was also analysed using a pairwise comparison model (assuming no particular dose-response relationship). The least square mean and 95% CI were estimated for each treatment group at each visit using a mixed

model fitting treatment, visit, treatment*visit, baseline gastric emptying t1/2 as fixed effects, and subject as a random effect. The difference between each active dose group and placebo and 95% CI was also estimated from the model.

Secondary outcomes:
GCSI-DD: For each individual symptom, response was defined as an improvement of at least 1 point on the scale of 0 (=no symptoms) to 5 (=very severe symptoms) from baseline to each week of measurement (weeks 1 to 4 are on treatment, weeks 5 to 6 are follow up). For each week, the proportion of responders in each of the active treatment groups was compared to placebo using a general estimating equation model fitting treatment, visit, treatment*visit and baseline score as fixed effects, and visit as a repeat effect. The odds ratio of treatment to placebo and the corresponding 95% confidence intervals were calculated for each dose group at each week.

Total gastric emptying time was analysed using the same approaches described for the primary outcome. The other WMC parameters were summarised using summary statistics.

Bowel movement parameters were analysed using the pairwise approach described for the primary outcome apart from time to first movement which was summarised using summary statistics.

Safety Analyses: These data are summarized descriptively.

Pharmacokinetic Analyses: Population PK modelling, using non-linear mixed effects methods was performed using NONMEM (Version VII) and appropriate model validation procedures. Individual camicinal concentration-time profiles for Days 1 and 28 were simulated using PK parameters and inter- and intra-individual variability estimates from the model. PK parameters where calculated from these concentration-time profiles using noncompartmental methods.

**Study Population:** Eligible subjects were males and females between 18 and 80 years of age with controlled T1 or T2DM (HbA1C <11%) with gastroparesis at screening and at least a 3 month history of relevant symptoms of gastroparesis (e.g., chronic post-prandial fullness, early satiety, post-prandial nausea); confirmed with a minimum mean GCSI-DD score (spanning 7 days) ≥ 2 (mild) for post prandial fullness. Gastroparesis was confirmed with a half time of gastric emptying > upper limit of normal or % $^{13}C$ dose recovered < lower limit of normal as determined by $^{13}C$ oral breath test.

| **Number of Subjects** | **Placebo** | **Camicinal** | | | **Total** |
|---|---|---|---|---|---|
| | | **10 mg** | **50 mg** | **125 mg** | |
| Number of subjects planned, N: | 20 | 20 | 20 | 20 | 80 |
| Number of subjects randomized, N: | 21 | 18 | 19 | 22 | 80 |
| Number of subjects included in All subjects (safety) population, n (%): | 21 (100) | 18 (100) | 18 (95) | 22 (100) | 79 (98) |
| Number of subjects included in PK population, n (%): | 0 | 18 (100) | 18 (95) | 22 (100) | 58 (72) |
| Number of subjects completed as planned, n (%): | 18 (86) | 16 (89) | 18 (95) | 22 (100) | 74 (93) |
| Number of subjects withdrawn (any reason), n (%): | 3 (14) | 2 (11) | 0* | 0 | 5 (6) |
| Number of subjects withdrawn for AE, n (%): | 0 | 0 | 0 | 0 | 0 |
| Withdrawn due to Lack of Efficacy n (%) | 0 | 0 | 0 | 0 | 0 |
| Reasons for subject withdrawal, n (%) | | | | | |
| Protocol Deviation | 1 (5) | 1(6) | 0 | 0 | 2 (3) |
| Lost to Follow-up | 1 (5) | 0 | 0 | 0 | 1 (1) |
| Withdrew consent | 1 (5) | 1 (6) | 0 | 0 | 2 (3) |
| **Demographics** | **Placebo** | **Camicinal** | | | **Total** |
| | | **10 mg** | **50 mg** | **125 mg** | |
| Females: Males | 14:7 | 14:4 | 10:8 | 9:13 | 47:32 |

| | | | | | |
|---|---|---|---|---|---|
| Mean Age in Years (sd) | 54.6 (14.2) | 54.0 (11.4) | 55.2 (12.2) | 51.4 (11.3) | 53.7 (12.2) |
| Mean Weight in Kg (sd) | 76.7 (12.00) | 87.7 (20.78) | 83.1 (18.63) | 84.8 (17.97) | 82.9 (17.62) |
| **Race, n (%)** | | | | | |
| White – White/Caucasian/European Heritage | 19 (90) | 15 (83) | 17 (94) | 20 (91) | 71 (90) |

*One subject that was allocated to Camicinal 50 mg, withdrew consent prior to dosing.

**Primary Efficacy Results:**

Pharmacodynamic results

**Summary of Statistical Analysis of Dose Response for Gastric Emptying Half Time (T½ (min)): Linear Model**

| Disease Type | Treatment (n) | | | | Slope | Intercept Est. | Slope Est. | 95% CI of Point Estimate | Between Subject SD |
|---|---|---|---|---|---|---|---|---|---|
| | Placebo | Camicinal | | | | | | | |
| | | 10 mg | 50 mg | 125 mg | | | | | |
| Type 1 Diabetes | 11 | 9 | 9 | 12 | Day 1 | 125.45 | -0.225 | (-0.320, -0.129) | 21.63 |
| | | | | | Day 28 | | -0.078 | (-0.171, 0.016) | |
| Type 2 Diabetes | 10 | 9 | 9 | 10 | Day 1 | 113.23 | -0.225 | (-0.320, -0.129) | |
| | | | | | Day 28 | | -0.078 | (-0.171, 0.016) | |

Due to the different response patterns at day 1 and day 28, separate slopes were fitted for each visit and due to an imbalance at baseline between diabetes types, different intercepts were fitted for each type (but same slopes).

**Summary of Statistical Analysis of Dose Response for Gastric Emptying Half Time (T½ (min)): Pairwise Comparison**

| Comparison (Test vs. Ref.) | Test N | LSM Test | Ref. N | LSM Ref. | Point Est. | 95% CI for True Diff. | Between Subject SD |
|---|---|---|---|---|---|---|---|
| Camicinal 10 mg vs Placebo Day 1 | 18 | 115.93 | 21 | 119.29 | -3.36 | (-21.96, 15.24) | 14.47 |
| Camicinal 50 mg vs Placebo Day 1 | 18 | 107.49 | | | -11.81 | (-30.01, 6.40) | |
| Camicinal 125 mg vs Placebo Day 1 | 21 | 93.64 | | | -25.65 | (-42.99, -8.32) | |
| Camicinal 10 mg vs Placebo Day 28 | 16 | 112.11 | 18 | 106.38 | 14.74 | (-5.06, 34.53) | |
| Camicinal 50 mg vs Placebo Day 28 | 18 | 110.60 | | | 4.22 | (-14.64, 23.08) | |
| Camicinal 125 mg vs Placebo Day 28 | 22 | 113.03 | | | 6.65 | (-11.18, 24.47) | |
| | | | | | | | |
| Day 28 vs Day 1 Placebo | 18 | 106.38 | 21 | 119.29 | -12.92 | (-28.73, 2.90) | 14.47 |
| Day 28 vs Day 1 Camicinal 10 mg | 16 | 121.11 | 18 | 115.93 | 5.18 | (-11.69, 22.05) | |
| Day 28 vs Day 1 Camicinal 50 mg | 18 | 110.60 | 18 | 107.49 | 3.11 | (-13.13, 19.36) | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Day 28 vs Day 1 Camicinal 125 mg | 22 | 113.03 | 21 | 93.64 | 19.39 | (4.47, 34.30) | |

LSM = Least Squares Means

**Secondary Outcome Results:**
**Pharmacokinetics (PK),pharmacodynamics (PD), PK/PD Endpoints:**
Pharmacokinetic parameters of Camicinal
**Summary of Selected Camicinal Plasma Pharmacokinetic Parameters**

| Parameter | Camicinal | | | | | |
|---|---|---|---|---|---|---|
| | 10 mg | | 50 mg | | 125 mg | |
| | Day 1 (n=15) | Day 28 (n=15) | Day 1 (n=18) | Day 28 (n=15) | Day 1 (n=21) | Day 28 (n=21) |
| AUC (0-24) (ng.h/mL)* Geom. Mean (CVb%) | 854.9 (36.6) | 1908.1 (46.1) | 4083.1 (23.6) | 7347.2 (24.3) | 12911.9 (30.0) | 22173.3 (31.8) |
| Cmax (ng/mL)* Geom. Mean (CVb%) | 70.21 (54.7) | 131.71 (52.9) | 385.73 (27.6) | 530.97 (34.0) | 1239.62 (40.0) | 1703.29 (38.0) |
| Tmax (h) Median (Min, Max) | 1.58 (1.40, 4.55) | 1.50 (1.50, 6.33) | 1.50 (1.50-4.52) | 2.5 (1.50, 3.50) | 1.67 (1.50-4.50) | 1.52 (0.00-5.50) |

*=Log-transformed
CVb%: coefficient of variation between subjects

**Summary of Result of Statistical Analysis of GCSI-DD Response: Generalised Estimating Equations Model**

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Nausea | Camicinal 10 mg vs Placebo | Week 1 | 4/11 (36%) | 7/19 (37%) | 0.63 | (0.105, 3.723) |
| | | Week 2 | 8/14 (57%) | 8/20 (40%) | 1.28 | (0.243, 6.751) |
| | | Week 3 | 10/15 (67%) | 8/19 (42%) | 2.29 | (0.452, 11.590) |
| | | Week 4 | 11/16 (69%) | 9/16 (56%) | 1.51 | (0.410, 5.555) |
| | | Week 5 (FU) | 9/15 (60%) | 8/18 (44%) | 1.26 | (0.259, 6.088) |
| | | Week 6 (FU) | 6/13 (46%) | 8/17 (47%) | 0.59 | (0.126, 2.794) |
| | Camicinal 50 mg vs Placebo | Week 1 | 8/17 (47%) | 7/19 (37%) | 1.26 | (0.273, 5.844) |
| | | Week 2 | 12/17 (71%) | 8/20 (40%) | 3.35 | (0.758, 14.833) |
| | | Week 3 | 11/17 (65%) | 8/19 (42%) | 2.20 | (0.503, 9.627) |
| | | Week 4 | 8/16 (50%) | 9/16 (56%) | 0.53 | (0.145, 1.932) |
| | | Week 5 (FU) | 11/16 (69%) | 8/18 (44%) | 2.40 | (0.545, 10.602) |
| | | Week 6 (FU) | 9/14 (64%) | 8/17 (47%) | 1.22 | (0.292, 5.135) |
| | Camicinal 125 mg vs Placebo | Week 1 | 6/21 (29%) | 7/19 (37%) | 0.75 | (0.150, 3.705) |
| | | Week 2 | 6/22 (27%) | 8/20 (40%) | 0.43 | (0.095, 1.957) |
| | | Week 3 | 7/22 (32%) | 8/19 (42%) | 0.54 | (0.107, 2.742) |
| | | Week 4 | 10/22 (45%) | 9/16 (56%) | 0.51 | (0.119, 2.195) |
| | | Week 5 (FU) | 8/22 (36%) | 8/18 (44%) | 0.50 | (0.097, 2.577) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | Week 6 (FU) | 6/21 (29%) | 8/17 (47%) | 0.27 | (0.056, 1.311) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Postprandial fullness | Camicinal 10 mg vs Placebo | Week 1 | 3/11 (27%) | 6/19 (32%) | 1.16 | (0.245, 5.522) |
| | | Week 2 | 6/14 (43%) | 5/20 (25%) | 2.07 | (0.455, 9.391) |
| | | Week 3 | 11/15 (73%) | 9/19 (47%) | 2.51 | (0.609, 10.347) |
| | | Week 4 | 11/16 (69%) | 6/16 (38%) | 3.39 | (0.819, 14.037) |
| | | Week 5 (FU) | 9/15 (60%) | 7/18 (39%) | 2.07 | (0.515, 8.278) |
| | | Week 6 (FU) | 7/13 (54%) | 8/17 (47%) | 1.04 | (0.261, 4.119) |
| | Camicinal 50 mg vs Placebo | Week 1 | 3/17 (18%) | 6/19 (32%) | 0.50 | (0.104, 2.419) |
| | | Week 2 | 11/17 (65%) | 5/20 (25%) | 6.02 | (1.387, 26.124) |
| | | Week 3 | 9/17 (53%) | 9/19 (47%) | 1.28 | (0.328, 5.002) |
| | | Week 4 | 9/16 (56%) | 6/16 (38%) | 2.24 | (0.559, 8.957) |
| | | Week 5 (FU) | 10/16 (63%) | 7/18 (39%) | 2.42 | (0.568, 10.331) |
| | | Week 6 (FU) | 8/14 (57%) | 8/17 (47%) | 1.53 | (0.383, 6.097) |
| | Camicinal 125 mg vs Placebo | Week 1 | 8/21 (38%) | 6/19 (32%) | 1.29 | (0.345, 4.817) |
| | | Week 2 | 10/22 (45%) | 5/20 (25%) | 2.58 | (0.651, 10.219) |
| | | Week 3 | 11/22 (50%) | 9/19 (47%) | 1.08 | (0.302, 3.891) |
| | | Week 4 | 12/22 (55%) | 6/16 (38%) | 1.83 | (0.505, 6.637) |
| | | Week 5 (FU) | 12/22 (55%) | 7/18 (39%) | 1.56 | (0.426, 5.682) |
| | | Week 6 (FU) | 10/21 (48%) | 8/17 (47%) | 0.77 | (0.218, 2.704) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Bloating | Camicinal 10 mg vs Placebo | Week 1 | 1/11 (9%) | 5/19 (26%) | 0.41 | (0.070, 2.434) |
| | | Week 2 | 4/14 (29%) | 6/20 (30%) | 0.80 | (0.184, 3.519) |
| | | Week 3 | 10/15 (67%) | 9/19 (47%) | 1.65 | (0.417, 6.548) |
| | | Week 4 | 11/16 (69%) | 5/16 (31%) | 3.69 | (0.917, 14.819) |
| | | Week 5 (FU) | 8/15 (53%) | 8/18 (44%) | 1.49 | (0.387, 5.718) |
| | | Week 6 (FU) | 6/13 (46%) | 8/17 (47%) | 0.72 | (0.170, 3.042) |
| | Camicinal 50 mg vs Placebo | Week 1 | 3/17 (18%) | 5/19 (26%) | 0.56 | (0.115, 2.737) |
| | | Week 2 | 11/17 (65%) | 6/20 (30%) | 3.74 | (0.969, 14.476) |
| | | Week 3 | 8/17 (47%) | 9/19 (47%) | 0.81 | (0.208, 3.121) |
| | | Week 4 | 10/16 (63%) | 5/16 (31%) | 2.83 | (0.687, 11.637) |
| | | Week 5 (FU) | 10/16 (63%) | 8/18 (44%) | 1.95 | (0.513, 7.424) |
| | | Week 6 (FU) | 7/14 (50%) | 8/17 (47%) | 1.42 | (0.344, 5.895) |
| | Camicinal 125 mg vs Placebo | Week 1 | 6/21 (29%) | 5/19 (26%) | 1.03 | (0.264, 4.004) |
| | | Week 2 | 8/22 (36%) | 6/20 (30%) | 1.22 | (0.343, 4.344) |
| | | Week 3 | 8/22 (36%) | 9/19 (47%) | 0.55 | (0.155, 1.952) |
| | | Week 4 | 9/22 (41%) | 5/16 (31%) | 1.16 | (0.335, 4.044) |
| | | Week 5 (FU) | 9/22 (41%) | 8/18 (44%) | 0.86 | (0.246, 2.972) |
| | | Week 6 (FU) | 7/21 (33%) | 8/17 (47%) | 0.48 | (0.133, 1.755) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Early satiety | Camicinal 10 mg vs Placebo | Week 1 | 4/11 (36%) | 5/19 (26%) | 1.66 | (0.358, 7.734) |
| | | Week 2 | 8/14 (57%) | 6/20 (30%) | 2.90 | (0.666, 12.628) |
| | | Week 3 | 11/15 (73%) | 6/19 (32%) | 4.99 | (1.171, 21.293) |
| | | Week 4 | 10/16 (63%) | 6/16 (38%) | 2.70 | (0.675, 10.836) |
| | | Week 5 (FU) | 11/15 (73%) | 10/18 (56%) | 1.83 | (0.424, 7.850) |
| | | Week 6 (FU) | 9/13 (69%) | 9/17 (53%) | 1.40 | (0.325, 5.992) |
| | Camicinal 50 mg vs Placebo | Week 1 | 3/17 (18%) | 5/19 (26%) | 0.58 | (0.107, 3.099) |
| | | Week 2 | 10/17 (59%) | 6/20 (30%) | 4.18 | (0.935, 18.671) |
| | | Week 3 | 8/17 (47%) | 6/19 (32%) | 2.03 | (0.514, 7.982) |
| | | Week 4 | 7/16 (44%) | 6/16 (38%) | 1.55 | (0.394, 6.121) |
| | | Week 5 (FU) | 8/16 (50%) | 10/18 (56%) | 0.68 | (0.172, 2.677) |
| | | Week 6 (FU) | 4/14 (29%) | 9/17 (53%) | 0.34 | (0.073, 1.625) |
| | Camicinal 125 mg vs Placebo | Week 1 | 5/21 (24%) | 5/19 (26%) | 0.97 | (0.221, 4.248) |
| | | Week 2 | 6/22 (27%) | 6/20 (30%) | 1.16 | (0.263, 5.095) |
| | | Week 3 | 7/22 (32%) | 6/19 (32%) | 1.23 | (0.301, 5.052) |
| | | Week 4 | 7/22 (32%) | 6/16 (38%) | 0.97 | (0.254, 3.722) |
| | | Week 5 (FU) | 6/22 (27%) | 10/18 (56%) | 0.33 | (0.081, 1.369) |
| | | Week 6 (FU) | 7/21 (33%) | 9/17 (53%) | 0.46 | (0.114, 1.821) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Retching | Camicinal 10 mg vs Placebo | Week 1 | 6/11 (55%) | 5/19 (26%) | 2.26 | (0.265, 19.240) |
| | | Week 2 | 8/14 (57%) | 5/20 (25%) | 2.11 | (0.365, 12.165) |
| | | Week 3 | 10/15 (67%) | 4/19 (21%) | 6.25 | (0.853, 45.723) |
| | | Week 4 | 9/16 (56%) | 6/16 (38%) | 1.16 | (0.299, 4.535) |
| | | Week 5 (FU) | 8/15 (53%) | 6/18 (33%) | 0.88 | (0.159, 4.896) |
| | | Week 6 (FU) | 7/13 (54%) | 5/17 (29%) | 1.27 | (0.249, 6.516) |
| | Camicinal 50 mg vs Placebo | Week 1 | 3/17 (18%) | 5/19 (26%) | 0.26 | (0.031, 2.212) |
| | | Week 2 | 10/17 (59%) | 5/20 (25%) | 4.67 | (1.066, 20.473) |
| | | Week 3 | 11/17 (65%) | 4/19 (21%) | 9.19 | (1.485, 56.825) |
| | | Week 4 | 9/16 (56%) | 6/16 (38%) | 1.99 | (0.475, 8.323) |
| | | Week 5 (FU) | 9/16 (56%) | 6/18 (33%) | 1.97 | (0.415, 9.379) |
| | | Week 6 (FU) | 5/14 (36%) | 5/17 (29%) | 0.71 | (0.139, 3.628) |
| | Camicinal 125 mg vs Placebo | Week 1 | 6/21 (29%) | 5/19 (26%) | 0.87 | (0.131, 5.831) |
| | | Week 2 | 7/22 (32%) | 5/20 (25%) | 0.85 | (0.149, 4.897) |
| | | Week 3 | 8/22 (36%) | 4/19 (21%) | 1.48 | (0.200, 10.988) |
| | | Week 4 | 9/22 (41%) | 6/16 (38%) | 0.59 | (0.132, 2.671) |
| | | Week 5 (FU) | 8/22 (36%) | 6/18 (33%) | 0.52 | (0.088, 3.119) |
| | | Week 6 (FU) | 7/21 (33%) | 5/17 (29%) | 0.51 | (0.085, 3.014) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|

| | | | | | | |
|---|---|---|---|---|---|---|
| Vomiting | Camicinal 10 mg vs Placebo | Week 1 | 2/11 (18%) | 3/19 (16%) | 0.90 | (0.033, 24.501) |
| | | Week 2 | 3/14 (21%) | 3/20 (15%) | 0.54 | (0.052, 5.650) |
| | | Week 3 | 5/15 (33%) | 3/19 (16%) | 2.81 | (0.365, 21.669) |
| | | Week 4 | 5/16 (31%) | 3/16 (19%) | 1.98 | (0.506, 7.727) |
| | Camicinal 50 mg vs Placebo | Week 1 | 3/17 (18%) | 3/19 (16%) | 2.20 | (0.119, 40.673) |
| | | Week 2 | 5/17 (29%) | 3/20 (15%) | 7.88 | (1.232, 50.419) |
| | | Week 3 | 4/17 (24%) | 3/19 (16%) | 2.63 | (0.348, 19.883) |
| | | Week 4 | 4/16 (25%) | 3/16 (19%) | 4.33 | (0.875, 21.449) |
| | Camicinal 125 mg vs Placebo | Week 1 | 2/21 (10%) | 3/19 (16%) | 0.16 | (0.001, 18.696) |
| | | Week 2 | 2/22 (9%) | 3/20 (15%) | 0.10 | (0.002, 5.440) |
| | | Week 3 | 2/22 (9%) | 3/19 (16%) | 0.12 | (0.004, 3.684) |
| | | Week 4 | 4/22 (18%) | 3/16 (19%) | 0.58 | (0.031, 10.875) |

*For Vomiting, the model could not run when follow-up data was included. Therefore only the odds ratios for weeks 1-4 are reported.

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Rati o |
|---|---|---|---|---|---|---|
| Stomach/belly visibly larger | Camicinal 10 mg vs Placebo | Week 1 | 3/11 (27%) | 6/19 (32%) | 0.72 | (0.130, 3.971) |
| | | Week 2 | 4/14 (29%) | 6/20 (30%) | 0.73 | (0.154, 3.482) |
| | | Week 3 | 6/15 (40%) | 8/19 (42%) | 0.78 | (0.203, 3.007) |
| | | Week 4 | 8/16 (50%) | 6/16 (38%) | 1.83 | (0.467, 7.175) |
| | | Week 5 (FU) | 6/15 (40%) | 6/18 (33%) | 1.08 | (0.278, 4.173) |
| | | Week 6 (FU) | 6/13 (46%) | 6/17 (35%) | 1.33 | (0.350, 5.081) |
| | Camicinal 50 mg vs Placebo | Week 1 | 4/17 (24%) | 6/19 (32%) | 0.90 | (0.211, 3.825) |
| | | Week 2 | 10/17 (59%) | 6/20 (30%) | 4.37 | (1.002, 19.025 |
| | | Week 3 | 6/17 (35%) | 8/19 (42%) | 0.86 | (0.229, 3.238) |
| | | Week 4 | 7/16 (44%) | 6/16 (38%) | 1.75 | (0.425, 7.194) |
| | | Week 5 (FU) | 8/16 (50%) | 6/18 (33%) | 2.09 | (0.536, 8.111) |
| | | Week 6 (FU) | 7/14 (50%) | 6/17 (35%) | 2.69 | (0.601, 12.065 |
| | Camicinal 125 mg vs Placebo | Week 1 | 6/21 (29%) | 6/19 (32%) | 0.92 | (0.232, 3.685) |
| | | Week 2 | 7/22 (32%) | 6/20 (30%) | 1.17 | (0.292, 4.660) |
| | | Week 3 | 7/22 (32%) | 8/19 (42%) | 0.64 | (0.180, 2.295) |
| | | Week 4 | 10/22 (45%) | 6/16 (38%) | 1.54 | (0.412, 5.735) |
| | | Week 5 (FU) | 9/22 (41%) | 6/18 (33%) | 1.30 | (0.369, 4.583) |
| | | Week 6 (FU) | 7/21 (33%) | 6/17 (35%) | 0.76 | (0.202, 2.825) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Stomach fullness | Camicinal 10 mg vs Placebo | Week 1 | 4/11 (36%) | 3/19 (16%) | 3.28 | (0.638, 16.900) |
| | | Week 2 | 5/14 (36%) | 6/20 (30%) | 0.98 | (0.222, 4.290) |
| | | Week 3 | 10/15 (67%) | 6/19 (32%) | 2.95 | (0.784, 11.081) |
| | | Week 4 | 11/16 (69%) | 4/16 (25%) | 5.82 | (1.445, 23.437) |
| | | Week 5 (FU) | 10/15 (67%) | 7/18 (39%) | 2.64 | (0.709, 9.828) |
| | | Week 6 (FU) | 6/13 (46%) | 7/17 (41%) | 1.05 | (0.251, 4.405) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Camicinal 50 mg vs Placebo | Week 1 | 7/17 (41%) | 3/19 (16%) | 3.50 | (0.760, 16.090) |
| | | Week 2 | 12/17 (71%) | 6/20 (30%) | 4.91 | (1.223, 19.674) |
| | | Week 3 | 12/17 (71%) | 6/19 (32%) | 4.20 | (1.118, 15.774) |
| | | Week 4 | 10/16 (63%) | 4/16 (25%) | 4.65 | (1.168, 18.495) |
| | | Week 5 (FU) | 9/16 (56%) | 7/18 (39%) | 2.14 | (0.562, 8.186) |
| | | Week 6 (FU) | 7/14 (50%) | 7/17 (41%) | 1.59 | (0.403, 6.282) |
| | Camicinal 125 mg vs Placebo | Week 1 | 5/21 (24%) | 3/19 (16%) | 1.59 | (0.342, 7.341) |
| | | Week 2 | 7/22 (32%) | 6/20 (30%) | 1.02 | (0.263, 3.944) |
| | | Week 3 | 7/22 (32%) | 6/19 (32%) | 0.90 | (0.251, 3.210) |
| | | Week 4 | 9/22 (41%) | 4/16 (25%) | 2.04 | (0.541, 7.697) |
| | | Week 5 (FU) | 11/22 (50%) | 7/18 (39%) | 1.74 | (0.473, 6.429) |
| | | Week 6 (FU) | 6/21 (29%) | 7/17 (41%) | 0.63 | (0.168, 2.354) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Loss of appetite | Camicinal 10 mg vs Placebo | Week 1 | 5/11 (45%) | 2/19 (11%) | 8.10 | (1.155, 56.875) |
| | | Week 2 | 7/14 (50%) | 4/20 (20%) | 3.65 | (0.796, 16.698) |
| | | Week 3 | 10/15 (67%) | 6/19 (32%) | 4.11 | (1.047, 16.128) |
| | | Week 4 | 11/16 (69%) | 5/16 (31%) | 4.78 | (1.131, 20.165) |
| | | Week 5 (FU) | 10/15 (67%) | 7/18 (39%) | 3.72 | (0.858, 16.123) |
| | | Week 6 (FU) | 10/13 (77%) | 7/17 (41%) | 3.47 | (0.742, 16.252) |
| | Camicinal 50 mg vs Placebo | Week 1 | 7/17 (41%) | 2/19 (11%) | 6.10 | (0.874, 42.598) |
| | | Week 2 | 13/17 (76%) | 4/20 (20%) | 14.84 | (3.562, 61.809) |
| | | Week 3 | 13/17 (76%) | 6/19 (32%) | 7.89 | (2.250, 27.639) |
| | | Week 4 | 13/16 (81%) | 5/16 (31%) | 10.29 | (2.725, 38.829) |
| | | Week 5 (FU) | 9/16 (56%) | 7/18 (39%) | 1.97 | (0.419, 9.313) |
| | | Week 6 (FU) | 7/14 (50%) | 7/17 (41%) | 1.74 | (0.375, 8.122) |
| | Camicinal 125 mg vs Placebo | Week 1 | 5/21 (24%) | 2/19 (11%) | 3.53 | (0.505, 24.712) |
| | | Week 2 | 8/22 (36%) | 4/20 (20%) | 3.07 | (0.679, 13.838) |
| | | Week 3 | 8/22 (36%) | 6/19 (32%) | 1.70 | (0.417, 6.911) |
| | | Week 4 | 6/22 (27%) | 5/16 (31%) | 0.90 | (0.220, 3.717) |
| | | Week 5 (FU) | 9/22 (41%) | 7/18 (39%) | 1.38 | (0.324, 5.882) |
| | | Week 6 (FU) | 7/21 (33%) | 7/17 (41%) | 0.74 | (0.174, 3.107) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Upper abdominal pain | Camicinal 10 mg vs Placebo | Week 1 | 2/11 (18%) | 8/19 (42%) | 0.41 | (0.093, 1.848) |
| | | Week 2 | 7/14 (50%) | 7/20 (35%) | 1.37 | (0.309, 6.087) |
| | | Week 3 | 8/15 (53%) | 7/19 (37%) | 1.31 | (0.314, 5.470) |
| | | Week 4 | 10/16 (63%) | 6/16 (38%) | 3.05 | (0.730, 12.735) |
| | | Week 5 (FU) | 8/15 (53%) | 7/18 (39%) | 0.97 | (0.215, 4.420) |
| | | Week 6 (FU) | 6/13 (46%) | 7/17 (41%) | 0.74 | (0.130, 4.241) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Camicinal 50 mg vs Placebo | Week 1 | 5/17 (29%) | 8/19 (42%) | 0.51 | (0.122, 2.113) |
| | | Week 2 | 10/17 (59%) | 7/20 (35%) | 2.12 | (0.509, 8.804) |
| | | Week 3 | 10/17 (59%) | 7/19 (37%) | 2.05 | (0.489, 8.638) |
| | | Week 4 | 7/16 (44%) | 6/16 (38%) | 1.64 | (0.373, 7.218) |
| | | Week 5 (FU) | 7/16 (44%) | 7/18 (39%) | 0.75 | (0.172, 3.267) |
| | | Week 6 (FU) | 5/14 (36%) | 7/17 (41%) | 0.56 | (0.120, 2.618) |
| | Camicinal 125 mg vs Placebo | Week 1 | 4/21 (19%) | 8/19 (42%) | 0.33 | (0.082, 1.363) |
| | | Week 2 | 6/22 (27%) | 7/20 (35%) | 0.51 | (0.120, 2.136) |
| | | Week 3 | 7/22 (32%) | 7/19 (37%) | 0.64 | (0.159, 2.536) |
| | | Week 4 | 8/22 (36%) | 6/16 (38%) | 1.10 | (0.283, 4.298) |
| | | Week 5 (FU) | 7/22 (32%) | 7/18 (39%) | 0.51 | (0.121, 2.158) |
| | | Week 6 (FU) | 8/21 (38%) | 7/17 (41%) | 0.67 | (0.160, 2.829) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Upper abdominal discomfort | Camicinal 10 mg vs Placebo | Week 1 | 2/11 (18%) | 7/19 (37%) | 0.48 | (0.100, 2.349) |
| | | Week 2 | 7/14 (50%) | 8/20 (40%) | 1.56 | (0.375, 6.492) |
| | | Week 3 | 10/15 (67%) | 7/19 (37%) | 3.20 | (0.790, 12.970 |
| | | Week 4 | 12/16 (75%) | 7/16 (44%) | 5.61 | (1.325, 23.748 |
| | | Week 5 (FU) | 9/15 (60%) | 7/18 (39%) | 1.76 | (0.447, 6.926) |
| | | Week 6 (FU) | 5/13 (38%) | 8/17 (47%) | 0.56 | (0.122, 2.573) |
| | Camicinal 50 mg vs Placebo | Week 1 | 5/17 (29%) | 7/19 (37%) | 0.80 | (0.204, 3.146) |
| | | Week 2 | 11/17 (65%) | 8/20 (40%) | 2.75 | (0.724, 10.406 |
| | | Week 3 | 11/17 (65%) | 7/19 (37%) | 3.21 | (0.877, 11.755 |
| | | Week 4 | 6/16 (38%) | 7/16 (44%) | 1.13 | (0.293, 4.373) |
| | | Week 5 (FU) | 7/16 (44%) | 7/18 (39%) | 1.26 | (0.339, 4.711) |
| | | Week 6 (FU) | 5/14 (36%) | 8/17 (47%) | 0.55 | (0.132, 2.297) |
| | Camicinal 125 mg vs Placebo | Week 1 | 5/21 (24%) | 7/19 (37%) | 0.67 | (0.176, 2.556) |
| | | Week 2 | 7/22 (32%) | 8/20 (40%) | 0.70 | (0.197, 2.498) |
| | | Week 3 | 8/22 (36%) | 7/19 (37%) | 1.05 | (0.297, 3.673) |
| | | Week 4 | 9/22 (41%) | 7/16 (44%) | 1.25 | (0.350, 4.493) |
| | | Week 5 (FU) | 9/22 (41%) | 7/18 (39%) | 1.01 | (0.285, 3.581) |
| | | Week 6 (FU) | 8/21 (38%) | 8/17 (47%) | 0.66 | (0.179, 2.408) |

| Parameter | Comparison (Treatment vs. Placebo) | Week | % Responders Treatment | % Responders Placebo | Odds Ratio | 95% CI for Odds Ratio |
|---|---|---|---|---|---|---|
| Overall severity | Camicinal 10 mg vs Placebo | Week 1 | 3/11 (27%) | 5/19 (26%) | 1.17 | (0.240, 5.704) |
| | | Week 2 | 7/14 (50%) | 6/20 (30%) | 1.60 | (0.374, 6.838) |
| | | Week 3 | 10/15 (67%) | 5/19 (26%) | 3.92 | (0.977, 15.686) |
| | | Week 4 | 11/16 (69%) | 5/16 (31%) | 4.88 | (1.203, 19.828) |
| | | Week 5 (FU) | 8/15 (53%) | 8/18 (44%) | 0.97 | (0.246, 3.795) |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | Week 6 (FU) | 7/13 (54%) | 9/17 (53%) | 0.85 | (0.198, 3.599) |
| | Camicinal 50 mg vs Placebo | Week 1 | 3/17 (18%) | 5/19 (26%) | 0.57 | (0.118, 2.712) |
| | | Week 2 | 9/17 (53%) | 6/20 (30%) | 2.37 | (0.636, 8.829) |
| | | Week 3 | 8/17 (47%) | 5/19 (26%) | 2.12 | (0.551, 8.183) |
| | | Week 4 | 9/16 (56%) | 5/16 (31%) | 3.41 | (0.823, 14.095) |
| | | Week 5 (FU) | 9/16 (56%) | 8/18 (44%) | 1.21 | (0.320, 4.557) |
| | | Week 6 (FU) | 5/14 (36%) | 9/17 (53%) | 0.52 | (0.130, 2.060) |
| | GSK962040 125 mg vs Camicinal | Week 1 | 6/21 (29%) | 5/19 (26%) | 1.17 | (0.314, 4.340) |
| | | Week 2 | 11/22 (50%) | 6/20 (30%) | 2.10 | (0.606, 7.251) |
| | | Week 3 | 9/22 (41%) | 5/19 (26%) | 1.63 | (0.461, 5.762) |
| | | Week 4 | 9/22 (41%) | 5/16 (31%) | 1.57 | (0.438, 5.640) |
| | | Week 5 (FU) | 8/22 (36%) | 8/18 (44%) | 0.56 | (0.153, 2.018) |
| | | Week 6 (FU) | 7/21 (33%) | 9/17 (53%) | 0.38 | (0.101, 1.440) |

**Summary of Statistical Analysis of Dose Response for 100% Gastric Emptying Time Measured via Wireless Motility Capsule: Linear Model**

| Disease Type | Treatment (n) | | | | Slope | Intercept Est. | Slope Est. | 95% CI of Point Estimate | Between Subject SD |
|---|---|---|---|---|---|---|---|---|---|
| | Placebo | Camicinal | | | | | | | |
| | | 10 mg | 50 mg | 125 mg | | | | | |
| Type 1 Diabetes | 11 | 9 | 9 | 12 | Day 1 | 730.04 | -4.745 | (-6.628, -2.863) | 281.08 |
| | | | | | Day 28 | | -4.921 | (-6.802, -3.039) | |
| Type 2 Diabetes | 8 | 8 | 9 | 10 | Day 1 | 453.77 | -2.164 | (-4.212, -0.116) | |
| | | | | | Day 28 | | -0.635 | (-2.701, 1.431) | |

**Summary of Statistical Analysis of Dose Response for 100% Gastric Emptying Time Measured via Wireless Motility Capsule: Pairwise Comparison**

| Comparison (Test vs. Ref.) | Test N | LSM Test | Ref. N | LSM Ref. | Point Est. | 95% CI for True Diff. | Betwee Subjec SD |
|---|---|---|---|---|---|---|---|
| GSK962040 10 mg vs Placebo Day 1 | 15 | 374.37 | 17 | 632.34 | -258.0 | (-493.41, -22.53) | 221.55 |
| GSK962040 50 mg vs Placebo Day 1 | 17 | 332.88 | | | -299.5 | (-531.11, -67.80) | |
| GSK962040 125 mg vs Placebo Day 1 | 22 | 209.83 | | | -422.5 | (-639.08, -205.95) | |
| GSK962040 10 mg vs Placebo Day 28 | 14 | 622.89 | 16 | 478.11 | 144.78 | (-99.91, 389.47) | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| GSK962040 50 mg vs Placebo Day 28 | 15 | 434.63 | | | -43.48 | (-288.19, 201.23) | |
| GSK962040 125 mg vs Placebo Day 28 | 22 | 249.51 | | | -228.6 | (-451.57, -5.64) | |
| | | | | | | | |
| Day 28 vs Day 1 Placebo | 16 | 478.11 | 17 | 632.34 | -154.2 | (-339.20, 30.74) | 221.55 |
| Day 28 vs Day 1 GSK962040 10 mg | 14 | 622.89 | 15 | 374.37 | 248.52 | (62.05, 435.00) | |
| Day 28 vs Day 1 GSK962040 50 mg | 15 | 434.63 | 17 | 332.88 | 101.75 | (-80.33, 283.83) | |
| Day 28 vs Day 1 GSK962040 125 mg | 22 | 249.51 | 22 | 209.83 | 39.68 | (-108.03, 187.39) | |

LSM = Least Squares Means

Small bowel transit, colonic transit, and total bowel transit times were summarized descriptively without formal statistical comparison between treatments (data not shown) however no meaningful differences were noted.

**Summary Statistics and Statistical Analysis (Pairwise Comparison) of Daily Mean Bowel Movement Parameters by Treatment and Visit**

**Consistency of stool 24 hrs**

| Comparison (Test vs. Ref) | Week | n test | LSM Test | n ref | LSM Ref. | Point Est. | 95% CI for True Diff. | Between Subject SD |
|---|---|---|---|---|---|---|---|---|
| GSK962040 10 mg vs Placebo | Week 1 | 7 | 3.17 | 9 | 3.04 | 0.13 | (-0.45, 0.70) | 0.571 |
| | Week 2 | 11 | 2.78 | 13 | 2.99 | -0.21 | (-0.72, 0.31) | |
| | Week 3 | 12 | 2.83 | 14 | 2.94 | -0.11 | (-0.61, 0.40) | |
| | Week 4 | 13 | 2.93 | 12 | 2.93 | -0.00 | (-0.51, 0.51) | |
| GSK962040 50 mg vs Placebo | Week 1 | 11 | 2.82 | 9 | 3.04 | -0.22 | (-0.76, 0.31) | |
| | Week 2 | 13 | 3.01 | 13 | 2.99 | 0.02 | (-0.48, 0.52) | |
| | Week 3 | 12 | 2.90 | 14 | 2.94 | -0.04 | (-0.54, 0.46) | |
| | Week 4 | 12 | 2.87 | 12 | 2.93 | -0.06 | (-0.57, 0.45) | |
| GSK962040 125 mg vs Placebo | Week 1 | 13 | 3.77 | 9 | 3.04 | 0.72 | (0.20, 1.24) | |
| | Week 2 | 17 | 3.29 | 13 | 2.99 | 0.30 | (-0.18, 0.78) | |
| | Week 3 | 16 | 3.22 | 14 | 2.94 | 0.28 | (-0.19, 0.76) | |
| | Week 4 | 14 | 3.43 | 12 | 2.93 | 0.49 | (-0.00, 0.98) | |

Note: Stool consistency 1 = Very hard, 2 = Hard, 3 = Formed, 4 = Loose, 5 = Watery

**Number of times passed stools in 24 hrs**

| Comparison (Test vs. Ref) | Week | n test | LSM Test | n ref | LSM Ref. | Point Est. | 95% CI for True Diff. | Between Subject SD |
|---|---|---|---|---|---|---|---|---|
| GSK962040 10 mg vs Placebo | Week 1 | 11 | 1.32 | 19 | 1.31 | 0.01 | (-0.61, 0.62) | 0.768 |
| | Week 2 | 14 | 1.53 | 19 | 1.44 | 0.08 | (-0.52, 0.68) | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Week 3 | 15 | 1.44 | 18 | 1.44 | 0.00 | (-0.60, 0.60) | |
| | Week 4 | 16 | 1.51 | 16 | 1.36 | 0.15 | (-0.45, 0.75) | |
| GSK962040 50 mg vs Placebo | Week 1 | 17 | 1.50 | 19 | 1.31 | 0.19 | (-0.40, 0.77) | |
| | Week 2 | 17 | 1.55 | 19 | 1.44 | 0.10 | (-0.48, 0.69) | |
| | Week 3 | 17 | 1.77 | 18 | 1.44 | 0.33 | (-0.26, 0.92) | |
| | Week 4 | 17 | 1.68 | 16 | 1.36 | 0.32 | (-0.28, 0.91) | |
| GSK962040 125 mg vs Placebo | Week 1 | 21 | 1.35 | 19 | 1.31 | 0.04 | (-0.51, 0.59) | |
| | Week 2 | 22 | 1.45 | 19 | 1.44 | 0.00 | (-0.55, 0.56) | |
| | Week 3 | 22 | 1.38 | 18 | 1.44 | -0.06 | (-0.61, 0.50) | |
| | Week 4 | 21 | 1.35 | 16 | 1.36 | -0.01 | (-0.58, 0.55) | |

**Time to first bowel movement (hrs)**

Time to first bowel movement was summarized descriptively without formal statistical comparison between treatments (data not shown) however no meaningful differences were noted.

| Treatment | N | Visit | n | Mean | SD | Median | Min. | Max. | Lower 95% CI | Upper 95% CI |
|---|---|---|---|---|---|---|---|---|---|---|
| Placebo | 21 | After first dose | 16 | 28.94 | 25.044 | 26.63 | 0.8 | 76.5 | 15.60 | 42.29 |
| Camicinal 10 mg | 18 | After first dose | 12 | 53.98 | 67.901 | 18.37 | 0.3 | 191.2 | 10.83 | 97.12 |
| Camicinal 50 mg | 18 | After first dose | 15 | 17.52 | 19.286 | 10.00 | 1.8 | 72.1 | 6.84 | 28.20 |
| Camicinal 125 mg | 22 | After first dose | 12 | 15.73 | 15.648 | 7.98 | 0.5 | 56.5 | 5.79 | 25.68 |

Note: 17 subjects who entered their time of first instance of bowel movement before taking first dose were excluded from the summary statistics of time to first bowel movement.

**Safety results:** AEs were collected from the start of Investigational Product and until the follow-up contact. SAEs were collected from the start of study procedures and until the follow-up contact.

The most common AEs (all treatment groups combined) were headache (20%) and GI symptoms (diarrhea (14%), nausea (14%), vomiting (8%)). In general, these were similar across treatment groups. The majority were assessed by the investigator as related to study medication.

Lab data was unremarkable overall including no significant LFT changes. ECGs and vital signs were similar across treatment groups.

There were no withdrawals due to AEs.

**Summary of Adverse Events in >=2 Subjects**

| All Adverse Events | Placebo (N=21) | Camicinal | | | Total (N=79) |
|---|---|---|---|---|---|
| | | 10 mg (N=18) | 50 mg (N=18) | 125 mg (N=22) | |
| | n (%) | n (%) | n (%) | n (%) | n (%) |
| Any AE | 13 (62) | 14 (78) | 13 (72) | 18 (82) | 58 (73) |
| Headache | 4 (19) | 2 (11) | 4 (22) | 6 (27) | 16 (20) |
| Diarrhea | 1 (5) | 4 (22) | 3 (17) | 3 (14) | 11 (14) |
| Nausea | 1 (5) | 4 (22) | 2 (11) | 4 (18) | 11 (14) |

| | | | | | |
|---|---|---|---|---|---|
| Vomiting | 2 (10) | 2 (11) | 2 (11) | 0 | 6 (8) |
| Fatigue | 2 (10) | 0 | 1 (6) | 2 (9) | 5 (6) |
| Gastroesophageal reflux disease | 1 (5) | 1 (6) | 2 (11) | 1 (5) | 5 (6) |
| Abdominal distension | 1 (5) | 3 (17) | 0 | 0 | 4 (5) |
| Abdominal pain upper | 1 (5) | 1 (6) | 1 (6) | 1 (5) | 4 (5) |
| Constipation | 1 (5) | 0 | 2 (11) | 1 (5) | 4 (5) |
| Dizziness | 0 | 0 | 1 (6) | 3 (14) | 4 (5) |
| Increased appetite | 0 | 0 | 2 (11) | 2 (9) | 4 (5) |
| Edema peripheral | 0 | 1 (6) | 2 (11) | 0 | 3 (4) |
| Migraine | 0 | 1 (6) | 1 (6) | 1 (5) | 3 (4) |
| Urinary tract infection | 0 | 1 (6) | 2 (11) | 0 | 3 (4) |
| Abdominal pain | 0 | 1 (5) | 0 | 1 (5) | 2 (3) |
| Asthma | 2 (10) | 0 | 0 | 0 | 2 (3) |
| Cough | 1 (5) | 0 | 0 | 1 (5) | 2 (3) |
| Disturbance in attention | 0 | 0 | 2 (11) | 0 | 2 (3) |
| Feeling of body temperature change | 1 (5) | 0 | 1 (6) | 0 | 2 (3) |
| Flatulence | 0 | 2 (11) | 0 | 0 | 2 (3) |
| Hypoglycemia | 0 | 1 (6) | 0 | 1 (5) | 2 (3) |
| Local swelling | 1 (5) | 0 | 0 | 1 (5) | 2 (3) |
| Muscle spasms | 1 (5) | 0 | 1 (6) | 0 | 2 (3) |
| Upper respiratory tract infection | 0 | 2 (11) | 0 | 0 | 2 (3) |

**Serious Adverse Events**

Three SAEs were reported. One subject, on placebo, experienced a SAE of pneumothorax following central line placement; this subject subsequently withdrew consent. One subject, on camicinal (50 mg), experienced a reoccurrence of breast cancer reported after the subject had completed the 28-day study medication treatment period. Neither SAE was assessed by the investigator as related to study medication. One subject reported an SAE of vomiting during the period between consent and randomization. This event was assessed by the investigator as possibly related to study participation because the subject was asked to stop the use of concomitant prokinetic drugs and it could not be excluded that the GI symptoms may have been exacerbated by the change in standard of care. The subject was excluded from study participation. No fatalities were reported during the study.

**Conclusion:**

Gastric emptying

Gastric emptying t1/2 (as determined by the Oral Breath Test):

- Linear dose-response modelling (study was statistically powered for this primary analysis): increasing response with increasing dose demonstrated at day 1 (95% CI for slope did not contain 0) but not day 28
- Pairwise comparisons: decreased t1/2 at day 1 with 125 mg only compared to placebo (95% CI did not contain 0); no differences for any dose at day 28

100% gastric emptying time (as assessed by the wireless motility capsule):

- Linear dose-response modelling: increasing response with increasing dose demonstrated at day 1 (95% CI for slope did not contain 0; type 1 and type 2 diabetics) and day 28 (type 1 but not type 2 diabetics)
- Pairwise comparisons: decreased t1/2 for all doses compared to placebo (95% CI did not contain 0) at day 1; same effect observed for 125 mg only at day 28

Pharmacokinetics

- Camicinal mean single dose exposures on Day 1 were similar to those observed in earlier studies enrolling healthy volunteers and Type 1 diabetic subjects with gastroparesis. Mean steady-state exposures evaluated at Day 28 were comparable to 14-day exposures observed in healthy volunteers; exposures exhibited low to moderate interindividual variability.

Symptoms

- GCSI Symptoms Response: Higher odds (>2, with 95% CIs generally containing 1) of a positive treatment response vs placebo observed for 10 mg and 50 mg doses (but not 125mg) for the majority of symptoms at weeks 2-4 but not weeks 5-6 during follow up.

Bowel effects

- No difference observed between any dose vs placebo on bowel movement consistency or frequency for the majority of visits.

Safety

- The most common adverse events noted in the study were headache and GI symptoms and were similar across treatment groups. There were no withdrawals due to AEs. Three serious adverse events were reported. Two were assessed by the investigator as unrelated to study medication. The third was reported prior to dosing with study medication and was assessed as possibly related to study participation. No fatalities were reported during the study.