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Granisetron Transdermal System for Gastroparesis: A Prospective Study using the GCSI-Daily Diary

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Jason Heckert, BS: statistical analysis, data interpretation, writing manuscript

Ron Schey, MD: patient recruitment, reviewing manuscript

Henry P. Parkman, MD: study conceptualization, patient recruitment, data interpretation, writing manuscript

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Henry Parkman has served as a consultant and on a product advisory board for ProStrakan, Inc. (now Kyowa Kirin, Inc.), makers of Sancuso®.
James Heckert and Ron Schey have nothing to disclose.

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Sancuso® in patients with nausea and/or vomiting from gastroparesis: An open label study.
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1) Abstract of the study

The aim of this study is to determine the efficacy of Sancuso® (granisetron transdermal system) 3.1 mg/24 hours in improving symptoms of nausea and vomiting in patients with gastroparesis. This will be a prospective open–label study using Sancuso® to treat symptoms of nausea and/or vomiting in patients diagnosed with gastroparesis. Symptomatic patients with diabetic or idiopathic gastroparesis with nausea and/or vomiting will be enrolled. The Gastroparesis Cardinal Symptom Index Daily Diary (GCSI-DD) will be used to capture the severity of symptoms, including nausea and vomiting, at baseline for one week. Patients will then be treated with Sancuso®. Patients will continue to fill out the GCSI-DD on a daily basis while undergoing treatment with Sancuso® for two weeks. To determine if Sancuso® treatment helps improve symptoms of nausea and vomiting, the symptoms at baseline will be compared to symptoms after the first week and the second week of treatment. Thirty patients diagnosed with gastroparesis (approximately 15 with diabetic and 15 with idiopathic gastroparesis) will be treated on an open label basis with Sancuso®. The goal of this study is to demonstrate the efficacy of Sancuso® in treating nausea and/or vomiting in gastroparesis patients. Safety information will also be collected regarding any adverse effects. If the results are encouraging, as we expect them to be based on personal experience, a larger double blind study would be appropriate.

2) Protocol Title

Sancuso® in patients with nausea and/or vomiting from gastroparesis: An open label study.

3) IRB Review History

No prior IRB submission

4) Investigator

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5) Objectives

The aim of this study is determine the efficacy of Sancuso® in improving symptoms of nausea and vomiting in patients with gastroparesis.
The specific objectives of this study are to determine:
1) Determine the treatment response of Sancuso® in gastroparetic patients with nausea and/or vomiting.
2) Determine which specific symptoms of gastroparesis improve – nausea, vomiting, early satiety, abdominal distension, abdominal pain
3) To determine symptomatic responses in both diabetic and idiopathic gastroparesis
4) To determine the time course of symptom improvement (with Sancuso® for symptoms of gastroparesis;

The hypotheses to be tested include:
1) Sancuso® improves symptoms of gastroparesis.
2) Symptoms of nausea and vomiting improve to a greater degree than abdominal pain.
3) The beneficial response of Sancuso® is seen in both diabetic and idiopathic gastroparesis.
4) The symptom reduction occurs on days 3 after starting treatment and continues throughout the treatment course.

6) Background

Gastroparesis is a chronic, symptomatic disorder characterized by delayed gastric emptying in the absence of mechanical obstruction. There is a common association with long-standing diabetes, which comprises a majority of gastroparesis cases. Idiopathic gastroparesis represents another common form.

Symptoms of gastroparesis can be debilitating, causing frequent hospitalizations and diminished quality of life. Major symptoms of gastroparesis include nausea, early satiety, bloating and vomiting. Although symptoms have been difficult to associate with delayed gastric emptying, nausea and vomiting are two symptoms that appear to relate to gastric retention. Nausea is among the most commonly reported symptoms in gastroparesis. In a recent study by Anaparthy et al, nausea was one of the most prevalent symptoms, reported in 96% of patients undergoing evaluation for gastroparesis. Nausea and vomiting also have a major impact on the reduction in quality of life that occurs in gastroparesis.

Treatment of gastroparesis involves the use of prokinetic agents and antiemetic agents. Prokinetic agents are used to accelerate gastric emptying and include metoclopramide, a dopamine type 2 receptor antagonist. Antiemetic agents are used to reduce nausea and vomiting and include Compazine and Phenergan. Recently, the 5HT3 receptor antagonists, such as ondansetron and granisetron have been used.

Sancuso® is a topical formulation of the 5HT3 receptor antagonist granisetron. The patch provides treatment for prevention of chemotherapy induced nausea and vomiting; the patch can be left in place for 7 days. The PI has used this in some patients to help improve the symptoms of nausea and vomiting in patients with gastroparesis. It is particularly helpful in patients with symptoms, such as vomiting, which precludes oral ingestion of an antiemetic. In addition, it is helpful when repeated doses of oral ondansetron or oral granisetron are needed to control symptoms.

The Gastroparesis Cardinal Symptom Index (GCSI) is a validated patient-reported outcome for gastroparesis using a two-week recall period. The nine symptom GCSI (nausea, vomiting, retching, stomach fullness, unable to finish a meal, feeling excessively full after meals, loss of appetite, bloating, belly visibly larger) is based on three subscales (postprandial fullness/early satiety, nausea/vomiting, and bloating). A larger symptom questionnaire, the Patient Assessment of GI Symptoms (PAGI-SYM) includes the 9 symptoms in the GCIS, and additional symptoms of gastroesophageal reflux disease and functional dyspepsia. A daily diary form of the GCSI has been developed (GCSI-DD) includes symptoms relevant to patients with gastroparesis, captures daily variability of those symptoms and has psychometric properties consistent with a good patient-reported outcome endpoint for gastroparesis clinical trials. Each of these questionnaires, the PAGI-SYM, the GCSI, and the GCSI-DD are in the public domain for use by investigators and physicians.

7) Setting of the Human Research

Patients are seen for clinical care by Dr. Parkman in the third floor of the Ambulatory Care Center of Temple University Hospital. For patients with refractory symptoms of nausea and/or vomiting from their gastroparesis, which comprise many of Dr. Parkman's patients, other off-label treatment options are discussed including the use of tricyclic antidepressant agents as symptom modulators, botulinum toxin injection into the pylorus, gastric electric stimulation, and more recently the use of Sancuso® (granisetron transdermal system). If it is elected to proceed with Sancuso® for their clinical care, then the patients will be approached about participating in this open label study which will be recording their response to treatment.

The clinical nurse practitioner, Aaron Roberts, has an office in the GI Section where she will see patients in this study. Patients will be seen in five visits for this study.

8) Resources Available to Conduct the Human Research

Patients are seen for clinical care by Dr. Parkman in the third floor of the Ambulatory Care Center of Temple University Hospital. There are 12 outpatient examining rooms to see patients. Dr. Parkman often has four of these rooms when he is seeing patients. Dr Parkman sees a sizable number of patients with gastroparesis. Dr. Parkman has five half day sessions in which he sees patients on the third floor of the ambulatory care building. The patients seen by Dr. Parkman often have gastroparesis. Several hundred patients with gastroparesis are seen in the course of a year. Most patients have refractory symptoms that are not being adequately treated; this is often the reason they are referred to Dr. Parkman. For patients with refractory symptoms of nausea and/or vomiting from their gastroparesis, other off-label treatment options are discussed including the use of tricyclic antidepressant agents as symptom modulators, botulinum toxin injection into the pylorus, gastric electric stimulation, and more recently the use of Sancuso®. If it is elected to proceed with Sancuso®, then the patients will be approached about this open label study.

In the GI Section, patients are seen by the physicians and also clinical nurse practitioners. For this project, one of the nurse practitioners will help with this study: Aaron Roberts. She has participated in studies before, particularly the NIH gastroparesis registry. She is adequately informed about the protocol, and the duties and functions. Aaron Roberts will spend approximately two half days per week seeing patients for this study. This study will take place in the GI Section of Temple University Hospital (3rd floor Ambulatory Care Center and 8th Floor of Parkinson Pavilion).

9) Prior Approvals

None.

10) Study Design

a) Recruitment Methods

For patients with refractory symptoms of nausea and/or vomiting from their gastroparesis, which comprise many of Dr. Parkman's patients, during the office visit, other treatment options are often discussed including the use of tricyclic antidepressant agents as symptom modulators, botulinum toxin injection into the pylorus, gastric electric stimulation, and more recently the use of Sancuso® . These patients are seen by Dr. Parkman on the third floor of Ambulatory Care Center (ACC). If it is elected to proceed with Sancuso®, then the patients will be approached about participating in this open label study. Informed consent will be reviewed and signed. There will be no advertisements for this study. There will be a $250 payment to help defray any travel related expenses for participation in the study ($50 for each study visit).

b) Inclusion and Exclusion Criteria

Inclusion Criteria

Age 18 to 65 years of age
Diagnosed gastroparesis patients with symptoms of gastroparesis for at least 3 months
Symptoms of nausea and vomiting of at least moderate severity using the GCSI
Prior history of delayed gastric emptying as determined by scintigraphy
Gastroparesis from either diabetic or idiopathic etiologies
Symptoms of nausea and vomiting that have not responded adequately to conventional antiemetic agents (Compazine®, Tigan®)

Exclusion Criteria

Post-surgical gastroparesis
Prolonged QTc on EKG

Prior intolerance to 5HT3 antagonists (ondansetron or granisetron)
Known hypersensitivity to granisetron or to any of the components of the patch
Current treatment with ondansetron or granisetron. Patients may stop these medications for one week to enter the study. Patients will not be allowed to take ondansetron or oral granisetron during the study.
Use of ketoconazole, a medications with known drug-drug interactions with granisetron
Women known to be pregnant, as determined on enrollment by a urine pregnancy test
Women of childbearing potential who do not agree to use a medically approved form of contraception
Nursing mothers

c) Local Number of Subjects

This study will enroll up to 30 patients to be treated in this open label study.

d) Study-Wide Number of Subjects

Single site study at Temple with 30 patients.

e) Study Timelines

Visit 1: Baseline information will be collected including History and Physical Examination, EKG, routine clinical blood work. Women will give a urine sample for a pregnancy test. Patients will fill out baseline questionnaires including the Patient Assessment of GI Symptoms (PAGI-SYM) for assessment of GI symptoms over the past 2 weeks. Inclusion and Exclusion criteria will be reviewed to determine if the patient is eligible for the study. Patients meeting the inclusion criteria will be asked to participate and sign informed consent. Patients will be shown how to apply Sancuso patch using a placebo-containing patch. This will be worn by the patients for one week. Patients will be given a notebook containing the GCSI-DD sheets and fill out the GCSI-DD as baseline for one week and not take any 5-HT3 receptor antagonist during this time. A follow up appointment in one week will be scheduled.

Visit 2: Patients will return after the one week baseline period. The daily symptom questionnaires will be collected. Patients will fill out baseline questionnaires including the Patient Assessment of GI Symptoms (PAGI-SYM) for assessment of GI symptoms over the past 2 weeks, SF-36 to assess their quality of life, HAD questionnaire to assess for symptoms of anxiety and depression, and a modified McGill Pain inventory to assess for abdominal pain. Patients will be given Sancuso® for one week. The placebo patch will be removed and the active Sancuso will be applied at the visit to ensure that it sticks. Patients will continue to fill out the GCSI-DD on a daily basis and not take any 5-HT3 receptor antagonist. A follow up appointment in one week will be scheduled.

Visit 3: Patients will be seen after one week of treatment. The GCSI daily diaries will be collected. The therapeutic response of the patients will be enquired using the simple Clinical Patient Grading Assessment Scale (CPGAS). Patient will be asked if any adverse or side effects occurred while being treated with Sancuso. Patient will then fill out a symptom side effect questionnaire that also asks about difficulty with wearing the patch. The old Sancuso patch will be removed and a new Sancuso® patch will be applied for another one week. A follow up appointment in one week will be scheduled.

Visit 4: Patients will be seen after the second one week of treatment. The GCSI daily diaries will be collected. The therapeutic response of the patients will be enquired using the simple Clinical Patient Grading Assessment Scale (CPGAS). Patients will fill out the Patient Assessment of GI Symptoms (PAGI-SYM), SF-36, HAD questionnaire, a modified McGill Pain

inventory, and a symptom side effect questionnaire. Patients will stop treatment with Sancuso® at this time, and be followed for an additional week of treatment off medication. Patients will continue to fill out the GCSI-DD on a daily basis and not take any 5-HT3 receptor antagonist. A follow up appointment in one week will be scheduled.

Visit 5: Patients will be seen after one week after cessation of treatment. The GCSI daily diaries will be collected. Patients will fill out the symptom side effect questionnaire. After this visit, the study period is over and the patient returns to clinical care.

f) Study Endpoints

Primary and Secondary Endpoints:

Primary: Nausea and Vomiting severity scores using the GCSI-DD
Secondary: Total Gastrointestinal Cardinal Symptom Index
Clinical Patient Grading Assessment Scale (CPGAS)

Patients will fill out daily information of their symptoms of gastroparesis using the Gastroparesis Cardinal Symptom Index Daily Diary (GCSI-DD). The Gastroparesis Cardinal Symptom Index (GCSI) is a validated patient-reported outcome for gastroparesis daily recording of symptoms. Several symptoms of gastroparesis including nausea, vomiting, retching, stomach fullness, unable to finish a meal, feeling excessively full after meals, bloating, belly visibly larger will be monitored. This is used in clinical practice and will be performed in this project.

For this study, the therapeutic response of the patients will also be enquired using the simple Clinical Patient Grading Assessment Scale (CPGAS). Patients will be asked if they improved, stayed the same, or worsened with Sancuso® treatment. The clinical response of their gastroparesis symptoms to Sancuso treatment with gradations from (+7) = completely better; (0) = no change, and (-7) = very considerably worse. Responders are defined as those with score of >0 and non-responders with score of $\leq$0 by CPGAS. Patients will be asked if they experienced any side effects with Sancuso® treatment and to describe any side effects. Other than your GI symptoms, how have you been feeling?

Adverse events will be recorded.

g) Procedures Involved in the Human Research

This will be an open label study of patients with gastroparesis. The study period will be approximately four weeks.

Patients meeting the inclusion criteria will be asked to participate and sign informed consent. Baseline information will be collected including History and Physical Examination, EKG, routine clinical blood work. The history will include prior 5-HT3 receptor antagonist treatment and the patient's response. Patients will fill out baseline questionnaires including the Patient Assessment of GI Symptoms (PAGI-SYM) for assessment of GI symptoms over the past 2 weeks, SF-36 to assess their quality of life, HAD questionnaire to assess for symptoms of anxiety and depression, and a modified McGill Pain inventory to assess for abdominal pain.

Patients will be treated with Sancuso® for two weeks (one patch every 7 days), being seen after each week. A copy of the package insert for Sancuso in in the appendix. Symptoms will be followed on a daily basis using the GCSI-DD

At the study visits, the GCSI daily diaries will be collected. At each of these visits, patients will fill out the Patient Assessment of GI Symptoms (PAGI-SYM), SF-36, HAD questionnaire, a modified McGill Pain inventory, and a symptom side effect questionnaire.

After the two weeks of active treatment, the patient will be followed for a further week off treatment, for a study period of 4 weeks (one week baseline off treatment, two weeks treatment with Sancuso®, then one week off treatment).

Adverse event reporting

The Principal Investigator will be responsible for the reporting and submission of serious (expected or unexpected) adverse events that occur during the conduct of this study to FDA on a MedWatch 3500a form. Additionally, the Principal Investigator will be responsible for providing the required study update reports to the Institutional Review Board (IRB). The Principal Investigator will also provide ProStrakan with a copy of the MedWatch 3500a completed for all serious adverse event reports. The information includes the investigator's assessment of causality. This information will be sent to the company within 10 days of receipt of the adverse event report by the Investigator. A copy of the completed MedWatch 3500a form submitted to FDA will be sent to Drugsafety@prostrakan.com. The company will enter all safety information in the Global Safety Database along with the investigator's assessment of relationship of the event to the study medication. Any follow up information will also be sent to the company within 10 days of receipt of the information by the Investigator on a completed MedWatch 3500a form.

h) Data and Specimen Banking

Data will be stored on encrypted password-protected computer using a Microsoft Excel data base. No specimens will be obtained.

i) Data Management

Data will be entered into an Excel spreadsheet in an encrypted password protected computer accessible only to the study coordinator and the PI.

Descriptive analysis of the outcome variables will be constructed using Excel and SPSS.

Outcome measures

The primary outcome measures in this study are the GCSI-DD nausea/vomiting symptom scores. The secondary outcome measures are Total Gastrointestinal Cardinal Symptom Index and Clinical Patient Grading Assessment Scale (CPGAS). The percent of patients treated with Sancuso® that have improved symptoms of nausea, vomiting will be calculated both as a positive score on the CPGAS as well as a 25% improvement in the nausea score compared to baseline.

Data Analysis

Descriptive analysis of the outcome variables will be constructed. Statistical analysis will be performed using SPSS. This study is designed to test the hypothesis that Sancuso® treatment provides improvement of gastroparetic symptoms. We will compare the absolute GCSI symptom scores before and after treatment using ANOVA for repeated measures. The symptom score improvement will be tested between the two treatment groups (diabetic and idiopathic gastroparesis) using ANOVA for repeated measures on ranks. Linear regression will be used to identify potential predictors of a beneficial symptomatic response to treatment.

Sample Size Determination

In a gastroparesis study at our institution with similar inclusion criteria, the average GCSI of 16 patients was 34.8 with standard deviation of 4.6. In a previous study at our institution, the absolute magnitude of symptom improvement for open label botulinum toxin was 38% (Miller 2002). The sample size in this study is calculated to show a benefit of Sancuso® by at least 30% reduction in the GCSI score. Assuming a standard deviation of 5 in the GCSI reduction of symptoms and with an α= .05 and β= .80, fifteen patients will be needed. We will recruit 15 diabetic patients and 15 idiopathic patients to enter this study to give adequate power to address the primary outcome variable - symptom response.

j) Confidentiality

Private health information (PHI) as defined by HIPAA will be collected as part of the research. These include: name, birthdate, telephone number, medical record number. All data will be kept confidential. Data will be entered into an Excel spreadsheet in an encrypted password protected computer accessible only be the study coordinator and the PI. The data will be de-identified.

k) Provisions to Monitor the Data to Ensure the Safety of subjects

This study involves minimal risk to the subjects. Patients will be monitored during the study in weekly study visits. The Sancuso® patch is being used to try to help reduce their symptoms of nausea and/or vomiting. The study is to allow recording of the response to treatment. All data will be kept confidential. Data will be entered into an Excel spreadsheet in an encrypted password protected computer accessible only be the study coordinator and the PI.

l) Withdrawal of Subjects

Patients have the option to not participate. Patients may elect at any time to stop treatment with Sancuso®.

11) Risks to Subjects

Risks of the Study: For the open label study, data is being recorded about their medical condition. All data will be kept confidential. Data will be entered into an Excel spreadsheet in a password protected computer accessible only be the study coordinator and the PI.

Risks of Sancuso®:

The decision to enroll a patient in this study with Sancuso® will be made after discussing all available treatment options with the patient. The following risks of Sancuso® might occur. The most common adverse reaction with Sancuso® is constipation. The patch may also cause some local skin irritation. In clinical trials with Sancuso®, application site reactions were reported which were generally mild in intensity and did not lead to discontinuation of use. The incidence of reactions was comparable with placebo. If severe reactions, or a generalized skin reaction occur (e.g. allergic rash, including erythematous, macular, papular rash or pruritus) the patch must be removed. Granisetron may be affected by direct natural or artificial sunlight. Patients must be advised to cover the patch application site, e.g. with clothing, if there is a risk of exposure to sunlight throughout the period of wear and for 10 days following its removal because of a potential skin reaction.

The safety of Sancuso® was evaluated in a total of 404 patients undergoing chemotherapy who participated in two double-blind, comparator studies with patch treatment durations of up to 7 days. The control groups included a total of 406 patients who received a daily dose of 2 mg oral granisetron, for 1 to 5 days. Adverse reactions considered by the investigators as drug-related occurred in 8.7% (35/404) of patients receiving Sancuso® and 7.1% (29/406) of patients receiving oral granisetron. The most common adverse reaction was constipation that occurred in 5.4% of patients in the Sancuso® group and 3.0% of patients in the oral granisetron group. Table 1 lists the treatment emergent adverse reactions that occurred in at least 3% of patients treated with Sancuso® or oral granisetron.

Table 1: Incidence of Adverse Reactions in Double-Blind, Active Comparator Controlled Studies in Cancer Patients Receiving Chemotherapy (Events ≥ 3% in either group)

Body System Preferred Term	Sancuso® TDS N=404 (%)	Oral granisetron N=406 (%)
Gastrointestinal disorders		
Constipation	5.4	3.0
Nervous system disorders		
Headache	0.7	3.0

No clinically relevant drug interactions have been reported in clinical studies with Sancuso®. Theoretically, co-administration of drugs that prolong the QTc interval may increase the risk of cardiac arrhythmias. 5-HT3 receptor antagonists, such as granisetron, may be associated with arrhythmias or ECG abnormalities. Three ECGs were performed on 588 randomized patients in the Phase 3 study: at baseline before treatment, the first day of chemotherapy, and 5 to 7 days after starting chemotherapy. QTcF prolongation greater than 450 milliseconds was seen in a total of 11 (1.9%) patients after receiving granisetron, 8 (2.7%) on oral granisetron and 3 (1.1%) on the Sancuso® patch. No new QTcF prolongations greater than 480 milliseconds ware observed in any patient in this study. No arrhythmias were detected in this study.

Granisetron does not induce or inhibit the cytochrome P-450 drug-metabolizing enzyme system *in vitro*. There have been no definitive drug-drug interaction studies to examine pharmacokinetic or pharmacodynamic interaction with other drugs. However, in humans, granisetron hydrochloride injection has been safely administered with drugs representing benzodiazepines, neuroleptics and anti-ulcer medications commonly prescribed with antiemetic treatments. In agreement with these data, no clinically relevant drug interactions have been reported in clinical studies with Sancuso®.

Because granisetron is metabolized by hepatic cytochrome P-450 drug-metabolizing enzymes (CYP1A1 and CYP3A4), inducers or inhibitors of these enzymes may change the clearance and hence, the half-life of granisetron. In addition, the activity of the cytochrome P-450 subfamily 3A4 (involved in the metabolism of some of the main narcotic analgesic agents) is not modified by granisetron hydrochloride *in vitro*. In *in-vitro* human microsomal studies, ketoconazole inhibited ring oxidation of granisetron hydrochloride. However, the clinical significance of *in-vivo* pharmacokinetic interactions with ketoconazole is not known. In a human pharmacokinetic study, hepatic enzyme induction with phenobarbital resulted in a 25% increase in total plasma clearance of intravenous granisetron hydrochloride. The clinical significance of this change is not known.

Because some medications may interact with 5HT3 receptor antagonists, if any new agents are being added for the patient's clinical care, they should contact the study physician.

12) Potential Benefits to Subjects

The patients may potentially benefit from the study, as they will receive two weeks of treatment with Sancuso®. In addition, after the study, if there was improvement with their symptoms, Sancuso® could be given as a prescription for their clinical care. If needed, the nurse practitioner can help assist them with preauthorization from their insurance company. In addition, if the patient is not responding to treatment, they can be given an appointment to be seen clinically by Dr. Parkman. Since patients are being treated, hopefully there is some possibility of symptom reduction.

13) Provisions to Protect the Privacy Interests of Subjects

Safety issues related to patient privacy: Every effort will be made to maintain patients' privacy. The subjects' privacy interests will be protected. The medical chart may be reviewed for the data – to assess age, gender, etiology of the gastroparesis, result of gastric emptying test, upper endoscopy. The study visits will take place in a closed office. Patients will be identified only by an identification code but not by their name, Social Security Number, or hospital medical record number. Investigators will maintain a separate confidential enrollment log that matches identifying codes with the patients' names and addresses (i.e., available only to local clinic staff). All study material will be maintained in strict confidence.

14) Compensation for Research-Related Injury

Injury Statement in the informed consent: If you are injured as a result of your participation in this research study, seek immediate medical care. However, there is no commitment by Temple University, Temple University Health System or its subsidiaries to provide monetary compensation or free medical care to you in the event of a study-related injury. By signing this consent form, you are not waiving any of the legal rights that you otherwise would have as a participant in a research study. If you have questions about the study or a research-related injury, please contact Dr. Parkman at (215) 707-3431.

15) Economic Burden to Subjects

The study requires five study visits. Patients will receive a stipend for their participation to cover travel expenses ($50 per visit, up to $250 for the study).

16) Consent Process

Informed consent and HIPAA will be obtained for this study. The patient will sign the consent form prior to their enrollment in the registry. The patient can take the consent form home to go over the form with their family. We will follow the "SOP: Informed Consent Process for Research." The patients will be told at the time of the prescription that they will be contacted in several weeks to assess their response. In addition, they will be told that their data may be used to be published anonymously. The patients voluntarily answer questions on the telephone.

17) Process to Document Consent in Writing

The patient will sign the consent form. We will follow the "SOP: Written Documentation of Consent."

18) Vulnerable Populations

Not applicable. This project will involve only adult patients that are not pregnant and not prisoners.

19) Drugs or Devices

The Sancuso® granisetron patch is given to try to help control their nausea and vomiting. A copy of the package insert is attached.

The Sancuo patches will be stored in a locked cabinet in the GI section; only the clinical coordinator and the PI have access to this locked cabinet. The drug will be given directly to the patient in this study. The Sancuso patches will be used only in subjects who have provided consent for this study.

20) Multi-Site Human Research

Not applicable.

21) Community-Based Participatory Research

The open-label study was developed by an investigator that sees patients with gastroparesis. The use of Sancuso® came up due to the need for additional treatments for their nausea and vomiting. This open label study came up, as many insurance companies do not allow this as treatment, as it is approved for chemotherapy-induced nausea and vomiting.

22) Sharing of Results with Subjects

New Findings: Patients will be told about new information that might change their decision to be in this study. Patients will also be told about new information that may have an effect on their future medical care. Patients may be asked to sign a revised informed consent form that contains the new information.

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Appendix A – Initial enrollment questionnaire including PAGI-SYM

Appendix B – GCSI-DD

Appendix C – Followup questionnaire – including PAGI-SYM

Appendix D - Package insert for Sancuso®