Clinical Outcome Assessments (COA) Qualification Program
DDT COA #000020: American Neurogastroenterology and Motility Society Gastroparesis Cardinal Symptom Index-Daily Diary (ANMS GCSI-DD)
March 8, 2018 Update

I. Background

Gastroparesis is a condition involving delayed gastric emptying when no mechanical obstruction is present. Patients with gastroparesis often experience a variety of symptoms including early satiety, postprandial fullness, nausea, vomiting, and abdominal pain. Gastroparesis of unknown etiology accounts for the largest number of cases, but is also frequently associated with conditions such as diabetes, and may occur after various types of gastrointestinal surgeries.

A symptom questionnaire, the Gastroparesis Cardinal Symptom Index (GCSI), was originally developed and validated in university-based clinical practices for quantifying symptoms in gastroparesis. The nine-symptom GCSI is based on three subscales (postprandial fullness/early satiety, nausea/vomiting, and bloating) and represents a subset of the longer 20-symptom Patient Assessment of Upper Gastrointestinal Disorders-Symptoms (PAGI-SYM). The GCSI and PAGI-SYM both ask patients to describe the severity of their symptoms over the last two weeks. The GCSI, GCSI-DD (the daily diary version of the GCSI), and PAGI-SYM are used in clinical trials for patients with gastroparesis.

The Food and Drug Administration (FDA) has been reevaluating symptom endpoints used in clinical trials of pharmaceutical agents for all disorders, including gastroparesis, and suggests using patient-reported outcomes (PROs) to assess symptom endpoints. In July 2015, the FDA Gastroparesis Guidance for Industry was released which contained recommendations for endpoints for gastroparesis studies (FDA 2015). The American Neurogastroenterology and Motility Society Gastroparesis Cardinal Symptom Index-Daily Diary (ANMS GCSI-DD) has been developed to meet these recommendations.

A daily diary version of the GCSI (ANMS GCSI-DD) has been developed by the ANMS GCSI-DD PRO Committee, consisting of representatives of ANMS interested in gastroparesis and Dr. Dennis Revicki (Evidera), the developer of the original GCSI questionnaire. The initial daily diary version was based on the existing two-week GCSI questionnaire that has undergone prior extensive psychometric evaluation. The development of the diary has involved changing the instructions and recall period; however, the item stems and response scales remain the same. In response to suggestions of clinical experts, the diary was revised to ask about symptoms of abdominal pain which was not present in the original GCSI. In some patients, abdominal pain and/or discomfort can be an important symptom (Hoogerwerf 1999), and has been used in other severity scores for gastroparesis (Punkkinen 2008; Lin 2008). The daily diary version is based on the PAGI-SYM questionnaire which has been previously tested and validated in patients with different gastrointestinal disorders. Suggestions from the FDA were also incorporated including changing the vomiting assessment from severity to frequency.

Based on the requirements of the FDA PRO guidance, the recent FDA guidance on gastroparesis, and the FDA feedback to date during the qualification guidance of the ANMS GCSI-DD, further

evaluation of the content validity and psychometric characteristics of the new GCSI-daily diary was suggested by the FDA to be completed for qualification of the ANMS GCSI-DD as a PRO endpoint for diabetic or idiopathic gastroparesis. The purpose of the present study is to determine if the appropriate symptoms are being addressed in the ANMS GCSI-DD using concept elicitation and to evaluate the understanding of this daily questionnaire with cognitive debriefing in patients with gastroparesis.

This protocol will involve processes termed concept elicitation and cognitive debriefing. Concept elicitation will be used by asking open-ended questions about the patient's symptoms of gastroparesis. This will be used to assess and confirm whether the relevant symptoms are included in the ANMS GCSI-DD. The current version of the ANMS GCSI-DD will be completed by the patient. Cognitive debriefing will be conducted to ensure that the instrument's instructions are clear, the content is relevant and comprehensive from the patient's perspective, the intended connotation of each item is consistent with the participant's interpretation or assigned meaning, and that the response scales are clear. The ANMS GCSI-DD will be the focus of the cognitive debriefing. In addition, patients will be asked if other symptoms should be added or any present symptoms should be removed.

II. Study Objectives

The purpose of the project is to further develop and confirm the content of a daily symptom diary for diabetic and idiopathic gastroparesis. The study will involve interviewing patients with either diabetic or idiopathic gastroparesis for concept elicitation of their symptoms of gastroparesis, evaluate a newly revised questionnaire for symptoms related to gastroparesis (ANMS GCSI-DD), and determine if the patients understand and respond appropriately to the questionnaire. The questionnaire has been modified from a previously developed questionnaire (i.e., GCSI-DD) that was further revised based on the input of patients and the FDA that reviews these types of questionnaires as PRO endpoints for drug approval. The primary objective of the study is to evaluate whether the revised ANMS GCSI-DD is understandable and relevant for patients with gastroparesis and to learn how and what patients think about the instructions, question content, and response options. We will also determine if other symptoms should be included or if any currently included symptoms should be removed from the daily diary. The information that patients provide will be used to improve or confirm the content of the ANMS GCSI-DD so that it can be used on a daily basis to assess gastroparesis symptoms.

References:

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