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# The Signal

## Signant Health Raises the Bar in Ulcerative Colitis Trials with eCOA

*The Mayo Clinic Score (MCS) is one of the most commonly used measures of disease activity in clinical trials for Ulcerative Colitis (UC). Sponsors use the MCS as it is a common primary endpoint in UC trials. However, it can be difficult to implement for various reasons. Our expert, Katie Garner, gives us her insights on the condition and how using electronic clinical outcome assessments (eCOA) in UC clinical trials can benefit the industry. In this Q&A, Katie addresses the complexities and challenges of implementing the MCS and provides recommendations for improving compliance, site workflows, and implementing eCOA in UC clinical trials.*

**Q: Can you set the scene for us? What is Ulcerative Colitis?**

Ulcerative colitis (UC) is a chronic relapsing inflammatory bowel disease (IBD) that causes inflammation of the digestive tract. It is characterized by abdominal pain and diarrhea. Like Crohn's disease, another common IBD, UC can be debilitating and sometimes lead to life threatening complications. It usually affects only the innermost lining of the large intestine (called the mucosa) and rectum. It occurs only through continuous stretches of colon, unlike Crohn's disease, which occurs in patches anywhere in the digestive tract and often spreads deep into the layers of affected tissues.

In the United States, it is currently estimated that about 1 –1.3 million people suffer from IBD.[1] A precise understanding of how many people experience Crohn's disease and UC is very difficult as there is no standard criteria for diagnosing IBD. Identifying cases of IBD is often inconsistent or the disease may be classified as another condition.

**Q: What is the MAYO score and why is it problematic?**

UC cannot be cured, but there are a range of drugs to treat the symptoms of the disease. Clinical trials designed to study the efficacy of therapeutic interventions require outcome measures that assess the activity of the disease. These measures frequently combine findings from invasive tests (sigmoidoscopy or colonoscopy) and clinical characteristics reported by the patient. The Mayo Clinic Score (MCS) is one of the most commonly used measures of disease activity in clinical trials for UC however it can be a problematic measure to implement. Challenges occur around data collection and MAYO score calculation, data selection for scoring purposes, data compliance and clinical site workflows.


With incidences of UC continuing to rise, it is likely that the number of UC clinical trials will continue to increase, and so a better solution for calculating the MAYO score is drastically needed. At Signant Health, we have developed a novel way of calculating the MAYO score using a seamless solution that is easy to implement and offers benefits for patients, sites, and sponsors. Clinical trials to assess the disease and find new treatments for UC are crucial and with Signant Health's help, these trials will be equipped to collect compliant, complete, quality data.

**Q: Can you give us any insights into how a UC clinical trial operates?**

The effects of treatment are often assessed through patient-reported signs and symptoms, as well as endoscopic evidence of inflammation. In clinical trial settings, MCS historically has been used to assess disease activity, combining endoscopic findings with physician-rated signs and symptoms, based on information provided by the patient and totaled into a single total score. Both the Food and Drug Administration (FDA) and European Medicines Agency (EMA) have issued guidelines specific to clinical trials of UC, noting the importance of including adequately validated patient-reported outcome measures (PROMs) to assess symptomatic relief as a primary outcome measure in pivotal clinical trials of UC.[5,6]

The clinical trial industry has adopted technology to improve the efficiency and quality of trials, including electronic clinical outcome assessments (eCOA) and more specifically, electronic patient-reported outcome assessments (ePRO). The eCOA market is predicted to grow significantly as the benefits of completeness of data, timeliness, accuracy and attributability are realized and regulators strengthen their recommendations with respect to electronic data collection.

Using electronic device systems, PROMs in IBD can be routinely measured before and between appointments in order to identify response or failure to therapies. The FDA has said that the MCS meets current regulatory requirements for drug development in UC. Although, it recognizes that there are limitations with this score and other scores because they incorporate the Physician Global Score (PGA). The FDA do not feel that a single score from a physician can accurately contribute to representing a patient's condition. The FDA has encouraged sponsors to develop alternative outcome measures based on patient reported outcomes and encourages use of the MCS in the meantime.[7]

**Q: What are the specific challenges of the MCS?**

There are many ways to implement the MCS. It is a composite score, which means that multiple components are combined into one score including patient-reported outcomes, clinician-reported outcomes and usually a medical imaging value from colonoscopy. In


terms of eCOA implementation, UC trials are like most other clinical trials. However, there are a couple of aspects that can be challenging, mainly related to implementation of the MCS. These include:

- Data aggregation from multiple sources
- Data collection and MCS calculation
- Data selection for scoring purposes
- Data compliance
- Site workflow

**Q: What issues are encountered during data collection?**

A lot of data needs to be collected from the patient before the site visit. From a sponsors' point of view, they want to achieve MAYO scoring on one system. Getting all the data combined and in one place for the calculation can be difficult. The subject data, the physicians/site data and often the endoscopy score (depending on whether it is the full or the partial Mayo score) must all be present in the same software environment for the Mayo calculation to be performed. Manual calculation is more time consuming, can lead to errors and is burdensome for site staff. This is especially important when the MCS is also used as an eligibility criterion.  A seamless eCOA solution that allows patient and site data to be combined and the MCS calculated is beneficial. This is what has driven our approach at Signant Health.

**Q: Are there any issues with data selection?**

Typically, a study protocol requires data from a fixed number of days prior to the site visit to calculate the MCS score. Several days are used rather than just one in order to ensure that the information is representative of the subject's experience. The FDA generally recommends using the most recent three-day consecutive period within the week before the visit to calculate the Stool Frequency and Rectal Bleeding sub scores.

The site is generally asked to input the date of visit for the system to calculate the right data collection window. It is important to highlight days in which endoscopy/bowel preparation was done so that this data can be excluded. These days are excluded because bowel preparation encourages bowel movement. There are likely to be more movements on these days and it is not truly representative of the subject's condition. The site should be asked "Was a bowel preparation preformed for this visit?" "Date of bowel preparation?" so that data can be excluded on these days from the Mayo score.


**Q: What compliance challenges do you encounter?**

Patient burden and engagement can be an issue. Due to the large amount of data that needs to be collected from the patient, this can lead to patient burden and a loss of engagement. Thus, PROM completion compliance can ultimately be affected. Non-compliance can in turn impact the MCS calculation. Some UC trials require patients to collect data during a pre-defined window prior to a site visit. Patients can forget to start completing data or don't complete all required data resulting in low compliance. Recording data only on some days can lead to patients forgetting to complete data entry (even when they are sent reminders). An eCOA solution can have audible alarms to remind patients to complete their data and lead them through data collection in an easy way, reducing some of the burden.

If an eCOA solution retrieves data from days when the subject did not complete their daily diary and there is no data or data missing, then the score will not be completed correctly. Therefore, the FDA has recommended that three-consecutive days are used 'from the week before a visit' and has not restricted their guidance to the three days immediately before a visit. This offers some flexibility and allows the most complete data set (working around the rules of consecutive days and excluding bowel prep) to be retrieved. An eCOA solution can select the required number of consecutive days where subject data was entered and avoid non-compliant days where no subject data was entered.

**Q: How can site workflow be impacted?**

The practical aspects of calculating the MCS score can be challenging, especially if subjects and sites have different devices which they use to enter data. Many UC studies also include other instruments such as the Inflammatory Bowel Disease Questionnaire (IBDQ) completed at site visits on a tablet. It is not always practical for the subject and the site to pass the one device backwards and forwards, requiring them to log in and out multiple times. Thus, it is important to be mindful of this burden and try to reduce it wherever possible.

**Q: Can you outline the Signant Health solution?**

Our clinical science and consulting expertise, including rater training experience in fields such as neuroscience, has provided a unique blueprint in understanding how to rate complex conditions and specific trial challenges. Ultimately, we want to take the burden away from sites, sponsors, and patients. We conducted a qualitative research study at Signant Health to assess how composite scores such as the MCS had been implemented over various studies and to identify current experience and attitudes, potential challenges,


opportunities, and best practices for using eCOA in UC clinical trials. After reviewing all the requirements and implementations, a best of breed UC eCOA web solution was identified combining of eDiary and Management components.

**An eDiary to:**

- Capture the patient's daily symptom responses
- Capture the patient's 'normal' number of stools per day while in remission
- Capture, if necessary, whether the patient took diarrhea/constipation medications (or anything else defined as an 'exclusion' day)

**A Management tool for sites to:**

- Capture Visit Dates, or allow users to 'Activate' a visit
- Capture PGA values
- Capture Endoscopy score values
- Capture any other relevant information such as Bowel Preparation dates and Procedure dates
- Calculate scores, once all the required information has been entered for a visit
- Capture, if necessary, criteria for eligibility or flare checks, and inform the user when these criteria are met, and
- Allow users to 'recalculate' if a value has been adjusted via a data correction form (DCF), or if a device has sent data that was previously unavailable

The seamless web UC solution uses an electronic daily diary to enable subjects to collect bowel movement and rectal bleeding data through an intuitive, easy to use diary. The diary entries are converted to sub scores and combined with physician and endoscopy scores to calculate and display the MCS score within the study management interfaces (our TrialMAx® system).

Clinical trial sponsors and investigators running a UC study continue to face many challenges when it comes to implementing an eCOA strategy. A sponsor's clinical trial technology should be about more than just collecting data. It should be about patient empowerment and engagement. It should help patients throughout the clinical trial journey. And, it should help sponsors and sites reach their goals.

There are so many advantages to using an integrated electronic solution, both in terms of efficiencies and data quality. It suits the subject and the site's data collection needs,


enables data pooling, calculation and management of site workflow issues

It is advantageous for subjects to complete a daily diary and not just on the required days before the site visit. In our experience, there is less burden to subjects in completing an activity which is familiar to them, rather than having to think and remember which days to complete information and which days not to complete. We believe this to be true even if they are given reminders. Overall compliance and data quality are likely to be higher with a daily diary.

A daily diary also reduces the potential for errors in implementing the opening, closing, and rescheduling of data entry windows. Data entry windows rely on good quality data being submitted during the specific data entry window. However, a daily diary approach allows the system to choose data and protocol compliant days.

**Q: How do you see this affecting the greater clinical trial industry?**

There is a key element that stands out for me here. This element runs through all the themes we've talked about – it is the importance of simplicity. Sponsors, CROs and research sites need technology that seamlessly connects their research programs into the flow of patients every day. The simpler it is for patients to participate in a trial, and for study teams and sites to run studies, the easier it is to ensure quality, improve efficiency and provide data and analytics that will help improve the future of healthcare for everyone. Blending solutions into the background simplifies every step of the patient journey and enables patients to provide the honest insights that today's research needs. At Signant Health, we're committed to technology and innovation. A unified solution, supported by expert developers, project managers, data analysts, scientists and clinicians, can truly improve key aspects of clinical research from planning and startup through closeout and beyond.

Often those running UC trials need to rely on technology providers with expertise and legacy credentials in this area. We have the answers, so you don't need to worry about finding a way forward. Staying ahead of potential risks takes experience, and eCOA platforms that handle data quality considerations one step ahead are advantageous. Few can claim in-depth experience in this field, so finding a partner with experience in the area would be the first step. If that can be backed by extensive experience in science, operations, and regulations, across therapeutic areas and countries, then sponsors should feel confident about using globally accessible technology that delivers seamless, usable solutions for many different types of patient populations.


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