

Title of Research

Evaluating the Placebo Endoscopic Response in Crohn's Disease Clinical Trials

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Summary of Research

Understanding the magnitude of placebo response and associating factors in inflammatory bowel disease (IBD) clinical trials is important for trial design and interpretation. Factors affecting the placebo response include patient expectations of treatment benefits, response to observation and assessment (Hawthorne effect), response to administration of a therapeutic ritual, the patient-physician relationship and intrinsic features of trial design.

In clinical trials for Crohn's disease (CD), the Crohn's Disease Activity Index (CDAI) has been used as the basis for approval of many treatments over the past four decades. The CDAI's properties are well defined, but subjective components of the score may contribute to measurement error. In contrast, endoscopic activity is a more objective measurement of disease activity, and mucosal healing – which may reduce relapse, hospitalization and surgery rates in CD patients – has emerged as an important therapeutic endpoint in CD clinical trials.

An understanding of the evolution of endoscopic activity in trial subjects randomized to placebo will help inform design of randomized trials, particularly in calculating sample sizes.

Study Design

This study is a retrospective analysis of three existing datasets from completed clinical trials of induction therapy for CD. Data will be analysed for research subjects who had baseline endoscopy, received placebo treatment, and then underwent a second colonoscopy after 10- 12 weeks. All three trials have ileo-colonoscopy videos recorded at baseline and follow-up for outcome assessment, read by a local and central reader blinded to treatment allocation and study visit. The study objectives will be to describe changes in endoscopic scores (measured using the Simplified Endoscopy Score for CD or SES-CD) in participants randomized to placebo in the three completed trials; provide a pooled estimate of the endoscopic placebo response rate; and identify factors associated with spontaneous improvement in endoscopic mucosal healing in CD patients randomized to placebo treatment.

Citation:

Evaluating the Placebo Endoscopic Response in Crohn's Disease Clinical Trials. Duijvestein M, Jeyarajah J, Guizzetti L, Zou G, Parker CE, van Viegen T, VandeCastele N, Khanna R, Van Der Aa A, Sandborn WJ, Feagan BG, D'Haens GR, Jairath V. [Clinical Gastroenterology and Hepatology](#) 2020 May;18(5):1121-1132.e2. doi: 10.1016/j.cgh.2019.08.025. Epub 2019 Aug 20