COMPUTER VISION MEASUREMENT OF DISEASE SEVERITY DISTRIBUTION OUTPERFORMS TRADITIONAL ENDOSCOPIC SCORING FOR DETECTING THERAPEUTIC RESPONSE IN A CLINICAL TRIAL OF USTEKINUMAB FOR ULCERATIVE COLITIS

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BACKGROUND: Endoscopic scoring is a cornerstone of disease assessment in ulcerative colitis (UC). Novel computer vision methods may provide a more sensitive measure of endoscopic activity, potentially improving therapeutic efficacy assessment compared to con-ventional scoring. **METHODS**: Endoscopic video from subjects completing through week 44 of the phase-three randomized placebo (PBO) controlled trial of ustekinumab (UST) for UC (UNIFI) underwent novel computer vision analysis. Pre-trained neural networks were used to detect UC severity, ulceration, and erythema at the frame-level. A fully automated anatomic positional neural network provided colon location data within videos and was fused with disease severity data to generate novel UC disease distribution scores (Figure 1). Disease distribution scores were compared to conventional Mayo endoscopic scoring (MES) for detecting therapeutic effect at study completion and the change between pre- and post-treatment. Endoscopic activity measurement differences between treatments were assessed using the Student's *t*-test, with therapeutic effect measured using Cohen's *d* values. Projected sample size estimates based on endoscopic effect detected assumed a power of 0.8 and alpha of 0.05. **RESULTS**: 362 subjects from UNIFI met selection criteria, including 276 standard-dose UST and 86 PBO users. At study completion mean MES scores were significantly lower for UST (1.36, SD 1.07) compared to PBO (1.72, SD 1.19, p=0.014). Mean novel disease severity distribution scores at week 44 were also significantly lower for UST (493, SD 344) compared to PBO (651, SD 440, p=0.003). The detected endoscopic healing effect size was greater using disease severity distribution scores (d=0.40) compared to conventional MES scoring (d=0.31). Examining the change in endoscopic activity between week 0 and 44, mean MES change was significantly greater for UST (1.34, SD 1.06) vs. PBO (0.97, SD 1.11, p=0.007). Alternatively, disease distribution scoring again captured an improved separation of therapeutic change for UST (455, SD 451) vs. PBO (252, SD 474, p=0.0006). Disease distribution measures better detected the change in endoscopic activity between UST and PBO, with an effect of d=0.44 compared to the effect assessed with traditional MES of d= 0.34. Using novel endoscopic disease distribution measures, the projected sample size estimated to detect a therapeutic difference between UST compared to PBO was reduced 39.4% from 274 to 166 subjects. **CONCLUSIONS**: Computer vision enabled endoscopic disease distribution measures better detects the significant therapeutic effect of UST over PBO in UC compared to traditional endoscopic scoring instruments. Objective computer-aided activity measures may improve efficiency in clinical trials and therapeutic disease monitoring in the care of UC.

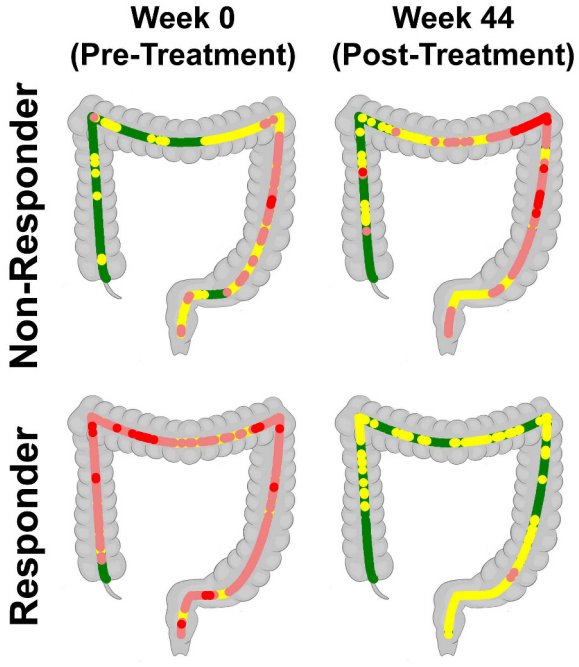

Figure 1. Disease Severity Distribution Scoring for UC Using Novel Computer Vision Methods. Shown is an example of the endoscopic disease severity distribution score for ulcerative colitis. Automated location inference is used to plot normal (green), mild (yellow), moderate (pink), and severe (red) disease activity (score values 0,1,2,3) at standardized relative intervals along the length of the colon and aggregated for a cumulative disease severity score. The clinical non-responder exhibited minimal change during the study and was assigned placebo (+161). The clinical responder assigned to ustekinumab had a reduction of cumulative endoscopic activity (-1044).