Table 1. Co–primary End Point Results: Global Improvement

Treatment	Responder Rate, %			
	Month 1	Month 2	Month 3	Last Point
Placebo	19.4	28.5	31.7	32.0
Ramosetron 2.5 μg	31.5*	41.8*	49.3**	50.7**

*$P = .001$.

**$P < .001$.

or placebo (n = 284) once a day before breakfast for 12 weeks. Co–primary end points included responder rates assessed by global improvement of irritable bowel syndrome symptoms and the Bristol Stool Scale. Secondary end points included abdominal pain or discomfort, abnormal bowel habit, stool frequency, and Japanese version of IBS-Quality of Life (IBS-QOL-J).

There were no significant differences between groups in baseline characteristics, including mean age (41 years), duration of disease (156 months), and symptoms. The co–primary end point results are shown in Table 1.

Ramosetron rapidly improved symptoms, with significant relief occurring by week 2. Stool consistency improved significantly with ramosetron treatment vs placebo at monthly assessments throughout the trial ($P < .001$). At the last point, 40.8% of the ramosetron group vs 24.3% of the placebo group showed significant improvement in stool consistency ($P < .001$). By day 2, patients in the ramosetron group showed an improved Bristol Stool Scale ($P = .018$ vs placebo). In addition, ramosetron significantly reduced daily stool frequency ($P < .001$). At study end, ramosetron also significantly improved abdominal pain and discomfort vs placebo (51.4% vs 37.7%; $P = .001$) and abnormal bowel habits during the study (50.3% vs 31.0%; $P < .001$). Ramosetron significantly improved some measures of IBS-QOL at study end, including overall quality of life, dysphoria, and food avoidance ($P < .01$ for all), as well as interference with activity ($P < .001$).

Ramosetron was associated with significantly more AEs than placebo, including gastrointestinal disorders ($P < .001$); however, there were no differences between treatment groups in infections and infestations. No ischemic colitis was observed, but the number of patients in the study may be too small to see this AE.

To conclude, ramosetron is effective in women with IBS-D at a dose half of that indicated for men, for reasons that are currently unclear. Improvements in IBS-QOL exceeded the minimal clinically important difference, further supporting ramosetron as therapeutic option for women as well as men.

High-Definition Chromoendoscopy Improves Dysplasia Detection in Ulcerative Colitis

Written by Lynne Lederman, PhD

Individuals with ulcerative colitis (UC) have an increased risk for colorectal cancer when compared with the general population [Jess T et al. *Clin Gastroenterol Hepatol*. 2012]. Surveillance endoscopy to detect dysplastic lesions is critical in reducing this risk. Image-enhanced endoscopy offers improved resolution and lesion detection during surveillance endoscopy [Subramanian V, Ragunath K. *Clin Gastroenterol Hepatol*. 2014]. Advances in image enhancement include improving contrast using dye-based chromoendoscopy (CE), using virtual CE that relies on filters or software manipulation, or using autofluorescence endoscopy based on filter technology with software manipulation.

CE increased the detection of dysplasia during surveillance endoscopy as compared with standard-definition white light endoscopy (SDWLE) in a pooled analysis [Soetikno R et al. *Gastroenterology*. 2013]. High-definition white light endoscopy (HDWLE) improved detection rates for dysplasia about 2.5-fold when compared with SDWLE [Subramanian V et al. *Inflamm Bowel Dis*. 2013]. HDWLE detected dysplasia in 24 (11.5%) of 209 patients, whereas SDWLE detected dysplasia in 8 (5.0%) of 160 patients (prevalence ratio, 2.3; 95% CI, 1.03 to 5.11).

Venkat Subramanian, MD, St James University Hospital, Leeds, United Kingdom, presented the results of a randomized trial [NCT02138318] to compare the rate of detection of dysplasia in patients with long-standing (> 8 years of disease) UC using HDWLE compared with high-definition chromoendoscopy (HDCE).

Adults were included if they had long-standing extensive UC (extending proximal to splenic flexure) and a surveillance colonoscopy. Exclusion criteria were pregnancy, unwillingness or inability to give informed consent, or severe active colitis as assessed by the endoscopist at the time of the procedure.

For HDCE, 0.2% indigo carmine dye spray was used on withdrawal. Targeted and random biopsies from each colonic segment were taken from all patients. Patients randomly assigned to the HDWLE group (n = 53) were matched with those in the HDCE group (n = 50) for baseline demographics, including age, duration of disease, smoking status, presence of primary sclerosing cholangitis, family history of colorectal cancer, and use of 5-aminosalicylates or immunomodulators. About two-thirds of patients in the HDWLE group and about half the patients in the HDCE group were women. Results are shown in Table 1.

Table 1. Detection of Dysplasia With HDCE vs HDWLE

	HDWLE (n = 53)	HDCE (n = 50)	*P* Value
Patients with dysplasia, n (%)	5 (9.4)	11 (22)	.04[a]
Total no. of dysplastic lesions detected on targeted biopsy	6[b]	14[c]	
No. of dysplastic lesions, mean ± SD	0.12 ± 0.4	0.26 ± 0.6	.04[d]
Right-sided dysplasia	2 of 6	5 of 14	
Withdrawal time, min, mean ± SD	13.6 ± 3.3	21.2 ± 5.8	< .001

HDCE, high-definition chromoendoscopy; HDWLE, high-definition white light endoscopy.
[a]Incremental yield of HDCE.
[b]All low grade.
[c]1 high grade, 13 low grade.
[d]Differences in means.

The increase in time for HDCE may be a result of the study's mandate to collect random biopsies. Since all of the dysplastic lesions detected arose from targeted biopsies rather than random biopsies, Dr Subramanian suggested that random biopsies could be omitted in practice.

HDCE significantly improves the detection of dysplastic lesions in patients with long-standing extensive UC who are undergoing surveillance endoscopy. This method could become the procedure of choice for these patients and has been recommended in recent guidelines [Shergill AK et al. *Gastrointest Endosc*. 2015]. One limitation of the study was its single-center design in a small number of patients. To confirm these results, a study enrolling about 1600 participants across the United Kingdom is being initiated.

Budesonide Shows Validated Promise in Patients With Eosinophilic Esophagitis

Written by Jaye Summers

Eosinophilic esophagitis (EoE) is a condition defined by symptoms of dysphagia or esophageal dysfunction, and an eosinophilic infiltrate that persists even after a trial of proton pump inhibitors. Evan Dellon, MD, MPH, University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA, reviewed data from a clinical trial [NCT01642212] comparing oral budesonide (OBS) with placebo in adolescents and adults with EoE.

Typical first-line medications for EoE include swallowed topical corticosteroids such as fluticasone or budesonide. Although observational data and randomized clinical trials support the use of these agents [Dellon ES, Liacouras CA. *Gastroenterology*. 2014; Liacouras CA et al. *J Allergy Clin Immunol*. 2011], neither is FDA approved for the indication of EoE. In addition, neither of these drugs has been assessed in patients using a validated measure of patient-reported outcomes.

This randomized, double-blind, multicenter placebo-controlled trial was designed to determine whether OBS was superior to placebo in generating both a histologic and a symptomatic response. Histologic response was measured by a finding of ≤ 6 eosinophils/high-power field (HPF); symptom response was measured using the Dysphagia Symptom Questionnaire (DSQ) over the 16-week course of therapy. The DSQ is a daily diary that asks 3 questions relative to a patient's symptoms and has been validated for dysphagia frequency and severity in patients with EoE [Dellon ES et al. *Aliment Pharmacol Ther*. 2013]. The histology assessment was based on biopsies obtained from the proximal, mid, and distal esophagus. All patients had a confirmed diagnosis of EoE per the 2011 updated consensus guidelines [Liacouras CA et al. *J Allergy Clin Immunol*. 2011].

Inclusion criteria included patients aged 11 to 40 years with a confirmed diagnosis of EoE, biopsy findings of ≥ 15 eosinophils/HPF at 2 esophageal levels, ≥ 4 days of dysphagia over 2 weeks during the 4-week blinded placebo run-in portion of the trial, and 70% completion of the DSQ. Key exclusion criteria included the presence of other gastrointestinal diseases, use of steroids within 4 weeks of the screening endoscopy, tight esophageal stricture, or pregnancy.

After a baseline endoscopy and biopsy, patients entered a 4-week placebo run-in period and their symptoms were assessed. Patients who met the symptom and biopsy criteria at that time were randomized to either OBS 2 mg/10 mL BID (n = 51) or placebo suspension for 12 weeks (n = 42); an open-label extension was also planned for an additional 24 weeks. Dr Dellon emphasized that this was a highly symptomatic and inflamed study group, with a mean DSQ score of 29 to 30 and a mean overall eosinophil count of 130 (placebo) and 156 (OBS).

Following the end of treatment, endoscopy and biopsy were reperformed. The coprimary outcomes were change in the DSQ from baseline and the proportion of patients with a histologic response defined as ≤ 6 eosinophils/HPF. Safety and adverse events were also monitored.

There were significant differences favoring OBS vs placebo in both the DSQ scores ($P = .0096$) and the histology results ($P < .0001$). Although the most common adverse event among both groups was nasopharyngitis, there were no safety signals evident in either group. In addition, although these results are encouraging, Dr Dellon noted several limitations to the study, including the short treatment course and the restricted age range of the patients.