



## Inflammatory Bowel Disease 10th International Meeting

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### Lessons on Optimizing 5-ASA Therapy and Bowel Preparation

**Vienna** - 5-ASA remains the mainstay of mild-to-moderate ulcerative colitis treatment. Non-adherence to treatment, however, can substantially reduce remission rates. Here at IBD 10, delegates discussed the importance of optimizing treatment regimens and endoscopy protocols in patients with inflammatory bowel disease. Key data presented showed that adherence can be improved with once-daily dosing of 5-ASA without loss of efficacy even in patients with active disease. Furthermore, evidence suggests that once-daily regimens may even lead to improved mucosal healing. Optimizing treatment with 5-ASA and thiopurines may also offer some degree of chemoprotection against colorectal cancer. Identifying tumours when they do arise, however, requires appropriate bowel cleansing to enhance visualization of lesions during endoscopy. One way in which this might be achieved is by optimizing protocol timing of bowel preparation.

Chief Medical Editor: Dr. Léna Coïc, Montréal, Quebec

When treating patients with inflammatory bowel disease (IBD), Prof. Michael Kamm, St. Vincent's Hospital, Melbourne, Australia, told delegates, "When things go wrong with patients, it's usually not the drugs that were at fault, it was how we used them." He encouraged physicians to make sure patients actually take their medication.

#### Optimizing Treatment Regimens

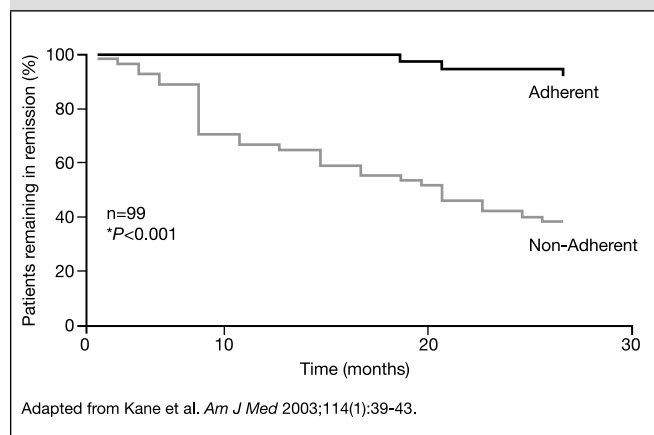
Improving adherence to 5-ASA therapy was the focus of a presentation by Prof. Axel Dignass, Markus Hospital, Frankfurt, Germany. After reminding delegates that more than 80% of patients with ulcerative colitis (UC) have mild-to-moderate disease, Prof. Dignass pointed out that failure to ensure adherence to 5-ASA therapy leads to a substantial reduction in the rate of remission, particularly in those with quiescent disease (Figure 1). One of the main risk factors for non-adherence is frequent dosing. However, as Prof. Dignass mentioned, by changing the 5-ASA regimen, adherence could be improved with no loss of efficacy.

The results of the PODIUM (Pentasa Once Daily In UC Maintenance) study (Dignass et al. *Clin Gastroenterol Hepatol* 2009;7:762-9) showed that clinical and endoscopic remission at 12 months was greater in patients receiving once-daily mesalamine (2 g) than in those following a twice-daily dosing regimen. Moreover, adherence and acceptability scores were significantly higher with the once-daily regimen. Recent studies have now extended those findings to patients with active disease, Prof. Dignass told delegates. Non-inferiority trials have now shown that once-daily dosing with mesalamine is at least as effective as repeated dosing in patients with active UC.

Most recently, the results of the MOTUS study, first presented at the 2011 UEGW in October, showed that once-daily mesalamine (2 x 2 g) was at least as effective

as twice-daily dosing in achieving clinical and endoscopic remission at 8 weeks. Importantly, the study also showed that mucosal healing was significantly better in patients receiving the once-daily regimen ( $P=0.007$ ) and that time to remission was also shorter with once-daily dosing ( $P=0.042$ ). According to Prof. Dignass, these data show that once-daily dosing is at least as effective as multiple dosing regimens, even in acute disease.

Figure 1. Non-Adherence and Risk of Relapse in UC



Irrespective of the dosing regimen, Prof. Dignass noted that the formulation used is also important. Citing a recent study by Leifeld et al., Prof. Dignass showed delegates that mesalamine granules are more effective than coated tablets in terms of both clinical and endoscopic remission (*Aliment Pharmacol Ther* 2011;34(9):1115-22). When asked about the applicability of the MOTUS trial to other 5-ASA formulations, Prof. Dignass pointed out that the effectiveness of once-daily treatment had not been investigated in all preparations and could not be considered

a class effect. Thus, ensuring that patients receive the right 5-ASA formulation and the most appropriate dosing regimen is critical to achieving sustained remission in patients with mild-to-moderate UC.

### Chemoprevention of Colorectal Cancer

Adherence is not only an issue for maintenance of remission but also to facilitate chemoprevention of colorectal cancer (CRC). In a discussion of the role of inflammation in the development of CRC, Dr. Gijs van den Brink, Academic Medical Center in Amsterdam, The Netherlands, showed delegates that agents used to treat IBD may also serve as chemoprotective agents against CRC. Citing a study by van Schaik et al., Dr. van den Brink presented evidence that thiopurine treatment is associated with a significant reduction in the prevalence of advanced colorectal neoplasia in patients with a confirmed diagnosis of UC or colonic Crohn's disease (*Gut* 2011 May 20;Epub ahead of print). In that study, 5-ASA therapy was also associated with a decreased risk of advanced neoplasia (adjusted HR 0.56; 95% CI, 0.22-1.40), although the effect was not statistically significant. Furthermore, there was some evidence of an additional protective effect of combination therapy with thiopurines and 5-ASA.

Overall, the effect of 5-ASAs on CRC remains unclear, Prof. Laurence Egan, University Hospital Galway, Ireland, told delegates. Although there is evidence of a modest effect, its duration may be limited. Nevertheless, as both Prof. Egan and Dr. van den Brink remarked, the chemoprotective effects of most IBD drugs on CRC are likely to be related to the control of inflammation and mucosal healing. Thus, the message for delegates at IBD 10 was that optimization of treatment regimens, including measures to promote adherence through improved dosing, is central to both disease management and chemoprotection.

### Bowel Preparation

Although chemoprotection is an important factor in reducing CRC-related morbidity and mortality, it is still crucial for neoplastic disease to be identified at the earliest possible opportunity. As Prof. Pradeep Bhandari, Queen Alexandra Hospital, Portsmouth, UK, reminded delegates, however, endoscopic identification of colorectal tumours is reliant upon high-quality bowel preparation.

In a study of almost 13,000 patients published earlier this year by Lebwohl et al., 24% had suboptimal bowel preparation,

yet only 17% of those had repeat colonoscopy within 3 years and only 7% within 1 year (*Gastrointest Endosc* 2011; 73(6):1207-14). According to Prof. Bhandari, this shows that poor bowel preparation is common and does not result in rescoping. In the same study, Prof. Bhandari told delegates, the miss rate for adenoma was 42%, irrespective of whether it occurred in the proximal or distal colon. Importantly, the rate for advanced adenoma was 27% in the cited study. "What this shows us," Prof. Bhandari emphasized, "is that poor bowel preparation is leading us to miss significant pathology."

Various approaches can be used to cleanse the bowel, ranging from large-volume isosmotic polyethylene glycol to low-volume hyperosmotic preparations. According to Prof. Bhandari, all of them can achieve good bowel cleansing but they differ substantially in acceptability for patients and their suitability in some cases is determined by comorbidities such as congestive heart failure and renal failure. Critical is the timing of the preparation and its acceptance by patients.

Prof. Bhandari described how good results with a high level of patient acceptability and adherence could be obtained using same-day bowel preparations. In a study involving 227 patients prepared for colonoscopy with Pico-Salax (sodium picosulphate), 95 patients were randomized to 3 sachets given at noon, 5:00 PM the day before and at 8:00 AM on the morning of the procedure; 132 patients were given 2 sachets of sodium picosulphate on the morning of the procedure at 07:00 and 10:00 (*J Clin Gastroenterol* 2011 Nov 4;Epub ahead of print). Mucosal visibility was superior with the same-day regimen ( $P=0.0049$ ) and there were fewer side effects compared to the split-dose regimen ( $P=0.002$ ). Furthermore, the impact on patient's daily activities was lower in patients who received the same-day regimen ( $P=0.0001$ ), mainly because they had less difficulty sleeping the previous night. When asked about their preferences, most patients stated that they would prefer the same-day regimen ( $P=0.014$ ).

According to Prof. Bhandari, the key to achieving the good mucosal cleansing demanded by endoscopists in order to identify lesions such as sessile serrated adenoma is to ensure a delay of less than 5 hours between the last dose of the bowel preparation and the procedure. This allows very good results to be achieved irrespective of the preparation used. "We also need to listen to what patients want, however," and according to Prof. Bhandari, this means a small volume of a palatable preparation that has no impact on their diet and minimal disruption of their daily life. Thus, in bowel cleansing as with 5-ASA dosing regimens, less may indeed be more. □

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