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File: ■ Andrographis (*Andrographis paniculata*)
■ HMPL-004
■ Ulcerative Colitis

HC 021131-420

Date: March 15, 2011

RE: Andrographis Extract HMPL-004 Improves Colitis Symptoms

Tang T, Targan SR, Li Z-S, Xu C, Byers VS, Sandborn WJ. Randomised clinical trial: herbal extract HMPL-004 in active ulcerative colitis – a double-blind comparison with sustained release mesalazine. *Aliment Pharmacol Ther*. 2011;33(2):194-202.

Ulcerative colitis (UC) is a chronic inflammatory disease of the colon. About 50% of patients with UC are treated with drugs that contain 5-aminosalicylic acid, including oral and rectal mesalazine, sulfasalazine, balsalazide, and olsalazine. Those for whom these drugs do not work are treated with steroids, azathioprine, or the anti-tumor necrosis factor-alpha (anti-TNF-α) agent infliximab. Risks for infection and malignancy have been associated with these therapies. Andrographis (*Andrographis paniculata*; AP) is widely used in Asian countries to treat various inflammatory and infectious diseases. The authors sought to determine if HMPL-004 (Hutchison Medipharma Ltd.; Shanghai, China), an aqueous ethanolic extract of AP, could significantly decrease the activity of UC and produce significant mucosal healing.

The 8-week study, which included 120 patients, was conducted at 5 sites in Shanghai, China, between November 2005 and November 2006. Eligible patients were aged 18 to 65 years, with a diagnosis of mildly to moderately active UC confirmed by colonoscopy within 1 week of the beginning of the study.

Baseline evaluation included disease history, physical examination, complete blood count (CBC), serum chemistry, urinalysis, and C-reactive protein (CRP) test for inflammation. CBC was repeated at 4 and 8 weeks; routine laboratory assessments and physical examination, at 8 weeks. Clinical symptoms were assessed at baseline and every 2 weeks by using the Chinese Gastroenterological Association's (CGA's) 2001 Standard for Diagnosis of UC Symptom Score Paradigm. Mucosal healing was evaluated by colonoscopy, and histopathology was evaluated by biopsy at baseline and at 8 weeks.

Sixty patients were randomized to receive HMPL-004, 400 mg 3 times daily; the other 60 patients received mesalazine SR granules (Etiasa®; Ethypharm Industries; France),

1500 mg 3 times daily. The 2 HMPL-004 lots used in this study contained 8-10% andrographolide (AG) by weight.

All analyses were conducted in the intention-to-treat (ITT) population—those patients who took 1 or more doses of study medication (53 in the HMPL-004 group and 55 in the mesalazine group). Consequently, patients with no treatment outcome due to discontinuation of the study were considered to have shown no efficacy.

Although no other UC medications were allowed during the study, about 50% of patients in each group had been on mesalazine at some time before the study. About half of those had failed to respond satisfactorily to it on at least one occasion. A post hoc analysis revealed that 70% of patients who responded to treatment (with remission and partial remission) in both groups had not received mesalazine previously.

Regarding safety, the authors report that 7 (13%) patients in the HMPL-004 group and 15 (27%) patients in the mesalazine group had at least 1 adverse event. Most of those events were mild to moderate and probably not related to the study medication, according to the authors.

At week 8, 11 (21%) patients treated with HMPL-004 and 9 (16%) patients treated with mesalazine were in remission. An additional cohort of 36% in both groups was classified as being in partial remission. Overall efficacy (remission, partial remission, or improvement) was reported in 40 (76%) patients in the HMPL-004 group and 45 (82%) patients in the mesalazine group ($P<0.001$).

Also, at week 8, results of the colonoscopy evaluation revealed 28% remission and 74% response rates in patients treated with HMPL-004, and 24% remission and 71% response rates in those treated with mesalazine.

Of the patients with available biopsies at week 8, 53% in the HMPL-004 group and 40% in the mesalazine group had decreased inflammation of at least 25%. Of those patients with CRP concentrations above the upper limit of normal at baseline, 80% in the HMPL-004 group and 66% in the mesalazine group had CRP concentrations within normal limits at week 8.

The authors conclude that both drugs significantly improved the clinical severity of UC and eliminated inflammation assessed by colonoscopy in about 25% of patients. The distribution between the percentage of patients who experienced remission, partial remission, or improvement was not different between the two groups. The limited sample size, however, did not power the study to demonstrate non-inferiority. Nevertheless, these results suggest that HMPL-004 could be used as a substitute for induction therapy with mesalazine or be used as induction therapy in patients who have a suboptimal response to mesalazine.

—Shari Henson

The American Botanical Council has chosen not to reprint the original article.