Mucosal Healing of Inflammatory Bowel Disease: Efficacy of Immunomodulatory Therapies Against Ulcerative Colitis and Crohn’s Disease

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Clinical efficacy of tacrolimus as a remission-induction therapy has been demonstrated in refractory ulcerative colitis (UC) in the placebo-controlled phase 2 study (Ogata H, et al. Gut 2006;55:1255-1262). Recently we have conducted phase 3 study, which consisted of placebo-controlled, double-blind study in refractory UC and the open-label study in severe refractory UC by oral administration of tacrolimus. In double-blind study, clinical response rate was 50.0% (16/32) in tacrolimus group (TG) and 13.3% (4/30) in placebo group (PG) (p=0.003), and the rate of mucosal healing observed was 43.8% (14/32) in TG and 13.3% (4/30) in PG (p=0.0117) at week 2. While in open-label study in severe patients, clinical response rate reached to 45.5% (5/11) and mucosal healing were observed in 18.2% (2/11) at week 2. As compared with the results at week 2, the rate of mucosal healing in the responder group of the double-blind study was increased to 56.3% (18/32) and clinical remission rate was 18.8% (6/32) at week 12. Of note, also in severe patients enrolled into the open-label study, mucosal healing was observed in 45.5% (5/11), and 36.4% (4/11) of the patients was successfully induced remission at week 12. Those results suggested that not only clinically remission-induction efficacy but also significant mucosal healing was demonstrated by oral tacrolimus therapy in refractory, moderate/severe UC.

Balloon endoscopy (BE) is an exciting new tool that has the distinct advantage of enabling biopsy or treatment of lesions detected during the procedure. This technique is at the forefront of the rapidly evolving field of imaging the gut in patients with Crohn’s disease (CD). BE offers the potential advantage of performing tissue biopsies or therapeutic balloon dilatation of small-bowel strictures associated with CD. Diagnostic uses of BE in the context of CD could include confirming suspected ulcerated lesions seen at capsule endoscopy or making definitive diagnoses of small-bowel lesions such as masses or strictures seen with other imaging techniques. Recently, using BE, Regueiro M, et al have demonstrated that infliximab (IFX) prevents CD recurrence after ileal resection (Gastroenterol 2009;136:441-450) by analyzing IFX maintenance therapy for 1 year after operation. We have also performed BE against CD patients at 3~15 months after ileal resection. Many of the patients (16/19) were clinically remission (CDAI<150), while 84% (16/19) of the patients showed endoscopically active findings. Of note, among 5 patients with early IFX maintenance therapy after surgery, 3 patients were endoscopically active regardless of clinically remission, and those active findings were observed mostly in anastomosis, which were not supposed to be CD involvement. And the cumulative incidence rate of re-surgery with IFX therapy was 7% (1/13) among the patients observed more than 3 years. Thus our analysis also suggests that IFX therapy is thought to be effective for maintained remission against CD after ileal resection.