



# Higher Mucosal Healing with Tumor Necrosis Factor Inhibitors in Combination with Thiopurines Compared to Methotrexate in Crohn's Disease

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## Abstract

**Background** The differential impact of anti-tumor necrosis factor (anti-TNF) therapy with methotrexate versus thiopurine co-therapy on endoscopic remission remains uncertain.

**Aims** To compare rates of endoscopic remission based on methotrexate or thiopurine co-therapy used with anti-TNF therapy in Crohn's disease.

**Methods** A retrospective observational study at two tertiary centers between 2010 and 2016 compared endoscopic remission rates and persistence on anti-TNF therapy in combination with methotrexate versus thiopurines for at least 3 months.

**Results** Of 412 patients on anti-TNF therapy, 278 (67%) received immunomodulator co-therapy for  $\geq 3$  months and 269 (65%) had complete data for analysis. Methotrexate was used in 77 (29%) and thiopurines in 192 (71%) patients plus either infliximab (156, 58%) or adalimumab (113, 42%), with median follow-up of 2.8 years. The methotrexate group had greater prior immunomodulator intolerance (62% vs 20%,  $p < 0.01$ ). Endoscopic remission rates were higher in those treated with thiopurine compared to methotrexate co-therapy at 12 m (58% vs 17%,  $p < 0.01$ ) and at last review (59% vs 40%,  $p = 0.03$ ). Endoscopic remission rates were higher with thiopurines than methotrexate when combined with adalimumab (49% vs 6%,  $p < 0.01$ ) but not with infliximab (65% vs 54%,  $p = 0.09$ ). In multivariate analysis, thiopurine co-therapy, elevated baseline CRP, and therapeutic anti-TNF drug levels were each associated with longer persistence of co-therapy (each  $p < 0.05$ ). There were no significant differences in adverse events, malignancy or infection rates.

**Conclusion** In this cohort, anti-TNF and thiopurine co-therapy resulted in higher rates of mucosal healing than methotrexate, the difference is most pronounced with adalimumab and conversely with low-dose methotrexate.

**Keywords** Infliximab · Adalimumab · Azathioprine · Mercaptopurine · Endoscopy

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