|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **Study drug**  | **Study design** | **Cohorts** | **Endpoints** | **Results** | **Conclusions** |
| Regueiro M et al[156] | IFX | Double blind RCT | Arm 1: 11 patients started IFX within 4 weeks after resectionArm 2: 13 patients received placebo.30% of both groups previously treated with IFX | Primary endpoint: proportion of patients with endoscopic recurrence at 1 year. Secondary endpoints: clinical recurrence, remission and histologic recurrence | At 12 mo: Endoscopic recurrence 9% vs 84%Clinical recurrence: 0% vs 38.5% | IFX superior to placebo in preventing endoscopic and clinical recurrence. |
| Regueiro M et al[255] | IFX | Open-label, long-term follow-up (5 years) study of previous study (1) | The 24 patients previously randomly assigned to receive infliximab for 1 year or placebo given the option to continue, stop, or start IFX | Primary endpoint: time to endoscopic recurrence from the initial assignment to IFX or placebo. Secondary endpoints: rate of endoscopic recurrence, time to reoperation, and rate of surgical recurrence in relation to the total time on IFX | Patients assigned to IFX had longer mean time to first endoscopic recurrence (1231 ± 747 days vs 460 ± 121 days, P = .003). Endoscopic recurrence in 22.2% of patients with long-term IFX vs 93.9% of those not on IFX (P < .0001).  | IFX maintenance beyond 1 year prevents recurrence of CD |
| Yoshida K et al[256] | IFX | RCT | Arm 1: 15 patients received scheduled IFX every 8 weeks for 36 monthsArm 2: 15 patients received no treatment | Primary endpoint: remission rate at 12 mo Secondary endpoints: remission rate at 36 mo, endoscopic recurrence at 12 and 36 mo  | At 12 and 36 mo, 100%, and 93.3% of IFX patients in remission vs. 68.8% and 56.3% in controls (P < 0.03).86.7% of IFX patients maintained serological remission (CRP <0.3 mg/dL) vs. 37.5% in controls (P < 0.02)The IFX group achieved higher endoscopic remission at 12 mo: 78.6% vs. 18.8% (P = 0.004) | IFX prevents clinical, serological, and endoscopic recurrence after ileocolic resection |
| Sorrentino D, et al[257] | IFX | Prospective series of patients | Arm 1:7 patients treated with IFX and MTXArm 2:16 patients treated with mesalamine | Primary endpoints: clinical and endoscopic recurrence at 2 years | At 2 years: 0% of clinical or endoscopic recurrence in patients treated with IFX and MTX vs 75% in the mesalamine group | Combination treatment with IFX and MTX is superior to mesalamine for preventing post-operative recurrence |
| Sorrentino D, et al[177] | IFX | Prospective cohort study | 12 consecutive patients, treated after surgery with IFX without recurrence after 24 mo, followed up for an additional year and then discontinued. Patients with disease recurrence, were given IFX again  | Recurrence while on IFX treatment and after discontinuation.Rates of remission after IFX re-initiation  | None of the patients had recurrence by 3 yrs. 83% endoscopic recurrence 4 mo after IFX discontinuation. All 10 patients treated again restored and maintained mucosal integrity for 1 year.  | Long-term IFX maintenance therapy maintains mucosal integrity after surgeryLow IFX doses (3 mg/kg) can avoid endoscopic recurrence at 1 year. |
| Savarino E, et al[258] | ADA | RCT | After 2 weeks from surgery patients received ADA every two weeks, azathioprine (AZA) or mesalamine, and they were followed up for 2 years. | Primary endpoint: proportion of patients with endoscopic and clinical recurrence. Secondary endpoint: assessment of QoL  | SIgnificantly lower rate of endoscopic recurrence in ADA (6.3%) compared with the AZA (64.7%) and mesalamine groups (83.3%). Significantly lower proportion of patients in clinical recurrence in the ADA group (12.5%) compared with the AZA (64.7) and mesalamine groups (50%). Higher QoL in the ADA than in the AZA and mesalamine groups  | ADA after intestinal resection is superior to AZA and mesalamine in preventing clinical and endoscopic recurrence |
| Savarino E, et al[259] | ADA | Prospective series of patients | 6 patients were given 2 weeks after the operation ADA and followed up | Clinical, radiological, endoscopic and histological recurrence rates in the series | All the patients disease-free for 3 years after surgery on clinical, radiological, and endoscopic/histological grounds | ADA seems to be effective in preventing recurrence after intestinal resection |
| Papamichael K, et al[260] | ADA | Prospective open-label, two-year study | Arm 1: 8 patients received ADA from post operative 14 day.Arm 2: 15 patients received ADA 6 mo post-operatively after confirmation of endoscopic recurrence despite treatment with AZA, IFX or mesalamine | Primary endpoints: maintenance (Arm I) or achievement of mucosal healing (Arm II). Secondary endpoints: prevention of clinical recurrence (Arm I) and endoscopic and clinical improvement (Arm II) | Arm 1: 2 patients on ADA had recurrence (at 6 and 24 months)Arm 2: after 24 mo, 60% achieved complete (n=3) or near complete (n=6) mucosal healing and 56% clinical remission | ADA may prevent postoperative endoscopic recurrence and treat postoperative endoscopic and clinical recurrence in high risk patients  |
| Aguas M, et al[261] | ADA | Prospective, observational study | 29 high-risk patients were given ADA every 2 weeks after intestinal resection | Endpoints: Clinical, endoscopic and morphological recurrence 1 year after intestinal resection | 4/29 (13.7%) developed clinical recurrence, 6/29 (20.7%) endoscopic recurrence and 7/19 (36.8%) morphological recurrence after 1-year.  | ADA is effective and safe in preventing postoperative recurrence in high-risk patients after intestinal resection  |
| De Cruz P, et al[153] | ADA | RCT (POCER) | Consecutive 174 patients received 3 months of metronidazole therapy after intestinal resection. High-risk patients also received a thiopurine, or ADA (if intolerant to thiopurines).Patients randomly assigned to 2 groups: colonoscopy at 6 mo (active care) or no colonoscopy (standard care).For endoscopic recurrence at 6 months, patients stepped-up to thiopurine, fortnightly ADA with thiopurine, or weekly ADA | Primary endpoint: endoscopic recurrence at 18 mo | At 18 months: endoscopic recurrence in 49% in the active care group vs 67% in the standard care group (p=0·03).Mucosal normality maintained in 22% in the active care group vs 8% in the standard care group (p=0·03). In the active care arm, of those with 6 mo recurrence who stepped up treatment, 38% were in remission 12 mo later; of those in remission at 6 mo who did not change therapy recurrence occurred in 31 41% recurrence 12 mo later. Incidence and type of adverse events did not differ significantly between groups  | Treatment according to clinical risk of recurrence, with early colonoscopy and treatment step-up for recurrence, is better than conventional drug therapy alone for prevention of postoperative recurrence. Selective immune suppression, adjusted for early recurrence, rather than routine use, leads to disease control in most patients.  |

Suppl Table 1. Table of evidence of publications on prophylactic anti-TNF use in postoperative recurrence