

Medical therapy perianal Crohn's disease

1999	Infliximab	RCT/ IFX 5 mg/kg vs 10mg/kg vs placebo / Induction N=94 Primary endpoint: $\geq 50\%$ reduction in draining fistulas. R: Achieved in 68% (5 mg/kg) and 56% (10 mg/kg) vs 26% in placebo ($p=0.002$ & $p=0.02$). Conclusion: Infliximab is an efficacious treatment for fistulas in patients with Crohn's disease.
2003	Oral Tacrolimus	RCT/Oral tacrolimus 0.2mg/kg/day vs placebo / Induction N=48 Primary endpoint: fistula improvement ($\geq 50\%$ closure of draining tracts for ≥ 4 weeks). R: Significantly higher with Tacrolimus vs placebo (43% vs 8%, $P=0.004$). Conclusion: Oral tacrolimus is effective for fistula improvement, but not fistula remission.
2003	Antibiotics & azathioprine	Prospective OL/ Ciprofloxacin AND/OR metronidazol (AB) +/- AZA / Induction N=52 Primary endpoint: Fistula drainage improvement by Perianal Disease Activity Index at w8 R: 50% patients responded to antibiotic treatment. AZA+ AB response 48% vs AB alone 18%, $p=0.03$ Conclusion: AB are useful to induce a short-term response in perianal CD and may provide a bridging strategy to AZA.
2004	Infliximab	RCT/ IFX vs placebo after response to induction/ Maintenance N=306 Primary endpoint: time to loss of response. R: IFX >40 weeks vs 14 weeks placebo, $p<0.001$. At w54 36% IFX vs 19% placebo complete fistula absence. Conclusion: IFX maintenance is better than placebo to maintain response and fistula complete healing.
2004	IFX +/- ciprofloxacin	RCT/ Ciprofloxacin 500mg BD + IFX vs placebo+IFX / Induction N=24. Primary endpoint: clinical response ($\geq 50\%$ reduction in draining fistulas) at week 18. R: CIPRO+IFX 73% vs 39% IFX+placebo, $p=0.12$. PDAI only improved in IFX+CIPRO $p=0.008$ Conclusion: A combination of CIPRO and IFX tended to be more effective than IFX alone.
2007	Topical tacrolimus	Exploratory RCT/topical tacrolimus 1 g BID vs placebo / perianal CD (fistula & ulcerating)/ Induction N=19 Primary endpoint: Global improvement $\geq 50\%$ reduction in draining fistulas. R: Improvement in ulcerating disease vs placebo but not fistulising. Conclusion: Preliminary data suggest that topical tacrolimus is effective in anal ulcerating CD. This therapy is unlikely to be beneficial in fistulizing perianal CD.
2008	AST-120	RCT/ Oral spherical adsorptive carbon (AST-120) vs placebo / Induction N=62 Primary endpoint: $\geq 50\%$ reduction in draining fistulas at w4 and w8 R: AST120 37% vs 10% placebo, $p=0.025$ Conclusion: AST-120 is useful for the control of intractable anal fistulas in CD patients.
2009	Ciprofloxacin or metronidazol	RCT/ ciprofloxacin 500mg BID vs metronidazol 500mg BID or placebo for 8 weeks/ Induction N=25 Primary endpoint: Remission at 10 weeks R: Ciprofloxacin 30% vs metronidazol 0% vs 12.5% placebo, $p=0.41$ Conclusion: Remission & response occurred more frequently in patients treated with CIPRO but not significantly.
2010	Metronidazol ointment	RCT/ Metronidazol 10% ointment (0.7g/8h) vs placebo ointment/ perianal CD/ Induction N=74 Primary endpoint: Mean reduction in PDAI score. R: Metronidazol 2.4 vs 2.2 placebo. $p=0.66$ Conclusion: Metronidazole 10% ointment was not effective in the reduction of PDAI score
2014	FHASt-1	RCT phase 3/ Oral spherical adsorptive carbon (AST-120) vs placebo/Induction N=249 Primary endpoint: 50% reduction in the number of draining fistulae, at both weeks 4 and 8 R: 13.9% AST120 vs 16.5% placebo, $p=0.6$ Conclusion: The efficacy of AST-120 could not be confirmed.
2014	ADAFI	RCT/ Adalimumab +/- ciprofloxacin 500mg BID for 12 weeks/ Induction N=76 Primary endpoint: $\geq 50\%$ reduction in draining fistulas at week 12 R: ADA+CIPRO 71% vs 47% ADA+placebo, $p=0.047$ Conclusion: ADA+CIPRO is more effective than ADA alone to achieve fistula closure. However, after CIPRO discontinuation, the beneficial effect is not maintained.
2020	PISA I	RCT/ seton vs antiTNF vs surgical closure after 2 months on antiTNF/Maintenance (stopped for fertility) N=44 Primary endpoint: rate of fistula re-interventions at 1-5 years R: reintervention seton 66.7% vs AntiTNF 40% vs AntiTNF+closure 21.4% Conclusion: Chronic seton treatment should not be recommended as the sole treatment for CD fistulas.
2022	ENTERPRISE	RCT/Standard vedolizumab (0,2,6,14,22) induction vs extra dose at week 10 / perianal CD/ Induction N=34 Primary endpoint: $\geq 50\%$ decrease in draining fistulas at week 30 R: VDZ standard 64.3% vs VDZ+w10 42.9%, $p=ns$. 53.6% $\geq 50\%$ decrease & 42.9% complete closure at w30. Conclusion: An additional dose at week 10 does not appear to alter treatment outcomes.
2022	PISA-II	Patient preference RCT/ 4-month antiTNF& surgical closure or antiTNF for 1y, after seton insertion N=94 Primary endpoint: Radiological healing on MRI R: MRI healing 42% antiTNF+surgical closure vs 18% antiTNF, $p=0.014$ Conclusion: AntiTNF treatment +surgical closure induces long-term MRI healing more frequently than anti-TNF therapy in patients with perianal CD.
2024	DIVERGENCE 2	Phase 2 RCT/ filgotinib 200mg vs 100mg vs placebo 24week trial/ Induction N=57 Primary endpoint: Reduction of draining openings+ MRI absence of fluid collections >1 cm R: Filgo 200mg 47.1% vs Filgo100mg 29.2% vs 25% placebo Conclusion: Filgotinib 200 mg was associated with numerical reductions in the number of draining perianal fistulas

