INFLIXIMAB I

1995	IFX-cA2	Open-label study /single IFX IV dose 10mg/kg or 20mg/kg/ CD/ Induction Conclusion: **Treatment with cA2 was safe and may be useful in patients with Crohn's disease who do not respond to steroids.**
1997	IFX	RCT /single dose of IFX 5 mg/kg vs IFX 10mg/kg vs 20mg/kg vs placebo/ CD/ Induction Conclusion: **A single infusion of cA2 was effective in the short-term in moderate-severe Crohn's disease.**
1999	IFX	RCT/ Responders to 1 dose randomized to 10mg/kg q8w or placebo /CD/ Maintenance Conclusion: **Long-term treatment with IFX is better than placebo maintaining remission in Crohn's disease.**
1999	IFX-Fistula	RCT/ IFX+5mg/kg vs 10mg/kg vs placebo/ fistulizing CD/ Induction Conclusion: **Infliximab is an efficacious treatment for fistulas in patients with CD.**
2002	ACCENT I	RCT /After response to 1 dose IFX: IFX 5mg/kg vs 10mg/kg vs placebo/ CD/ Maintenance Conclusion: **CD who respond to an initial dose of infliximab more likely to be in remission at w30 & 54, to discontinue corticosteroids, & maintain response, if IFX is maintained q8w.**

INFLIXIMAB II

2004 — ACCENT II

RCT /Responders at w10 randomized to: IFX 5mg/kg q8w vs placebo/ CD/ Maintenance
Conclusion:
Patients with fistulizing CD who have a response to induction therapy with IFX have an increased likelihood of a sustained response over a 54-week period if iIFX treatment is continued every 8 weeks.

2005 — ACT I&II

RCT / IFX 5 mg/kg vs IFX 10mg/kg vs placebo/ Mod-Severe UC/ Induction & Maintenance
Conclusion:
IFX at w0,2&6 and q8w thereafter better achieving clinical response at w8,30&54 compared to placebo in mod-severe UC.

2007 — REACH

OL/ IFX 5 mg/kg q8w vs IFX 5mg/kg q12w after induction Mod-sev pediatric CD/ Induction&Maintenance
Conclusion:
IFX in pediatric CD q8w more likely to achieve clinical response & remission at w54 than q12w

2008 — SUTD

Open randomized trial/ IFX+AZA vs conventional (steroids)/ New CD/ Induction remission
Conclusion:
Combo therapy more effective than conventional for induction & reduction of steroid use in recently diagnosed CD.

2009 — IFX-postop

RCT/ IFX vs placebo after ileocolonic resection/ CD/ Disease recurrence
Conclusion:
Administration of infliximab after intestinal resective surgery was effective at preventing endoscopic and histologic recurrence of Crohn's disease.

INFLIXIMAB III

2010 — SONIC

RCT/ IFX vs AZA vs IFX+AZA/ Mod-Severe CD/ Remission
Conclusion:
Patients with mod-severe CD treated with IFX+ AZA or IFX monotherapy were more likely to have steroid free remission than AZA alone. Combotherapy superior to both monotherapies.

2012 — IFX-postop

Open label / IFX 5mg/kg induction and q8w vs placebo after surgery/ CD/ Disease recurrence
Conclusion:
An early intervention with IFX monotherapy should prevent clinical, serological, and endoscopic CD recurrence following ileocolic resection. Thiopurine naivety and eliminating the initial loading dose of IFX might minimize serious AEs.

2012 — STORI

Prospective cohort/ stop IFX in CD in remission & maintenance on AZA/ Relapse
Conclusion:
Aprox 50% of patients with CD treated for a year with IFX+AZA relapsed within 1 year after discontinuation.

2012 — SWITCH

OL/ IFX vs switch to ADA/ CD/ Relapse
Conclusion:
Elective switching from IFX to ADA associated with loss of tolerance and loss of efficacy within 1 year. Adherence to the first antiTNF is recommended.

2012 — CYSIF

OL RCT/Ciclosporin vs IFX/ASUC/Induction
Conclusion:
Ciclosporin was not more effective than IFX in patients with ASUC refractory to intravenous steroids. In clinical practice, treatment choice should be guided by physician and centre experience.

INFLIXIMAB IV

2013 — **IFX kids**

Open label/ IFX 5mg/kg /pediatric UC / Induction
Conclusion:
IFX shows similar pharmacokinetics and exposure/response in kids and adults. A positive relationship was noted between serum infliximab level and clinical effect following induction therapy similar to adults.

2013 — **AZA-IFX postop**

Open label/IFX standard dose vs AZA 2.5mg/kg/d / CD /Disease relapse
Conclusion:
Infliximab was more effective than azathioprine in reducing histological, but not endoscopic and clinical recurrence after curative ileocolonic resection in "high risk" CD patients.

2014 — **UC-SUCCESS**

RCT/AZA vs IFX vs AZA+IFX / UC/ Induction
Conclusion:
IFX+AZA combotherapy superior to IFX or AZA alone achieving steroid free remission w16.

2014 — **COMMIT**

RCT/IFX+MTX vs IFX alone/ CD
Conclusion:
The combination of infliximab and methotrexate, although safe, was no more effective than infliximab alone in patients with CD receiving treatment with prednisone.

2014 — **ADA-IFX postop**

OL RCT/IFX vs ADA /postsurgery CD/ Disease recurrence
Conclusion:
IFX and ADA were similar in preventing histological, endoscopic and clinical recurrence after curative ileocolonic resection in high risk CD patients.

INFLIXIMAB V

2015 — TAXIT

RCT/IFX dose change based on clinical symptoms or trough concentration/IBD remission 1year
Conclusion:
Targeting IFX TCs to 3–7 mg/mL results in a more efficient use of the drug. After dose optimization, continued concentration-based dosing was not superior to clinically based dosing for achieving remission after1 year, but was associated with fewer flares during the course of treatment.

2015 — REACT

OL RT/ antiTNF+AZA early treatment vs conventional/ CD/ Maintenance
Conclusion:
Lower risk of major adverse outcomes in early combined immunosuppresion in CD vs conventional treatment. However, no differences in remission rates at 12 months.

2016 — CONSTRUCT

OL RT/ IFX vs cicloscporin/ ASUC
Conclusion:
There was no significant difference between ciclosporin and infliximab in clinical effectiveness.

2016 — PREVENT

RCT/ IFX vs placeboy/ posturgical CD / Disease recurrence
Conclusion:
IFX is not superior to placebo in preventing clinical recurrence after CD-related resection. However, infliximab does reduce endoscopic recurrence

2017 — ENCORE-CD

Observational/ IFX vs conventional treatment/ CD / Safety
Conclusion:
IFX exposure related to increased risk of infections & haematological conditions, whereas mortality may be decreased.

INFLIXIMAB VI

2017 NOR-SWITCH

Phase 4/ CT-P13/ IMIDs/ non-inferiority
Conclusion:
Switching from IFX originator to CT-P13 was not inferior to continued treatment with IFX originator.

2017 LIRIC

OL-RCT/ IFX vs Surgery/ active ileal CD / QoL
Conclusion:
No differences in: QoL at 12 months, social life problems, hospital admission between IFX vs Surgery. Laparoscopic resection in limited (<40 cm) ileocaecal CD, could be considered as an alternative to IFX.

2018 SECURE

Open label RCT/In remission at w30 onIFX originator switch to CT-P13/ IBD
Conclusion:
Switching to CT-P13 is safe and well tolerated in patients with inflammatory bowel disease in remission.

2018 TEDDY

Observational/ antiTNF exposed newborn/ IBD/ Safety
Conclusion:
In utero exposure to anti-TNF drugs does not seem to be associated with increased short-term or long-term risk of severe infections in children.

2018 IFX-postop

Open laber RCT/ IFX vs placebo/ postsurgical CD / Disease recurrence
Conclusion:
The postoperative use of IFX is effective in preventing Crohn's disease recurrence for 2 years.

INFLIXIMAB VII

2018 — TAILORIX

Proof-of-concept RCT / IFX/ CD/ Steroid-free remission
Conclusion:
Increasing dose of IFX based on a combination of symptoms, biomarkers, and serum drug concentrations does not lead to corticosteroid-free clinical remission in a larger proportion of patients than increasing dose based on symptoms alone

2019 — PANTS

Observational/ antiTNF/CD/ Predictors of failure
Conclusion:
Anti-TNF treatment failure is common & is predicted by low drug concentrations, mediated in part by immunogenicity.

2019 — CT-P13

RCT/ IFX originator vs CT-P13/ CD/ Induction
Conclusion:
This study showed non-inferiority of CT-P13 to infliximab in patients with active Crohn's disease. Biosimilar CT-P13 could be a new option for the treatment of active Crohn's disease.

2020 — PISA-I

Open label RCT/seton drainage vs IFX vs seton+IFX/ perianal CD/ Induction and Maintenance
Conclusion:
The results imply that chronic seton treatment should not be recommended as the sole treatment for perianal Crohn's fistulas (study stopped due to futility as antiTNF showed clear superiority)

2020 — PIANO

Observational/Biologics &/or thiopurines/ IBD pregnant/ Safety
Conclusion:
Biologic, thiopurine, or combination therapy exposure during pregnancy was not associated with increased adverse maternal or fetal outcomes at birth or within the first year of life.

INFLIXIMAB VIII

2021 GARDENIA

Phase 3/ ETR vs IFX/ UC/ Maintenance
Conclusion:
Etrolizumab did not met primary endpoint for superiority against IFX in clinical response w10 &clinical remission w54.

2021 PRECISION

RCT/IFX dosing guided by Bayesian pharmacokinetic vs standard /IBD patients in remission / Maintenance
Conclusion:
The use of a Bayesian dashboard for IFX dosing in maintenance treatment for IBD reduced the incidence of LOR compared to standard dosing. Precision dosing also resulted in lower FCP levels.

2021 IFX IV/SC

RCT/ IFX (CT-P13) IV vs SC /IBD/ Maintenance
Conclusion:
The pharmacokinetic non-inferiority of CT-P13 SC to CT-P13 IV, and the comparable efficacy, safety, and immunogenicity profiles, support the potential suitability of CTP13 SC treatment in IBD.

2021 CLARITY

Observational/ Biologis and immunosupressants/ IBD and SARS-CoV2/ antibody response
Conclusion:
IFX is associated with attenuated serological response to SARS-CoV-2 that were further blunted by immunomodulators used as concomitant therapy.

2022 STOP-IT

RCT/Stop IFX/ CD/ Relapse
Conclusion:
Discontinuation of infliximab for patients with Crohn's disease receiving long-term infliximab therapy and in clinical, biochemical, and endoscopic remission leads to a considerable risk of relapse.

INFLIXIMAB IX

2022 PUCCINI

Observational /AntiTNF/ IBD needing surgery / Infection risk
Conclusion:
Preoperative antiTNF exposure was not associated with postoperative infectious complications in a large prospective multicenter cohort.

2022 VIP

Observational /Biologics & immunosupressants/ IBD and COVID vaccine / Response to vaccine
Conclusion:
For patients with IBD, the immunogenicity of COVID-19 vaccines varies according to immunosuppressive drug exposure, and is attenuated in recipients of IFX, IFX+thiopurines and TOFA.

2022 REMSWITCH

Observational/ IFX subcut/ IBD in remission/ relapse
Conclusion:
Switching from IV to SC IFX 120 mg every other week is safe and well accepted, leading to a low risk of relapse in IBD patients except for those receiving 10 mg/kg q4w requiring 240 mg every other week.

2022 TISkids

RCT/ IFX /paediatric CD/Induction
Conclusion:
First line-IFX was superior to conventional treatment in achieving short-term clinical and endoscopic remission, and had greater likelihood of maintaining clinical remission at week 52 on azathioprine monotherapy.

2022 PISA-II

RT/antiTNF and surgical closure or antiTNF alone/ CD perianal / Long term response
Conclusion:
Short-term anti-TNF treatment combined with surgical closure induces long-term MRI healing more frequently than anti-TNF therapy in patients with CD and perianal fistulas.

INFLIXIMAB X

2023

SPARE

OL RCT/antiTNF or AZA withdrawal/ CD

Conclusion:

IFX withdrawal should only be considered after careful assessment of risks/benefits, whereas withdrawal of immunosuppressant therapy could generally be preferable when considering de-escalation.