IBD Trials

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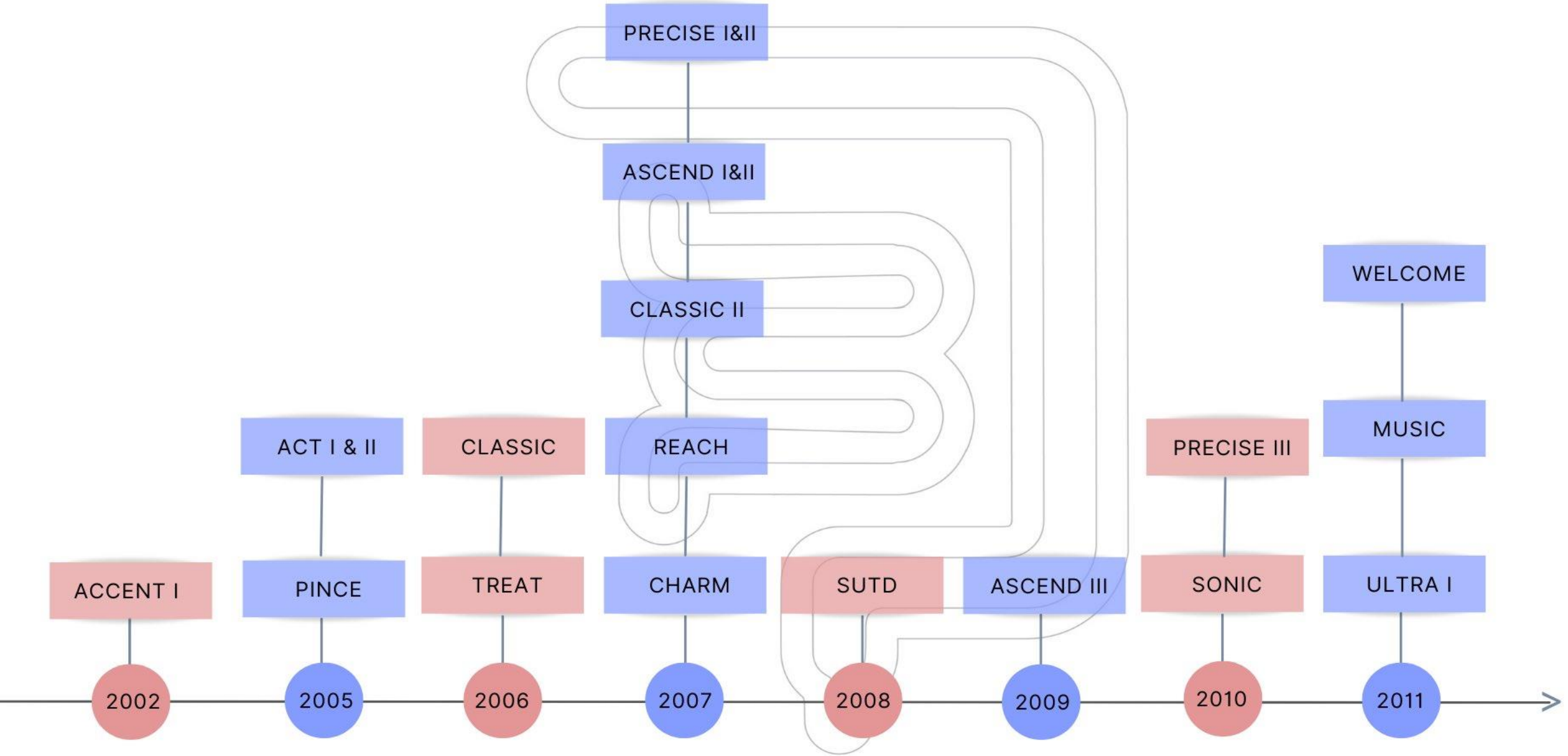

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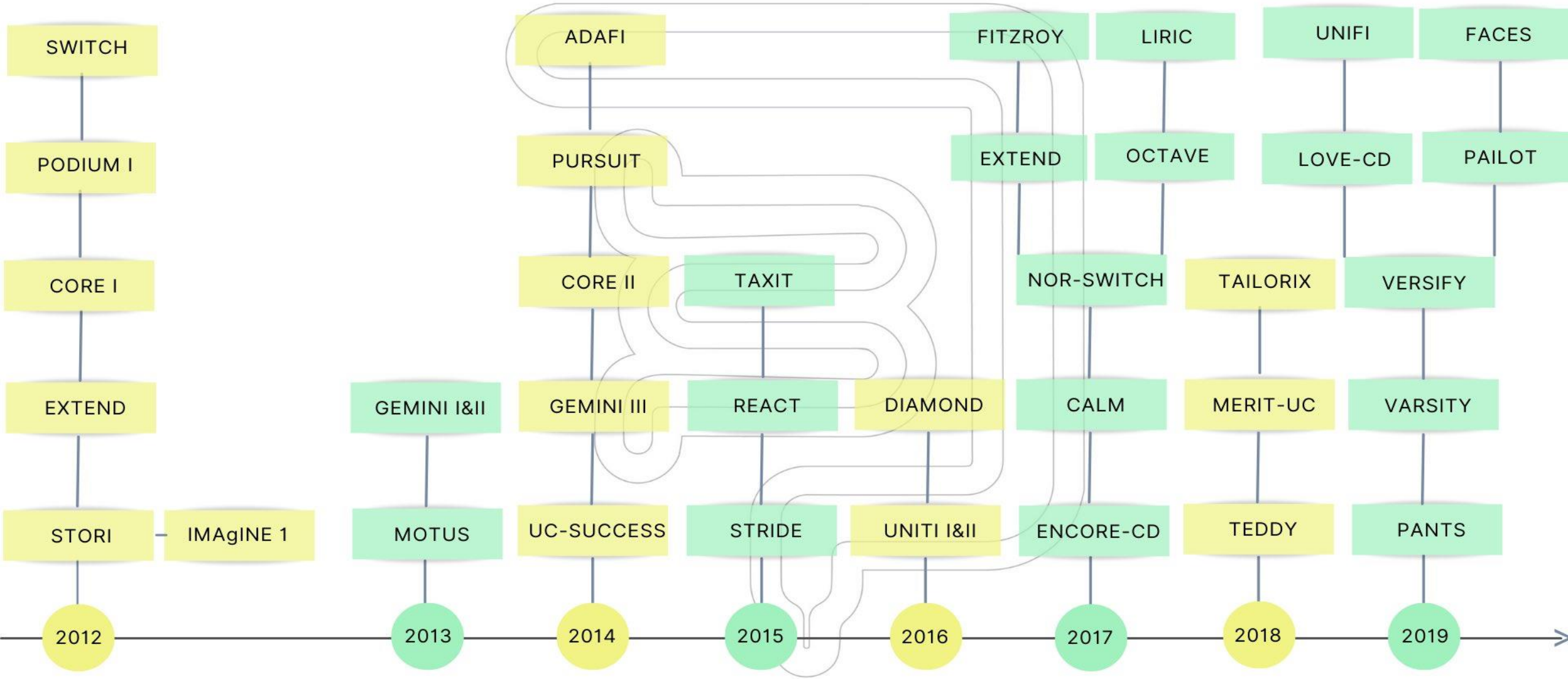

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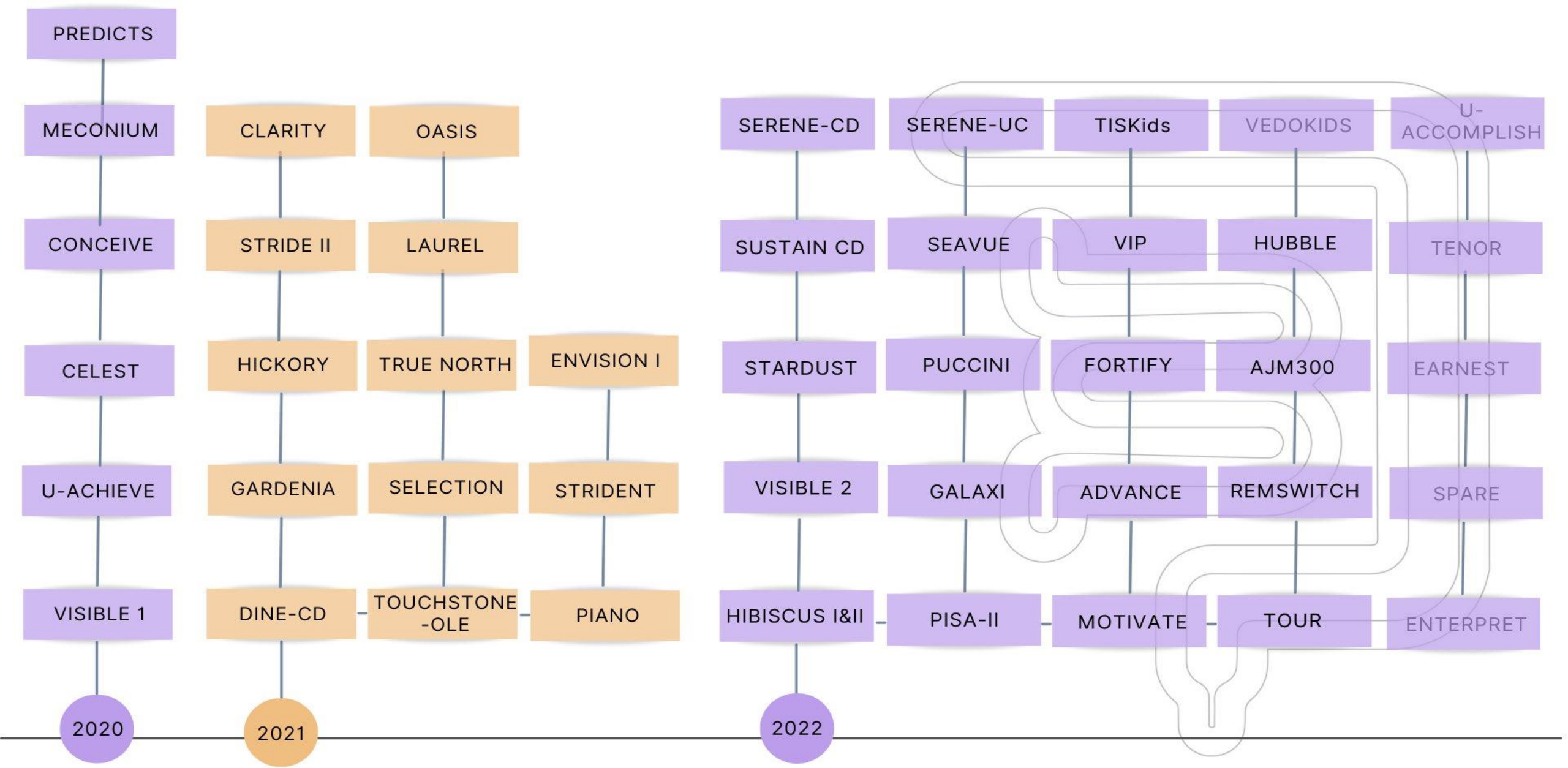

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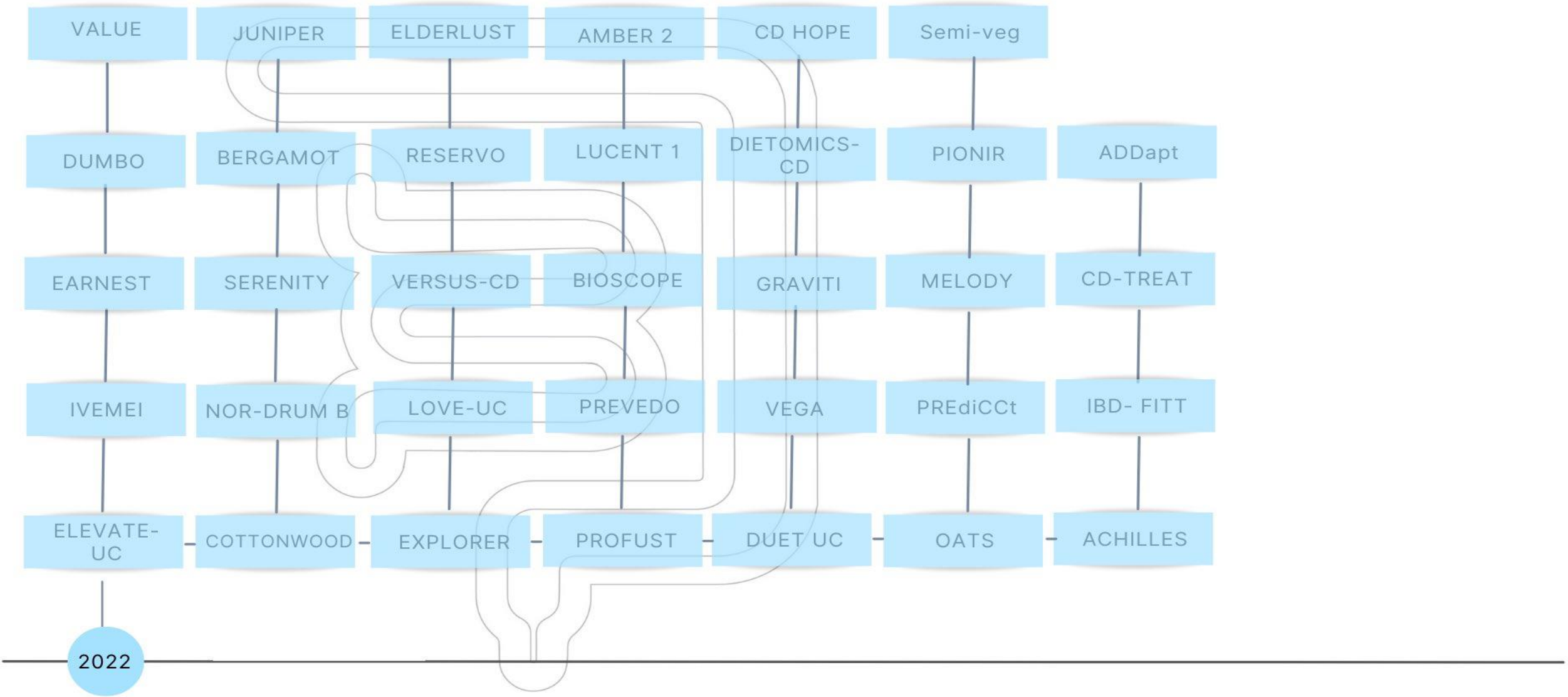

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5ASA studies

2005 PINCE

RCT / 5ASA oral+ enema/ Mild-Mod UC/ Induction of remission
Conclusion:
In extensive mild-moderate active UC, enema + oral mesalazine superior than oral 5ASA alone.

2007 ASCEND I

RCT/ 5ASA/ Mild-mod active UC/ Induction
Conclusion:
Preliminary evidence supporting the use of an initial 4.8 gr dose to treat moderate active UC.
This data were later confirmed in the ASCEND II (2007) and ASCEND III (2009) trials.

2012 PODIUM I

RCT/ 5ASA OD vs BD/ Mild-mod left sided-UC/ Maintenance
Conclusion:
Once daily slow-release mesalazine similarly effective to twice daily schedule in left-sided UC.

2013 MOTUS

RCT/ 5ASA OD vs BD/active UC/ Induction of remission
Conclusion:
Prolonged-release mesalazine OD 4 gr as effective and well tolerated as 2 gr BD for inducing remission in mild-to-moderately active UC.

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Thiopurines

2008	SUTD	Open randomized trial/ IFX+AZA vs conventional (steroids)/ New CD/ Induction remission Conclusion: **Combined therapy more effective than conventional for induction and reduction of steroid use in recently diagnosed CD.**
2010	SONIC	RCT/ IFX vs AZA vs IFX+AZA/ Mod-Severe CD/ Remission Conclusion: **Patients with moderate to severe active CD treated with IFX+ AZA or IFX monotherapy were more likely tohave steroid free remission than AZA alone. Combotherapy superior to both monotherapies.**
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.**
2015	REACT	RCT/ Early ADA+AZA vs conventional (steroids+/- thiopurine or ADA if no remission w12)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	DIAMOND	OL RCT/ ADA vs ADA+AZA / active CD / Efficacy & safety Conclusion: **Clinical efficacy of ADA+AZA did not differ from ADA monotherapy in CD naïve to both medications.**

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INFLIXIMAB I

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.

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.

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.

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INFLIXIMAB II

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.**
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.**
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.**
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.**

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INFLIXIMAB III

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 — 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.

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.

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.

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ADALIMUMAB

2006 — CLASSIC I

RCT/ ADA vs placebo dose ranging trial/ CD/ Induction
Conclusion:
ADA better than placebo for induction of remission. Optimal induction dosing regimen for ADA in this study was 160 mg at week 0 followed by 80 mg at week 2. Adalimumab was well tolerated.

2007 — CLASSIC II

RCT/ ADA ew vs eow vs placebo/ CD/ Maintenance & Safety
Conclusion:
ADA induced and maintained clinical remission for up to 56 weeks in patients with mod-severe Crohn's disease naive to anti-TNF treatment.

2007 — CHARM

OL induction, then double blind RCT/ ADA/ Mod-sev CD/ Maintenance
Conclusion:
Among patients who responded to ADA, both ADA eow & ew more effective than placebo in maintaining remission in mod-severe CD through 56w. ADA was well tolerated and safe.

2011 — UTRA I

RCT/ADA vs. pbo/ Mod-Severe UC/ Induction
Conclusion:
ADA160/80 was safe and effective for induction of clinical remission in patients with mod-severe active UC failing treatment with corticosteroids and/or immunosuppressants.

2012 — ULTRA 2

RCT/ADA vs. pbo/ Mod-Severe UC/ Maintenance
Conclusion:
ADA was more effective than placebo in inducing and maintaining clinical remission in patients with mod-severe UC that was not responsive to conventional therapy.

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ADALIMUMAB II

2012 — EXTEND

RCT/ ADA vs Pbo/ Mod-Sev CD/ Induct+Maintain
Conclusion:
Following induction therapy with ADA, patients with mod-severe active CD who continue with ADA are more likely to achieve mucosal healing than those given placebo.

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.

2015 — REACT

RCT/ ADA+AZA vs conventional/ CD/ Remission+Maintain
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 — DIAMOND

OL RT/ ADA vs ADA+AZA / active CD / Efficacy & safety
Conclusion:
Clinical efficacy of the combination of ADA+AZA did not differ from ADA monotherapy in CD naïve to both medications.

2017 — CALM

OL/ tight control vs clinical management with ADA+/- AZA/ CD / Efficacy & safety
Conclusion:
Timely escalation with ADA on the basis of clinical symptoms and biomarkers in patients with early CD results in better clinical an endoscopic outcomes than symptom-driven decisions alone.

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ADALIMUMAB III

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.

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 — VARSITY

Phase 3b/ VEDO vs ADA/ UC/Remission
Conclusion:
VEDO superior to ADA in moderate-severe UC with respect to clinical remission and endoscopic improvement but not steroid-free clinical remission.

2021 — HIBISCUS I&II

Phase 3/ ETR vs ADA/ UC/ Induction
Conclusion:
ETR (Etrolizumab) met primary endpoint of remission w10 in HIBISCUS I but not HIBISCUS II
ETR induced endoscopic improvement and histologic remission w10 vs pblo in HIBISCUS I
Etrolizumab not superior to Adalimumab for induction of remission at w10

2022 — SERENE-CD

RCT/ ADA 40mg eow vs 40 mg ew clinical adjusted or based in TDM / CD / Induction & maintenance
Conclusion:
No differences between clinical adjusted or TDM regimens with respecto to the key exploratory efficacy endpoitns. Both dosing regimens were generally well-tolerated with a similar safety profile.

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ADALIMUMAB IV

2022 — SERENE-UC

RCT/ higher induction (ADA 160mg w0,1,2&3) or standard induction + w8 randomization to 40 mg eow or 40 mg ew/ UC / Remission

Conclusion:

No statistical difference between higher induction and standard at week 8. No statistical differences between responders to induction receiving 40 mg eow or ew for clinical remission at w52.

2022 — RAPIDA

OL/ single arm ADA/ mod-severe luminal CD/Remission

Conclusion:

Rapid clinical response & remission, improvement in QoL & fatigue & reduction of inflammatory biomarkers achieved with ADA as early as day 4 in adult anti-TNF naïve patients with mod-severe CD

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VEDOLIZUMAB

2013 — GEMINI I

Phase 3 RCT/ VEDO vs placebo /active UC/ Induction+ Maintenance.
Conclusion:
VEDO more effective than placebo as induction and maintenance therapy for UC.

2014 — GEMINI II

Phase 3 RCT/ VEDO vs placebo/ active CD/ Induction+ Maintenance
Conclusion:
VEDO in CD better than placebo to achieve remission but not CDAI-100 response w6.
Those who responsed to induction & continued on VEDO more likely to be in remission at w52.

2014 — GEMINI III

Phase 3/ VEDO/ CD-failed to antiTNF/ Induction
Conclusion:
VEDO not more effective than placebo in inducing clinical remission at w6 in CD with previous TNF antagonists exposure. The therapeutic benefits of VEDO in these patients were detectable at week 10.

2019 — VARSITY

Phase 3b/ VEDO vs ADA/ active UC/ Induction of remission
Conclusion:
VEDO was superior to ADA in mod-sev UC with respect to clinical remission and endoscopic improvement but not steroid-free clinical remission.

2019 — VERSIFY

Phase 3b / VEDO / CD / Endoscopic remission
Conclusion:
Treatment with Vedolizumab in moderate-severe CD induces endoscopic, radiologic and histologic healingat 26 and 52w.

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VEDOLIZUMAB II

2020 — GEMINI LTS

Phase 3 OL/ UC and CD active disease/ from previous GEMINItrials
Conclusion:
The safety profile of VEDO remains favourable with no unexpected or new safety concerns. These results further establish the safety of VEDO and support its long-term use

2021 — VISIBLE 1

Phase 3/ VEDO IV vs SC vs placebo/ active UC / efficacy and safety
Conclusion:
Subcutaneous VEDO is effective as maintenance therapy in mod-sev active UC who had a clinical response to IV VEDO induction therapy. It has a favorable safety and tolerability profile.

2021 — TRAVELESS

Observational/ VEDO IV vs SC / CD and UC/ Maintenance
Conclusion:
Transitioning patients established on IV VEDO to SC appears to be safe and effective, with high patient satisfaction and multiple benefits for the health service.

2022 — VISIBLE 2

Phase 3b/ VEDO IV vs SC/ active CD / efficacy and safety
Conclusion:
Vedolizumab SC is an effective and safe maintenance therapy in patients with CD who responded to two infusions of vedolizumab intravenous induction therapy

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USTEKINUMAB

2016 — UNITI 1&2

Phase 3 RCT/ UST vs placebo in mod-severe CD / Induction& Maintenance
Conclusion:
UST better than placebo. Subcutaneous UST maintained remission in patients who had a clinical response to induction therapy.

2016 — IM-UNITI

Phase 3 RCT/ UST / CD / Safety & Maintenance
Conclusion:
UST better than placebo to maintain remission in moderate-active CD.
No safety concerns compared to placebo.

2019 — UNIFI

Phase 3 RCT/ UST vs placebo in mod-severe UC/ Induction & Maintenance
Conclusion:
UST more effective than placebo for inducing & maintaining remission in patients with mod-severe UC.

2022 — STARDUST

OL-phase 3b trial/ T2T vs SoC (standard of Care) in CD with UST.
Conclusion:
Timely escalation of UST in CD, based on early endoscopic response, clinical symptoms, and biomarkers, not better endoscopic outcomes at week 48 than symptom-driven decisions alone

2022 — SUSTAIN

Observational study/ UST/ CD / Effectiveness
Conclusion:
UST was demonstrated to be effective in real-world use in the short and long run. Safety was consistent with the known profile of UST.

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USTEKINUMAB
II

2022

SEAVUE

Phase 3b RCT/ ADA vs UST/ mod-severe CD naïve to biologics/ Induction & Maintenance
Conclusion:
ADA and UST monotherapies highly effective in CD biologic-naive, with no difference in the clinical remission w52 between the drugs.

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TOFACITINIB

2017 — OCTAVE 1

RCT / TOFA 10mg BD vs placebo/ Mod-Severe UC/ Induction
Conclusion:
In patients with moderately to severely active UC, tofacitinib more effective as induction therapy than placebo.

2017 — OCTAVE 2

RCT / TOFA 10mg BD vs placebo/ Mod-Severe UC/ Induction
Conclusion:
In patients with moderately to severely active UC, tofacitinib more effective as induction therapy than placebo.

2017 — OCTAVE sustain

RCT / TOFA 5mg BD vs 10mg BD vs placebo/ Mod-Severe UC (responders from OCTAVE 1&2)/Maintenance
Conclusion:
In patients with moderately to severely active UC, tofacitinib more effective as maintenance therapy than placebo.

2020 — OCTAVE OPEN

OL/ Tofa dose de-escalation or escalation/ Mod-Severe UC /Maintenance
Conclusion:
Following TOFA de-escalation in patients in remission on 10 mg BD,25.4% lost remission by m12. For induction responders who dose-escalated following failure on 5 mg BD, 49.1% achieved remission by m12.

2021 — RIVETING

RCT/Tofa de-escalation to 5 mg BD after 2y on 10 mg BD being in stable remission vs continue 10mgBD
Conclusion:
Remission at 6m: 77.1% and 90.0% in 5 & 10 mg BID groups, respectively. For those de-escalated, those in deep endoscopic remission & those without prior TNFi failure were more likely to maintain remission.

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