

Case #3

- Worsened pain 4/4, Semi urgent lap colectomy on 4/5 with end ileostomy. Rocky course with fluid collections requiring abx (no clear abscess) but ultimately d/c'd 4/21 on DVT prophylaxis for 1 month and continues to improve

FINAL DIAGNOSIS

A. Colon, total colectomy:

Extensive severe chronic active colitis with ulceration; see comment.

The distal resection margin shows chronic active colitis, but appears viable.

The proximal margin (terminal ileum) appears viable.

Appendix with acute serositis and partial fibrous obliteration of the lumen.

Twenty-six benign lymph nodes.

B. Omentum:

Benign omentum with vascular congestion and recent hemorrhage

DIAGNOSIS COMMENT

The patient's history of ulcerative colitis refractory to medical management is noted. Gross dissection of the colectomy shows an area of inflamed, cobblestone mucosa involving the majority of the colon (~77cm). The inflamed areas are submitted extensively for histologic evaluation. Sections show severe chronic active colitis. These findings are not entirely specific, but are compatible with the patient's known UC. No viral inclusions or granulomas are seen. There is no evidence of malignancy.

Case #3

- Plan is for eventual IPAA
- Could we have saved his colon or should he have had surgery much sooner? Tofa chosen given availability of samples over Upadacitinib
- In retrospect, wish we had him transferred earlier but not sure it would have changed the outcome....2 out of 3 ain't bad...
- For IBD Live: What combinations are you using? How about ASUC?
- Multiple trials underway (Vedo + Jak, Vedo + Adalimumab, Vedo + Uste, IL-23 + Jak, IL-23 + anti-TNF, etc...)

Table 1. Studies investigating the effectiveness and safety of dual biologic therapy in IBD.

Authors	Year of publication	Type of study	Number of participants	Combination of drugs	Duration of the DBT	Effectiveness
Feagan et al. ³¹	2023	Randomized controlled trial	214 Patients with moderate to severe UC	GOL/GUS (71, 33.1%)	12Weeks	Endoscopic results: Improvement 49% Remission 18% Clinical presentation: Improvement 83% Remission 37%
Sands et al. ⁹	2007	Randomized controlled trial	79 Patients with CD	IFX/NAT (52, 65.8%)	10Weeks	Clinical remission 46%
Colombel et al. ⁴³	2023	Single-arm open-label study	55 Biologic naïve patients with newly diagnosed, moderate to severe CD	VED/ADA/MTX (55, 100%)	26Weeks	Endoscopic remission 34.5% Clinical improvement 43.6% Clinical remission 54.5%
Eronen et al. ³⁴	2022	Retrospective cohort study	15 Patients with CD 1 with UC	ADA/UST (8, 36.3%) ADA/VED (5, 22.7%) GOL/VED (2, 9.1%) GOL/UST (2, 9.1%) VED/UST 5, 22.7%)	2–5 Months	Clinical remission 32% Clinical improvement 13%
Stone et al. ⁵⁰	2021	Retrospective chart review	9 Patients with CD 1 Patient with UC	UST/VED (5, 50%) UST/anti-TNF- α (5, 50%)		90% of patients reported significant symptomatic improvement
Yang et al. ³²	2020	Retrospective cohort study	22 Patients with intractable, complicated CD	VED/anti-TNF- α (13, 54%) VED/UST (8, 33.0%) UST/anti-TNF- α (3, 12.5%)	191–365 Days (MD 274 days)	Endoscopic results: Improvement 43% Remission 23% Clinical presentation: Improvement 50% Remission 41% (steroid-free remission in 36% of cases) Presence of perianal fistulas: 50% at baseline to 33% after DBT 33% of patients required surgery (treatment failure)
Glassner et al. ⁴⁶	2020	Retrospective cohort study	18 Patients with UC 32 Patients with CD 1 Patient with IBD-U	VED/UST (25, 47.2%) VED/TOFA (8, 15.0%) VED/ADA (3, 5.7%) VED/CERT (2, 3.8%) VED/GOL (2, 3.8%) TOFA/IFX (4, 7.5%) TOFA/GOL (4, 7.5%) TOFA/UST (3, 5.7%) TOFA/CERT (1, 1.9%) ADA/APR (1, 1.9%)	Median of 8 months (IQR 5.5–13 months)	Clinical improvement: Remission 50% Endoscopic improvement: Remission 34%
Kwapisz et al. ³⁵	2021	Case series	14 Patients with recurrent CD, 1 patient with UC	VED/UST (5, 33.3%) VED/GOL (3, 20%) VED/ADA (2, 13.3%) VED/IFX (2, 13.3%) VED/CERT (1, 6.7%) UST/ADA (1, 6.7%) UST/GOL (1, 6.7%)	2–48Months (MD 6 months)	Endoscopic/radiographic improvement 74% Steroid use reduction 67% Symptomatic improvement 73% 20% of patients required surgery

(Continued)

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Authors	Year of publication	Type of study	Number of participants	Combination of drugs	Duration of the DBT	Effectiveness
Biscaglia et al. ⁴⁷	2020	Case report	1 Patient with CD and Psoriasis 1 Patient with UC and psoriasis	VED/UST (2, 100%)	~2Years	Remission of intestinal and extraintestinal symptoms in both patients
Elmoursi et al. ³¹	2020	Case report	A 35-year-old male with refractory CD	VED/UST (1, 100%)	>12Months	Steroid-free deep remission after 8months of DBT
Fumery et al. ⁴⁰	2020	Case series	5 Patients with CD and ankylosing spondylitis/psoriasis 2 Patients with UC and multiple sclerosis/psoriasis	UST/ADA (1, 14.3%) UST/IFX (2, 28.6%) UST/GOL (2, 28.6%) VED/ETA (1, 14.3%) VED/OCRE (1, 14.3%)	3–30Months	Intestinal symptoms: Deep remission 57% Clinical remission 29% Coexisting diseases: Improvement 14% Remission 29%
Privitera et al. ³³	2020	Case series	11 Patients with CD 5 Patients with UC Participants were divided into two groups: with active IBD and active extraintestinal manifestations	VED/UST (3, 18.8%) VED/ADA (3, 18.8%) VED/SEC (2, 12.5%) UST/IFX (2, 12.5%) VED/CERT (1, 6.3%) VED/IFX (1, 6.3%) UST/ADA (1, 6.3%) VED/APR (1, 6.3%)	3–28Months (MD 7 months)	Clinical improvement of intestinal and extraintestinal symptoms in all patients at the end of the induction phase At 6months clinical improvement was observed in 43% of patients with intestinal symptoms, 14% achieved remission; extraintestinal manifestations improved in 22% of cases, and 56% reported remission
Buer et al. ³⁹	2018	Case series	6 Patients with UC 4 Patients with CD	VED/IFX (9, 90%) VED/ADA (1, 10%)	6Months	Endoscopic results: Improvement 40% Remission 50% Clinical remission 80%
Mao et al. ³⁷	2018	Case series	4 Patients with CD, one of whom suffered from coexisting ankylosing spondylitis	VED/ETA and UST/ETA (1, 25%) VED/UST (1, 25%) VED/GOL (2, 50%)	2–37Months	75% of patients achieved clinical remission
Bethge et al. ⁵²	2017	Case report	A 56-year-old male with refractory pouchitis and spondylarthritis	VED/ETA (1, 100%)	10Months	Remission of both intestinal and extraintestinal symptoms
Fischer et al. ⁵³	2017	Case report	A 33-year-old male with intractable UC and spondyloarthritis	VED/CERT (1, 100%)	21Months	Clinical and endoscopic remission was obtained
Huff-Hardy et al. ⁴⁸	2017	Case report	A 22-year-old female with severe CD and vulvo-perianal disease	VED/UST/MTX) (1, 100%)	>12Months	Clinical and endoscopic remission
Liu and Loomes ⁴⁹	2017	Case report	A 27-year-old female with refractory ileocolonic CD	VED/UST (1, 100%)	6Months	Decrease in FC, improvement of clinical symptoms, mucosal healing
Roblin et al. ⁴⁸	2017	Case report	A 48-year-old female with severe UC and ankylosing spondylitis	GOL/VED (1, 100%)	12Months	Clinical and endoscopic remission
Afzali and Chiorean ³⁴	2016	Case report	A 23-year-old female with steroid-dependent CD	ADA/VED (1, 100%)	6Months	Clinical and endoscopic improvement

Table 1. (Continued)

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Yzet et al. ¹³	2016	Case reports	2 Patients with CD, 1 patient with UC All patients in clinical remission of IBD, with paradoxical psoriasis during anti-TNF therapy	ADA/UST (1, 33.3%) IFX/UST (2, 66.6%)		No effect on skin lesions, all patients stayed in intestinal remission
Hirten et al. ⁵⁵	2015	Case report	A 43-year-old male with complicated CD and erythema nodosum	INF/VED (1, 100%)	~8Weeks	Remission of erythema nodosum, clinical, and endoscopic improvement

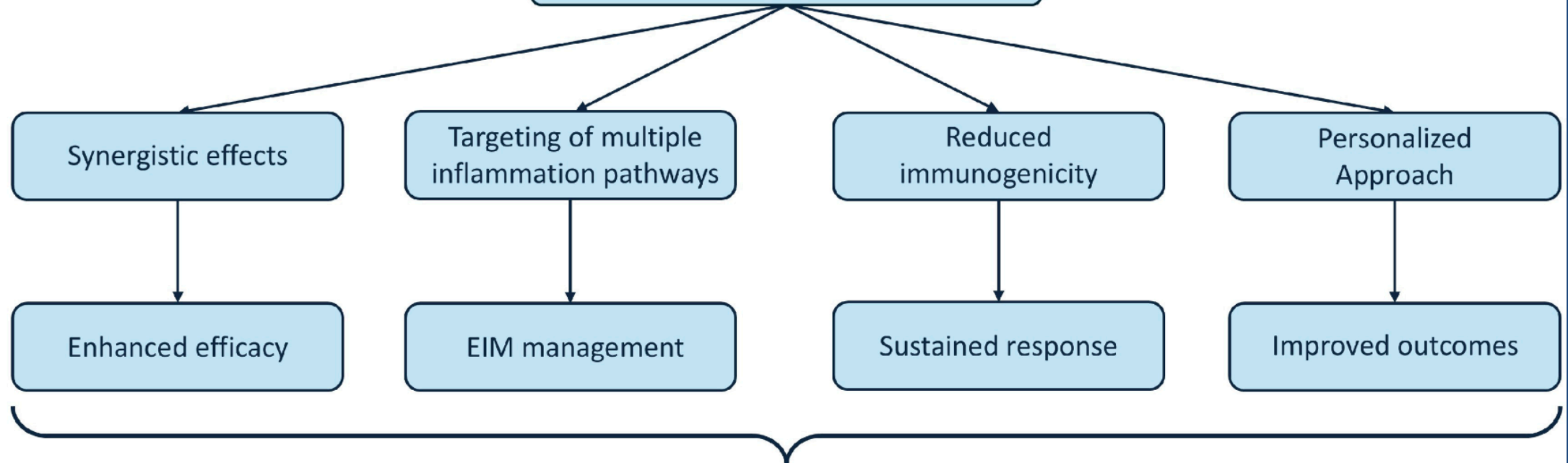
ADA, adalimumab; APR, apremilast; CD, Crohn’s disease; CERT, certolizumab; DBT, double biological therapy; ETA, etanercept; FC, fecal calprotectin; GOL, golimumab; GUS, guselkumab; IBD, inflammatory bowel disease; IFX, infliximab; IQR, interquartile range; MD, median; MTX, methotrexate; NAT, natalizumab; OCRE, ocrelizumab; SEC, secukinumab; TNF- α , tumor necrosis factor α ; UC, ulcerative colitis; UST, ustekinumab; VED, vedolizumab.

Biologics and SMDs with different targets and mechanisms of action

- Anti-TNF α
- Anti-integrin
- Anti-IL12/23
- JAK inhibitors
- S1P modulators



DUAL-TARGETED THERAPY



OVERCOMING THE THERAPEUTIC CEILING