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Table 2: Comparative characteristics of CD and UC with coexisting celiac disease on follow-up

Characteristic		CD N= 32	UC N= 73
Age at diagnosis, median (IQR)		27.7 (16.9 - 39.5)	29.8 (19.7 – 45.2)
Age at Celiac diagnosis, median (IQR)		35.5 (23.4 – 54.1)	34.9 (24.9 – 49.7)
Male gender, N (%)		11 (34.4)	45 (61.6)
Coexisting Primary Sclerosing Cholangitis		4 (12.5)	20 (27.4)
Baseline	5-ASA ever use	17 (53.1)	49 (67.1)
	Corticosteroid ever use	12 (37.5)	32 (43.8)
	Immunomodulator ever use	4 (12.5)	8 (11)
	Biologics ever use	10 (31.3)	9 (12.3)
1 year follow-up CD, N = 24 UC, N = 54	5-ASA ever use	8 (33.3)	31 (57.4)
	Corticosteroid ever use	8 (33.3)	10 (18.5)
	Immunomodulator ever use	5 (20.8)	9 (16.7)
	Biologics ever use	7 (29.2)	5 (9.3)
Change in disease location/phenotype		7 (29.2)	-
Disease activity	Remission	21 (87.5)	50 (92.6)
	Refractory	3 (12.5)	4 (7.4)
2 year follow-up CD, N = 19 UC, N = 48	5-ASA ever use	4 (21.1)	25 (52.1)
	Corticosteroid ever use	5 (26.3)	7 (14.6)
	Immunomodulator ever use	5 (26.3)	6 (12.5)
	Biologics ever use	7 (36.8)	6 (12.5)
Change in disease location/phenotype		5 (26.3)	-
Disease activity	Remission	17 (89.5)	45 (93.7)
	Refractory	2 (10.5)	3 (6.3)
5 year follow-up CD, N = 14 UC, N = 26	5-ASA ever use	3 (21.4)	12 (46.2)
	Corticosteroid ever use	4 (28.6)	5 (19.2)
	Immunomodulator ever use	4 (28.6)	2 (7.7)
	Biologics ever use	7 (50)	2 (7.7)
Change in disease location/phenotype		6 (42.9)	-
Disease activity	Remission	10 (71.4)	25 (96.1)
	Refractory	4 (28.6)	1 (3.9)
IBD-related hospitalization		16 (50)	17 (23.3)
IBD-related surgery		17 (53.1)	23 (31.5)

Footnotes: 5-ASA, 5 –Aminosalicylates; CD, Crohn's disease; IBD, Inflammatory bowel disease; UC, Ulcerative colitis

Results: All patients developed extraintestinal symptoms between the first and sixth dose, and the three patients receiving more than three infusions all responded well to the therapy regarding to their intestinal symptoms (decline in Harvey-Bradshaw-Index or modified Mayo-Score). One female patient with ulcerative colitis was diagnosed with thyreoiditis de Quervain, a granulomatous inflammation of the thyroid, based on pathognomic ultrasound features after six doses. The second female patient developed vasculitis of the eye after receiving one dose of Vedolizumab for Crohn's disease (CD). Two male patients, both with Crohn's colitis, presented predominantly with pulmonary symptoms: One suffered from rapidly progressive acute respiratory distress syndrome requiring mechanical ventilation after receiving the fourth infusion; the other presented with dyspnoea and dry cough after the third dose. In both cases, CT-scan showed bilateral infiltrates and hilar lymphadenopathy. Extensive work-up identified no infectious or other specific cause (including repeat cultures and PCR for Mycobacterium tuberculosis complex DNA, Quantiferon assay, urine histoplasmosis antigen, HIV testing, negative autoantibodies; and soluble IL-2 receptor, ACE and CD4/CD8-ratio within normal range). In the latter case, lung tissue obtained during thoracoscopic wedge resection showed multiple characteristic non-caseating epithelioid-granulomas, highly suspicious for pleural and pulmonary manifestation of CD. Analysis of integrin-expression on PBMCs demonstrated a distinct CD29+ (i.e. integrin β 1+) population, an integrin necessary for lymphocyte homing into the lung. After treatment with prednisolone, both the β 1+ cells as well as pulmonary infiltrates vanished, along with complete resolution of clinical symptoms. Likewise, the other patients fully recovered after cessation of Vedolizumab plus administration of steroids, if needed.

Conclusions: Shifts in integrin-expression triggered by Vedolizumab and consequently altered migrational behaviour of immune cells into other organs than the gut might explain the excellent intestinal response to the drug accompanied by extraintestinal manifestation of the disease in our patients.

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Rapidity of onset of response to adalimumab in luminal Crohn's disease. Data from RAPIDA trial

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Background: Rapidity of response to treatment in Crohn's disease (CD) is now considered a field of major interest, due to the importance of achieving the highest benefit in the shortest possible time. There are no studies specifically designed to evaluate the rapidity of

response to ADA neither other anti-TNF therapies. The aim of this trial was to evaluate the rapidity of onset of clinical response to adalimumab (ADA) therapy.

Methods: Adult anti-TNF naïve patients with active luminal (Harvey-Bradshaw Index (HBI) ≥8) moderate-to-severe CD (excluding penetrating and stricturing disease), with no response to a full and adequate course of therapy with corticosteroids and/or immunosuppressants, were enrolled in this interventional, prospective, open label, single arm and multicenter clinical trial. Patients received standardized ADA treatment (160 mg – 80 mg – 40 mg eow).

The HBI was evaluated to determine the response at day 4 and week 1; and clinical remission at weeks 2, 4 and 12. Response was defined as a decrease of, at least, 3 points in the HBI global score and remission was defined as HBI global score <5.

CRP (C Reactive Protein) and fecal calprotectin (FC) were analyzed at baseline, day 4, week 1, 2, 4, 12.

The modified intention to treat (mITT) population was the primary population for efficacy analysis and consisted of those patients enrolled in the study who had received at least one dose of ADA.

Treatment-emergent serious adverse events (AEs) were recorded to assess safety throughout the study until 70 days after last treatment dose. All patients who received at least one dose of ADA were included in the safety population.

Statistical analyses were performed by the t-test or the Wilcoxon signed rank test, as applicable. Time to clinical response was analyzed using a Kaplan-Meier survival analysis model.

Results: 80 anti-TNF naïve patients were analyzed. 62.5% and 71.3% of patients experienced a response at day 4 and week 1, respectively. Remission was achieved by 50.0% of patients at week 2, 62.5% at week 4 and 42.5% at week 12. The median time to obtain response was 4.0 days (95% confidence interval (CI): 1.0, 4.0) and the median time to remission was 7.0 days (95% CI: 4.0–18.0).

Table 1

	Median CRP levels (mg/L)	Median FC levels (µg/g)	p-value vs baseline for CRP and FC
Baseline	5.50	732	<0.0001
Day 4	1.71	453	<0.0001
Week 1	1.71	465	<0.0001
Week 2	1.66	448	<0.0001
Week 4	2.47	279	<0.0001
Week 12	2.38	346	<0.0001

37.50% of the patients suffered from any adverse event (AE) during the study. Only 1 patient (1.25%) showed a serious AE.

Conclusions: ADA produces rapid clinical remission and response since day 4 in patients with moderate-to-severe CD unresponsive to therapy with corticosteroids and/or immunosuppressants.

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Tofacitinib for the treatment of resistant ulcerative colitis: the University of Chicago experience

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Background: Many inflammatory bowel disease (IBD) patients are unresponsive to medical therapy or lose response. Tofacitinib is a selective inhibitor of the Janus kinase (JAK) family, focused on JAK 1–3. Its effectiveness for rheumatoid arthritis and for induction and maintenance of remission of ulcerative colitis (UC) has been demonstrated in pivotal trials, but 2 separate phase 2 trials for Crohn's disease (CD) were negative. Here we describe our off-label experience with the use of tofacitinib for the treatment of anti-TNF refractory moderate to severe IBD patients.

Methods: This is a retrospective, observational study of the off-label use of tofacitinib for IBD. Patients with medically resistant IBD were treated with 5 mg twice daily or 10 mg twice daily. Clinical response and adverse events were assessed at 8 weeks and at subsequent visits until the last follow up encounter. Response to treatment was determined as defined by the patient's provider. Partial response was symptomatic improvement but not resolution and remission was defined as resolution of clinical symptoms.

Results: Between December 2014 and September 2016, 12 IBD patients (9 UC, 2 CD (colon), 1 IBD-U; 7 male; median age 36.5 years IQR 25.5) were treated with tofacitinib.

All patients had failed treatment with anti-TNF and anti-integrin previously. The initial dose for the patients was 5 mg PO twice daily. At 8 weeks of treatment, 8 patients (66.7%) had a clinical response to treatment. Of those, 3 achieved clinical remission. 3 patients (25%) did not respond to treatment and a single patient stopped treatment after 4 weeks due to an adverse event. Dose escalation to 10 mg PO twice daily was tried in 2 patients, with no clinical response in one patient and subsequent clinical remission in the other. The patients were followed for a mean 6.3 + 6.6 (range 2–23) months. No loss of response was noted in clinical follow-up. Two episodes of systemic infections were noted, both while on concomitant steroids: cellulitis and parainfluenza which required hospitalization and cessation of treatment. No other adverse effects were observed including changes in the levels of hemoglobin, neutrophil count, creatinine clearance,

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Table 1 Clinical and demographic characteristics of the patients

Gender (M/F)		7/5
Age at induction (median (IQR)), years		36.5 (25.5)
Duration of disease (median (IQR)), months		76 (158)
Previous medications (no. (percentile))	anti TNF	12 (100)
	thiopurines	8 (67)
	MTX	7 (58)
	vedolizumab	10 (83)
Concomitant medications	systemic corticosteroids (no. (percentile))	8 (67)
	prednisone dose (median (IQR)), mg	22.5 (15)
	azathioprine (no. (percentile))	1 (8)
	vedolizumab (no. (percentile))	1 (8)