Comparative Effectiveness of Vedolizumab versus Ustekinumab in Anti-TNF Experienced Patients With Crohn's Disease

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Introduction

- Many patients with Crohn's disease (CD) lose response or become intolerant to anti-TNF therapy.
- Newer classes of biologics have demonstrated efficacy in anti-TNF experienced patients.
- There is a paucity of research comparing vedolizumab and ustekinumab as subsequent therapy.
- Prior studies, limited to tertiary care centers in Europe, have yielded conflicting results and did not include reported outcomes (PROs).

Objective

We sought to compare the effectiveness of vedolizumab and ustekinumab in anti-TNF experienced CD patients, focusing on patient-prioritized patient reported outcomes (PROs).

Methods and Materials

- We utilized the IBD Partners internet-based research infrastructure to conduct a prospective, direct-to-patient cohort study in a geographically diverse U.S. population.
- Within IBD Partners, participants report disease characteristics, current and prior treatments, and PROs every 6 months.
- For this analysis, we identified anti-TNF experienced patients with CD initiating vedolizumab or ustekinumab and analyzed PROs reported approximately 6 months later (minimum 4 months, maximum 10 months).
- Co-primary outcomes were Patient Reported Outcome Measurement Information System (PROMIS) domains of Fatigue and Pain Interference.
- Secondary outcomes included patient-reported short Crohn's Disease Activity Index (sCDAI) and treatment persistence and corticosteroid use at the time of follow-up.
- Inverse probability of treatment weighting (IPTW) was used to control for potential confounders and incorporated into linear and logistic regression models for linear and categorical outcomes, respectively.

Table 1: Demographic and Baseline Characteristics of Patients with Crohn's Disease Initiating Treatment with Vedolizumab versus Ustekinumab following anti-TNF Therapy

	Vedolizumab n=141		Ustekinumab n=219		SMD	SMD after IPTW
	N/mean	%/SD	N/mean	%/SD		
Index year (N, %)					0.331	0.003
2017	55	39%	45	21%		
2018	31	22%	56	26%		
2019	26	18%	65	30%		
2020	29	21%	53	24%		
Age (Mean, SD)	46.4	15.46	46.0	14.98	0.024	0.001
Sex (N, %)					0.121	0.009
Male	41	29%	52	24%		
Female	100	71%	167	76%		
Race/ Ethnicity (N, %)					0.173	0.008
Hispanic	3	2%	3	1%		
Non-Hispanic White	129	91%	193	88%		
Non-Hispanic Black	2	1%	2	1%		
Other/unknown	7	5%	21	10%		
Years from diagnosis (Mean, SD)	19.6	14.17	18.0	12.00	0.119	0.009
Number of prior anti-TNF (N, %)						
1	70	50%	97	44%	0.105	0.008
2	51	36%	87	40%		
3+	20	14%	35	16%		
Smoking status (N, %)					0.023	0.002
Nonsmoker	97	69%	153	70%		
Former smoker	41	29%	58	26%		
Current smoker	3	2%	8	4%		
BMI prior to index (Mean, SD)	25.3	6.45	25.4	5.85	0.018	0.016
Prior hospitalization (N, %)	97	75%	144	75%	0.018	0.005
Prior surgery (N, %)	71	55%	114	60%	0.103	0.013
Prior use of steroids (pred, bud) (N, %)	127	98%	187	98%	0.018	0.007
Prior use of 6MP/AZA (N, %)	103	79%	147	77%	0.022	0.009
Prior use of MTX (N, %)	40	31%	58	30%	0.036	0.011
Prior use of tacrolimus/cyclosporine (N, %)	7	5%	6	3%	0.002	0.004
Baseline sCDAI (Mean, SD)*	186	105.2	172	90.0	0.147	0.144
Baseline PROMIS (Mean, SD)*						
Anxiety	52.1	10.49	50.7	8.70	0.151	0.140
Depression	49.4	9.94	48.5	8.29	0.102	0.112
Fatigue	56.3	11.52	55.0	10.74	0.118	0.125
Sleep Disturbance	51.4	8.86	50.0	7.69	0.169	0.138
Pain Interference	53.1	10.11	52.8	9.71	0.029	0.021
Social Role Satisfaction	48.5	10.57	49.3	8.90	0.084	0.125

*Baseline measures of Short Crohn's Disease Index (sCDAI) and Patient Reported Outcome Measurement Information System (PROMIS) measures were evaluated in the 6 months prior to index date.

Table 2: Unadjusted outcomes at 6-months among Patients with Crohn's Disease Initiating Treatment with Vedolizumab versus Ustekinumab following anti-TNF Therapy

	Vedolizumab n=141		Ustekinumab n=219		P-value
	N/mean	%/SD	N/mean	%/SD	
Primary Outcomes					
PROMIS Fatigue* (Mean, SD)	54.7	11.73	54.4	12.31	0.778
PROMIS Pain interference* (Mean, SD)	51.2	10.17	51.6	9.94	0.751
Secondary Outcomes					
Index medication persistence (N, %)	119	84%	203	93%	0.012
Corticosteroid use at follow-up (N, %)	27	19%	28	13%	0.103
Short Crohn's Disease Activity Index	147	89.6	144	85.8	0.785
PROMIS Social satisfaction (Mean, SD)* (Mean, SD)	49.1	10.59	49.3	10.06	0.887

*Patient Reported Measurement Information System

Table 3. Average Treatment Effects (adjusted) at 6-months among Patients with Crohn's Disease Initiating Treatment with Vedolizumab versus Ustekinumab following anti-TNF Therapy

	Estimate (95% Confidence Intervals) *	P-value
Primary Outcomes		
Fatigue	0.6 (-1.9.0-3.0)	0.657
Pain Interference	-0.2 (-2.3-1.9)	0.824
Secondary Outcomes		
Index medication persistence	0.36 (0.22-0.60)	<0.001
Corticosteroid use	1.69 (1.13-2.56)	0.010
sCDAI	6.0 (-13.36-25.36)	0.688
Social satisfaction	-0.9 (-3.0-1.3)	0.435

*Estimates for Patient Reported Measurement Information System (PROMIS) measures of Fatigue, Pain Interference, and Social Satisfaction and the Short Crohn's Disease Activity Index (sCDAI) represent adjusted mean differences comparing treatment with vedolizumab versus ustekinumab. Estimates for persistence and corticosteroid use represent adjusted odds ratios for treatment for vedolizumab versus ustekinumab.

Conclusions

- This real-world comparative effectiveness study of anti-TNF experienced CD patients initiating vedolizumab or ustekinumab showed similar treatment persistence rates beyond 52 weeks.
- Secondary outcomes such as all-cause hospitalization, non-surgical CD hospitalizations, and hospitalizations for infection favored ustekinumab initiation.
- We therefore advocate for individualized decision making in this medically refractory population, considering patient preference, prior Anti-TNF experience and other factors such as cost and route of administration.

Results

- Overall, 141 vedolizumab and 219 ustekinumab initiators were included in our analysis.
- After adjustment, we found no differences between treatment groups in our primary outcomes of Pain Interference or Fatigue or the secondary outcome of sCDAI.
- Vedolizumab was associated with lower treatment persistence (OR 0.4, 95% CI 0.2-0.6) and higher corticosteroid use at follow-up assessment (OR 1.7, 95% CI 1.1-2.6).

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