Real World Evidence Comparing Vedolizumab and 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.
- Real-world comparative effectiveness studies are limited and have yielded conflicting results.

Objective

We sought to compare the effectiveness and safety of ustekinumab to vedolizumab in a large, geographically diverse United States (U.S.) population of adult patients with CD previously treated with TNF inhibitors.

Methods and Materials

- We conducted a retrospective cohort study using longitudinal claims data from a large U.S. insurer (Anthem, Inc.)
- We identified CD patients initiating vedolizumab or ustekinumab with anti-TNF treatment in the prior 6 months.
- Our primary outcome was treatment persistence > 52 weeks.
- Secondary outcomes included: 1) all-cause hospitalization; 2) hospitalization for CD with surgery; 3) hospitalization for CD without surgery, and 4) hospitalization for infection.
- Propensity score fine stratification was used to control for demographic and baseline clinical characteristics and prior treatments.

Results

- We identified 885 new users of ustekinumab and 490 new users of vedolizumab
- We observed no difference in treatment persistence [adjusted RR 1.09 (95% CI 0.95 -1.25)]
- Ustekinumab was associated with lower all-cause hospitalization (adjusted HR 0.73 [0.59-0.91]) and non-surgical CD hospitalizations (adjusted HR 0.58 [0.40-0.83])
- Ustekinumab initiators were also less likely to be hospitalized for infection (adjusted HR 0.56 [0.34-0.92]).

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.

Figure 1: Propensity Score Distributions Before and After Trimming and Weighting in Primary Analysis of Treatment Persistence

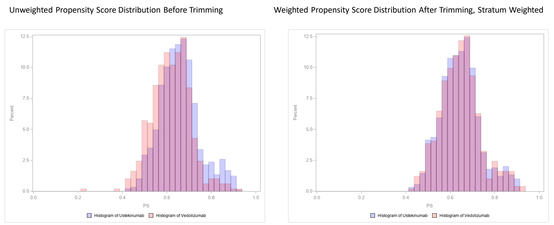


Table 1. Baseline Characteristics of Adults with Crohn's Disease Newly Initiating Treatment with Ustekinumab or Vedolizumab After Failure of Anti-TNF Before and After Propensity Score Stratum Weighting

	Untrimmed, Unweighted					Trimmed, Weighted				
	Ustekinumab		Vedolizumab		Standardized Difference	Ustekinumab		Vedolizumab		Standardized Difference
	N/Mean	%/Std Dev	N/Mean	%/Std Dev		N/Mean	%/Std Dev	N/Mean	%/Std Dev	
Patients (N)	885	100.0%	490	100.0%		884	-	484	-	
Demographics										
Mean age	41.6	14.6	43.8	14.2	-0.17	42.3	14.7	42.6	14.0	-0.02
Sex (Female)	497	56.2%	278	56.7%	-0.01	501	56.7%	270	55.8%	0.02
Comorbidity Burden										
Charlson/Elixhauser Combined Comorbidity Score	1.1	1.7	1.0	1.6	0.01	1.0	1.7	1.1	1.7	-0.01
Inflammatory Bowel Disease-Related Characteristics										
Severe perianal disease	88	9.9%	38	7.8%	0.08	82	9.3%	45	9.3%	0.00
Anemia	231	26.1%	131	26.7%	-0.01	234	26.5%	129	26.6%	-0.00
Malnutrition	37	4.2%	13	2.7%	0.08	37	4.2%	17	3.5%	0.03
C. difficile testing	171	19.3%	105	21.4%	-0.05	173	19.6%	97	20.0%	-0.01
Inflammatory Bowel Disease-Related Health Care Utilization										
Crohns disease (any outpatient diagnosis)	885	100.0%	490	100.0%	-	884	100.0%	484	100.0%	-
Crohns disease (any inpatient diagnosis)	181	20.5%	89	18.2%	0.06	175	19.8%	96	19.8%	0.00
Crohns disease (principal inpatient diagnosis)	117	13.2%	59	12.0%	0.04	112	12.7%	65	13.3%	-0.02
Crohns disease surgery	75	8.5%	34	6.9%	0.06	72	8.2%	37	7.7%	0.02
Any endoscopic procedure	367	41.5%	188	38.4%	0.06	363	41.1%	191	39.6%	0.03
Recent Use (-30,-1) of Immunosuppressive Therapy										
Thiopurines (recent)	72	8.1%	40	8.2%	-0.00	75	8.5%	41	8.5%	-0.00
Methotrexate (recent)	45	5.1%	13	2.7%	0.13	38	4.3%	21	4.4%	-0.00
Calcineurin inhibitors (recent)	2	0.2%	1	0.2%	0.01	3	0.3%	1	0.1%	0.04
Systemic corticosteroids (recent)	230	26.0%	142	29.0%	-0.07	242	27.3%	127	26.2%	0.03
Oral budesonide (recent)	95	10.7%	48	9.8%	0.03	95	10.8%	48	9.9%	0.03
Rectal corticosteroids (recent)	5	0.6%	2	0.4%	0.02	4	0.5%	2	0.3%	0.02
Any of the above	377	42.6%	213	43.5%	-0.02	383	43.4%	206	42.5%	0.02
Prior anti-TNF use										
1 unique anti-TNF inhibitor used at baseline	639	72.2%	366	74.7%	-0.06	647	73.1%	351	72.6%	0.01
2+ unique anti-TNF inhibitors used at baseline	246	27.8%	124	25.3%	0.06	237	26.9%	133	27.4%	-0.01
Adalimumab	621	70.2%	304	62.0%	0.17	595	67.3%	330	68.1%	-0.02
Certolizumab	137	15.5%	59	12.0%	0.10	131	14.8%	69	14.2%	0.02
Golimumab	8	0.9%	3	0.6%	0.03	7	0.8%	3	0.6%	0.03
Infliximab	401	45.3%	260	53.1%	-0.16	422	47.8%	226	46.7%	0.02

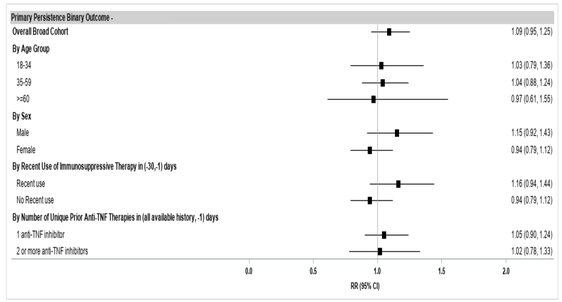
Table 2: Incidence and Effect Estimates for Primary and Secondary Endpoints in New Users of Ustekinumab vs Vedolizumab

	Crude new users	Incidence rate*	Effect estimate** (95% CI) before weighting	Effect estimate** (95% CI) after weighting
Primary Outcome-Treatment persistence > 52 weeks				
Ustekinumab	884	45.7	1.08 (0.91-1.28)	1.09 (0.95-1.25)
Vedolizumab	484	42.3	(Ref)	(Ref)
Secondary measures of effectiveness				
All-cause hospitalization				
Ustekinumab	1217	267.80	0.73 (0.60, 0.90)	0.73 (0.59, 0.91)
Vedolizumab	667	366.70	(Ref)	(Ref)
Hospitalization for Crohn's disease without surgery				
Ustekinumab	1217	76.25	0.56 (0.40, 0.79)	0.58 (0.40, 0.83)
Vedolizumab	667	136.19	(Ref)	(Ref)
Hospitalization for Crohn's disease with surgery				
Ustekinumab	1217	87.96	0.90 (0.62, 1.29)	0.83 (0.57, 1.22)
Vedolizumab	667	97.78	(Ref)	(Ref)
Safety Outcomes				
Hospitalization for any infection				
Ustekinumab	1217	40.72	0.53 (0.34, 0.85)	0.56 (0.34, 0.92)
Vedolizumab	667	76.23	(Ref)	(Ref)
Hospitalization for thrombotic event				
Ustekinumab	1217	3.34	0.56 (0.11, 2.76)	0.57 (0.11, 2.94)
Vedolizumab	667	6.00	(Ref)	(Ref)

* Incidence rates are per 100 new users for the primary outcome and per 1000 person-years for other outcomes

** Effect estimates are risk ratios for the primary outcome and hazard ratios for other outcomes

Figure 2: Forest Plot of Adjusted Risk Ratios (RR) and 95% Confidence Intervals (CI) for Treatment Persistence among New Users of Ustekinumab vs. Vedolizumab (Reference), Overall and by Subgroups (Propensity Score Stratum Weighted Analyses)



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