Ustekinumab Therapeutic Drug Monitoring in Inflammatory Bowel Disease

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BACKGROUND

- In the setting of inflammatory bowel disease (IBD), therapeutic drug monitoring (TDM) is a commonly used clinical tool to guide anti-TNF therapy; however, the use of TDM for ustekinumab (UST) has yet to be fully defined

AIMS

- The goal of this study is to analyze possible correlations between UST drug levels and patient characteristics, disease activity, and clinical outcomes in a population of both Crohn's disease (CD) and ulcerative colitis (UC) patients.

METHODS

- A retrospective cohort study was performed for IBD patients who had UST trough levels drawn at maintenance dosing.
- Data collected:
  - Trough levels
  - Patient demographics (age, gender, BMI)
  - UST dosing schedule
  - Concurrent IBD medications
  - Prior failed biologics
  - Treatment outcomes (biomarkers, clinical scores, and endoscopy scores)

RESULTS

TABLE 1. Patient data relationship to ustekinumab levels

	Adequate Ustekinumab levels	Low Ustekinumab levels	Total N	Statistical Test	p-value
Inflammatory Markers					
ESR (mm/hour)	10.93 (N=60)	22.48 (N=54)	114	t-test	**0.002**
CRP (mg/L)	6.44 (N=62)	17.18 (N=55)	117	t-test	**0.005**
Albumin (g/dL)	4.20 (N=59)	4.03 (N=42)	101	t-test	0.182
Fecal Calprotectin (µg/g)	511.67 (N=9)	1105.13 (N=8)	17	t-test	0.160
Combined Labs (# of patients)					
Lab Flare	17	27	125	χ^2	**0.011**
Lab Remission	55	34			
Endoscopy					
Mayo Endoscopy	3 (N=2)	1.5 (N=2)	4	t-test	0.095
SES-CD	1.5 (N=4)	8.5 (N=4)	8	t-test	**0.018**
Anti-TNF					
Anti-TNF Exposure	68	73	177	χ^2	**0.048**
Anti-TNF Naive	24	12			
Infliximab					
Infliximab Exposure	27	48	177	χ^2	**0.006**
Infliximab Naïve	58	44			
Adalimumab					
Adalimumab Exposure	46	37	177	χ^2	0.388
Adalimumab Naive	46	48			
Certolizumab					
Certolizumab Exposure	13	24	177	χ^2	**0.021**
Certolizumab Naive	79	61			
Golimumab					
Golimumab Exposure	2	6	177	χ^2 Fisher exact (two-sided)	0.118 0.156
Golimumab Naive	90	79			
Prednisone (#of patients)					
Concomitant Prednisone	4	12	177	χ^2 Fisher exact (two-sided)	**0.024** **0.034**
No Prednisone	73	88			

RESULTS

- 177 IBD patients had an average UST trough level of 4.742 µg/mL (range 0 µg/mL - 25 µg/mL)
- No patients had anti-drug antibody to UST.
- Higher frequency dosing schedules (i.e. Q4, Q6) were significantly associated ($p<0.001$) with increased UST trough levels compared to standard (Q8 week) maintenance dosing.
- Naiveté to anti-TNFs correlated with higher UST titer levels ($p=0.048$) with 67% adequate UST titer for anti-TNF naïve patients vs 48% for those with previous exposure to anti-TNFs.
- A higher erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were significantly related to lower UST titer levels ($p=0.002$ and $p=0.005$, respectively).
- HBI, Mayo Score, and UCAI did not correlate with UST trough levels.
- Lower SES-CD correlated with adequate titer levels ($p=0.018$).
- Mayo and Rutgeerts endoscopic scores did not correlate with titer levels.

CONCLUSIONS

- **Prior anti-TNF exposure was associated with lower UST levels.**
- **Higher UST drug levels correlated with lower SES-CD scores and ESR and CRP levels.**
- **Based on these findings, therapeutic drug monitoring of UST trough levels and corresponding dosing schedule adjustments to reach target levels may ensure more adequate response from UST therapy.**