#P2259

Therapeutic Drug Monitoring of Biologics in Patients with Inflammatory Bowel Disease: A Real-World Experience

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Background

Therapeutic drug monitoring (TDM) is recommended by the American Gastroenterological Association to guide treatment changes with anti-TNF agents in patients (pts) with inflammatory bowel disease (IBD).[1] Previous studies have shown that changes in treatment regimen of biologics in response to TDM are beneficial in achieving enhanced pt clinical response and remission.[2-5]

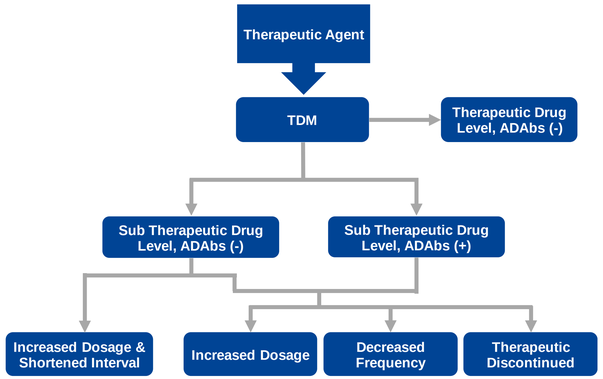
Aim

- To examine utilization of TDM in IBD pts treated at a large GI private practice
- Assess changes in disease activity post therapeutic intervention
- To present clinical remission as a function of TDM directed dose modifications

Methods

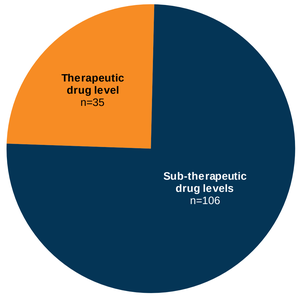
We conducted a chart review of 141 IBD pts who had TDM during maintenance therapy while on adalimumab (ADA), certolizumab pegol (CZP), infliximab (IFX), or vedolizumab (VDZ) between March$_T$ 2016 and March$_T$ 2018. We analyzed demographics, disease characteristics, serum drug concentrations, and presence of anti-drug antibodies (ADAbs). Target concentrations for ADA, CZP, IFX, and VDZ were ≥7.5ug/mL, ≥20ug/mL, ≥5ug/mL and ≥12ug/mL, respectively.[1, 6-8] Pts with therapeutic drug levels were not further evaluated. Pts with sub-therapeutic drug levels were assessed 6 months (mo) post TDM intervention for clinical response and remission. Clinical remission was defined as a Harvey-Bradshaw Index score less than 5 for Crohn's disease and a Partial Mayo score less than 2 for ulcerative colitis. -Changes in disease activity and biomarkers were evaluated using the Wilcoxon signed rank test. We analyzed categorical data using frequency distributions and continuous variables, such as mean±SD with range.

Study Design



Results

TDM Study Population



- Of the total 141 pts, 35 (25%) had therapeutic drug levels vs 106 (75%) with sub-therapeutic drug levels.

Baseline Characteristics

Characteristics	CD (n=85)	UC (n=56)	Total (n=141)
Demographics			
Mean age (range)	45 (16-76)	45 (19-79)	45 (16-79)
Female Gender, n (%)	52 (61)	21 (38)	73 (52)
Months from biologic initiation to TDM, median (IQR)	10.8 (31.5)	7.2 (10.7)	9.2 (17.7)
Biologic Agent with TDM, n (%)			
ADA	1 (1)	0	1 (1)
CZP	2 (2)	0	2 (1)
IFX	75 (88)	45 (80)	120 (85)
VDZ	7 (8)	11 (20)	18 (13)
Type of TDM, n (%)			
Proactive	23 (27)	22 (39)	45 (32)
Reactive	62 (73)	34 (61)	96 (68)

- TDM was primarily reactive (68%) and largely conducted in pts receiving IFX (85%).

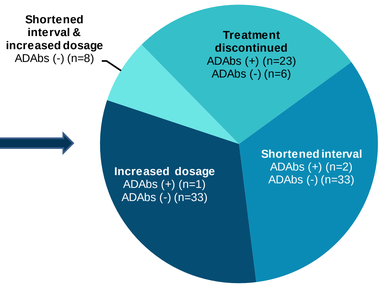
Initial TDM by Drug

- TDM characteristics of the 106 pts with sub-therapeutic drug levels are noted below:

TDM Characteristics	Biologic			
	ADA (n=1)	CZP (n=2)	IFX (n=90)	VDZ (n=13)
Drug Levels				
Mean ug/mL, (range)*	-	16.2 (-)	2.3 (0.3-4.8)	8.4 (4.9-11.7)
Detectable levels, n	0	1	60	11
Undetectable levels, n	1	1	30	2
Anti-drug Antibodies				
Mean ng/mL, (range)*	17 (-)	30 (-)	139 (13-200)	-
Detectable antibodies, n	1	1	24	0
Undetectable antibodies, n	0	1	66	13

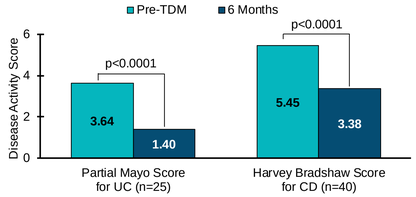
*mean of detectable levels/antibodies

TDM Intervention



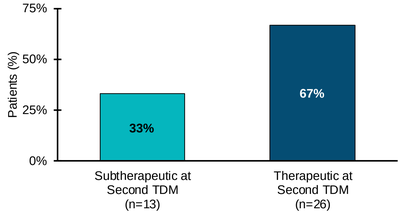
- 77/106 (73%) underwent dose intervention. These pts were followed for 6 mo for clinical outcomes.
- Shortened interval was the largest (33%) subset of dose changes.
- Overall, 26/106 (24%) were ADAbs (+).

Disease Activity Following TDM Intervention



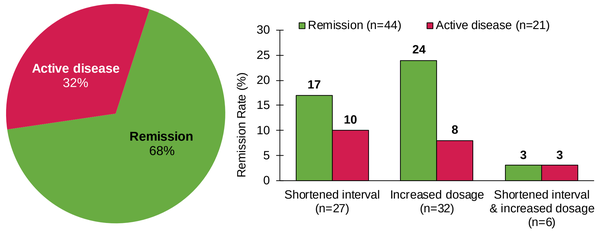
- Both UC and CD pts showed significant decreases in disease activity following TDM dose intervention (p<0.0001).
- CRP significantly lowered following TDM dose intervention (median of 0.375 vs 0.23 mg/dl; p=0.0423).
- ESR did not change significantly (mean of 24.8 vs 24.5 mm/hr; p=0.9863).

Drug Concentrations at Time of Repeat TDM



- 39 pts had repeat TDM following dose intervention; 29 within 6 mo, 10 > 6 mo.
- Median IFX and VDZ serum levels increased following TDM dose intervention (IFX 0.9 to 3.9 ug/mL; VDZ 1.7 to 5 ug/ml).
- Of the 29 pts with repeat levels in the 6 mo outcome assessment, 17 (58%) achieved clinical remission.

Remission Rate Following TDM Intervention



- Significant remission occurred in 44/65 pts (68%) who continued on therapy following TDM intervention (p<0.0001).
- 12 pts discontinued the current therapeutic agent prior to the 6 mo follow-up evaluation, primarily due to loss of clinical response (median 3.6 mo; IQR 2.9-4.1).

Discussion

- 75% of TDM performed demonstrated sub-therapeutic serum levels.
- At our centers, the majority (85%) of TDM assessments were for IFX.
- 68% of TDM assessments were induced reactively, while 32% were induced proactively.
- 25% of pts (26/109) with sub-therapeutic levels were ADAbs (+), and of those with undetectable serum drug levels, 71% (24/34) were ADAbs (+).
- 27% of pts (29/106) with sub-therapeutic levels had the therapeutic agent discontinued, with 79% (23/29) due to being ADAbs (+).
- In the pts who continued the therapeutic agent (n=65), therapy interventions were distributed equally between dose increases (42%) and shortening of dosing interval (49%).
- At the outcome assessment following TDM dose intervention:
  - 68% achieved clinical remission, which was statistically significant (p<0.001).
  - CD (n=40) and UC (n= 25) pts experienced significant reductions in disease activity score (p<0.0001).
  - CRP levels were significantly reduced (p<0.0423).
  - Pts administered a higher dose achieved higher rates of remission (71%) in comparison to pts administered a shortened interval (49%).
- Following a repeat TDM post dose intervention, 58% (17/29) of pts achieved clinical remission.

Conclusion

- TDM-guided dosage changes led to enhanced clinical outcomes in pts treated with biologic therapy.
- Disease activity and CRP significantly improved following TDM-guided intervention.
- Use of TDM with biologic treatment modifications in our IBD population is consistent with published reports and supports the need for TDM in optimizing treatment for these pts.
- Our results suggest increasing drug dosage leads to a higher probability of clinical remission, however further studies are necessary.

References

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