EVALUATION OF RESPONSE TO ADALIMUMAB DOSE INTENSIFICATION IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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BACKGROUND

Adalimumab has a well-established role in the treatment of pediatric inflammatory bowel disease (IBD)

In clinical practice, it is common to increase the frequency of adalimumab in patients who experience a disease exacerbation, waning or loss of response

Previously reported data related to dose escalation of adalimumab by increasing the frequency in pediatric patients is lacking

OBJECTIVES

Primary Endpoint
- Frequency of patients requiring a change in adalimumab therapy

Secondary Endpoints
- Time to change in adalimumab therapy
- Clinical characteristics of patient before and after the adalimumab change

METHODS

Design Single-center retrospective chart review

Sample Pediatric patients (age <18) in Monroe Carell Jr. Children's Hospital at Vanderbilt (MCCHV) Pediatric IBD Program prescribed adalimumab from January 2008 to February 2019

Exclusion Criteria
No adalimumab levels
No baseline labs
Patients not taking adalimumab as prescribed
Adalimumab initiated outside of MCCHV

Analysis The Wilcoxon signed rank test and Chi-square test were used to compare characteristics of those requiring dose intensification before and after dose change

Kaplan-Meier estimates were used to calculate the probability of no change in dose after accounting for censored patients

Adalimumab dose intensification (+/- reinduction) → 40mg biweekly to 40mg weekly; 20mg biweekly to 40mg biweekly

RESULTS

Figure 1. Patients requiring dose intensification

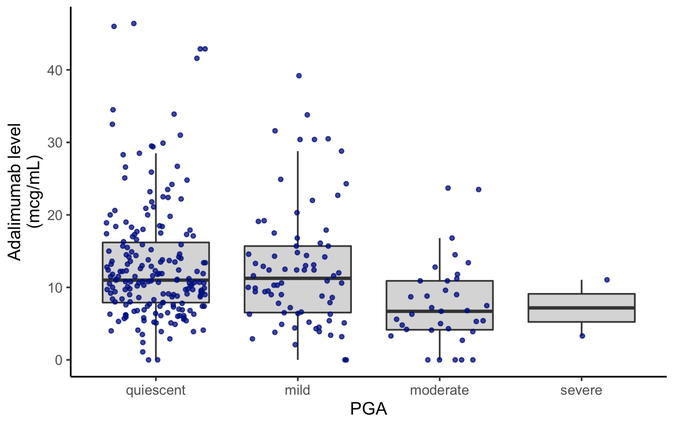
109 patients met inclusion criteria → 29 patients required change in therapy (27%)

10 patients received a reinduction prior to dose intensification (9.2%)
- 30% (3): Full reinduction (complete starting dose again)
- 70% (7): Micro reinduction (80mg x 1)

Table 1. Medication History of Sample (n=109)

	% (n)
Prior biologic therapy	
No	68% (74)
Yes - Remicade	32% (34)
Adalimumab starting dose	
160mg on day 1, 80mg on day 15, then 40mg every 14 days	*83% (90)*
80mg on day 1, 40mg on day 15, then 20mg every 14 days	*17% (19)*
Concomitant therapy at initiation (MTX, AZA, or corticosteroids)	
At least one	*27% (29)*
None	*73% (80)*

Figure 2. PGA severity and associated adalimumab levels

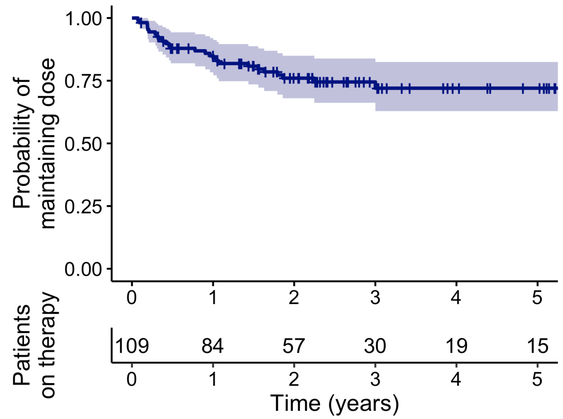


PGA (physician global assessment) severity score and adalimumab levels. Among the 109 patients in the study, there were a total of 366 patient visits. Of those, there are 305 observations with both a valid PGA score and adalimumab level.

Table 2. Baseline characteristics stratified by any change in therapy, %(n) or [mean ± SD]

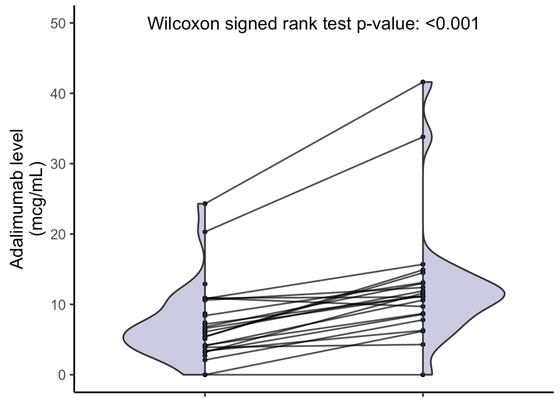
Characteristic	No change in therapy (n=80)	Change in therapy (n=29)
Age at adalimumab start	13.8±2.9	12.8±2.6
Gender (male)	55% (44)	41% (12)
Race (White)	89% (71)	90% (26)
Diagnosis		
Crohns Disease	83% (66)	83% (24)
Indeterminate	3% (2)	0% (0)
Ulcerative Colitis	15% (12)	17% (5)
PGA		
Quiescent	9% (7)	10% (3)
Mild	47% (36)	45% (13)
Moderate	40% (30)	41% (12)
Severe	3.9% (3)	3% (1)
Missing	4	0
Extraintestinal manifestations at any point in disease course	49% (39)	48% (14)
Adalimumab level median [quartile 1, quartile 3]	16.1±8.7 10.9 [14.2-20.6]	10.1±5.9 6.1 [9.2-10.9]
Missing	3	0

Figure 3. Kaplan-Meier estimates for time to dose intensification



Kaplan-Meier estimates for the probability of patients on adalimumab not requiring dose intensification. Each step down denotes an event while a vertical tick mark denotes the time when a patient was censored. The probability that a patient will maintain the same dose at 3 years is 0.76 (95% confidence interval 0.68-0.85).

Figure 4. Adalimumab levels before and after dose intensification, median [IQR]



Adalimumab level: 6.1 [3.9-8.7]

Adalimumab level: 11.2 [8.6-13.1]

CONCLUSIONS

This study characterizes patients who required dose intensification when using adalimumab for management of pediatric IBD.

Adalimumab dose intensification may improve clinical and biochemical response in pediatric IBD patients who experience waning or loss of response. However, future studies need to be conducted to further explore this response.

Proactive therapeutic drug monitoring (TDM) may prolong adalimumab response, particularly in patients whose trough levels decline ≤6 mcg/mL.

REFERENCES

1. Humira. Package insert. AbbVie Inc; 2020.
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