Primary Non-response to Initial Biologic in Inflammatory Bowel Disease does not Predict Subsequent Biologic Failure

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BACKGROUND

- The armamentarium of medical therapies to treat inflammatory bowel disease (IBD) has given patients more options if they fail their first biologic
- Currently, limited studies investigate the predictive value of first biologic primary nonresponse (PNR) on subsequent biologic success
- It is important to understand if PNR to the first biologic predicts response to subsequent biologics both within and outside of the initial biologic class

STUDY OBJECTIVE

- Our objective was to compare IBD patients with PNR, secondary loss of response (SLOR), and intolerance to their first biologic to determine predictors for response to subsequent biologics

METHODS

- Study Design:
  - Multicenter retrospective study on IBD patients that received more than two biologics were identified from the Johns Hopkins Hospital and UCLA Health IBD Database
- Population
  - PNR was defined as patients with no improvement clinically or on endoscopy leading to cessation of drug
  - Exclusion criteria - J-pouch, received any biologic other than adalimumab, infliximab, or vedolizumab for first biologic, or had missing data for major endpoints
- Data Collection/Main Outcomes
  - Patient characteristics identified included - age, sex, race, ethnicity, BMI, smoker status, IBD diagnosis, year of diagnosis, disease location, disease behavior, PSC, concomitant medication use including steroids and immunomodulator
  - For each biologic extracted - start date, stop date, dosage and frequency, dose/frequency escalation, endoscopy changes before and after biologic, physician global assessment, drug and antibody level, new or escalated steroid prescription, and serum and stool inflammatory markers
- Statistical Analysis
  - Python was used for analysis. Results were calculated by Odds Ratio (PNR/ SLOR + intolerance)

RESULTS

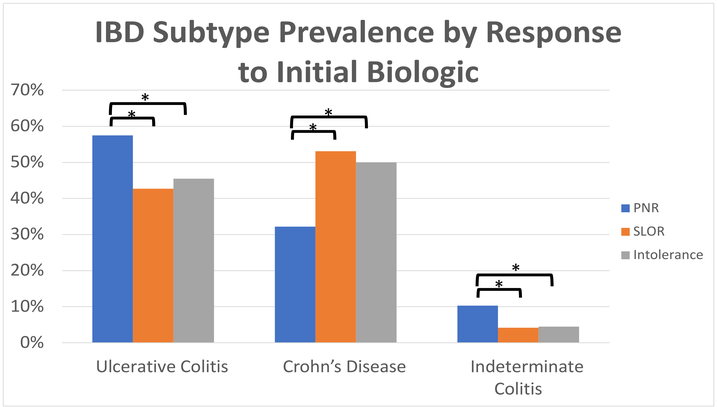
Table 1. Demographics

	Patients w/ PNR for first biologic	Patients w/ SLOR for first biologic	Patients w/ Intolerance for first biologic	p value from Chi-squared test
Total Number of Patients	87	96	66	
Age	47.6	45.2	46.3	0.5953 (ANOVA)
Male %	35/87 (40.2%)	36/96 (37.5%)	24/66 (36.3%)	0.8755
Race				0.8023
Caucasian	70/87 (80.5%)	78/96 (81.2%)	50/66 (75.8%)	
African American	3/87 (3.4%)	3/96 (3.1%)	5/66 (7.6%)	
Asian	4/87 (4.6%)	6/96 (6.3%)	5/66 (7.6%)	
Other	10/87 (11.5%)	9/96 (9.4%)	6/66 (9.1%)	
Hispanic	6/87 (6.9%)	9/96 (9.4%)	7/66 (10.6%)	0.7055
Smoking Status				0.4287
Current	8/87 (9.2%)	3/96 (3.1%)	6/66 (9.1%)	
Former	15/87 (17.2%)	18/96 (18.8%)	14/66 (21.2%)	
Never	64/87 (73.6%)	75/96 (78.1%)	46/66 (69.7%)	
BMI at diagnosis	24.8	24.8	26.1	0.2396 (ANOVA)
Subtype of IBD				*0.0344**
Ulcerative Colitis	50/87 (57.5%)	41/96 (42.7%)	30/66 (45.5%)	
Crohn's Disease	28/87 (32.2%)	51/96 (53.1%)	33/66 (50.0%)	
Indeterminate Colitis	9/87 (10.3%)	4/96 (4.2%)	3/66 (4.5%)	
Perianal	3/87 (3.4%)	17/96 (17.7%)	9/66 (13.6%)	*0.0093**
PSC	3/87 (3.4%)	3/96 (3.1%)	2/66 (3.0%)	0.9876
C. difficile infection	17/87 (19.5%)	18/96 (18.8%)	19/66 (28.8%)	0.2614
Immunomodulator during first biologic	25/87 (28.7%)	29/96 (30.2%)	23/66 (34.8%)	0.7068
Time between diagnosis and first biologic (years)	6.34	6.64	6.94	0.9225 (ANOVA)
Time on first biologic (months)	9.93	36.75	27.28	*<0.0001 (ANOVA)**

Table 2. Univariate Analysis

	n	Odds Ratio (Confidence Interval) PNR / (SLOR + Intolerance)	p value
Response to 2nd biologic			
All biologics changes	258	1.06 (0.58 – 1.91)	0.859
Anti-TNF to anti-TNF	110	0.70 (0.29 – 1.66)	0.419
IFX to ADA	60	0.36 (0.09 – 1.55)	0.171
ADA to IFX	48	0.89 (0.24 – 3.31)	0.868
Anti-TNF to non-TNF (class switch)	113	1.26 (0.47 – 3.38)	0.645
Subanalyses by Disease			
Crohn's Disease			
All biologic changes	116	0.98 (0.40 – 2.45)	0.974
Anti-TNF to anti-TNF	69	0.52 (0.17 – 1.58)	0.248
IFX to ADA	35	0.48 (0.06 – 3.89)	0.489
ADA to IFX	32	0.57 (0.12 – 2.60)	0.469
Anti-TNF to non-TNF (class switch)	33	n too small to calculate	
Ulcerative Colitis			
All biologic changes	142	0.86 (0.37 – 2.01)	0.735
Anti-TNF to anti-TNF	41	1.01 (0.24 – 4.26)	0.986
IFX to ADA	25	0.28 (0.04 – 2.17)	0.226
ADA to IFX	16	1.80 (0.09 – 35.42)	0.699
Anti-TNF to non-TNF (class switch)	80	0.81 (0.26 – 2.51)	0.718

- In patients with PNR, there was a significantly (p=0.0344) higher percentage of patients with ulcerative colitis and indeterminate colitis (UC: 57.5%, IC: 10.3%) compared to Crohn's disease (CD: 32.2%)
- Higher presence of perianal disease in SLOR and intolerance
- Among patients who had PNR, SLOR, or intolerance of their first biologic, there was no significant difference in those that demonstrate non-response to their second biologic
- Univariate and multivariate analyses showed no difference in rates of PNR to second biologic when switching intra-class or out of class



CONCLUSIONS

- Our results are reassuring that despite PNR to first biologic, there is a high chance of response to second biologic
- Subanalyses evaluating intraclass and out of class medication switches showed similar success
- Ulcerative colitis and indeterminant colitis have higher rates of PNR compared to Crohn's disease, but still have high response to second biologic agents