

# Characterization of Crohn's Patients That Are Multiple Primary Non-Responders to Biologic Therapies

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## Introduction

- Many patients with Crohn's Disease (CD) remain non-responders despite availability of new therapies.
- Few studies have characterized medically refractory CD.
- Identifying patients that are true primary non responders to multiple therapies may reveal novel mechanisms on which future therapies can be built.

## Aim

- Here we describe the clinical characteristics of CD patients that are primary non-responders to all 3 FDA approved classes of biologics from a tertiary center.

## Methods

- Two datasets were used: a randomly selected cross sectional dataset of 783 patients and a dataset of 42 patients screened for a clinical trial that permitted failure of 3 biologics.
- Datasets were reviewed for medication use and primary failure of 3 or more medications as defined by the following criteria 1 - Demonstrated endoscopic disease activity. 2 - Trial of therapy > 6 months and 3 - No record of adverse event.

## Results

- 19 patients met criteria for primary non-response across three biologic classes.
- The refractory patients had more upper tract disease and penetrating (B3) disease compared to the non-refractory group.
- There were otherwise no significant differences in clinical factors between responders and refractory patients.

Table 2: Treatment strategies employed after multiple biologic failure.

Treatment Strategy	Number of Times Used
Trial Referral	16
Recycling Biologic Class	10
Medication Optimization	5
Surgery	2
Use of Off-Label Med	2
Combination Biologics	1

Table 1: Comparison of clinical characteristics between refractory group (primary non-response to 3+ classes of biologics) vs general population of cross sectional study participants.

	Multiple Primary NR Patients (n = 19)	Non-Multiple Refractory Patients (n = 787)	P value
Mean age at Dx (yrs)	24.7	26.17534943	0.999
# Male	10 (52.6%)	427 (54.2%)	0.883
# Female	9 (47.4%)	360 (45.7%)	0.883
# Ileocolitis	13 (68.4%)	413 (52.4%)	0.278
# Colitis	4 (21.1%)	173 (22.0%)	0.278
# Ileal	2 (10.5%)	201 (25.5%)	0.278
# Upper GI	2 (10.5%)	9 (1.14%)	0.0005
# B1	5 (26.3%)	455 (57.8%)	---
# B2	5 (26.3%)	225 (28.6%)	---
# B3	9 (47.4%)	106 (13.5%)	0.00002
# Perianal	3 (15.8%)	69 (8.77%)	0.289
Prior CD Surgery	11 (0.58%)	340 (43.2%)	0.202

## Conclusions

- This retrospective review demonstrates there is a small subset of highly medically refractory CD patients that are true primary non-responders to multiple biologics.
- Common clinical characteristics don't allow the identification of these patients, suggesting the need for molecular phenotyping in order to identify rational rescue therapies for this unique subset of patients.