Long-term Outcomes of Treatment with and De-escalation from a Combination of Vedolizumab and another Biologic or Tofacitinib for Inflammatory Bowel Disease

Jenny Jan MD[1], Ernesto Llano MD[2], Shreeju Shrestha MSN[2], Ezra Burstein MD PhD[2], Moheb Boktor MD[2], David Fudman MD[2]

[1]Department of Internal Medicine and [2]Division of Digestive and Liver Diseases, University of Texas Southwestern Medical Center, Dallas TX

UT Southwestern Medical Center

Background

- Combining advanced therapies with different mechanisms of action is a potential approach for treatment of refractory inflammatory bowel disease (IBD).
- There are scarce data on long-term outcomes of combining advanced therapies, including safety, efficacy, and de-escalation.

Goals

- We sought to examine the long-term outcomes of patients with IBD being treated with a combination of advanced therapies at a single tertiary medical center, including after de-escalation of combination therapy. Short-term outcomes of this cohort were previously reported

Methods

- We identified patients with IBD at a tertiary center who began therapy with vedolizumab (VDZ) in combination with another advanced therapy (biologic or JAK inhibitor) between 2016 and 2020 and examined their outcomes through June 2022.
- We defined biochemical remission as CRP <5mg/L and calprotectin <150 mcg/g, and endoscopic remission as Mayo endoscopic subscore 0 or simple endoscopic score for Crohn's disease (CD) 0.

Results

- We identified a total of 14 patients on combination therapy
  - 10 patients had ulcerative colitis (UC), 3 patients had CD, and 1 patient had indeterminate colitis (IC)
  - VDZ was combined with tofacitinib (TOF) in 9 patients, ustekinumab (UST) in 3 patients, and adalimumab (ADA) in 2 patients.
- Median follow up was 322 (IQR 251-322) weeks. Median time on combination therapy was 94 (IQR 17-133) weeks.
- 8 patients achieved objective remission (3 biochemical, 5 endoscopic), 1 changed combination with subsequent endoscopic remission, 2 had primary non-response, 1 had secondary non-response, and 1 lacked follow-up data.
- 8 patients de-escalated to a single agent, 4 at physician direction and 4 due to insurance denial.
  - Before de-escalation, 6 patients had objective remission (2 biochemical, 4 endoscopic)

Table 1: Outcomes Summary Table

	IBD type	Initial Biologic	2nd biologic	Efficacy of Combination Therapy	Outcome	Discontinued therapy	Outcome of de-escalation
1	CD	UST	VDZ	Biochemical remission	De-escalation (insurance denial)	Stopped VDZ	Flare
2	CD	UST	VDZ	Changed combination	Ongoing combination now with endoscopic remission	VDZ changed to ADA	-
3	CD	TOF	VDZ	Primary non-response	Surgery	No discontinuation	-
4	IC	ADA	VDZ	Biochemical remission	De-escalation (insurance denial)	Stopped ADA	Biochemical remission
5	UC	VDZ	TOF	Stopped therapy after 1 month	De-escalation (adverse effect [parasthesias])	Stopped TOF	Flare
6	UC	TOF	VDZ	Endoscopic remission	De-escalation (insurance denial)	Stopped VDZ	Flare
7	UC	TOF	VDZ	Primary non-response	De-escalation (insurance denial)	Stopped VDZ	Flare requiring surgery
8	UC	VDZ	ADA	Endoscopic remission	De-escalation (physician-directed)	Both, now on UST alone	Endoscopic remission
9	UC	VDZ	TOF	Endoscopic remission	De-escalation (physician-directed)	Stopped TOF	Biochemical remission
10	UC	TOF	VDZ	Biochemical remission	De-escalation (physician-directed)	Stopped TOF	Transferred care after de-escalation
11	UC	TOF	VDZ	Endoscopic remission	De-escalation (physician-directed)	Stopped TOF	No updated data (recently de-escalated)
12	UC	TOF	VDZ	Lacks data	Lacks data	Lacks data	Lacks data
13	UC	TOF	VDZ	Secondary non-response	Ongoing combination with moderate endoscopic disease	TOF changed to UST	-
14	UC	VDZ	UST	Biochemical remission	Transferred care while on combination therapy	No discontinuation	-

Results, cont.

  - After de-escalation, 3 patients maintained objective remission (2 biochemical, 1 endoscopic), 3 had disease flare, of which 1 required colectomy, and 2 lacked data
  - All 3 patients with disease flare had de-escalated following an insurance denial
- 2 patients remained on combination therapy through follow-up: 1 has endoscopic remission after changing one drug of their combination, and 1 has ongoing moderate endoscopic disease despite combination therapy
- There were 2 infections requiring hospitalization (rotavirus, C.difficile), and 8 non-serious infections (5 mild SARS-COV2, 1 peristomal cellulitis, 1 pneumonia, 1 sinus) while on combination therapy

Conclusions

- In long-term follow up of this small cohort treated with vedolizumab and another advanced agent, there were no new signals on effectiveness or safety
- This treatment strategy continues to appear effective despite the population's previously refractory disease
- Half of patients with follow-up data tolerated de-escalation; all patients who flared following de-escalation had adjusted therapy due to insurance denial
- More data is needed to inform de-escalation decisions

Table 2: Outcomes of combination therapy

Outcome	Number of Patients
Objective remission	8
Endoscopic	5
Biochemical	3
Change of combination	1
Primary non-response	2
Secondary non-response	1
Stopped therapy (AE)	1
No data	1

Table 3: Outcomes of de-escalation

Before de-escalation	Number of Patients
Objective Remission	6
Endoscopic	4
Biochemical	2
De-escalation	8
Physician direction	4
Insurance denial	4
After de-escalation	
Objective Remission	3
Endoscopic	1
Biochemical	2
Disease flare	3
De-escalation due to insurance denial	3
Required surgery	1
Lacked data	2