crohn's colitis

Name of Clinical Care Pathway

Loss of Response or Partial Response for Patients on Advanced Therapy

Objective

Achieve and maintain remission with advanced therapy

Patient Population

Patients diagnosed with inflammatory bowel disease (IBD) on advanced therapy

Dr. Jesse Siffledeen MD MSc (Oxon) FRCPC (University of Alberta &
Covenant Health / Grey Nuns Hospital Edmonton)
Dr. Vivian Huang MD, FRCPS (University of Toronto & Mount Sinai Hospital)

These clinical decision support tools were developed by Canadian experts in IBD, based on their interpretation of current evidence and considerations specific to Canadian healthcare. International guidelines from Europe and the United States are available. However, these may reflect regional factors not directly applicable in Canada.

Abbreviations

5-ASA	5-Aminosalicylic acid
6-MMP	6-methylmercaptopurine
6-TGN	6-thioguanine nucleotides
ADA	Anti-drug antibodies
BID	Twice daily
IBD	Inflammatory bowel disease
IBS	Irritable bowel syndrome
IV	Intravenous
MTX	Methotrexate
N/A	Not applicable
PO	By mouth
q4w	Every 4 weeks
TDM	Therapeutic drug monitoring
TNF	Tumor necrosis factor
TPMT	Thiopurine methyltransferase
µg/g	Micrograms per gram

Version: June 25, 2025

crohn's colitis

Highlights from this CCP

New IBD therapies are continuously becoming available. However, the approach to the loss of response or partial response for patients on advanced therapy remains inconsistent. The main objective is to achieve and maintain remission by dose optimization, reassessment of response to medications, and switching therapies as required.

Introduction

This CCP recommends a common approach to any IBD patient who is on advanced therapy and who is exhibiting symptoms of loss of response or partial response. While initially developed for guidance regarding drug level monitoring and dose optimization for patients losing response to anti-TNF therapies, this CCP also provides suggestions for how to approach patients who are on newer biologics and small molecules. Where applicable, the guidance reflects published data and recommendations established by the global IBD community.

The algorithms below are best practice clinical pathways for loss of response or partial response for patients on advanced therapy (Refer to Flowchart 1 and Flowchart 2).

Confirm clinically relevant active IBD

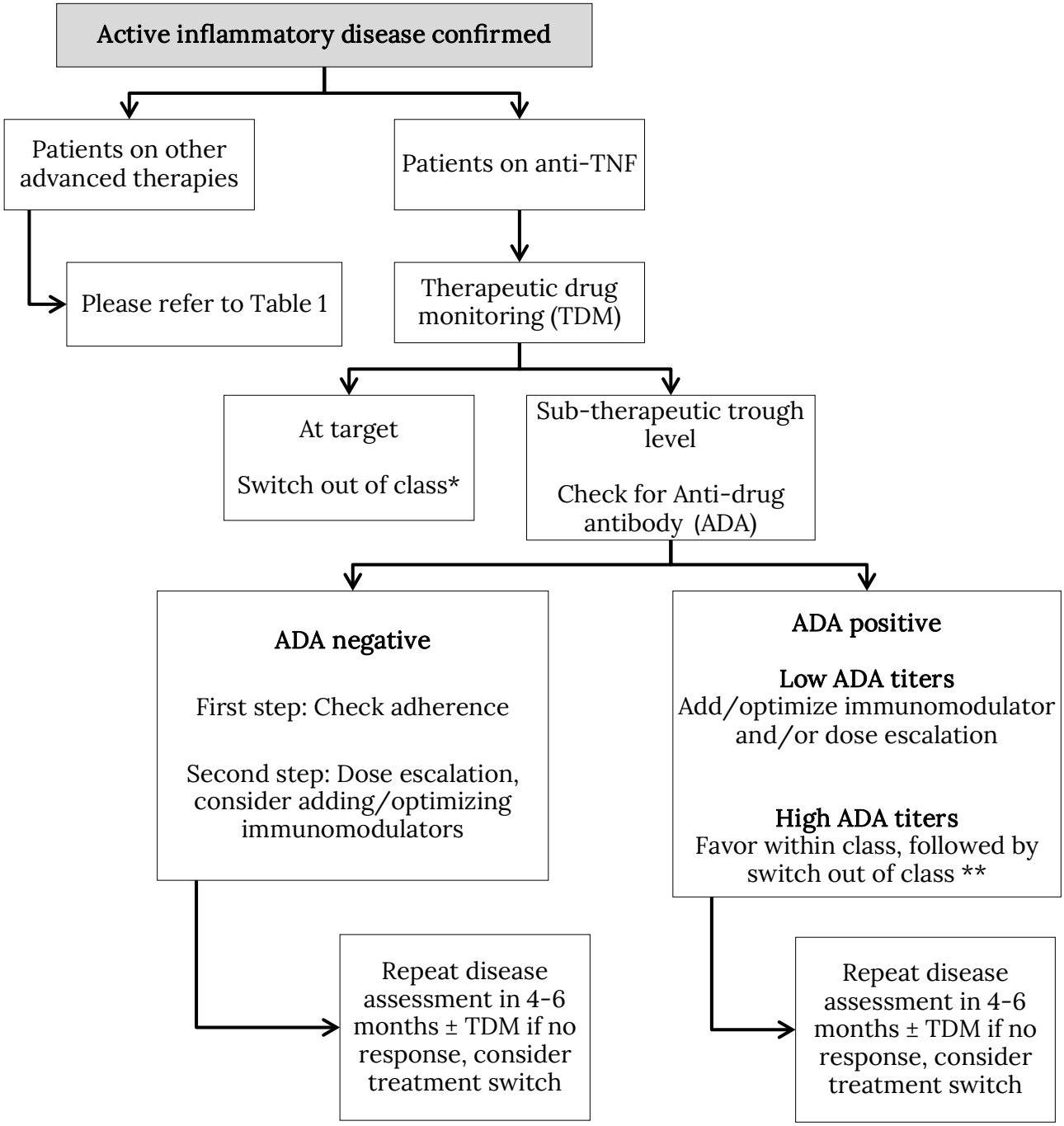
- Clinical symptoms
- Fecal Calprotectin/stool testing (Table 2)
- Blood (Routine, drug trough levels and ADA)
- Endoscopy/radiology (ultrasound)
- Clinical symptoms

Exclude IBS, infection, malignancy and fibrostenotic stricture

In the absence of clinically relevant active IBD, treat the alternative diagnosis. For confirmed active IBD, proceed to Flowchart 1.

crohn's colitis

Flowchart 1: For patients with confirmed active IBD



*Consider adding an immunomodulator if switching to another advanced therapy agent to prevent ADA formation.

**Add an immunomodulator if switching to another advanced therapy agent to prevent ADA formation.

Version: June 25, 2025

Table 1: Approach to managing other advanced therapies

Drug	Dose optimization	Time to reassess
Vedolizumab	Escalate to q4w dosing*	At the 3rd q4w dosing
Ustekinumab	Escalate to q4w dosing OR request IV reloading dose	At the 3rd q4w dosing OR 3 to 4 months after IV reloading dose
Tofacitinib	10mg po BID	After 8 weeks
Upadacitinib	30 mg/daily	After 8-12 weeks
Risankizumab	N/A***	12-24 weeks
Ozanimod**	N/A***	
Etrasimod	N/A***	

q4w: every 4 weeks N/A: not applicable IV: intravenous PO: by mouth BID: twice daily

*Optimization has limited benefits based on evidence.

**If there is no response or loss of response after 10 weeks, switch out of the class. Note that its availability may be limited, which could impact access for patients.

***There is insufficient observational data to make a recommendation.

Always discuss the potential risks associated with changing advanced therapies with the patient, including the risk of a lesser response and potential side effects.

Table 2: Fecal calprotectin results and clinical approach

Fecal Calprotectin (µg/g)	Interpretation	Suggested management
<50-100	Quiescent disease likely	Continue current therapy
>100-250	Inflammation possible	Investigate (e.g., colonoscopy) to confirm inflammation
>250	Inflammation likely	Optimize/switch therapy

Table 3: Approach to managing thiopurine therapy

Etiology of thiopurine Failure	6-TGN level (pmol/10^8 erythrocytes)	6-MMP level (pmol/10^8 erythrocytes)	6-MMP/6-TGN ratio	Proposed treatment strategy
Inadequate dose	Low (<230)	Low (<5700)	Normal (4-24)	Increase dose
Excessive TPMT	Low (<230)	High (>5700)	High (>24)	TPMT modulation by the addition of allopurinol or 5-ASA, dose splitting, switch to an alternative agent, such as MTX
Lack of adherence	Low (<230)	Low (<5700)	Normal (4-24)	Verify adherence
True drug ineffectiveness	Normal (230-400)	Normal (<5700)	Normal (4-24)	Alternative therapy

5-ASA: Mesalamine 6-MMP:Methyl mercaptopurine 6-TGN: 6-Thioguanine nucleotides
MTX: Methotrexate TPMT: Thiopurine methyltransferase

References

Bressler et al. Clinician's guide to the use of fecal calprotectin to identify and monitor disease activity in inflammatory bowel disease. Canadian Journal of Gastroenterology and Hepatology 2015;29(7):369-372. https://doi.org/10.1155/2015/852723

Feuerstein et al. American Gastroenterological Association Institute Guideline on Therapeutic Drug Monitoring in Inflammatory Bowel Disease. Gastroenterology 2017;153(3):827-834. https://doi.org/10.1053/j.gastro.2017.07.032

Kopylov, U., Ben-Horin, S., & Seidman, E. (2014). Therapeutic drug monitoring in inflammatory bowel disease. Annals of gastroenterology, 27(4), 304–312.PMCID: PMC4188926

Mitrev et al. Review article: Consensus statements on therapeutic drug monitoring of anti-tumour necrosis factor therapy in inflammatory bowel diseases. Aliment Pharmacol Therapeutics 2017; 46(11-12):1037-1053. https://doi.org/10.1111/apt.14368

Papamichael et al. Appropriate Therapeutic Drug Monitoring of Biologic Agents for patients with inflammatory bowel diseases. Clinical Gastroenterology Hepatology. 2019; 17(9):1655-1668. https://doi.org/10.1016/j.cgh.2019.03.037

crohn's colitis

Turner et al. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. Gastroenterology 2021 Apr;160(5):1570–1583. https://doi.org/10.1053/j.gastro.2020.12.031