# Diverting loop ileostomy as an alternative to emergent colectomy in acute severe ulcerative colitis flare due to immunotherapy

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## Introduction

- **Checkpoint inhibitors** including cytotoxic T lymphocyte antigen 4 (CTLA-4) inhibitors and programmed cell death 1 (PD-1) inhibitors are increasingly prescribed for malignancies.
- Checkpoint inhibitors may cause immune-related adverse events (irAE) including immunotherapy-induced colitis, and can worsen pre-existing ulcerative colitis in up to 40% of patients[1]. This risk is higher for CTLA-4 inhibitors compared to PD-1 inhibitors[1].
- The disease phenotype for checkpoint inhibitor worsening of ulcerative colitis can be severe, with most patients requiring corticosteroids, one-third requiring checkpoint inhibitor discontinuation and escalation to biologic therapy (most commonly infliximab and vedolizumab), and **up to 5% requiring gastrointestinal surgery such as colectomy[1,2].**
- **Diverting loop ileostomy** is an uncommonly performed procedure for patients with refractory ulcerative colitis, with successful reversal described in a small minority of patients[3]
- In checkpoint-inhibitor colitis, diverting loop ileostomy has been described, with reversal unsuccessful due to recurrence of severe colitis[4]
- We describe the first case to our knowledge of successful reversal of ileostomy in checkpoint inhibitor worsening of ulcerative colitis.

## Case

An Australian born 81-year-old man with previously **well-controlled ulcerative proctitis** diagnosed in 1970, with documented symptomatic, endoscopic and histologic remission on sulfasalazine 500mg daily, was referred in 2022 with increased blood-stained diarrhoea of up to 5 per day for the previous week. He had been diagnosed with metastatic melanoma 4 months earlier with a subcutaneous upper back primary, with lesions to the liver, left lung and right adrenal. He was commenced on nivolumab 3 months earlier with partial response and ipilimumab added on 6 weeks earlier. He was otherwise independent in activities of daily living, had never smoked and had no significant comorbidities.

Despite withholding immunotherapy, maximising oral and topical 5-ASA therapy, as well as commencement of oral steroids, he progressed to severe left sided colitis over the following 6 weeks, with >10 blood-stained bowel actions/day, Mayo endoscopic subscore 3, with CRP > 100 mg/L and albumin < 20g/L. He also had severe inflammatory peripheral arthritis. Stool cultures were negative for infections including Clostrioides difficile. Cytomegalovirus immunohistochemistry on biopsies was negative. **His UC remained refractory** despite accelerated infliximab (x3 doses of 5mg/kg) and vedolizumab (x2 doses of 300mg) over 3 weeks with persistent bloody diarrhoea of 6-8 bowel actions per day, CRP 40 mg/L and albumin 22g/L.

A decision was made to perform a **rescue diverting loop ileostomy** instead of a colectomy. This was performed at the same time as left hemi-hepatectomy for a 58mm Segment 4a metastatic melanoma deposit which showed no residual cancer on histology, suggesting a complete response.

His disease activity was subsequently controlled with 8-weekly vedolizumab, Asacol 4.8g daily, salofalk enemas 2g nocte and suppositories 1g mane, reaching histological remission. **His ileostomy was reversed 14 months later**. He had a complicated postoperative course with ileus, pseudo-obstruction and superimposed *Clostroides difficile* infection treated with a combination of oral vancomycin and intravenous metronidazole, continuing with a 4-week weaning course of vancomycin to prevent relapse.

He achieved clinical remission with one to two soft bowel motions a day without blood or mucus, improvement of energy levels and a return to normal functional status two months later. Colonoscopy one year following ileostomy reversal showed his UC to be in endoscopic and histological remission on maintenance 8-weekly vedolizumab. His melanoma remains in remission 3 years after the last dose of immunotherapy.

## References

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