A User Guide for Inflammatory Bowel Disease
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ULCERATIVE COLITIS
Clinical remission:
Resolution of symptoms (stool frequency ≤ 3/day, no bleeding and no urgency)

Endoscopic remission:
Absent or minimal endoscopic lesions

Relapse:
Flare of symptoms (blood in stool, tenesmus, diarrhea) with or without evidence of mucosal inflammation and in the absence of concomitant infection

Steroid-resistant:
Patients who have active disease despite prednisolone of up to 0.75 mg/kg/day over a period of 4 weeks

Steroid-dependent:
Patients who are either:
- Unable to reduce steroids below the equivalent of prednisolone 10 mg/day within 3 months of starting steroids, without recurrent active disease, or
- Who have a relapse within 3 months of stopping steroids
Anatomic Extent of Ulcerative Colitis

**Pancolitis**
- Beyond splenic flexure or > 60cm

**Left-sided disease**
- Extends to splenic flexure or <60cm

**Proctitis**
- Rectum only
### Severity of active colitis

<table>
<thead>
<tr>
<th>Severity</th>
<th>Stool per day</th>
<th>Blood in stool</th>
<th>Erythrocyte sedimentation rate</th>
<th>Systemic toxicity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&lt;4</td>
<td>Present or absent</td>
<td>Normal</td>
<td>Absent</td>
</tr>
<tr>
<td>Moderate</td>
<td>4 to 6</td>
<td>Present or absent</td>
<td>Normal or elevated</td>
<td>Absent</td>
</tr>
<tr>
<td>Severe</td>
<td>7 to 10</td>
<td>Present</td>
<td>Elevated</td>
<td>Present</td>
</tr>
<tr>
<td>Fulminant</td>
<td>&gt;10</td>
<td>present</td>
<td>Elevated</td>
<td>Present</td>
</tr>
</tbody>
</table>

* - Fever, tachycardia, leukocytosis, or anemia
  - Fulminant disease may also manifest as abdominal tenderness or distension, continuous bleeding with transfusion requirement or colonic dilatation

### UC Endoscopic Spectrum of Severity

<table>
<thead>
<tr>
<th>Severity</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No friability or granularity</td>
<td>Erythema</td>
<td>Marked erythema</td>
<td>Marked erythema</td>
</tr>
<tr>
<td></td>
<td>Intact vascular pattern</td>
<td>Decreased vascular pattern</td>
<td>Absent vascular pattern</td>
<td>Absent vascular markings</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mild friability</td>
<td>Friability</td>
<td>Friability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Erosions</td>
<td>Granularity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Friability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Spontaneous bleeding</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ulcerations</td>
</tr>
</tbody>
</table>
Treatment Algorithm for Ulcerative Colitis

Patient diagnosed with Ulcerative Colitis

Determine severity and extent

- Mild to moderate left distal colitis/proctitis
- Mild to moderate extensive colitis
- Moderate to severe extensive colitis
- Severe to fulminant colitis
## Medical therapies for UC

<table>
<thead>
<tr>
<th>Medication (form)</th>
<th>Dosage for Active disease</th>
<th>Maintenance dosage</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>5ASA (oral)</td>
<td>2 to 4.8g/day in 3 divided doses</td>
<td>1.2 to 2.4 g/day</td>
<td>Interstitial nephritis</td>
</tr>
<tr>
<td>5ASA (suppository)</td>
<td>1g once per day</td>
<td>0.5g once or twice per day</td>
<td>Anal irritation, discomfort</td>
</tr>
<tr>
<td>5ASA (enema)</td>
<td>1 to 4 g per day</td>
<td>1 to 4 g daily to every third day</td>
<td>Difficulty retaining, rectal irritation</td>
</tr>
<tr>
<td>Hydrocortisone (10% foam)</td>
<td>90mg once or twice per day</td>
<td>Not recommended</td>
<td>Rectal irritation</td>
</tr>
<tr>
<td>Prednisone (oral)</td>
<td>40 to 60 mg per day until clinical improvement then taper by 5 to 10mg per week</td>
<td>Not recommended</td>
<td>Adrenal suppression, bone disease, cataracts, cushingoid features, glaucoma, impaired wound healing, infections, metabolic abnormalities</td>
</tr>
<tr>
<td>Methylprednisolone (solumedrol, IV)</td>
<td>40 to 60 mg per day</td>
<td>Not recommended</td>
<td></td>
</tr>
</tbody>
</table>
# Medical therapies for UC

<table>
<thead>
<tr>
<th>Medication (form)</th>
<th>Dosage for active disease</th>
<th>Maintenance dosage</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab (IV)</td>
<td>5 mg per Kg on weeks 0, 2, and 6</td>
<td>5mg per Kg every 8 weeks</td>
<td>Increased risk of infection and lymphoma, infusion reaction</td>
</tr>
<tr>
<td>Adalimumab (sc)</td>
<td>160mg W0, 80mg W2, than 40mg EOW</td>
<td>40mg EOW</td>
<td>Increased risk of infection and lymphoma</td>
</tr>
<tr>
<td>Godilumab</td>
<td>200mg (w0), 100mg (w2)</td>
<td>50-100mg (e4w)</td>
<td>Increased risk of infection and lymphoma</td>
</tr>
<tr>
<td>Azathiopyrine (oral)</td>
<td>Not recommended</td>
<td>1.5 to 2.5 mg per Kg per day</td>
<td>Allergic reactions, bone marrow suppression, infection, pancreatitis</td>
</tr>
<tr>
<td>Ciclosporine (IV)</td>
<td>2 to 4 mg per Kg per day</td>
<td>Not recommended</td>
<td>Infection, nephrotoxicity, seizures</td>
</tr>
</tbody>
</table>

Zocco MA, Aliment Pharmacol ther. 2006;
Treatment Algorithm for Ulcerative Colitis

Patient diagnosed with Ulcerative Colitis

Determine severity and extent

Mild to moderate left distal colitis/proctitis
Proctitis/distal colitis

- Colitis limited to the rectum with mild or moderate activity should be initially treated topically.
  

- 5-ASA suppository
  - is the drug of first choice
    
    ECCO EL 1b, RG B; DGVS EL A
  - induces remission in 31-80% of patients compared to 7-11% in the placebo-treated group.
    
    Marshall JK, Gut 1997; 40: 775-781

- There is no dose response to topical therapy above 1 g mesalazine daily.
Proctitis/distal colitis

- Topical corticoids are less effective than topical mesalazine.
  
  Gionchetti P, Aliment Pharmacol Ther 1997; 11: 1053-1057

- If no therapeutic effect is observed, treatment escalation using a combination of:
  
  – oral mesalazine (2-6 g/d for induction),
  – with topical mesalazine and/or a topical steroid is recommended as second-line therapy

  ECCO EL 1b, RG B; DGVS A
Proctitis/distal colitis

- If symptoms do not resolve within 2-4 weeks, the patient’s adherence to medical treatment should be evaluated.

- Confirmed persistent proctitis, in spite of combined local and topical therapy, is best treated as if it were more extensive or severe colitis.
Left-sided UC

- Left-sided active UC of mild-to-moderate severity should be initially treated with topical aminosalicylates combined with > 2 g/d oral mesalazine
  
  (ECCO EL1b, RG B; ACG EL A)
  
- Comparative trials
  
  - revealed a dose-response of oral mesalazine (< 2.4 g vs 4.8 g/d) with more rapid clinical improvement and cessation of rectal bleeding in patients taking a higher dose (16 d vs 9 d, P < 0.05)
  
  - failed to show significant differences in remission rates 20.2% vs 17.7% (not significant)
    
    - Hanauer SB, Am J Gastroenterol 2005; 100: 2478-2485
    - Sutherland L, Cochrane Database Syst Rev 2006; CD000543
Active left-sided UC: combination therapy superior to solo therapy with oral mesalamine 2.4g or mesalamine enemas 4.0g

percent of patient reporting no blood seen in stool

Safidi et al, Am J Gastroenterol. 1997, 92(10) 1867-1871
Induction of response:
2.4g to 4.8g/day
Left-sided UC

• If rectal bleeding persists after 10-14 d despite combined treatment, systemic steroids should be introduced
  
  ECCO EL 1b, RG C; DGVS EL B; ACG EL C

• Steroid starting dose is 40-60 mg orally once daily. Marked differences between 40 and 60 mg starting doses have not been found
  
  DGVS EL A
Left-sided UC

- Severe left-sided colitis is usually an indication for hospital admission and systemic therapy

(ECCO EL 1b, RG B)
Maintenance of remission proctitis/ left side colitis

• First-line medical therapy for proctitis and left sided colitis consists of topical 5-ASA with a minimum dose of 1 g 3 times a week

  ECCO EL 1b, RG B; ACG EL A

• Oral mesalazine can be added as second-line therapy and has been shown to be superior compared with monotherapy, or it can be given alone if long-term rectal treatment is not accepted by the patient.

  ECCO EL 1b, RG B
Remission maintenance UC: combination therapy superior to solo therapy with oral mesalamine 1.6g
Mild to Moderate Distal Colitis

**Proctitis**
- 5-ASA suppositories for 4 to 6 weeks
- Remission
  - Yes: 5-ASA suppositories maintenance dose
  - No: Add topical steroid and/or oral 5-ASA
  - Remission
    - Yes: Oral + topical 5-ASA maintenance dose
    - No: Oral steroid + oral 5-ASA + rectal ASA
    - Remission
      - Yes: Oral + topical 5-ASA maintenance dose (± Azathioprine)
      - No: Anti-TNF alpha

**Proctosigmoiditis**
- Oral 5-ASA (induction dose) + 5-ASA enema for 4 to 6 weeks
- Remission
  - Yes: Oral +/- enema 5-ASA maintenance dose
  - No: Oral steroid + 5-ASA
    - Maintenance dose 5-ASA
    - Steroid dose induction + Azathioprine + 5-ASA
    - Remission
      - Yes: Azathioprine + 5-ASA
      - No: Anti-TNF alpha

5-ASA: 5-aminosalicylic acid
Treatment Algorithm for Ulcerative Colitis

Patient diagnosed with Ulcerative Colitis

Determine severity and extent

Mild to moderate extensive colitis

Moderate to severe extensive colitis
Extensive UC of mild-to-moderate severity

- Systematic review and meta analysis that investigated the effect of high or standard dose 5ASA (≥ 2 g) vs low dose 5ASA (< 2 g) on induction of remission demonstrated
  
  – that doses of ≥ 2 g/d were more effective than doses of < 2 g/d for inducing remission with a RR of failure to achieve remission of 0.91 (95%CI: 0.850.98).
  
  • Ford AC, Am J Gastroenterol 2011; 106: 601-616

- This finding was based on data showing that
  
  • 380 (58.7%) of 647 patients receiving high or standard dose 5ASA failed to achieve remission
  • compared with 257 (69.8%) of 368 patients assigned to low dose 5ASA

Hanauer S, Am J Gastroenterol 1993; 88: 1188-1197
Levine DS,. Am J Gastroenterol 2002; 97: 1398-1407
D’Haens G,. Aliment Pharmacol Ther 2006; 24: 1087-1097
Extensive UC of mild-to-moderate severity

- Initially treated with oral sulfasalazine at a dose titrated up to 4-6 g/d (ACG EL A)
  
  or

- A combination of oral and topical mesalazine (ECCO EL 1a, RG A; DGVS EL A).

- **Oral 5-ASA formulas induce remission in only approximately 20% of patients.**

  Bebb JR, Aliment Pharmacol Ther 2004; 20: 143-149

- Patients who do not respond to this treatment within 10-14 d or who are already taking appropriate maintenance therapy should be treated additionally with a course of oral steroids (ECCO EL 1b, RG C; ACG EL B).
Extensive UC of mild-to-moderate severity

- **Standard corticosteroids were superior to placebo** for UC remission with a
  - RR of failure to achieve remission of 0.65 (95%CI: 0.450.93).

- This finding was based on analysis of data showing that
  - 122 (54.0%) of 226 patients assigned to standard oral glucocorticoids failed to achieve remission compared with
  - 173 (79.0%) of 219 patients allocated to placebo.

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Ford AC, Am J Gastroenterol 2011; 106: 590-599
Truelove SC, Gut 1992; 33: 711-714
Rizzello F, Aliment Pharmacol Ther 2002; 16: 1109-1116
Bossa F, Am J Gastroenterol 2008; 103: 2509-2516
Maintenance of remission
Extensive UC of mild-to-moderate severity

- Systematic review and meta analysis of the efficacy of 5ASA vs placebo in preventing relapse in quiescent UC demonstrated that
  - 5ASA is highly effective for preventing relapse in UC with a RR of relapse of 0.65 (95%CI: 0.550.76).
  - finding was based on data showing that
    - 342 (40.3%) of 849 patients randomized to 5ASA relapsed
    - compared with 409 (62.6%) of 653 patients allocated to placebo.
      - Misiewicz JJ, Lancet 1965; 285: 185-188
      - Lichtenstein GR, Aliment Pharmacol Ther 2010; 32: 990-999
  - Doses of $\geq 2$ g/d may be more effective than doses of < 2 g/d for preventing relapse with a RR of relapse of 0.79 (95%CI: 0.640.97). finding based on data showing that:
    - 225 (34.7%) of 649 patients receiving high or standard dose 5ASA relapsed, compared with 379 (42.8%) of 885 patients assigned to low dose 5ASA.
      - Ford AC, Am J Gastroenterol 2011; 106: 601-616
Maintenance of remission
Extensive UC of mild-to-moderate severity

• **Oral mesalazine is the therapy of first choice.** It is effective and well tolerated

  Sutherland L,. Cochrane Database Syst Rev 2006; CD000543

• In the case of:

  – steroid-dependency

  ECCO EL 1a, RG A

  or

  – Steroid refractory course

  ECCO EL 1a, RG B, ACG A

• **Azathioprine (2.5 mg/kg per day)** or 6-mercaptopurine (1.5 mg/kg per day) should be introduced for induction of remission and remission maintenance.
Azathioprine in the Management of Chronic UC

Mean Activity Score at Baseline and 6 mo

- Placebo: n = 20, Mean Activity Score = 7.7
- Azathioprine: n = 24, Mean Activity Score = 8.1

Reduction in Prednisone Dose at Baseline and 6 mo

- Placebo: n = 20, Reduction in Prednisone Dose = 23.2 mg/d
- Azathioprine: n = 24, Reduction in Prednisone Dose = 22.2 mg/d

Comparison between azathioprine and placebo at 6 mo.

Azathioprine vs 5-ASA for Corticosteroid-Dependent, Active UC

Treatment Success* After 6 mo

- **5-ASA 3.2 g/d (in 3 divided doses)†**: 19%
- **AZA 2 mg/kg/d**: 53%

*Defined as clinical remission (Powell-Tuck Index score of 0) and endoscopic remission (Baron Index score ≤ 1) plus corticosteroid discontinuation. Patients treated with a concurrent tapering dose of corticosteroids. AZA = azathioprine
†Doses were taken as 0.8 g at breakfast and lunch and 1.6 g at dinner.

Extensive UC of mild-to-moderate severity

- Azathioprine have been proven to be effective in steroid-dependent or steroid-refractory UC patients.

- Other indications of thiopurines for UC patients include:
  - Patients with severe relapses
  - Patients who need ≥2 courses of steroid within a 12 months period
  - Patients with relapses when the dose of steroid is < 15 mg
  - Patients with relapses <3 months of discontinuing steroids

Extensive UC of mild-to-moderate severity

- Systematic review and meta analysis of the effect of AZA on active UC demonstrated
  - A trend to benefit of AZA over placebo in a total of 130 UC patients allocated to AZA or placebo with no statistical significance (RR = 0.85; 95%CI: 0.711.01; P = 0.07).
  - AZA is of benefit in preventing relapse in quiescent UC (RR = 0.60; 95%CI: 0.370.95; P = 0.03). This finding was based on data
    - that 26 (39.3%) of 66 patients receiving AZA experienced a relapse of UC,
    - compared with 40 (65.6%) of 61 patients allocated to placebo, with a statistically significant benefit of AZA

- AZA/6-MP appears to be of little benefit for inducing remission in active UC, but may prevent relapse in quiescent UC.

Khan KJ, Am J Gastroenterol 2011; 106: 630-642
Sood A, Indian J Gastroenterol 2000; 19: 14-16
Sood A, Indian J Gastroenterol 2002; 37: 270-274
Extensive UC of mild-to-moderate severity

- Comparing AZA with placebo or 5-ASA for the:

  - induction of remission in UC patients did not show statistically significant benefit of AZA over placebo
    - OR= 1.59, 95% CI, 0.59-4.29

  - maintenance of remission in UC, demonstrated a benefit of AZA with statistically significant results
    - OR=2.56; 95% CI, 1.51-4.34


- Generally, thiopurines should not be used for induction of remission in active UC patients.
Extensive UC of mild-to-moderate severity

Systematic review and network meta analysis of the efficacy of biological agents on UC in a total of 2282 mild to moderate UC patients randomized to

- biological agents (n = 1167) or placebo (n = 1115) demonstrated that
  - all biological agents (ADA, golimumab, IFX, and vedolizumab) were superior to placebo for
    - induction of clinical response,
    - clinical remission,
    - mucosal healing.

- IFX was shown to be more likely to induce a favorable clinical outcome than ADA for induction of
  - clinical response (OR = 2.36, 95%CI: 1.22-4.63),
  - clinical remission (OR = 2.79, 95%CI: 0.95-8.83),
  - mucosal healing (OR = 2.02, 95%CI: 1.13-3.59).

- All biological agents also suggested superiority over placebo for maintenance.

Danese S, Ann Intern Med 2014; 160: 704-711
Moderate to Severe Extensive UC

- Systematic review and meta analysis of the efficacy of all anti-TNF-α antibodies on moderately to severely active UC demonstrated that
  - **Anti-TNF-α antibodies are superior to placebo in inducing remission** (RR of failure to achieve remission, 0.72; 95%CI: 0.57-0.91).
  - This is based on data showing that remission of UC was not achieved
    - in 231 (42.9%) of 539 patients that were randomized to receive IFX for 6 to 12 wk, compared with
    - 201 (69.8%) of 288 patients allocated to placebo.

  Probert CS, Gut 2003; 52: 998-1002
  Gastroenterology 2005; 128: 1805-1811
  Ford AC, Am J Gastroenterol 2011; 106: 644-659

- **Anti-TNF-α antibodies are effective in maintaining improvement and remission** and is therefore recommended for those patients who initially respond to the Anti-TNF-α antibodies induction regime

  ECCO EL 1b, RG A
Moderate to Severe Extensive UC

• Anti-TNF-α antibodies and cyclosporine are effective for the treatment of patients with moderate or severe corticosteroid dependent/refractory UC.

• Whether cyclosporine therapy should precede Anti-TNF-α antibodies as a second line therapy currently remains controversial.
Mild to Moderate Extensive Colitis

Oral + topical 5-ASA

Remission

Yes

Oral 5-ASA maintenance dose

No

Oral steroid + oral 5-ASA

Remission

Yes

5-ASA maintenance dose

No

Check adherence/reassess disease activity

Oral steroid (taper dose) + Azathioprine

Relapse

Add Azathioprine

5-ASA: 5-aminosalicylic acid
Moderate to Severe Extensive Colitis

Oral steroid + oral 5-ASA

Remission

Yes
Azathioprine + 5-ASA maintenance dose

Yes
Oral steroids + Azathioprine + oral 5-ASA

No
Hospital admission, IV steroid

Objective response after 3-5 days

Yes
Consult surgery Cyclosporine or Anti-TNF alpha

Remission

Yes
Azathioprine (if CsA ) or Anti-TNF alpha

No
Surgery

5-ASA: 5-aminosalicylic acid
CsA: Cyclosporine
Treatment Algorithm for Ulcerative Colitis

Patient diagnosed with Ulcerative Colitis

Determine severity and extent

Severe to fulminant colitis
Severe to Fulminant Ulcerative Colitis

• Patients should be hospitalized for intensive treatment and surveillance as the development of a toxic mega colon and perforation is a potentially life-threatening condition.
  
  ECCO EL 5, RG D

• Intravenous steroids (e.g. methylprednisolone 60 mg/d or hydrocortisone 400 mg/d) remain the mainstay of conventional therapy to induce remission.
  
  ECCO EL 1b, RG D; DGVS C
Severe to Fulminant Ulcerative Colitis

- Colectomy rates are as high as 29% in patients with severe UC and who need intravenous corticosteroids.

- They should therefore be presented to the colorectal surgeon on the day of admission.

- In the case of a worsening condition or a lack of amelioration after 3 d of steroid therapy, colectomy should be discussed.

- Extending steroid therapy beyond 7 d without clinical effect carries no benefit, but causes otherwise preventable postoperative wound healing disorders.

Turner D, Walsh CM, Clin Gastroenterol Hepatol 2007; 5: 103-110
Aberra FN, Gastroenterology 2003; 125: 320-327
Severe to Fulminant Ulcerative Colitis

• The response to intravenous steroids is best assessed by:
  – stool frequency
  – CRP
  – abdominal radiography on day 3

  ECCO EL 2b, RG B.

• If drug therapy fails, either
  – proctocolectomy

  DGVS EL C, ACG EL B
  or
  – rescue therapy with TNF-α blocker or CsA is recommended.

  ACG EL A
Severe to Fulminant Ulcerative Colitis

• ECCO and ACG guidelines:
  – IFX may be effective in the prevention of colectomy.

• Patients who required IFX to induce remission should receive regular maintenance therapy with IFX for at least 6 months.
Severe to Fulminant Ulcerative Colitis

• Continuous intravenous CsA monotherapy with 4 mg/kg per day is effective

• Effect of cyclosporine on severely active UC, in which a response was defined as symptomatic improvement demonstrated that
  – **cyclosporine was of benefit over placebo in improving symptoms** (RR no improvement with cyclosporine, 0.22; 95%CI: 0.07-0.67).
  – This finding was based on data showing that
    • 2 (18%) of 11 patients receiving cyclosporine had no response as compared with
    • 9 of 9 patients allocated to placebo.

  Khan KJ, Am J Gastroenterol 2011; 106: 630-642

• After successful induction of remission, azathioprine (2.5 mg/kg per d) should soon be added, CsA switched to oral therapy with tacrolimus and tapered over a period of 3-6 months

  DGVS C.
Severe to Fulminant Ulcerative Colitis

Open label randomized controlled trial compared the efficacy of cyclosporin and IFX on acute severe UC that was refractory to intravenous corticosteroid.

115 severe UC (CsA: 58, IFX: 57)

Failed to respond to treatment by day 98

CsA: 60%

IFX: 54%

achieved a clinical response by day 7

CsA: 50 (86%)

IFX: 48 (84%)

OR = 1.3; 95%CI: 0.62-2.7; P = 0.52

OR = 1.2; 95%CI: 0.43-3.3; P = 0.76

Severe to Fulminant Ulcerative Colitis

- 13 patients receiving IFX for severe or moderate UC who showed refractoriness or loss of response to cyclosporine, or no tolerance

  - the mean partial Mayo score of UC activity was significantly decreased (P < 0.05) to
    - 5.69 at baseline
    - 3.07, at 8 wk
    - 2.77, at 30 wk

  - Clinical remission:
    - 46.2% at 8 wk
    - 30.8% at 30 wk

  - rates of clinical remission at 8 and 30 wk of IFX therapy were
    - 60.0% and 40.0%, respectively in cyclosporine responders
    - 37.5% and 25.0%, respectively, were also obtained in cyclosporine no responders

Tsukamoto H, Eur J Gastroenterol Hepatol 2013; 25: 714-718
Severe to Fulminant Ulcerative Colitis

- IFX salvage therapy following cyclosporine tended to be more efficacious in cyclosporine responders (loss of response or no tolerance) than in nonresponders (refractoriness), and that sequential therapy may prove useful and well tolerated.
Severe to Fulminant Ulcerative Colitis

IV steroid + initiate DVT prophylaxis + consult surgery

Objective response 3rd day

Yes

Oral steroid (taper dose) + Azathioprine

No relapse

Azathioprine + 5-ASA maintenance dose

Recurrence or steroid-resistant or steroid-dependent

Anti-TNF alpha or Cyclosporine (CsA)

Anti-TNF alpha or Azathioprine (if CsA)

Remission

No

Surgery

5-ASA: 5-aminosalicylic acid
CsA: Cyclosporine
DVT: Deep Venous Thrombosis