Treatment of

Mild to moderate

Extensive

Ulcerative Colitis

Philippe Marteau, Paris, France
Mild to moderate Extensive UC

Oral ASA are needed as local treatments cannot cover all lesions

**Recommendation:**

1\(^{st}\) line: oral 5-ASA 4 g/d

Obtaining endoscopic remission or frank improvement usually takes more than 4 weeks

2\(^{nd}\) line: if severe or resistant: consider oral steroids

Extensive ulcerative colitis of mild-moderate severity should initially be treated with mesalazine >2g/day [EL1a, RG A], combined with topical mesalazine [EL1b, RG A].

Oral aminosalicylates alone induce remission only in a minority of patients [EL1a, RG A].
Optimise the first line treatment of extensive UC?

- Many symptoms originate from the distal colon (blood in stools, tenesmus...)
- Is association of local and oral salicylates better than oral treatment alone?

*Combined oral and enema treatment with Pentasa (mesalazine) is superior to oral therapy alone in patients with extensive mild/moderate active ulcerative colitis: a randomised, double blind, placebo controlled study*

P Marteau, C S Probert, S Lindgren, M Gassul, T G Tan, A Dignass, R Befrito, G Midhagen, J Rademaker, M Foldager

Patients

- 116 patients

- Mild to moderate exacerbation of extensive UC (UCDAI $\geq 3$ and $\leq 8$)

- Exclusion criteria:
  - maintenance treatment with aminosalicylates $> 3$ g/d
  - corticosteroids
  - immunosuppressive agents

Methods

- Double-blind, parallel-group, placebo-controlled RCT
- For 8 weeks, each patient received 4 g/d pentasa orally
- During the initial 4 weeks, each patient additionally applied daily a 100 mL enema at bedtime, either containing 1 g Pentasa or placebo
- Evaluation
  - at inclusion, 4 weeks and 8 weeks
  - UCDAI score (clinical signs and endoscopic evaluation of the distal colon)

Pentasa orally + pentasa enema

P = 0.308

Pentasa orally + placebo enema

P = 0.0008

Time to cessation of rectal bleeding

Patients with frank bleeding at baseline

Systemic corticosteroids are appropriate if

- symptoms of active colitis do not respond rapidly to mesalazine [EL1b, RG C],

or for patients who are already taking appropriate maintenance therapy
Patients with persistently active, steroid-refractory disease should be treated with azathioprine / mercaptopurine [EL1b, RG B],
  – Although surgical options should also be discussed
  – intravenous steroids,
  – infliximab [EL1b, RG B]
  – or calcineurin inhibitors [EL3, RG C]
    should also be considered
Active disease
ECCO Statement: Thiopurine-intolerant or refractory ulcerative colitis

- Infliximab [EL1b, RG B] or surgical options should be considered
- Continued medical therapy that does not achieve steroid-free remission is not recommended [EL5, RG D]
Infliximab in Ulcerative colitis ACT1 & ACT2

- 2 RCTs 364 patients in each

- Patients with active UC (extensive 40% - 46%):
  - Mayo score of 6 to 12 points - Endoscopic subscore ≥2

- Either
  - Concurrent treatment with ≥1 of the following:
    - Steroids, azathioprine, 6-MP, or aminosalicylates (ACT 2 only)
  - Failure to tolerate or respond to ≥1 of:
    - Steroids, azathioprine, 6-MP, or aminosalicylates (ACT 2 only)

- Infliximab 5mg/kg vs 10mg/kg vs placebo
  At weeks. 0,2,6 then every 8 weeks. 46 weeks
Infliximab (keep thiopurines)
or calcineurine inhib.

Algorithm

1. Oral 5-ASA (4g/d)
2. Oral 5-ASA (4g/d) + 5-ASA enema (or suppos?)
3. Oral steroids (40-60mg/d) (keep 5-ASA ?)
   Tapering ... consider thiopurines (keep 5-ASA !)
4. Infliximab (keep thiopurines) or calcineurine inhib.
5. Surgery

What happened before ?
How many episodes ?
Resistance to treatments ?

Severity ?
Patient preferences ?
Personal view on the risk/benefit
Algorithm

Directly?

- Oral 5-ASA (4g/d)
- Oral 5-ASA (4g/d) + 5-ASA enema (or suppos?)
- Oral steroids (40-60mg/d) (keep 5-ASA?)
- Tapering ... consider thiopurines (keep 5-ASA!)
- Infliximab (keep thiopurines) or calcineurine inhib.
- Surgery

What happened before?
How many episodes?
Resistance to treatments?

Severity?
Patient preferences?
Personal view on the risk/benefit

No improvement after 2 weeks
Infliximab (keep thiopurines)
or calcineurine inhib.

Algorithm

Directly?

If previous failure to
5-ASA
If « rapid remission
needed »?
If nocturnal stools?

Oral 5-ASA (4g/d)
No improvement
after 2 weeks
Oral 5-ASA (4g/d) + 5-ASA enema (or suppos?)
4-8 weeks
Oral steroids (40-60mg/d) (keep 5-ASA ?)
Tapering ... consider thiopurines (keep 5-ASA !)
Infliximab (keep thiopurines) or calcineurine inhib.
Surgery

What happened before?
How many episodes?
Resistance to treatments?

Severity?
Patient preferences?
Personal view on the risk/benefit
**Algorithm**

Directly?

If previous failure to 5-ASA
If <= rapid remission
If...

Oral 5-ASA (4g/d)
Oral 5-ASA (4g/d) + 5-ASA enema (or suppos?)
Oral steroids (40-60mg/d) (keep 5-ASA ?)
Tapering...
consider thiopurines (keep 5-ASA !)
Surgery

No improvement after 2 weeks
4-8 weeks
4 weeks
4 - **** weeks

What happened before?
How many episodes?
Resistance to treatments?
Severity?
Patient preferences?
Personal view on the risk/benefit