Medical management of ulcerative colitis

Gerhard Rogler, Zürich
Step up approach to therapy of Ulcerative colitis

- Surgery
- Cyclosporine
- Tacrolimus
- Infliximab

AZA/6-MP (topical/systemic)

Corticosteroids (topical/systemic)

Aminosalicylates (topical/systemic)
Meta-analysis of drug treatment of ulcerative colitis

Kornbluth, 1993
Case 1: Musician with proctosigmoiditis

- Started 5-ASA enemas with initial success
- Switched to oral 5-ASA 2.4 g for flare
- Steroids 40 mg/day for subsequent flares
- Still has 8 BM/day, malaise without fever. Works but wants to feel good.

What next ???
ASCEND I, II
Treatment Success at Weeks 3 & 6
Pooled Moderate Population

% of Patients Improved

Week 3
p=0.058

Week 6
p=0.0034

N=223 N=198
N=223 N=200

53% 62%
58% 72%

2.4 g/day
4.8 g/day

Hanauer et al. Am J Gastroenterol 2005
# Dose finding for 5-ASA in active ulcerative colitis

Kruis et al., Clin Gastroenterol Hepatol 2003

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Remission (CAI &lt; 4)</th>
<th>Time to response (days, mean)</th>
<th>Endoscopic remission (%)</th>
<th>Histological improvement (%)</th>
<th>Stop due to side effects (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 x 0.5 g (n = 104)</td>
<td>50</td>
<td>27.5</td>
<td>28</td>
<td>42</td>
<td>11</td>
</tr>
<tr>
<td>3 x 1.0 g (n = 104)</td>
<td>66 *</td>
<td>26.5</td>
<td>48 *</td>
<td>56 *</td>
<td>7</td>
</tr>
<tr>
<td>3 x 1.5 g (n = 104)</td>
<td>55</td>
<td>21.6</td>
<td>49</td>
<td>63</td>
<td>9</td>
</tr>
</tbody>
</table>
5-ASA topical therapy is preferable

5-ASA: Combination is better

Corticosteroids: Short and Long Term Efficacy

1-Month Outcomes* (n=63)

- Complete Remission 54% (n=34)
- Partial Remission 30% (n=19)
- No Response 16% (n=10)

1-Year Outcomes (n=63)

- Prolonged Response 49% (n=31)
- Steroid Dependent 22% (n=14)
- Surgery 29% (n=18)

*30 days after initiating corticosteroid therapy

Risk of Resection in UC After 1st Course of Steroids:

*185 patients in Olmsted County, MN diagnosed with UC from 1970 to 1993

Infliximab for the induction of remission in active ulcerative colitis

Rutgeerts et al. NEJM 2005;353:2462-76

Infliximab 5 mg/kg or 10 mg/kg in ACT 1 and 2 significantly better than placebo

remission after 8 weeks (%)
Infliximab for the induction of remission in active ulcerative colitis

Rutgeerts et al. NEJM 2005;353:2462-76
Case 2: Actor with refractory pan-colitis

Formerly in remission on AZA

10-20 BM/day
Progressive weight loss
Transferred by air ambulance
IV steroids, PRBC, TPN
Does anti-viral therapy help?

64 non-refractory IBD pts (UC 23:CD 43)¹

- 42 (66%) had + serology
- 1 had CMV Ag and biopsy-proven CMV colitis
  - only this patient had benefit

47 inpatients with UC checked for CMV Ag in blood²

- 12/16 UC pts with +CMV treated
- 8 (66.7%) responded

62 pts with severe colitis (55 UC;7 CD)³

- 7 (5UC,2 CD) out of 19 (36%) pts with refractory disease: CMV found in rectal bx
- 5/6 treated patients went into remission after antiviral treatment; 1 did not->surgery

¹ de Saussure P.  APT 2004; 20; 1323
Current therapeutic choices in severe UC

CyA/Tacrolimus
Infliximab
Clinical Trial
Colectomy

Choice will depend on center expertise with drug choices and availability of expert surgical support

Arseneau K. Clin Gastro Hep 2006. 4(9);1135-1142
## 5-ASA orally for relapse prevention in ulcerative colitis

<table>
<thead>
<tr>
<th></th>
<th>5-ASA</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 103)</td>
<td>(n = 102)</td>
</tr>
<tr>
<td>Remission at 12 months (%)</td>
<td>64</td>
<td>38</td>
</tr>
<tr>
<td>Left sided (%)</td>
<td>63</td>
<td>41</td>
</tr>
<tr>
<td>Extensive colitis (%)</td>
<td>67</td>
<td>31</td>
</tr>
</tbody>
</table>

Miner, 1995
E. coli Nissle in UC

Acute flare within 12 months

222 patients

36 %
E. Coli Nissle

33 %
5-ASA

E. coli Nissle (Mutaflor)
200 mg

Kruis et al, GUT, Nov 2004
Carcinoma prevention in UC: Role of 5-ASA

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continous 5-ASA intake</td>
<td>0.25 (0.13 - 0.48)*</td>
</tr>
<tr>
<td>Continously 5-ASA &gt; 1.2 g/day</td>
<td>0.19 (0.05 - 0.61)*</td>
</tr>
<tr>
<td>&lt; 1.2 g/day</td>
<td>0.18 (0.02 - 1.92)</td>
</tr>
<tr>
<td>SASP 2g/day</td>
<td>0.85 (0.32 - 2.26)</td>
</tr>
<tr>
<td>Regular visit to physician (&gt; 2/year)</td>
<td>0.16 (0.04 - 0.60)*</td>
</tr>
<tr>
<td>Number of colonoscopies after diagnosis</td>
<td>no effect</td>
</tr>
<tr>
<td>Positive family history</td>
<td>5.0 (1.10 - 22.82)**</td>
</tr>
</tbody>
</table>

* p < 0.01        ** p < 0.04
Compliance is crucial!!

There is no “one size fits all” to UC therapy
• Therapy and decision making are tailored to the individual

Mild to moderate disease:
• Remember topical therapy

Success of algorithms depends upon optimization of each step of therapy and considerable judgment about each outcome
• Skillful application of medical therapy makes the difference in outcomes: **topical therapy, combination of oral and rectal administration, appropriate dosage**
Thank you for your attention!!