Severe Crohn's disease: Medical options

Gerhard Rogler, Department of Gastroenterology and Hepatology, UniversitätsSpital Zürich
Disclosure

Conflict of interests

Gerhard Rogler has consulted to Abbott, Abbvie, Boehringer, Calypso, Essex, FALK, Genentech, MSD, Novartis, Pfizer, Roche, UCB, Takeda, Tillots, Vifor and Zeller;

Gerhard Rogler has received speaker's honoraria from Astra Zeneca, Abbott, Abbvie, FALK, MSD, Phadia, Takeda, Tillots, UCB, and Vifor;

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Timing of anti-TNF introduction in IBD: Proposed algorithm

Diagnosis of IBD

Mild disease
40% CD
60% UC

Moderate disease
40% CD
30% UC

Directly severe disease
20% CD
10% UC

Step-up
5ASA, topical steroids, occasional systemic steroids

Accelerated step-up
Close monitoring (clinical biomarkers, imaging)

Targeted top-down

No need for anti-TNF

Secondary benign disease

Secondary severe disease

Anti-TNF

Anti-TNF

No need for anti-TNF

Numbers given in this slide represent an approximate estimation from several cohorts and population-based data.

ECCO statement 5D

Severely active localised ileocaecal Crohn’s disease should initially be treated with systemic corticosteroids [EL1]. For those who have relapsed, an anti-TNF based strategy is appropriate [EL1]. Surgery is a reasonable alternative for patients with disease refractory to conventional medical treatment and should also be discussed [EL3]. For some patients who have infrequently relapsing disease restarting steroids with an immunomodulator may be appropriate [EL2]. In patients refractory to steroids and/or anti-TNF vedolizumab is an appropriate alternative [EL1]
ECCO statement 5F

Extensive small bowel Crohn’s disease should initially be treated with systemic corticosteroids, but early therapy with an anti-TNF based strategy should also be evaluated [EL5]. For patients with severe disease who have relapsed, an anti-TNF based strategy is appropriate [EL5]

ECCO statement 5G

Patients who have clinical features suggesting a poor prognosis appear the most suitable for early introduction of immunosuppressive therapy. Early anti-TNF therapy [EL2] should be initiated in patients with high disease activity and features indicating a poor prognosis [EL3]
ECCO statement 5l

Patients with objective evidence of active disease refractory to corticosteroids should be treated with an anti-TNF based strategy [EL1], although surgical options should also be considered and discussed at an early stage [EL5]
REACT: time to initiation of treatment

REACT: time to first hospitalisation, surgery or complication

HR (95% CI) = 0.73 (0.62, 0.86), p<0.001

Khanna R, et al. ECCO 2014, Copenhagen; OP004
Side effects of prolonged GCS therapy

- Hypertension <20%
- Diabetes 2.33 relative risk for beginning insulin
- Infection 13-20%
- Osteoporosis <50%
- Myopathy 7%
- Cataracts 22% (dose-dependent)
- Psychosis (3-5%)

*Overall GCS therapy (not only therapy for CD).

Anti-TNF drug safety

- Infection and malignancy
  - Black-box warning for serious infection and malignancy for all anti-TNF therapies\(^1-3\)
- Black-box warning for HSTCL (ADA and IFX)\(^1,2\)
- Reactivation of hepatitis B\(^4\)
- Skin cancer\(^4\)
- Psoriasis\(^4\)
- Autoimmunity (lupus-like syndrome <1%)\(^4\)
- Immunogenicity—antibodies to anti-TNF\(^4\)
- Demyelinating disorders, CHF, liver toxicity\(^4\)

Anti-Integrin Drug Safety

Increased risk for progressive multifocal leukoencephalopathy (PML) (Natalizumab)

Headache, fatigue, depression, rash, nausea, abdominal discomfort, UTI, arthralgia, respiratory infection
Clinical Response to Ustekinumab (UNITI I)

Clinical response (a decrease from BL in CDAI score of ≥100 points or a CDAI score <150)

<table>
<thead>
<tr>
<th>Week 3</th>
<th>Week 6</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBO (n=247)</td>
<td>UST 130mg (n=245)</td>
<td>UST ~6mg/kg* (n=249)</td>
</tr>
<tr>
<td>17.8%</td>
<td>25.3%</td>
<td>30.1%</td>
</tr>
<tr>
<td>21.5%</td>
<td>34.3%</td>
<td>33.7%</td>
</tr>
<tr>
<td>20.2%</td>
<td>33.5%</td>
<td>37.8%</td>
</tr>
</tbody>
</table>

p=0.001*  
p=0.049*  
p=0.003  
p=0.002  
p<0.001  
p=0.001

Primary Endpoint

Secondary Endpoint

*Weight-range–based doses of ustekinumab approximating 6 mg/kg; UST: Stelara

TREATMENT ALGORITHM FOR CROHN’S DISEASE

Swiss expert recommendation – Based on ECCO guidelines 2010¹,² and other published literature

Developed by:
Luc Biedermann, Stephan Brand, Emanuel Burri, Petr Hruz, Pascal Juillerat, Michael Manz, Michel Maillard, Gerhard Rogler, Bernhard Sauter, Alain Schoepfer, Frank Seibold, Stephan Vavricka.
Evaluate response every 10–12 weeks°

Maintenance with Anti-TNF

1. Optimize by dose escalation
2. Evaluate combination + AZA/6-MP
3. Change to other biologic

Inadequate response or Loss of response

Intolerance

No response

Change to other Anti-TNF or Anti-Integrin

Consider surgery

Maintenance with Anti-TNF or Anti-Integrin

Evaluate response every 10–12 weeks°

Consider Pharmacokinetics

* Swiss expert recommendation
# See page "Risk for severe disease progression"
* See page "Target for CD treatment"

Response/remission
No response/no remission
FISTULATING DISEASE\textsuperscript{1-3}

Perianal Fistula without symptoms

Therapy optional

Simple perianal Fistula*
Excluded perianal abscess or treat if present

Antibiotics (Metronidazol or Ciprofloxacin) and/or Seton\textsuperscript{o} or Fistulotomy

If indicated
no Medication

Complex perianal Fistula*

Seton\textsuperscript{o} and/or Antibiotics and AZA/6-MP or Antibiotics and Anti-TNF

AZA/6-MP and/or Anti-TNF and/or Seton\textsuperscript{o}
Thank you for your attention