Achieving Deep Remission In Crohn’s Disease

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How do we define remission? Clinical (CDAI) versus mucosal healing versus sustained deep remission

What are impacts of these endpoints on other outcomes?

How do we achieve deep remission in Crohn’s disease?
How Do We Define Remission?

Clinical (CDAI)
vs
Mucosal Healing
vs
Sustained Deep Remission
Assessment Of Efficacy Of Medical Therapy: CDAI Versus CDEIS During Treatment With Prednisolone

CDAI, Crohn's Disease Activity Index; CDEIS, Crohn's disease endoscopic index of severity


Figure 1. Correlation of CDAI vs. CDEIS at D₀ (n = 142)

CDAI, Crohn's Disease Activity Index;
CDEIS, Crohn’s disease endoscopic index of severity
Correlations Between hsCRP, IL-6, Fecal Markers, CDAI, and Endoscopic Activity in CD

(N=164)

<table>
<thead>
<tr>
<th></th>
<th>IL-6</th>
<th>Calprotectin</th>
<th>Lactoferrin</th>
<th>CDAI</th>
<th>SES-CD</th>
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</thead>
<tbody>
<tr>
<td>hsCRP</td>
<td>0.65</td>
<td>0.47</td>
<td>0.52</td>
<td>0.16</td>
<td>0.46</td>
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<tr>
<td>IL-6</td>
<td></td>
<td>0.45</td>
<td>0.55</td>
<td>0.15</td>
<td>0.43</td>
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<tr>
<td>Calprotectin</td>
<td>0.76</td>
<td>0.23</td>
<td>0.45</td>
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<tr>
<td>Lactoferrin</td>
<td></td>
<td>0.19</td>
<td>0.46</td>
<td></td>
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<tr>
<td>CDAI</td>
<td></td>
<td></td>
<td></td>
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</table>

Correlation coefficients highlighted in red were significant ($P<0.05$).
When stratified by extent, correlation coefficients were highest for colonic disease.

CDAI, Crohn’s Disease Activity Index; SES-CD, Simple Endoscopic Score for Crohn’s Disease
Inflammatory Activity and Progression of Damage in a Theoretical Patient with CD

CDAI, Crohn’s Disease Activity Index; CDEIS, Crohn’s disease endoscopic index of severity; CRP, C-reactive protein.

The Evolving Goal of Therapy is Disease Modification

• In patients with no bowel damage
  – Prevention of bowel damage (stricture, fistula, abscess)
  – No surgical resection

• In patients with existing bowel damage (stricture, fistula, abscess, prior surgical resection)
  – Prevent further damage and reverse damage if possible
  – Prevention additional surgical resection
Working Definition of Deep Remission

• Overall, aiming for deep remission (DR) is managing disease beyond symptom control
  – In patients with no bowel damage or disability, DR is resolution of one or more objective measures of inflammation (endoscopy, markers, imaging) AND resolution of symptoms
    • To prevent damage and disability
  – In patients with existing bowel damage and disability, DR is resolution of one or more objective measures of inflammation (endoscopy, markers, imaging) AND improvement of symptoms if possible
    • To prevent further damage and disability, and reverse damage if possible
What Are the Impacts of These Endpoints on Other Outcomes?
Impact of Therapy will Depend on Degree of Structural Damage & Velocity of Progression

Cumulative Probability (%)

Patients at risk:
N = 2002

High Potential
Low Potential

Penetrating
Stricturing
Inflammatory

Months
0 12 24 36 48 60 72 84 96 108 120 132 144 156 168 180 192 204 216 228 240

Cosnes J et al. Inflamm Bowel Dis. 2002;8:244-254.
Cumulative Probability of Surgery for Crohn’s Disease and for Recurrence Following Surgery

Sx=surgery

Probability of Sx for CD

Probability (%) ± 2 SD

% of Patients

Time in years

No Sx 1 Sx 2 Sx >3 Sx

Sx=surgery
Classification of the Sequelae of Bowel Resection for Crohn’s Disease

Correlation between fecal weight and postoperative handicap index in the retrospective series. The regression equation was: \( y = 3793 - 866 \times \log [75 - x] \). \((n = 112, r = 0.60, P < 0.001)\)
Development of the Crohn’s Disease Digestive Damage Score, the Lémann Score


Development of the first disability index for inflammatory bowel disease based on the international classification of functioning, disability and health

Laurent Peyrin-Biroulet,1 Alarcos Cieza,2,3,4 William J Sandborn,5 Michaela Coenen,2,3 Yehuda Chowers,6 Toshifumi Hibi,7 Nenad Kostanjsek,8 Gerold Stucki,3,4,9 Jean-Frédéric Colombel,10 the International Programme to Develop New Indexes for Crohn’s Disease (IPNIC) group*

ABSTRACT

Objective The impact of inflammatory bowel disease (IBD) on disability remains poorly understood. The World Health Organization’s integrative model of human functioning and disability in the International Classification of Functioning, Disability and Health (ICF) makes disability assessment possible. The ICF is a hierarchical coding system with four levels of details that includes over 1400 categories. The aim of this study was to develop the first disability index for IBD by selecting most relevant ICF categories that are affected by IBD.

Significance of this study

What is already known about this subject?

- Inflammatory bowel disease (IBD) is a frequent disorder known to affect physical, psychological, familial, and social dimensions of life.
- Disability refers to the problems (objective) that a patient may have in different areas or health domains, whereas quality of life (subjective) refers to how he/she feels about these issues.

* Correspondence to Professor Jean-Frédéric Colombel, Département d’Hépato-gastroentérologie, Hôpital Claude Huriez, Centre Hospitalier Universitaire de Lille, France.
How Do We Achieve Deep Remission in Crohn’s Disease?
Net Remission at Six Months: Certolizumab Pegol; Adalimumab; Infliximab

Deep remission defined as clinical remission (CDAI <150) and complete mucosal healing in EXTEND

All patients (n=135) received adalimumab 160/80 mg induction therapy, before randomisation (n=129) to adalimumab 40 mg eow or to placebo. Deep remission was assessed in those who had ulceration at baseline (n=123).

CDAI: Crohn’s disease activity index; eow: every other week

eow=every other week

EXTEND: Patients Who Achieved Deep Remission* With Adalimumab at Week 12 and Hospitalization Rates

All-cause hospitalization through Week 52

<table>
<thead>
<tr>
<th>All hospitalization (%)</th>
<th>Deep remission* (Week 12)</th>
<th>Non-deep remission* (Week 12)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>0/11</td>
<td>9/53</td>
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CD-related hospitalization through Week 52

<table>
<thead>
<tr>
<th>CD-related hospitalization (%)</th>
<th>Deep remission* (Week 12)</th>
<th>Non-deep remission* (Week 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0/11</td>
<td>5/53</td>
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* Deep remission defined as clinical remission (CDAI <150) and complete mucosal healing in EXTEND
CD: Crohn’s disease; CDAI: Crohn’s disease activity index

CHARM Adalimumab in Active Crohn’s Disease Clinical Remission at 26 and 54 Weeks in Week 4 Responders by Duration of Crohn’s Disease

Schreiber S. Gastroenterology 2007 Abstract #985

*P=.002; **P<.001; †P=.014; ‡P=.001; all vs placebo
<2 years: PBO n=23, Adalimumab n=39; 2 to <5 years: PBO n=36, Adalimumab n=57; ≥5 years: PBO n=111, Adalimumab n=233

Schreiber S. Gastroenterology 2007 Abstract #985
PRECISE 2 Certolizumab Pegol in Active Crohn’s Disease
Clinical Response at 26 Weeks in Week 6 Responders by Duration of Crohn’s Disease

Mucosal Healing at Week 26

AZA = azathioprine

**Proportion of Patients (%)**

- AZA + placebo: 18/109
- IFX + placebo: 28/93
- IFX + AZA: 47/107

Significance levels:
- P < 0.001
- P = 0.023
- P = 0.055
Conclusions

- Remission is best defined by endoscopy, or the composite definition of deep remission
- Preliminary evidence suggests that deep remission reduces hospitalization, and may reduce surgery, bowel damage, and disability
- Maintenance therapy with a combination of azathioprine and an anti-TNF agent yields the best long term outcomes, discontinuation of either agent increases the risk of relapse