Vedolizumab-induced endoscopic remission in anti-TNF exposed and anti-TNF naïve IBD patients: a large single center experience

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- Consultancy fees Janssen.
- Research grant Pfizer.
**Introduction**

- **Vedolizumab**, targeting the $\alpha 4\beta 7$ integrin, has proven **efficacy** in both Crohn’s disease and ulcerative colitis during the GEMINI phase III program\(^1,2\)

- In the pivotal trials and in real-life series, **anti-TNF exposed patients** experienced **significantly less frequent clinical response or remission**, compared to anti-TNF naive patients\(^1,2,3,4\)

- **Real-life endoscopic remission data** are **limited**\(^5,6\)

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Aims

To report **real-life single center data** in **vedolizumab** treated IBD patients, focusing on **endoscopic remission** and comparing **anti-TNF naive** and **anti-TNF exposed** patients.
Methods - Recruitment

• Retrospective cohort study

• All consecutive IBD patients
  – who initiated vedolizumab therapy between Jan 2015 and April 2018
  – with active (endoscopic and/or biochemical) disease at baseline
  – who had a minimal follow-up of 6 months at our center

• Exclusions
  – patients with an ostomy
  – ileal pouch anal anastomosis

* For patients with Crohn’s disease
Methods - Outcomes

• Primary endpoint: endoscopic remission
  – UC: Mayo endoscopic sub-score 0 – 1 (at week 14)
  – CD: complete absence of ulcerations (at month 6)

• Primary non-response: no clinical improvement at week 14 (UC) or week 26 (CD)

• Loss of response: clinical impairment following initial clinical response

All performed by 3 IBD-specialized staff members
Results - Inclusion

408 patients exposed to vedolizumab

- 41 patients without baseline disease activity
  - 11 patients with an ostomy
  - 20 patients with ileo-anal pouch anastomosis

336 patients included
Results – Endoscopic remission overall

- Majority of the included patients (96.1%) underwent endoscopic assessment after vedolizumab induction.

- Median (IQR) time to endoscopic assessment:
  - UC: 14.0 (13.6-14.6) weeks
  - CD: 22.1 (21.6 – 25.0) weeks

Non-responder imputation was applied.
Non-responder imputation was applied.

Results – Endoscopic remission, the role of previous anti-TNF exposure

- **Anti-TNF naive**
  - No remission: 30.8%
  - Yes remission: 69.2%
  - 67 patients

- **Anti-TNF exposed**
  - No remission: 56.0%
  - Yes remission: 44.0%
  - 269 patients

**OR 2.9 (95% CI 1.6-5.2)**

*p = 0.0003*
Results – Endoscopic remission

Non-responder imputation was applied.

CD: $p = 0.03$

UC: $p = 0.02$

<table>
<thead>
<tr>
<th>Group</th>
<th>Anti-TNF Naive</th>
<th>Anti-TNF Exposed</th>
<th>Endoscopic Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD</td>
<td>61.5%</td>
<td>38.3%</td>
<td></td>
</tr>
<tr>
<td>UC</td>
<td>73.7%</td>
<td>51.3%</td>
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</tbody>
</table>

n = 26, n = 141, n = 39, n = 117

Non-responder imputation was applied.
Results – Long term outcome

• **61.9%** (n=208) were **still** on **vedolizumab maintenance therapy** after a median of **103.1** (61.8-143.5) weeks

• **38.1%** (n=128) **discontinued therapy** after **23.0** (14.1-46.9) weeks, mainly because of
  • Primary non-response (n=55)
  • Secondary loss-of-response (n=53)
  • Adverse events and/or inadequate control of extra-intestinal manifestations (n=14)
  • Patient preference due to deep remission (n=3)
  • Colectomy due to high risk colon (n=3)
Results – Long term outcome influenced by initial response

Hazard ratio 7.5 [95% CI 4.7 – 12.2], p=4.8 x10^{-22}

Endoscopic remission at the end of induction

No endoscopic remission at the end of induction
Conclusions

• This is the biggest, real-life, single-center cohort study confirming that vedolizumab can induce endoscopic remission in both Crohn’s disease and ulcerative colitis.

• Although anti-TNF naive patients had a significantly better outcome, 44% anti-TNF exposed patients did achieve endoscopic remission.

• No new safety signals have been observed.
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Marc Ferrante. MD. PhD.

@bverstockt
Back up
## Results – Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Anti-TNF naïve</th>
<th>Anti-TNF exposed</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 67)</td>
<td>(n = 269)</td>
<td></td>
</tr>
<tr>
<td>Women, (n) (%)</td>
<td>27 (40.3)</td>
<td>163 (60.6)</td>
<td>0.90</td>
</tr>
<tr>
<td>Age, years, median (IQR)</td>
<td>38.9 (25.2 – 55.8)</td>
<td>41.7 (30.3 – 52.3)</td>
<td>0.52</td>
</tr>
<tr>
<td><strong>Disease duration, years, median (IQR)</strong></td>
<td>4.8 (1.3 – 11.3)</td>
<td>10.8 (5.2 – 19.7)</td>
<td>2.9 (\times 10^{-6})</td>
</tr>
<tr>
<td>Diagnosis, (n) (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Crohn’s disease</td>
<td>28 (41.8)</td>
<td>151 (56.1)</td>
<td>0.04</td>
</tr>
<tr>
<td>- Ulcerative colitis</td>
<td>39 (58.2)</td>
<td>118 (43.9)</td>
<td></td>
</tr>
<tr>
<td>Disease location, (n) (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Ileal (L1)</td>
<td>6 (21.4)</td>
<td>29 (19.2)</td>
<td></td>
</tr>
<tr>
<td>- Colonic (L2)</td>
<td>6 (21.4)</td>
<td>18 (11.9)</td>
<td>0.40</td>
</tr>
<tr>
<td>- Ileocolonic (L3)</td>
<td>16 (57.2)</td>
<td>104 (66.9)</td>
<td></td>
</tr>
<tr>
<td>- Upper GI (L4)</td>
<td>1 (3.6)</td>
<td>30 (19.9)</td>
<td>0.05</td>
</tr>
<tr>
<td>- Proctitis (E1)</td>
<td>6 (15.4)</td>
<td>14 (11.9)</td>
<td></td>
</tr>
<tr>
<td>- Left-sided colitis (E2)</td>
<td>16 (41.0)</td>
<td>47 (39.8)</td>
<td>0.52</td>
</tr>
<tr>
<td>- Pancolitis (E3)</td>
<td>17 (43.6)</td>
<td>57 (48.3)</td>
<td></td>
</tr>
<tr>
<td>Disease behaviour, (n) (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Inflammatory (B1)</td>
<td>19 (67.9)</td>
<td>49 (32.5)</td>
<td></td>
</tr>
<tr>
<td>- Fibrosenotic (B2)</td>
<td>4 (14.2)</td>
<td>72 (47.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>- Penetrating (B3)</td>
<td>5 (17.9)</td>
<td>30 (19.3)</td>
<td></td>
</tr>
<tr>
<td>- Perianal (p)</td>
<td>9 (32.1)</td>
<td>66 (43.7)</td>
<td>0.40</td>
</tr>
</tbody>
</table>
## Results – Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Anti-TNF naïve</th>
<th>Anti-TNF exposed</th>
<th>p value</th>
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<tbody>
<tr>
<td></td>
<td>(n = 67)</td>
<td>(n = 269)</td>
<td></td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Active</td>
<td>44 (65.7)</td>
<td>132 (49.1)</td>
<td>0.11</td>
</tr>
<tr>
<td>- Former</td>
<td>3 (4.5)</td>
<td>46 (17.1)</td>
<td></td>
</tr>
<tr>
<td>- Never</td>
<td>18 (26.8)</td>
<td>80 (29.7)</td>
<td></td>
</tr>
<tr>
<td>Previous biological agents, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Previous infliximab</td>
<td></td>
<td>130 (48.3)</td>
<td></td>
</tr>
<tr>
<td>- Previous adalimumab</td>
<td>N.A.</td>
<td>169 (62.8)</td>
<td>NA.</td>
</tr>
<tr>
<td>- Previous certolizumab</td>
<td></td>
<td>9 (3.3)</td>
<td></td>
</tr>
<tr>
<td>- Previous golimumab</td>
<td></td>
<td>13 (8.3)</td>
<td></td>
</tr>
<tr>
<td>Previous anti-TNF agents, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- None</td>
<td></td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>- One</td>
<td>N.A.</td>
<td>125 (46.5)</td>
<td>N.A.</td>
</tr>
<tr>
<td>- Two</td>
<td></td>
<td>131 (48.7)</td>
<td></td>
</tr>
<tr>
<td>- Three</td>
<td></td>
<td>13 (4.8)</td>
<td></td>
</tr>
<tr>
<td>Steroids during induction, n (%)</td>
<td>36 (53.7)</td>
<td>124 (46.0)</td>
<td>0.26</td>
</tr>
<tr>
<td>Immunomodulators during induction, n</td>
<td>7 (10.4)</td>
<td>30 (11.1)</td>
<td>0.96</td>
</tr>
<tr>
<td>(%)</td>
<td></td>
<td></td>
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</tbody>
</table>
Results – Biological response and remission

**All patients with elevated CRP (n=147)**

- **Anti-TNF naive**
  - **No**: 44.0%
  - **Yes**: 68.2%
  - **Total**: 22
  - **p = 0.04**
  - **OR 2.7 (95% CI 1.0 – 7.2)**

- **Anti-TNF exposed**
  - **No**: 50.0%
  - **Yes**: 36.0%
  - **Total**: 125
  - **p = 0.21**
  - **OR 1.8 (95% CI 0.7 – 4.4)**
Results – (Steroid) free clinical remission

OR 3.9 (95% CI 2.2 – 6.82) p < 0.0001

OR 3.6 (95% CI 2.0 – 6.4) p < 0.0001
Results – Long term outcome influenced by previous anti-TNF exposure

Hazard ratio 1.6 [95% CI 1.0 - 2.8], p=0.05
Results – Endoscopic remission

• **No difference** in remission rates between patients failing 1 vs ≥ 2 anti-TNF agents (p=0.26).

• **No effect** of corticosteroids or immunomodulators during induction could be observed with regard to endoscopic remission (p=0.61, p=0.86 respectively).

• **No difference** in disease duration could be found between remitters and non-remitters (p=0.70).
Results – Endoscopic remission