Is Tofacitinib an Option for Salvage Therapy in Acute Severe Ulcerative Colitis?

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Ulcerative colitis is a chronic disease that originates in the rectum and progressively involves other areas, leading to episodes of bloody stools and diarrhea. The primary treatment for ulcerative colitis is mesalamine, known for its excellent safety profile. Additionally, other therapeutic options include thiopurines, tumor necrosis factor alpha (TNF) antagonists, anti-integrin agents, and monoclonal antibodies targeting IL 12 and 23.1 Steroids are also employed, primarily for inducing remission rather than maintaining it. Despite the availability of these treatments, some patients do not achieve remission. In such cases, colectomy is considered.

The JAK family activates the STAT pathway through autophosphorylation, regulating numerous immune mediators, including Type 1 Interferon (IFN), IFN-γ, and interleukins 2, 4, 6, 7, 9, 12, 15, 21, and 23.2,3 Tofacitinib, an oral medication that inhibits all JAKs, primarily targets JAK 1 and 3.4 Our study focused on assessing the effectiveness of tofacitinib induction therapy as a salvage treatment in patients with severe active ulcerative colitis, particularly those who have previously been treated with more than one biological agent. We present the efficacy of tofacitinib in a small case series.

Four patients from the Gastroenterology clinic were included in the study. All were diagnosed with Acute Severe Ulcerative Colitis (ASUC) and had previously been treated with at least three biological agents. The average age of the patients was 33.2 ± 16.5 years, and all were male. The demographic and clinical characteristics of the patients are shown in Table 1. No washout period was permitted from the last biological treatment before starting tofacitinib. Treatment began with a dose of 2x10 mg of tofacitinib, accompanied by enoxaparin prophylaxis for all patients. The tofacitinib dose was reduced to 2x5 mg in the second week of treatment to minimize adverse reactions. Colonoscopy revealed that all patients had pancolitis with Mayo 3 activation. CMV colitis was assessed in each procedure and excluded by immunostainings.

Total colectomy was performed on two patients due to nonresponsiveness by the eighth week of tofacitinib treatment. Conversely, two patients exhibited a dramatic clinical response in the first week of treatment, with the number of stools per day decreasing to three. By the end of the eighth week, while two patients underwent surgery, the other two were in clinical remission on a dose of 2x5 mg. None of the patients developed any adverse events such as herpes zoster infection, thromboembolism, or other infectious diseases during the 8-10 month follow-up period. Colonoscopy has not yet been performed.

Table 1. Demographic and Clinical Characteristics of Patients

<table>
<thead>
<tr>
<th>Case ID</th>
<th>Involvement</th>
<th>Age of UC (months)</th>
<th>SSACI Before Tofacitinib</th>
<th>Colonoscopy</th>
<th>Biologic Treatment Experiences</th>
<th>SSACI After 2 Weeks of Tofacitinib</th>
<th>CRP Before and After 2 Weeks of Treatment (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1 (MK)</td>
<td>Pancolitis</td>
<td>60</td>
<td>10</td>
<td>Mayo 3</td>
<td>Adalimumab, Vedolizumab, Ustekinumab, Infliximab</td>
<td>9</td>
<td>33-65</td>
</tr>
<tr>
<td>Case 2 (HA)</td>
<td>Pancolitis</td>
<td>60</td>
<td>8</td>
<td>Mayo 3</td>
<td>Adalimumab, Vedolizumab, Ustekinumab</td>
<td>3</td>
<td>3.4-2.8</td>
</tr>
<tr>
<td>Case 3 (YC)</td>
<td>Pancolitis</td>
<td>36</td>
<td>10</td>
<td>Mayo 3</td>
<td>Adalimumab, Vedolizumab, Ustekinumab, Infliximab</td>
<td>2</td>
<td>10-0.6</td>
</tr>
<tr>
<td>Case 4 (SO)</td>
<td>Pancolitis</td>
<td>36</td>
<td>11</td>
<td>Mayo 3</td>
<td>Infliximab, Vedolizumab, Ustekinumab</td>
<td>10</td>
<td>0.8-42</td>
</tr>
</tbody>
</table>
As a result, our study included four ulcerative colitis patients experiencing acute severe attacks. All had previously been treated with at least three biological agents, and colectomy was being considered for each. Clinical remission was achieved in half of the patients with tofacitinib treatment. The literature offers limited data on the efficacy of tofacitinib for ASUC. Our experience suggests that tofacitinib can serve as a salvage therapy in ASUC cases. Despite the small size of our patient group, a success rate of 50% was achieved.

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**REFERENCES**