Adalimumab dose intensification in refractory and flaring hidradenitis suppurativa

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Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory condition of apocrine gland-bearing skin that is characterized by recurrent painful inflammatory nodules, with abscess and sinus tract formation. Estimates of the prevalence of HS remains greatly variable, but it is believed to affect 1% of the population in Europe.

The pathophysiology of HS is complex and multifactorial; however, immunologic abnormalities remain the primary hypothesis as a causal role in the disease. Significant elevations in levels of pro-inflammatory cytokines, such as tumour necrosis factor-α (TNF-α) have been detected and described in HS lesional skin.

This has ultimately led to the therapeutic use of TNF-α antagonists in the treatment of HS. Adalimumab, a human monoclonal antibody against TNF-α, is the only approved biologic for the treatment of patients with moderate-to-severe HS who have failed prior systemic treatment. Despite its documented efficacy, a percentage of primary responders experience a progressive loss in efficacy.

It has been established that weekly adalimumab treatment is significantly more effective than adalimumab every second week in HS. Therefore, it is plausible that adalimumab dose intensification to 80mg weekly can induce or return efficacy in HS patients who had an insufficient response or a progressive loss of efficacy to adalimumab.

The aim of our study was to evaluate adalimumab dose intensification to 80mg/weekly in HS patients who exhibited progressive loss of efficacy after an initial primary response to adalimumab 40mg/weekly.

Methods

We conducted a single-centre retrospective review to assess clinical response and tolerability amongst this cohort of patients.

All patients who underwent dose intensification previously had an initial response to adalimumab but were experiencing a progressive loss of efficacy or a severe flare in disease.

Results

Demographics

A total of 8 patients received adalimumab dose intensification to 80mg/weekly between 2019 and 2020. All patients attended the specialist HS clinic. All 8 patients were female. The median age was 38 years (range 27-58), and the median weight was 105kg (range 90-135). All patients had Hurley stage III disease.

<table>
<thead>
<tr>
<th>Female</th>
<th>8 (100%)</th>
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<tbody>
<tr>
<td>Median Age</td>
<td>38 years</td>
</tr>
<tr>
<td>Median Weight</td>
<td>105kg</td>
</tr>
<tr>
<td>Hurley Stage III</td>
<td>8 (100%)</td>
</tr>
<tr>
<td>Active Smokers</td>
<td>3 (37.5)</td>
</tr>
</tbody>
</table>

Prior treatment

All patients failed first-line treatments prior to commencing adalimumab 40mg/weekly, Table 2.

<table>
<thead>
<tr>
<th>Prior treatment</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>8 (100%)</td>
<td></td>
</tr>
<tr>
<td>Doxycycline</td>
<td>8 (100%)</td>
<td></td>
</tr>
<tr>
<td>Rifampicin/Clindamycin</td>
<td>4 (50%)</td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>2 (25%)</td>
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Clinical response

The median duration of treatment with adalimumab 40mg/weekly prior to dose intensification was 12 months (range 6 - 36). These patients experienced a progressive loss of efficacy and then received dose intensification.

Dose intensification had a substantial impact on patient quality of life (QoL). Median pre-dose intensification DLQI was 14 (range 9 - 18) and the median post-dose intensification DLQI was 3 (range 0 - 6), this was significantly reduced, p < 0.001.

The one patient who did not demonstrate any clinical response to dose intensification was the only patient to developed adverse effects, including nausea and fatigue. No other adverse effects were reported amongst the remaining patients.

Discussion

• This study has found adalimumab dose intensification to 80mg/weekly subcutaneous to be an effective way at restoring efficacy and preventing adalimumab response loss in severe HS.
• A clinical response was seen in 7 out of 8 patients.
• QoL was substantially improved, with a significant reduction in DLQI from 14 to 6, p < 0.001.
• Adverse events were low, with one patient developing fatigue and nausea at the higher adalimumab dose of 80mg/weekly.
• In a similar multi-centre study, 14 patients received adalimumab dose intensification to 80mg/weekly. A significant improvement of IHS4, DLQI and HS-PGA was observed. In this study, 2 patients with HS and Cronh’s disease developed paradoxical psoriasis during dose intensification.
• We concluded that adalimumab dose intensification to 80mg/weekly in HS patients may recover efficacy loss of adalimumab 40mg/weekly in primary dose responders.
• Although larger scale randomized controlled studies are required for confirmation, the effectiveness and safety of dose intensification from this single centre study raise the possibility of offering our patients more individualized treatment regimens.

References