Tofacitinib Citrate for Refractory Cutaneous Dermatomyositis: An Alternative Treatment

Dermatomyositis is an uncommon autoimmune disorder with distinctive cutaneous manifestations that are frequently challenging to manage. Although a number of therapies including hydroxychloroquine, methotrexate, mycophenolate mofetil, and intravenous immunoglobulin have demonstrated efficacy, few alternative treatments are available when these agents fail.

Recently, tofacitinib, an oral Janus kinase (JAK)-1/3 inhibitor, was approved for use in rheumatoid arthritis and has demonstrated efficacy for treating inflammatory skin diseases including psoriasis, alopecia areata, vitiligo, and atopic dermatitis.1,2 Studies suggest that tofacitinib suppresses interferon signaling,3 a pathway that has been found to be abnormally upregulated in dermatomyositis.4 With this context in mind, we sought to evaluate the utility of tofacitinib for treating cutaneous dermatomyositis.

Methods | We identified patients with multidrug-resistant cutaneous dermatomyositis and assessed their response to treatment with twice-daily oral tofacitinib. Improvement was measured using the validated Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score.5 Secondary end point measures included tolerability, adverse events, and necessity for concurrent therapies. The Brigham and Women’s Hospital institutional review board approved this study, waiving the requirement for written informed consent.

Results | Three patients with refractory cutaneous dermatomyositis were identified and treated with tofacitinib (Table). Clinical response was observed after 4 weeks, and the mean treatment period was 9.6 months. The CDASI activity scores decreased in all 3 patients, with a mean improvement of 12 points. No adverse events occurred. Tofacitinib was given as monotherapy in 2 patients, and 1 patient continued using hydroxychloroquine. All 3 patients reported decreased pruritus, and 2 patients with classic dermatomyositis reported subjective improvement in strength and fatigue.

Discussion | Overexpression of interferons and their transcription products has been found in lesional tissues and serum samples of patients with dermatomyositis.4 Through blockade of interferon-mediated activation of JAK/signal transducer and activator of transcription (STAT), JAK inhibitors may be capable of downregulating the inflammatory signals responsible for dermatomyositis, as was seen clinically in our small cohort. To date, these agents have been relatively unexplored in dermatomyositis apart from a single case in which ruxolitinib given for myelofibrosis also resulted in improvement in the patient’s dermatomyositis.6

According to the most recent validation study, a 4- to 5-point change in CDASI activity reflects a clinically significant response.5 Furthermore, a decrease to an activity score of 14 or lower signifies a transition from moderate-to-severe to mild disease.5 In our series, improvement from moderate-to-severe to mild disease was seen in 2 patients, both of whom used tofacitinib as a monotherapy. The third experienced a lesser but still clinically significant response. The greatest degree of improvement was seen in the patient receiving higher doses of tofacitinib (Figure), suggesting that its effect may be dose dependent. This observation has been reported for other inflammatory skin diseases treated with tofacitinib.1

Table. Patient Characteristics, Other Treatments, and CDASI Activity Scores

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, y, and Ethnicity</th>
<th>DM Subtype</th>
<th>Previous Therapies</th>
<th>Disease Duration, y</th>
<th>Tofacitinib Dose, mga</th>
<th>Time From Initiation to Improvement, wk</th>
<th>Follow-up, mo</th>
<th>CDASI Activity Before</th>
<th>CDASI Activity After</th>
<th>Concomitant Therapies</th>
<th>Treatment Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/30s White Clinically amyopathic</td>
<td></td>
<td>Prednisone, HCO, MTX, MMF, IVIG, dapson, isotretinoin, lenalidomide</td>
<td>5</td>
<td>10</td>
<td>4</td>
<td>15</td>
<td>30</td>
<td>14</td>
<td>None</td>
<td>Pruritus improved</td>
</tr>
<tr>
<td>2/F/40s White Classic</td>
<td></td>
<td>Prednisone, HCO, MTX, MMF, IVIG, SCIG</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>6</td>
<td>23</td>
<td>10</td>
<td>None</td>
<td>Pruritus improved</td>
</tr>
<tr>
<td>3/F/50s White Classic</td>
<td></td>
<td>Prednisone, HCO, quinacrine, MTX, MMF, azathioprine, IVIG, rituximab, thalidomide</td>
<td>8</td>
<td>5</td>
<td>4</td>
<td>8</td>
<td>32</td>
<td>25</td>
<td>HCQ</td>
<td>Pruritus improved</td>
</tr>
</tbody>
</table>

Abbreviations: CDASI, Cutaneous Dermatomyositis Disease Area and Severity Index; DM, dermatomyositis; HCO, hydroxychloroquine; IVIG, intravenous immunoglobulin; MMF, mycophenolate mofetil; MTX, methotrexate; SCIG, subcutaneous immunoglobulin.

a Oral tofacitinib dose taken twice daily.
series, tofacitinib was well tolerated, without any adverse effects. Although some studies indicate a higher incidence of herpes zoster during tofacitinib therapy, we did not observe this complication in our small cohort.

These 3 patients represent several of the most treatment-refractory patients from our institution’s large dermatomyositis cohort. More pronounced benefit from tofacitinib might be observed in a more typical cutaneous dermatomyositis cohort. More pronounced benefit from tofacitinib treatment, 10 mg, twice daily, marked improvement is seen.

Conclusions | In conclusion, our series represents the first to successfully use tofacitinib as a treatment for refractory cutaneous dermatomyositis. Given the limited number of agents available for the management of recalcitrant skin disease, alternative options are needed. By mitigating the signaling cascades that are likely responsible for dermatomyositis, tofacitinib and other JAK inhibitors may represent a rational therapeutic approach. Additional studies evaluating the efficacy and long-term safety of tofacitinib in larger dermatomyositis cohorts are needed to validate our observations.

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Accepted for Publication: March 2, 2016.


Author Contributions: Drs Kurtzman and Vleugels had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Conflict of Interest Disclosures: Dr Merola has served as consultant for Biogen IDEC, Amgen, Janssen, AbbVie, Eli Lilly, Momenta; and as speaker for AbbVie and Eli Lilly. He has received a grant from Biogen IDEC. No other disclosures are reported.