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**An open-label trial of abatacept in mild relapsing granulomatosis with polyangiitis (Wegener’s) (GPA)**


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*Introduction.*—Treatment options for patients with mild relapsing GPA has been an area of unmet need. As T-cell activation has been implicated in the pathophysiology of GPA, we conducted an open-label trial to examine the safety and efficacy of abatacept in patients with mild relapsing GPA.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value at study entry</th>
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</thead>
<tbody>
<tr>
<td>Age (range)</td>
<td>45 years (17–73)</td>
</tr>
<tr>
<td>Female/Male</td>
<td>9/11</td>
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<tr>
<td>PR3-cANCA</td>
<td>80%</td>
</tr>
<tr>
<td>MPO-pANCA</td>
<td>10%</td>
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<tr>
<td>GPA duration mean (range)</td>
<td>100 months (5–326)</td>
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<tr>
<td>BVAS/WG mean (range)</td>
<td>3.1 (1–6)</td>
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<tr>
<td>VDI mean (range)</td>
<td>2.5 (0–7)</td>
</tr>
</tbody>
</table>

**Method**—Twenty patients with mild relapsing GPA were treated with abatacept 10 mg/kg given by vein on days 1, 15, 29 and monthly thereafter. Patients on methotrexate, azathioprine, or mycophenolate mofetil at enrolment continued these agents without dosage increase. Prednisone ≤ 30 mg daily was permitted at entry, but the dose had to be tapered down to the pre-relapse dose by month 2. Disease activity was assessed using the BVAS/WG. Patients received abatacept until meeting criteria for early termination or until the common closeout date of 6 months after enrolment of the last patient.

*Results.*—Disease characteristics of the 20 enrolled patients are outlined in *Table 1*. Of the 20 patients, 18 (90%) had disease improvement, 16 (80%) achieved remission (BVAS/WG = 0) at a median of 3.75 months (range 1–19), and 14 (70%) reached common closing. Six (30%) met criteria for early termination due to increased disease activity but none had severe disease; three of these six achieved remission and relapsed at a median of 8.33 months (range 6–10). The median duration of remission before common closing was 12 months (range 4–21). During the study, 11 of the 15 patients on prednisone reached a dose of 0 mg. Ten of the 14 patients who had been on prednisone during the 12 months prior to enrolment were able to discontinue prednisone and seven of these remained off prednisone until common closing. Nine serious adverse events occurred in seven patients, including seven infections that were successfully treated.

*Conclusion.*—In this population of patients with mild relapsing GPA, abatacept was well tolerated and was associated with disease remission and discontinuation of prednisone in a high percentage of patients.

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**Lactoferrin inhibits formation of neutrophil extracellular traps in inflammation**

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*Introduction.*—Neutrophils are endowed with microbicidal functions including phagocytosis, degranulation and neutrophil extracellular traps (NETs), a recently identified web-like structure composed of their own chromatin fibers and proteases. Dysregulated NETs system is associated with development of inflammatory diseases. In this report, we have found that lactoferrin, a multifunctional protein and one of the neutrophil proteases, is an inhibitor of NETs formation.

*Methods.*—We used human neutrophils and Human leukemia 60 (HL-60) cells to observe NETs formation under fluorescent microscopy and to determine the release of NET-DNA in vitro. Two different neutrophil-dependent vasculitis models: a spontaneous ANCA-associated vasculitis and a thrombohemorrhagic vasculitis in the skin were employed to evaluate the NETs formation in vivo.

*Results.*—Lactoferrin translocated from cytoplasm to cytoplasmic membrane of neutrophils upon stimulation and strongly suppressed NETs formation and its release independently of oxygen radicals generation. Furthermore exogenous lactoferrin critically shrunk the chromatin fibers in the released NETs probably via charge-charge interaction. Oral administration of lactoferrin significantly inhibited release of NET-DNA into circulation and prevented development of the diseases.

*Conclusion.*—In this study, we identified that lactoferrin is a strong inhibitor of NETs formation in vitro and in vivo. We propose that lactoferrin is a new therapeutic option to control NETs in autoimmune and inflammatory diseases.

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