Letters to the Editor

Abatacept as Adjunctive Therapy in Refractory Polymyalgia Rheumatica

To the Editor:

Glucocorticoids (GCs) are the mainstay of treatment for patients with polymyalgia rheumatica (PMR). Despite their efficacy, GCs are associated with well-known adverse events and a substantial proportion of patients with PMR do not respond adequately, or are refractory, to initial GC treatment. GC-sparing agents in PMR are limited to methotrexate (MTX). More recently, favorable results were reported with tocilizumab (TCZ), an interleukin (IL)-6 receptor blocking agent, in patients with steroid-dependent/resistant PMR. The results of a randomized clinical trial of abatacept (ABA) suggested that this agent could be an adjunctive therapy in patients with giant cell arteritis (GCA). In this study, we aimed to evaluate the efficacy of ABA in patients with isolated PMR and who had GC-refractory disease.

According to the French Regulatory Authority for clinical studies, prospective and retrospective studies consisting of observational analyses only do not need to obtain approval from ethics committees. The cases reported in this paper and this study design received no statement of opposition from the local ethics committee. As this study is a case series, written informed consent was not required due to its retrospective design.

A call for observations of all cases of patients with PMR who received at least 1 injection (intravenously or subcutaneously) of ABA was sent to the members of a specialized French rheumatism and inflammation network (Club Rhumatismes et Inflammation: www.cri-net.com; including rheumatologists and specialists in internal medicine). Patients had to satisfy the European Alliance of Associations for Rheumatology (EULAR)/American College of Rheumatology criteria for PMR and have isolated PMR, aiming to evaluate the ability of ABA alone to improve disease activity in patients with isolated PMR and who had GC-refractory disease.

We observed that ABA may improve disease activity and may have a steroid-sparing effect in certain patients with PMR. MTX is strongly recommended by the EULAR group as a steroid-sparing drug, especially in patients with high risk of relapse. However, this conventional synthetic disease-modifying antirheumatic drug is generally associated with moderate response and overall, the reported benefits are usually small. There are numerous reports of the benefit of IL-6 blockade in PMR using TCZ. However, results stem from limited series of patients or an open-label clinical trial. In addition, TCZ is not currently approved in PMR, and results of a randomized clinical trial are still pending. It is now established that Th17 lymphocytes are implicated in the pathogenesis of PMR and GCA. Together with experimental data, it is thought that PMR and GCA are antigen-driven diseases in which not only activated T lymphocytes but also macrophages and dendritic cells play a critical role. This led to the initiation of a randomized trial evaluating ABA, a costimulatory inhibitor, in patients with GCA.

The results of that trial showed that in patients with GCA who achieved remission under GC and ABA, the maintenance of ABA, on top of standardized prednisone taper, significantly reduced the risk of relapse compared to patients randomized to receive placebo and GC. All in all, ABA would appear to have therapeutic potential in PMR that warrants further investigation. The results in our series are mixed, with an improvement in disease activity in 2 patients, and drug failure for the 2 others. Based on these findings, ABA may be considered as a potential adjunctive therapy in selected or difficult cases of PMR. It may also be considered as an alternative to an IL-6 blocking agent, especially when this drug class has failed or is contraindicated. A clinical trial is currently ongoing in patients with early-onset PMR, aiming to evaluate the ability of ABA alone to improve PMR and its capacity to provide a steroid-sparing effect after this induction treatment.

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REFERENCES


Table 1. Clinical features, therapies, and outcomes of patients with isolated PMR treated by ABA.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, yrs/sex</th>
<th>GC Therapy</th>
<th>ABA</th>
<th>Duration, months</th>
<th>Previous csDMARD</th>
<th>bDMARD Before ABA</th>
<th>Previous bDMARD</th>
<th>ABA</th>
<th>Treatment</th>
<th>CRP, mg/L</th>
<th>GC Dosage, mg</th>
<th>PMR-AS</th>
<th>At Last ABA</th>
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ABA: abatacept; AS: activity score; bDMARD: biologic disease-modifying antirheumatic drug; CRP: C-reactive protein; csDMARD: conventional synthetic disease-modifying antirheumatic drug; GC: glucocorticoids; IV: intravenous; M: month; MTX: methotrexate; NA: not available; PMR: polymyalgia rheumatica; QM: once a month; QW: once a week; SC: subcutaneously; TCZ: tocilizumab.