Assessment of Bone and Cartilage Turnover Markers Following Treatment With Repository Corticosteroid Injection in Patients With Persistently Active Rheumatoid Arthritis
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Introduction
Persistently active rheumatoid arthritis (RA) is an autoimmune disorder characterized by progressive joint destruction.

Although systemic administration of corticosteroids is recommended alongside use of diseasemodifying antirheumatic drugs (DMARDs) for active disease, corticosteroid use is often associated with exacerbation of bone loss.

Replicating corticosteroid injection (CSI) is increasingly used by the US Food and Drug Administration for short-term csA use in the treatment of RA. However, data on the impact of CSI on bone metabolism in patients with persistently active RA are limited.

Aims
To evaluate Bone and cartilage turnover markers following repository corticosteroid injection (CSI) in patients with persistently active RA.

Methods
Study design
A total of 44 patients with persistently active RA despite DMARDs and corticosteroid use were enrolled and received the current biweekly DMARD and corticosteroid doses throughout the study (ClinicalTrials.gov identifier: NCT02919761). In part (1), all patients received abiraterone (Abir) (250 mg, 2 tablets, twice daily) for 12 weeks (Figure 1).

Methods (cont’d)
Those who achieved low disease activity (CDAI ≤ 2.8 in part 1) were excluded from further study participation. All subjects had a 12-week follow-up until the last visit of study drug and/or DMARDs (part 1, 20 weeks).

Statistical analysis
Statistical analyses were performed on the modified intent-to-treat (mITT) population (all enrolled subjects who received ≥ 1 dose of study drug and who contributed any efficacy or safety data). A one-sample t-test was used to compare the change from baseline in bone turnover markers. Linear regression was used to examine the correlation of bone turnover markers at baseline with changes in bone turnover markers. A linear mixedmodel was used to evaluate the treatment change in the double-blind randomized period.

Results
Open-label period
(1) 20 patients entering the open-label period; 16 (82.2%; P=0.001) achieved low disease activity (CDAI ≤ 2.8 in part 1) were excluded from further study participation. 12 of the patients were randomized to receive Abir in part 2 (76.4%; baseline mean: 20.28; week 12 mean: 20.15; P=0.004). Double-blind randomized period

Double-blind randomized maintenance period
(2) Of the 10 patients who achieved low disease activity, 12 entered the double-blind period. 12 entered the double-blind period and were randomized to treatment with Abir or placebo (Abir: n=6, placebo: n=6). In this study, patients were randomized to receive weekly subcutaneous injections of Abir (50 mg) or placebo (50 mg) for 24 weeks. Double-blind randomized period

Figure 1. Study Design

Table 1. Bone and Cartilage Biomarker Levels From the Open-Label Period (N=259)

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Week 12</th>
<th>Mean (SD)</th>
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<tbody>
<tr>
<td>CTX</td>
<td>0.8 (3.1)</td>
<td>0.8 (3.1)</td>
</tr>
<tr>
<td>NTX</td>
<td>0.8 (3.1)</td>
<td>0.8 (3.1)</td>
</tr>
<tr>
<td>PINP</td>
<td>32.2 (29.2)</td>
<td>32.2 (29.2)</td>
</tr>
<tr>
<td>saP</td>
<td>204.5 (306.2)</td>
<td>204.5 (306.2)</td>
</tr>
<tr>
<td>DIP</td>
<td>4.7 (4.0)</td>
<td>4.7 (4.0)</td>
</tr>
<tr>
<td>Carboxylation</td>
<td>5.2 (4.8)</td>
<td>5.2 (4.8)</td>
</tr>
</tbody>
</table>

Table 2. Bone and Cartilage Biomarker Levels Randomized in the Double-blind Period (RCI vs Placebo)

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>RCI</th>
<th>Placebo</th>
<th>Mean (SD)</th>
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</thead>
<tbody>
<tr>
<td>CTX</td>
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<td>0.8 (3.1)</td>
<td></td>
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<tr>
<td>NTX</td>
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</tr>
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</table>

Conclusions
Overall, bone and cartilage turnover markers were mostly stable throughout this study of patients with persistently active RA, suggesting that any demographic effects of RCIs were not present.

During the open-label phase, corticosteroid degenerative markers significantly decreased, suggesting a potential therapeutic effect, whereas bone degradation markers remained stable.

Some evidence of increased osteodifferentiation in response to RCIs was noted during the double-blind phase. However, markers of bone remodeling remained stable, suggesting no effect of RCIs on bone loss.

References

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Disclosures
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