**Background**

- Patients with autoimmune or inflammatory diseases (AIID) have higher CV risk due to systemic inflammation.
- In prior trials, patients with inflammatory conditions derived potentially greater relative benefit from statins, which may be attributable to an anti-inflammatory effect, greater atherosclerotic burden, and/or endothelial cell dysfunction.
- Trials of PCSK9 inhibitors provide an opportunity to study an alternative lipid-lowering therapy, without a clear effect on systemic markers of inflammation, in patients with AIID.

**Methods**

- We compared the efficacy of evolocumab vs. placebo in pts with and without AIID using data from the FOURIER trial.
- Key eligibility criteria: established ASCVD on statins, LDL-C ≥70 mg/dL or non-HDL-C ≥100 mg/dL.
- AIID defined as any autoimmune or chronic inflammatory condition (investigator-reported with blinded central review).
- Statistical analysis: Cox model adjusted for randomization stratification factors (region, screening LDL-C).

**Results**

**Results (cont.)**

- 3.2% of patients in each arm had an AIID at baseline, most commonly rheumatoid arthritis (34%) and psoriasis (16%).
- Patients with AIID were older, more commonly female; other baseline characteristics were largely comparable (Table, left).
- Baseline LDL-C was slightly lower in pts with an AIID, and percent reduction with evo was similar; baseline hsCRP was higher in AIID pts and unaffected by evo (Table, below).

**Laboratory value**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AIID</th>
<th>Not AIID</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline LDL-C, mg/dL</td>
<td>90.0 (80, 106)</td>
<td>91.5 (80, 109)</td>
<td>0.03</td>
</tr>
<tr>
<td>% change with evo</td>
<td>-62% (-65, -58)</td>
<td>-61% (-61, -60)</td>
<td>0.60</td>
</tr>
<tr>
<td>Baseline hsCRP, mg/L</td>
<td>2.1 (1.0, 4.5)</td>
<td>1.7 (0.9, 3.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% change with evo</td>
<td>17% (-65, 99)</td>
<td>11% (-4, 26)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

Baseline reported as median (IQR); change reported as mean (%). % change calculated as placebo-adjusted least-squares mean % change.

- EVO consistently reduced the primary endpoint in pts with and without AIID, with a trend toward greater relative (Fig, upper) and absolute (Fig, lower) reductions in pts with AIID.
- Endpoints CV death/MI/stroke, MI, and coronary revascularization were reduced to greater degree in pts with AIID (P int <0.05).

**Conclusions**

- Intensive LDL-C lowering with evolocumab may lead to greater relative and absolute CV event reduction in patients with autoimmune or inflammatory diseases, despite comparable LDL-C lowering.
- Patients with AIID may derive particular CV benefit from earlier, more intensive lipid-lowering interventions.

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