Increased Expression of T-Cell-Associated Genes in Baseline Biopsies from TNF Antagonist-Naive Patients with Moderately to Severely Active Ulcerative Colitis Who Undergo Remission in Response to Etrolizumab in a Phase 2 Trial

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OBJECTIVES

To identify expression patterns associated with clinical remission in response to etrolizumab in the EUCALYPTUS Study.

To evaluate expression of genes associated with clinical remission in EUCALYPTUS as sorted IB/IBD- and negative controls from naïve patients and control patients (n = 70 total patients) and control patients in the non-EUCALYPTUS patients with active UC (n = 30 patients with active UC, n = 5 patients with inactive UC).

RESULTS

Gene Set Enrichment Analysis

Results of the gene set enrichment analyses are summarized in Table 1. T-cell genes were significantly enriched in patients with active UC and multiple genes were significantly regulated associated with remission, whereas enterocyte, B-cell and dendritic cell genes did not exhibit significant enrichment in Table 1.

Table 1. Top Gene Sets Enriched in EUCALYPTUS Patients with Active UC

<table>
<thead>
<tr>
<th>Gene Set</th>
<th>Description</th>
<th>Q-Value</th>
<th>Beta</th>
<th>Adjusted Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-cells</td>
<td>T-cell genes</td>
<td>0.01</td>
<td>0.61</td>
<td>0.99</td>
</tr>
<tr>
<td>T-lymphocytes</td>
<td>T-cell genes</td>
<td>0.01</td>
<td>0.61</td>
<td>0.99</td>
</tr>
<tr>
<td>IRF1-TGF-β genes</td>
<td>0.016</td>
<td>0.66</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>RelA</td>
<td>0.06</td>
<td>0.56</td>
<td>0.60</td>
<td></td>
</tr>
</tbody>
</table>

METHODS

To determine expression patterns associated with clinical remission in response to etrolizumab in the EUCALYPTUS Study.

To evaluate expression of genes associated with clinical remission in EUCALYPTUS as sorted IB/IBD- and negative controls from naïve patients and control patients (n = 70 total patients) and control patients in the non-EUCALYPTUS patients with active UC (n = 30 patients with active UC, n = 5 patients with inactive UC).

Table 2. Differentially Expressed Genes in Remitters and Non-Remitters

<table>
<thead>
<tr>
<th>Gene</th>
<th>Description</th>
<th>log2FC</th>
<th>P-Value</th>
<th>Beta</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSTR2</td>
<td>Somatostatin receptor 2</td>
<td>1</td>
<td>0.04</td>
<td>0.72</td>
</tr>
<tr>
<td>CASP4</td>
<td>Caspase 4, apoptosis-related</td>
<td>-1</td>
<td>0.03</td>
<td>0.78</td>
</tr>
</tbody>
</table>

DISCLOSURES

All authors declare no financial and non-financial conflicts of interest. The findings and opinions expressed in this paper are those of the authors and do not necessarily reflect the views of Genentech, Inc., a member of the Roche Group.

REFERENCES

1. Etrolizumab Treatment Untreated IBD Patients with Moderately to Severely Active Ulcerative Colitis (EUCALYPTUS).

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