Unraveling Vedolizumab mechanism of action in Ulcerative Colitis

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DOP25
Copenhagen, March 07 2019
Hypothesis: Vedolizumab induces changes in the migration and integrin expression of lymphocytes that may correlate with disease remission in UC patients.

Objectives:
1. Determine the occupancy of α4β7 achieved by Vedolizumab
2. Analyze the number of lymphocytes in the intestine and peripheral blood and how they change with Vedolizumab treatment.
3. Characterize the expression of integrins α4β7 and αEβ7 before and after Vedolizumab treatment.
UC patients receiving Vedolizumab show full α4β7 occupancy

**BLOOD**

- % CD4+ VDZ+β7+

**COLON**

- % CD4+ VDZ-β7+

- Remitter
- Non-remitter
- No data

Graphs showing the percentage of CD4+ T cells expressing α4β7 integrin in UC patients before (Week 0) and after (Week 46) treatment with Vedolizumab.
Vedolizumab reduces the number of total T and B lymphocytes in the colon without affecting their numbers in blood.

<table>
<thead>
<tr>
<th></th>
<th>CD3+CD4+</th>
<th>CD3+CD8+</th>
<th>CD19+</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total cells/µl</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>BLOOD</strong></td>
<td></td>
<td></td>
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<tr>
<td>HC</td>
<td>w0</td>
<td>w14</td>
<td>w46</td>
</tr>
<tr>
<td><strong>Total cells/µl/mg</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>COLON</strong></td>
<td></td>
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<tr>
<td>HC</td>
<td>w0</td>
<td>w14</td>
<td>w46</td>
</tr>
</tbody>
</table>

- **Remitter**
- **Non-remitter**
- **No data**
VDZ treatment reduces intestinal $\alpha 4\beta 7^+$ CD4$^+$ T cells without affecting $\alpha 4\beta 7^+$ plasma cells.

**Graphs:**
- **BLOOD**:
  - CD3+CD4+
  - CD3+CD8+
  - CD19+
- **COLON**:
  - CD3+CD4+
  - CD3+CD8+
  - CD19+

**Legend:**
- **Remitter**
- **Non-remitter**
- **No data**
αEβ7+ cells are reduced in the colon of active UC patients

**COLON. Flow cytometry %αEβ7**

<table>
<thead>
<tr>
<th></th>
<th>αEβ7</th>
<th>a-β7 APC</th>
<th>CD3+CD4+</th>
<th>CD3+CD8+</th>
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<tr>
<td>HC</td>
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<td>w46</td>
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</table>

**Non-remitter**

**Remitter**

**COLON. Immunohistochemistry αE**

<table>
<thead>
<tr>
<th></th>
<th>CD103 signal</th>
<th>Epithelium</th>
<th>Lamina propria</th>
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</thead>
<tbody>
<tr>
<td>HC</td>
<td></td>
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<tr>
<td>VDZ w0</td>
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<td>VDZ w14</td>
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<td>VDZ w46</td>
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</table>

Non-remitter

Remitter
Conclusions

- Lack of response to Vedolizumab in UC patients is not due to α4β7 unoccupied integrin.

- Vedolizumab diminishes the total number of lymphocytes in the intestine without affecting their numbers in blood. This might explain the safety profile of Vedolizumab in comparison to other drugs used in IBD.

- Vedolizumab has a large effect on intestinal recirculating populations like CD4+ T cells without affecting plasma cells, despite full occupancy of α4β7 in all populations.

- Inflammation reduces the presence of αEβ7+ cells in the intestine of UC patients. Vedolizumab treatment does not affect this population, either in the epithelium or in the lamina propria.
Thank you for your attention!