Laquinimod is owned by Active Biotech, Lund Sweden.

**Disclosures**

CHDI-Foundation, DFG, EU-FP7, EHDN, DZNE, BMBF, and consultancy and clinical trial services for Actelion, Amarin Neuroscience, AOP Orphan, Cure Huntington Disease Initiative Foundation (CHDI), Desitin, Roche, Restoration (NECTAR), Evaluation Committee of PRTS of the French National Research Agency, Canada Research Chairs Program, France Parkinson "Grand Appel d’Offres and research consultancies from Teva and Prana.

**OBJECTIVE**

To evaluate the effect of laquinimod on putaminal and frontal white matter markers of neuronal integrity and astrocytosis using MRS in patients with early HD.

**METHODS**

Eligible participants from selected LEGATO-HD sites included men and women (aged 21-65 years) with adult onset HD. MRS scans were performed on 3T scanners in patients at baseline and week 52.

Two voxels of interest in the putamen (2.25mL) and a frontal white matter region (2.25mL) using a PRESS sequence (TR=3000ms, TE=50ms and NEX=128) using the same protocol that was used in the metabolite study for the TRACK-HD study and its extension 4 (see Fig 1a and 1b).

The MRS results were analyzed at the UBC site using LCModel (Version 6.3-0L)4 and poor quality spectra were rejected. Metabolite concentrations were derived for N-acetyl aspartate (NAA, a marker of neuronal integrity), NAA (NAA & N-acetyl aspartyl glutamate), Creatine (Cr, a marker of brain energy metabolism), total Choline (Cho, a marker for neuron, neurofilament and myelin turnover), Glutamate (Glu, an CNS excitatory neurotransmitter), Glx (glutamate and Glutamine) and Myo-inositol (m, an astrocyte marker) using an internal water standard (NAA=18) and assumed tissue water content.

Mean metabolite concentrations were compared between placebo and each laquinimod dose group using an ANCOVA with treatment, site (North America or Europe) and baseline value as fixed effects.

As no adjustment for multiplicity was defined for this ancillary study, the analysis results are presented with nominal p-values and cannot be interpreted intermediately.

**RESULTS**

**Table 1. Patient Demographics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo (n=18)</th>
<th>LAQ 0.5 mg (n=18)</th>
<th>LAQ 1.0 mg (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, Male (%)</td>
<td>9.0 (50.0)</td>
<td>11.0 (56.2)</td>
<td>9.0 (50.0)</td>
</tr>
<tr>
<td>Weight kg</td>
<td>76.2 (18.1)</td>
<td>73.5 (15.1)</td>
<td>70.0 (13.6)</td>
</tr>
<tr>
<td>Height cm</td>
<td>170.5 (12.6)</td>
<td>171.4 (12.7)</td>
<td>172.8 (10.7)</td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>26.1 (5.1)</td>
<td>24.9 (4.0)</td>
<td>23.3 (3.0)</td>
</tr>
<tr>
<td>Number of CAG repeats</td>
<td>43.8 (3.0)</td>
<td>43.1 (3.5)</td>
<td>43.1 (3.6)</td>
</tr>
<tr>
<td>Months from HD diagnosis</td>
<td>32.8 (32.5)</td>
<td>60.9 (32.6)</td>
<td>67.2 (72.6)</td>
</tr>
<tr>
<td>Months from first HD symptoms</td>
<td>53.6 (33.7)</td>
<td>58.1 (44.3)</td>
<td>63.5 (60.1)</td>
</tr>
<tr>
<td>UHDRS-TMS</td>
<td>22.2 (11.4)</td>
<td>24.9 (12.0)</td>
<td>25.6 (12.6)</td>
</tr>
<tr>
<td>UHDRS Total Functional Capacity (TFC)</td>
<td>11.4 (1.5)</td>
<td>11.2 (1.4)</td>
<td>11.0 (1.5)</td>
</tr>
</tbody>
</table>

**Fig 1a. Sample Voxel Placement in Left Putamen**

**Fig 1b. Sample Voxel Placement in Left Frontal White Matter**

**Table 2. Metabolite Concentrations**

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Placebo</th>
<th>LAQ 0.5 mg</th>
<th>LAQ 1.0 mg</th>
<th>Nominal p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>tCr (mM)</td>
<td>30.6 (2.8)</td>
<td>30.4 (2.7)</td>
<td>30.6 (2.8)</td>
<td>0.80</td>
</tr>
<tr>
<td>NAA (mM)</td>
<td>10.7 (2.7)</td>
<td>10.5 (2.6)</td>
<td>10.6 (2.7)</td>
<td>0.53</td>
</tr>
<tr>
<td>MI (mM)</td>
<td>2.2 (0.5)</td>
<td>2.2 (0.5)</td>
<td>2.1 (0.5)</td>
<td>0.70</td>
</tr>
<tr>
<td>Glx (mM)</td>
<td>2.5 (0.6)</td>
<td>2.5 (0.6)</td>
<td>2.5 (0.6)</td>
<td>0.98</td>
</tr>
<tr>
<td>Glutamate (mM)</td>
<td>26.2 (6.3)</td>
<td>25.0 (6.0)</td>
<td>25.1 (6.2)</td>
<td>0.54</td>
</tr>
<tr>
<td>GABA (mM)</td>
<td>18.4 (3.6)</td>
<td>19.1 (3.9)</td>
<td>18.5 (3.7)</td>
<td>0.40</td>
</tr>
<tr>
<td>Glutamine (mM)</td>
<td>23.0 (4.5)</td>
<td>23.0 (4.5)</td>
<td>22.9 (4.4)</td>
<td>0.99</td>
</tr>
<tr>
<td>tNAA (mM)</td>
<td>11.0 (1.8)</td>
<td>11.0 (1.8)</td>
<td>10.9 (1.8)</td>
<td>0.94</td>
</tr>
<tr>
<td>tCr/ NAA</td>
<td>2.7 (0.4)</td>
<td>2.7 (0.4)</td>
<td>2.7 (0.4)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

**Fig 2. Metabolite Concentrations**

**CONCLUSIONS**

The reduction in the glial cell metabolite mi in the putamen of early HD patients taking laquinimod compared to the increased mi levels of HD patients in the placebo group over 52 weeks suggests that laquinimod treatment decreases astrocytosis and gliosis, consistent with its known in vitro and in vivo effects on neuroinflammation.

**References**


**Disclosures**

Research sponsored by Teva Pharmaceutical Industries Ltd. August 2015. Investigator initiated study. All authors report no conflicts of interest.

**Presented at the International Congress of Parkinson's Disease and Movement Disorder in Nita France, September 22-26, 2019**