Tesamorelin Effect on Skeletal Muscle Fat in HIV+ Patients

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Background

Due to the successes of antiretroviral therapy (ART), individuals infected with human immunodeficiency virus (HIV) are living longer. They are also accumulating visceral adipose tissue (VAT) to a greater extent than their uninfected peers.

Accumulation of VAT is associated with HIV, ART, and lifestyle.

Prior studies have shown that VAT accumulation correlates with skeletal muscle fat. Both VAT and skeletal muscle fat have been associated with cardiovascular disease, liver fibrosis, type 2 diabetes, and physical functional impairments.

Tesamorelin is a growth-hormone-releasing hormone analog, and is found to be effective in reducing VAT in some HIV-infected patients, however, its effect on skeletal muscle fat is unknown.

The goal of this study is to examine the changes in truncal (i.e. skeletal) muscle fat, pre- and post- 26 weeks tesamorelin treatment.

We hypothesize tesamorelin can also decrease skeletal muscle fat compared to placebo.

Methods

• This retrospective study combines datasets from two multicenter, randomized (2:1) tesamorelin vs. placebo clinical trials of tesamorelin for its effect on VAT among HIV-infected adults with lipodystrophy.

• In the tesamorelin arm, only participants that were defined as ‘responders’ were included (VAT decrease of 28%). A total of 341 paired scans (baseline and week 26) were re-analyzed to quantify skeletal muscle area (cm²) and density (Hounsfield Unit, HU) using a semi-automatic segmentation image analysis program (developed in-house usingIDL).

• Differences between muscle area and density before and after treatment, for both study arms, were compared using t-tests.

Results

Table 1. Participants characteristics at baseline.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Tesamorelin (N = 193)</th>
<th>Placebo (N = 148)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.8 (±7.3)</td>
<td>48 (±7.6)</td>
<td>0.792</td>
</tr>
<tr>
<td>Male (%)</td>
<td>86.1</td>
<td>83.8</td>
<td>0.105</td>
</tr>
<tr>
<td>White (%)</td>
<td>86</td>
<td>78.6</td>
<td>0.208</td>
</tr>
<tr>
<td>Black or African American (%)</td>
<td>11.5</td>
<td>10.4</td>
<td>0.664</td>
</tr>
<tr>
<td>Other (%)</td>
<td>4</td>
<td>10</td>
<td>0.004</td>
</tr>
<tr>
<td>site of lipodystrophy (%)</td>
<td>65.6</td>
<td>66.8</td>
<td>0.132</td>
</tr>
<tr>
<td>VAT cell count at baseline (cells/µL)</td>
<td>125.5 (±73.6)</td>
<td>120 (±70)</td>
<td>0.102</td>
</tr>
<tr>
<td>VAT cell count at baseline (cells/µL)</td>
<td>875.4 (±456.1)</td>
<td>953 (±389.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Site of VAT cell count (module)</td>
<td>171.1 (±46.1)</td>
<td>158 (±46.1)</td>
<td>0.103</td>
</tr>
<tr>
<td>Duration of ART therapy (months)</td>
<td>59 (±38)</td>
<td>62 (±48.8)</td>
<td>0.173</td>
</tr>
</tbody>
</table>

Figure 4. Changes in muscle area following 26 weeks of tesamorelin (solid) vs placebo treatment (dashed).

Figure 5. Changes in muscle density following 26 weeks of tesamorelin (solid) vs placebo treatment (dashed).

Conclusion

Tesamorelin is effective in reducing skeletal muscle fat in a HIV-infected group but further studies are required to investigate the impact of these changes on physical function and long-term effectiveness.

Limitations

• Participant characteristics were not significantly different from one another, however, this study population included few women or minorities, thus the study results may not be generalizable to global HIV populations.

• Increase in truncal muscle density is associated with better physical performance, however, physical function and strength assessments were not obtained.

• For this preliminary analysis, the tesamorelin arm was restricted to responders, thus for the next step, a larger cohort should be used.

• Approximately 30% of participant’s data was either missing week-26 data or unreadable. This may contribute to why the tesamorelin and placebo study arms start at different mass/density at baseline.

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Summary

• Participants receiving tesamorelin experienced an increase in total muscle area, and these increases were significantly different for the psoas major compared to placebo (p < 0.005).

• Treatment with tesamorelin was associated with an increase of lean muscle area for all truncal muscles compared to placebo (p < 0.005).

• Participants receiving tesamorelin treatment experienced increases in muscle density (less fat infiltration), with significant differences in all of the truncal muscles compared to placebo (p < 0.005).

• Participants in the tesamorelin study group experienced gains in lean muscle density in the anterolateral abdominal wall muscles, and rectus abdominis compared to placebo (p < 0.005).