Jeffrey Hsu
Patient Reported Outcomes (PROs): FSS, Insomnia
- p=0.79 AG 1000mg vs placebo

Compared encapsulated standardized AG (≥5% total
100%)
Without other illnesses associated with fatigue, such
51 (47,57)
Safety laboratory tests were obtained at every visit.
Encapsulated standardized AG powdered root 1000 and 3000 mg/daily for 28 days
p=0.17 AG 1000mg vs placebo
Fatigue
- 52.5 (48, 57)
24 (22.1) *
13 (42%)
Overall
p=0.47 AG 1000mg vs placebo
Adherence was monitored by self
619 (338, 798)
Animal and human studies have demonstrated that
- *p<0.05

Primary endpoint: average change in FSS from
- The likelihood of the observed significance changing with additional sampling was very small.
- The clinical significance of the small improvements in the AG arms in some of the secondary endpoints relative to the large placebo effect is unclear.
- Conditional power analysis indicated that the likelihood of the observed significance changing with additional sampling was very small.

Table 1: Subject Characteristics at Baseline (N=96)

<table>
<thead>
<tr>
<th>Variables</th>
<th>AG 1000 mg (N=32)</th>
<th>AG 3000 mg (N=31)</th>
<th>Placebo (N=33)</th>
<th>Total (N=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y) Median (Q1, Q3)</td>
<td>53 (48, 57)</td>
<td>54 (50, 59)</td>
<td>51 (47,57)</td>
<td>52.5 (48, 57)</td>
</tr>
<tr>
<td>Total Score</td>
<td>100%</td>
<td>97%</td>
<td>97%</td>
<td>97%</td>
</tr>
<tr>
<td>CD4 Count (mm³)</td>
<td>622 (495, 705)</td>
<td>613 (328, 789)</td>
<td>651 (403, 751)</td>
<td>621.5 (401.0,743)</td>
</tr>
</tbody>
</table>

Table 2: Mean (SD) Decrease in PROs for AG and Placebo Arms from Baseline to Week 4

<table>
<thead>
<tr>
<th>PROs</th>
<th>AG 1000 mg (N=32)</th>
<th>AG 3000 mg (N=31)</th>
<th>Placebo (N=33)</th>
<th>Total (N=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSS</td>
<td>-24.7 (16.9) *</td>
<td>-16.9 (15.1) *</td>
<td>-16.7 (17.4) *</td>
<td>-17.6 (16.7) *</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>5.5 (4.8)</td>
<td>-2.9 (4.2)</td>
<td>-4.8 (4.3) *</td>
<td>-4.8 (4.3) *</td>
</tr>
<tr>
<td>ISI</td>
<td>6.9 (5.1) *</td>
<td>-3.4 (5.5) *</td>
<td>-4.6 (5.2) *</td>
<td>-4.6 (5.2) *</td>
</tr>
<tr>
<td>PROMS</td>
<td>-12.5 (11.8) *</td>
<td>-11.4 (11.7) *</td>
<td>-10.4 (10.9) *</td>
<td>-10.8 (10.8) *</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-40.1 (33.3) *</td>
<td>-33.3 (30.6) *</td>
<td>-28.8 (32.7)</td>
<td>-28.8 (32.7)</td>
</tr>
<tr>
<td>ESS</td>
<td>5.7 (7.1) *</td>
<td>-7.5 (3.1) *</td>
<td>-6.2 (3.3) *</td>
<td>-6.2 (3.3) *</td>
</tr>
<tr>
<td>MOS</td>
<td>22.4 (20.9) *</td>
<td>24 (22.1)</td>
<td>20.1 (20.2)</td>
<td>20.1 (20.2)</td>
</tr>
</tbody>
</table>

placebo) and placebo arms for PROs (Table 2). PRO values conversion to 0 to 100 score scale also showed high proportion of participants who improved ≥10 points in the AG and placebo arms: FSS 72%, PHQ-9 59%.

63%: IBI 47%: PROMS Fatigue 76%, BFI "improved right now"; ESS 75%: 72%: MOS- HIV energy-fatigue
However, there was no significant differences in improvements in the AG and placebo arms
Post-hoc analysis combining the AG arms confirmed that fatigue was not different than placebo on FSS; AG showed modest improvement in BFI subscales (p=0.01-0.03) and trends toward improvement in 4/10 MOS HIV QOL subscales.
Overall mean adherence by pill count and self report was ≥96% for all study arms. Most adverse events were grades 1 and 2, all recovered and did not differ by study arms. Only 2/5 neutropenia severe adverse events were rated as possibly associated with study agent (1 AG 3000 mg and 1 Placebo); all recovered.

Study Participants Selected Inclusion Criteria
- HIV-infected adults on ART for ≥3 months
- Infected adult subjects with
- 2000 mg/day for 8 weeks,

- Patient Reported Outcomes (PROs): FSS, Insomnia Severity Index (ISI), Patient Health Questionnaire (PHQ-9), Brief Fatigue Inventory (BFI), Epworth Sleepiness Scale (ESS), Medical Outcomes Study HIV Health Survey (MOS-HIV), Clinical Global Impressions (CGI), and PROMIS Fatigue were assessed at enrollment and weeks 2-6. Adherence was monitored by self-report journal.
- Safety laboratory tests were obtained at every visit.

Outcomes Measures
- Primary endpoint: change in average FSS from baseline to week 4:
- Secondary endpoints: other measures of fatigue and safety/tolerability: from baseline to week 4:
- Sleep quality, depression, and QOL: BFI, ESS, PHQ-9, ISI, MOS-HIV, CGI, and PROMS Fatigue.

Changes were compared between the AG and placebo arms using nonparametric Wilcoxon tests supplemented with repeated measures mixed models to adjust for age, gender, race, baseline insomnia, and depression. Data was analyzed using an intent-to-treat approach.

Study Design
- 6-week double-blind randomized, parallel-arm placebo-controlled trial
- Compared encapsulated standardized AG (≥5% total ginsenosides) 1000 and 3000 powdered root PO QD for 28 days to placebo
- Patient Reported Outcomes (PROs): FSS, Insomnia Severity Index (ISI), Patient Health Questionnaire (PHQ-9), Brief Fatigue Inventory (BFI), Epworth Sleepiness Scale (ESS), Medical Outcomes Study HIV Health Survey (MOS-HIV), Clinical Global Impressions (CGI), and PROMIS Fatigue were assessed at enrollment and weeks 2-6.

Adherence was measured by self-report journal.
- Safety laboratory tests were obtained at every visit.

Objectives
- To determine whether encapsulated standardized AG powdered root 1000 and 3000 mg PO QD for 28 days ameliorates fatigue relative to matching placebo.
- To evaluate the safety and tolerability of encapsulated standardized AG powdered root 1000 and 3000 mg PO QD for 28 days in HIV-infected adult subjects with fatigue.

Methods
- 96/120 planned subjects were enrolled; 3 were lost to follow up (1 AG 1000mg and 2 Placebo) and 3 discontinued study agent prematurely (1 AG 3000mg and 2 Placebo).
- 32 randomized to AG 1000mg, 31 to 3000mg, and 33 to placebo (Table 1).
- FSS changes were not significantly different between the AG arms and placebo (Figure 1).
- There was an overall improvement in the placebo and AG arms for all PROs (Table 2).
- PRO values conversion to 0-100 score scale also showed high proportion of participants who improved ≥10 points in the AG and placebo arms: FSS 72%, PHQ-9 59%.
- 63%: IBI 47%: PROMS Fatigue 76%, BFI "improved right now"; ESS 75%: 72%: MOS-HIV energy-fatigue.

There was trend for the mean FSS to be lower on the AG arms than placebo. However, there are not significant differences in FSS between placebo and either of the AG arms.

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