**INTRODUCTION**

Donepezil, a reversible acetylcholinesterase inhibitor, is the most prescribed medication for the treatment of dementia of the Alzheimer's type in patients with mild, moderate, and severe dementia. The initial dose of donepezil is 5 mg/d for mild to moderate dementia, which can be increased to 10 mg/d after 4 weeks. Both doses are administered orally once a day screening period followed by 3 treatment days in 21 days. Ratio of once TDSs and 10 mg/d donepezil TDS application with once daily oral donepezil (10 mg/d, 10 mg/d oral donepezil). The initial dose of donepezil is 5 mg/d for mild to moderate dementia, which can be increased to 10 mg/d after 4 weeks. Both doses are administered orally once a day screening period followed by 3 treatment days in 21 days. Ratio of once TDSs and 10 mg/d donepezil TDS application with once daily oral donepezil (10 mg/d, 10 mg/d oral donepezil).

**METHODS**

**Study Design**

This was an open-label, randomized, 3-period, 3-investigator, crossover phase 1 study (NCT00126870) in healthy volunteers. The study consisted of a 28-day screening period followed by 3 treatment periods of 36-day week (Figure 1).

**Safety and Pharmacokinetic Comparison of Once-Weekly Donepezil Transdermal System (TDS) with 10 mg/d Oral Donepezil**

For 5-mg-d donepezil TDSS (dose normalised to 10 mg/d donepezil TDS, and oral donepezil) treatments.

**RESULTS**

**Participant Demographics**

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.6 (12.3)</td>
<td>60.9 (13.3)</td>
<td>59.8 (13.3)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>75.2 (16.7)</td>
<td>72.6 (13.9)</td>
<td>74.1 (15.7)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.70 (0.09)</td>
<td>1.68 (0.10)</td>
<td>1.70 (0.09)</td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
<td>26.2 (4.8)</td>
<td>26.3 (5.1)</td>
<td>26.2 (4.9)</td>
</tr>
</tbody>
</table>

**Pharmacokinetics and Relative Bioavailability**

- **10 mg/d oral donepezil**
  - **Cmax,ss**: 41.0 (14.2) µg/mL
  - **tmax**: 12.0 (4.0) h

- **10 mg/d donepezil TDS**
  - **Cmax,ss**: 64.9 (23.7) µg/mL
  - **tmax**: 24.0 (8.4) h

**Safety**

- **Related TEAEs**
  - **Nervous system disorders**: Abdominal pain, DIarrhea
  - **Muscle spasms**: 2 (3.6)
  - **Other tissue disorders**: Skin abrasion

**CONCLUSIONS**

- For 10-mg-d donepezil TDSS versus oral donepezil, the 80% CI for the geometric mean ratio of 1.00 to 1.25 range for key plasma concentration time points was contained within the range for bioequivalence (Table 3).
- **Table 3. Relative bioavailability of 10 mg/d and 5 mg/d donepezil TDS and oral donepezil**

**Table 4. Overview of treatment-emergent AEs and most frequently reported AEs in ≥ 15% of participants**

**Table 5. AEs in ≥ 10% of participants**

**Table 6. Overview of treatment-emergent AEs and most frequently reported AEs in ≥ 15% of participants**

**Figure 1. Study design**

- **Logistic regression**
- **Multiple regression**

- **Figure 2. Mean steady-state (5 week) plasma concentration-time curves for 5 mg/d donepezil TDS, 10 mg/d donepezil TDS, and 10 mg/d oral donepezil**

- **Figure 3. Mean steady-state (5 week) plasma concentration-time curves for 5 mg/d donepezil TDS, 10 mg/d donepezil TDS, and 10 mg/d oral donepezil**

**Poster P3.384**

- **Bioequivalence and Safety Comparison of Once-Weekly Donepezil Transdermal System (TDS) with 10 mg/d Oral Donepezil**

**References**

- ProPhase Associates, Inc. and KemPharm, Inc. and funded by Corium, Inc, Grand Rapids, MI, USA.
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