A Pilot Study of a New Thrombolytic Agent for Acute Ischemic Stroke in Taiwan Within A Five-Hour Window

Han-Hwa Hu, MD; Michael Mu-Huo Teng, MD; Li-Chi Hsu, MD; Wen-Jang Wong, MD; Lee-Min Wang, MD; Yun-On Luk, MD; Chang-Ming Chern, MD; Bing-Wen Soong, MD, PhD; Wen-Yung Sheng, MPH

Background and Purpose—This study was the first clinical trial in Taiwan of a new thrombolytic agent human tissue urokinase type plasminogen activator (HTUPA) in patients with acute ischemic stroke.

Methods—Patients were treated with a single bolus intravenous HTUPA under an open-label dose escalation design within 5 hours after symptom onset. Safety outcomes were assessed by symptomatic and asymptomatic intracerebral hemorrhage (ICH) as well as other bleeding episodes. Preliminary efficacy was measured by National Institutes of Health Stroke Scale (NIHSS).

Results—Three doses of HTUPA (0.3 mg/kg, 0.35 mg/kg, and 0.4 mg/kg) were administered to 33 patients, with the majority of patients (n=29) receiving 0.3 mg/kg. Two cases of fatal ICH occurred: 1 in the patient who received 0.4 mg/kg and the other in the 0.3 mg/kg group. Asymptomatic ICH occurred in 6 patients. Other treatment-related serious adverse events were ecchymosis, hematuria, and upper gastrointestinal bleeding, which were completely recovered. At day 90, in patients treated with 0.3 mg/kg within a 0- to 5-hour window, 34% reached NIHSS scores 0 to 1, whereas of those treated within 0 to 3 hours, 86% reached this score.

Conclusion—Intravenous HTUPA, given at 0.3 mg/kg as a bolus injection within 5 hours after symptom onset, had an acceptable safety and efficacious profile in patients with acute ischemic stroke. (Stroke. 2006;37:918-919.)

Key Words: stroke, ischemic thrombolytic therapy
incidences in Taiwanese patients treated with HTUPA at 0.3 mg/kg with 1 intravenous bolus injection (Table) were within the limits of those reported for t-PA trials performed mostly in Western countries. However, interpretation of this study is limited because of the small number of patients and the lack of placebos. Further assessment of HTUPA would include using lower dosages, comparison with t-PA in Taiwanese patients, as well as trials of HTUPA in patients of other ethnic origins.

### Discussion

This study was the first clinical trial of a new thrombolytic agent in Taiwanese patients with acute ischemic stroke. When the study began, there were 2 major concerns: 1 being the newness of the test agent HTUPA and the other, the preponderance of intracranial vascular lesion in the Orientals over the Occidental people. Our study showed that the ICH incidences in Taiwanese patients treated with HTUPA at 0.3 mg/kg with 1 intravenous bolus injection (Table) were within the limits of those reported for t-PA trials performed mostly in Western countries. However, interpretation of this study is limited because of the small number of patients and the lack of placebos. Further assessment of HTUPA would include using lower dosages, comparison with t-PA in Taiwanese patients, as well as trials of HTUPA in patients of other ethnic origins.

### Table: Incidence of ICH Within 24 Hours After HTUPA Administration and Its Clinical Outcomes

<table>
<thead>
<tr>
<th>Outcomes of Dosage of HTUPA</th>
<th>0.3 mg/kg (n=29)</th>
<th>0.35 mg/kg (n=3)</th>
<th>0.4 mg/kg (n=1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic ICH, n (%)</td>
<td>5 (17)</td>
<td>1 (33)</td>
<td>0</td>
</tr>
<tr>
<td>Symptomatic ICH, n (%)</td>
<td>1 (3)</td>
<td>0</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Person who had symptomatic ICH died at day 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Person who had symptomatic ICH died at day 10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIHSS at baseline median (range)</td>
<td></td>
<td>19 (12–20)</td>
<td>13 (11–16)</td>
</tr>
<tr>
<td>NIHSS at day 90 median (range)</td>
<td>15 (5–22)</td>
<td>5 (4–12)</td>
<td>38 (38)</td>
</tr>
</tbody>
</table>

### References

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