Noncompartmental Pharmacokinetics of Tigecycline in Phase 3 Studies of Patients with Complicated Skin and Skin-Structure and Intra-Abdominal Infections

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ABSTRACT

Tigecycline is the first glycylcycline to reach Phase 3 clinical trials and is active against multidrug-resistant organisms. Four Phase 3 studies have examined tigecycline for the treatment of complicated skin and skin-structure infections (cSSSI) and intra-abdominal infections (IAI). Pharmacokinetics (PK) of multiple-dose tigecycline in subsets of patients with cSSSI and cIAI from these three studies have been examined and compared.

Patients enrolled in Studies 3074A1-301-WW and 3074A1-306-WW consisted of hospitalized patients with cSSSI. Patients enrolled in Study 3074A1-305-WW had clinical signs and symptoms of cIAI. Patients enrolled in Study 3074A1-101-US had clinical signs and symptoms of cIAI, but had received placebo (100 mL normal saline) IV doses for 5 days followed by IV tigecycline (100 mg) every 12 hr for 14 days.

RESULTS

24 patients from Study 3074A1-301-WW (12 cIAI, 12 cSSSI), 40 patients from Study 3074A1-306-WW (18 cIAI, 22 cSSSI), and 10 patients from Study 3074A1-305-WW (3 cIAI, 7 cSSSI) were included in this PK analysis.

Patients received either cSSSI or cIAI participating in one of three Phase 3 trials.

OBJECTIVE

To evaluate the noncompartmental PK parameters of tigecycline in subsets of patients with either cSSSI or cIAI participating in one of three Phase 3 trials.

METHODS

Patients enrolled in Studies 3074A1-301-WW and 3074A1-306-WW consisted of hospitalized patients with cSSSI. Patients enrolled in Study 3074A1-305-WW had clinical signs and symptoms of cIAI. Patients enrolled in Study 3074A1-101-US had clinical signs and symptoms of cIAI, but had received placebo (100 mL normal saline) IV doses for 5 days followed by IV tigecycline (100 mg) every 12 hr for 14 days.

Patients were randomly assigned (in a 1:1 ratio) to receive:

- TIG (intravenous [IV] or intramuscular [IM] for up to 2 weeks) for patients with cSSSI
- TIG or placebo (IV) for a minimum of 48 hr in patients with cSSSI

Patients had hospitalization until the end of the test article administration.

The subsets of patients receiving IV tigecycline are included in this presentation.

Studies 3074A1-301-WW and 3074A1-306-WW:

- Patients received a 100-mg IV infusion of tigecycline followed 12 hr later by 50 mg IV tigecycline twice a day (approximately every 12 hr).
- Additionally, patients received placebo (100 mL normal saline) for doses during the first 48 hr after the first IV tigecycline dose.
- All patients received tigecycline 0.5 hr in duration.

Studies 3074A1-305-WW:

- Patients received a 100-mg IV infusion of tigecycline followed 12 hr later by 50 mg IV tigecycline twice a day (approximately every 12 hr).
- All patients received tigecycline 1 hr in duration.

RESULTS

Concentrations of Tigecycline within a Dosage Interval After a 100-mg Loading Dose Followed 12 hr Later by 50 mg tigecycline (n = 24) in Patients with cIAI (Study 3074A1-301-WW).

Table 2: Comparison of Mean PK Parameters at Steady-State of Tigecycline in Healthy Subjects and Patients with cSSSI

<table>
<thead>
<tr>
<th>PK Parameter</th>
<th>Healthy Subjects</th>
<th>Patients with cSSSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (µg/mL)</td>
<td>0.145 (16)</td>
<td>0.162 (31)</td>
</tr>
<tr>
<td>Cmin (µg/mL)</td>
<td>0.140 (52)</td>
<td>0.152 (31)</td>
</tr>
<tr>
<td>AUCss (µg·hr/mL)</td>
<td>3.07 (12)</td>
<td>3.04 (27)</td>
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</table>

CONCLUSIONS

These studies demonstrate no substantial differences in steady-state PK parameters of tigecycline between healthy subjects and patients with cSSSI and cIAI, suggesting similar exposures to tigecycline among all groups studied.