PHASE I DOSE-ESCALATION STUDY OF MONOCLONAL ANTIBODY VRC07-523LS IN HEALTHY ADULTS

1061

METHODS AND SUBJECTS

20 mg/kg IV or 5 mg/kg SC. Determination of serum neutralization activity and detection of anti-VRC07 antibodies were one of the outcomes of this clinical trial. The study included 20 mg/kg IV or 5 mg/kg SC administrations, with three doses per group. Safety was assessed in the first 12 weeks after the single administration of VRC07-523LS.

RESULTS: Neutralization

Table 3. Serum concentration and potency of VRC07-523LS and VRC01LS at 12 weeks post administration

<table>
<thead>
<tr>
<th>Virus and group</th>
<th>Serum concentration (mg/mL)</th>
<th>MEAN (SD)</th>
<th>AUC (mg*d/mL)</th>
<th>Fold difference*</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRC07-523LS</td>
<td>40 mg/kg IV</td>
<td>1.103 (0.492)</td>
<td>20 mg/kg IV</td>
<td>1.37 (0.71)</td>
<td>1.78</td>
</tr>
<tr>
<td>VRC01LS</td>
<td>1.164 (0.51)</td>
<td>1.23 (0.79)</td>
<td>1.44</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

CONCLUSIONS AND RESULTS

25 subjects were evaluated for safety, PK parameters, and serum neutralizing activity following VRC07-523LS administration. Both local and systemic reactogenicity were mild to moderate when reported. No serious adverse events or dose-limiting toxicities were observed.

Maximum (Fold) and 4 weeks post-infection serum concentrations increased proportionally with antibody dosages from 1.40 to 4.08 mg/kg IV.

VRC07-523LS rapidly achieved concentrations greater than 10 mg/mL following 5 mg/kg SC administration. Later concentrations in this group were about half of those seen following 5 mg/kg IV.

The overall compartmental half-life (t1/2) of VRC07-523LS is currently estimated to be 330 days.

Analysis of PK data after multiple administrations is ongoing.

Serum concentrations at 4 weeks post administration demonstrated greater persistence and were more than 4 times higher than levels from prior studies with VRC01 in healthy adults.

While the serum concentrations of VRC07-523LS were lower than previous studies with VRC01LS at 12 weeks (7), the increased potency of VRC07-523LS may allow for lower antibody concentrations to achieve the same functional neutralization.

The potent neutralizing activity and breadth of VRC07-523LS make this antibody a leading candidate for inclusion in HIV-1 prevention and therapeutic strategies.

REFERENCES


ACKNOWLEDGMENTS

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