Phase Ib study of NGR-hTNF, a selective vascular targeting agent (VTA), in combination with cisplatin in patients with refractory solid tumors

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Table 1. Patients characteristics and preliminary antitumour activity by dose levels

<table>
<thead>
<tr>
<th>Grade</th>
<th>DL=0.2 µg/m²</th>
<th>DL=0.4 µg/m²</th>
<th>DL=0.8 µg/m²</th>
<th>DL=1.6 µg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PR</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PD</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Safety

- 77 cycles of NGR-hTNF (mean, 3.3; median, 2; range, 1-10).
- 65% of cycles were evaluable (mean, 3.0; median, 2; range, 1-10).

Method

- Phase I trial
- Standard 3×3 escalation
- Dosing scheme for NGR-hTNF
- Fixed dose of cisplatin 80 µg/m²

Results

- At dose level of 0.8 µg/m², a lung cancer patient pretreated with cisplatin, had a partial response, lasting 7.2 months. A further lung cancer patient, pretreated with 6 regimens including cisplatin, had a significant tumor shrinkage (-28%) maintained for 7.1 months. Additionally, 4 patients had stable disease for a median time of 4.7 months.

Pharmacokinetics and pharmacodynamics

- NGR-hTNF and soluble TNF receptors R-1 and R-2 observed with a 2-hour delay between NGR-TNF and cisplatin administration.

CONCLUSION

- The combination of NGR-hTNF at 0.8 µg/m² with cisplatin at 80 µg/m² showed a favorable toxicity profile and promising activity in heavily pre-treated patients, and will be further developed in platinum-sensitive tumours.

References