Innovative less invasive therapeutic arteriogenesis induced by nanoparticle-mediated endothelial cell-selective drug delivery system

Target disease: chronic limb ischemia

Department of Surgery and Science, Kyushu University Hospital

Synopsis

The objective of this project is to conduct exploratory translational research and an investigator-initiated trial to establish an innovative less-invasive nano-medical treatment for chronic limb ischemia.

We developed endothelial cell selective nano-DDS technology and demonstrated the efficacy of curative angiogenic treatment based on this technology in three hindlimb ischemic models (mouse, rabbit, cynomolgus monkey). In the NEDO Translational Research Project, we conducted a safety study of PLGA nanoparticle incorporated with pitavastatin in compliance with GLP and obtained the maximum no observed adverse effect level. Manufacturing of this nanoparticle preparation in compliance with IND GMP has been determined and an investigator-initiated trial is in progress. This promising nanoparticle preparation will be a world standard treatment developed in Japan if its efficacy is demonstrated in the clinical trials. This project is expected to improve QOL and life prognoses for patients with severe ischemic diseases. Moreover, establishment of internationally competitive nano-medical technology will enable development of new medical industries and employment generation that will enhance the competitiveness of Japanese industries.

Promotion of collateral arteries in the rabbit/monkey chronic hindlimb ischemic models

Rabbit model: introduction of curative angiogenesis with Pitava-NP (no response to statin alone)

Eight weeks after initiation of administration

Number of collateral arteries

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Single dose group</th>
<th>3-day administration group</th>
<th>6-day administration group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pitava-NP 0.5 mg/kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P&lt; 0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiogenesis score</td>
<td>0.2</td>
<td>0.6</td>
<td>1.0</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Non-human primate (cynomolgus monkey) model: efficacy of Pitava-NP supported by angio-CT finding of angiogenesis

Promotion of collateral arteries

Intellectual property information: Patented

Related keywords: pitavastatin, vascular endothelial cell selective nano-DDS, angiogenesis, chronic limb ischemia