

International Conference on

Pharmaceutical Chemistry

September 05-07, 2016 Frankfurt, Germany

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Promising clinical outcome of HPMA-polymer conjugated-pirarubicin (THP) [P-THP], which exerts three steps for cancer selective delivery

The HPMA-polymer-conjugated-THP [P-THP] showed sustain drug (pirarubicin) release only at tumor tissue, but no significant delivery to normal tissues was seen. The drug uptake studied by human pancreatic cancer cells showed that THP is taken-up more than 30-40 fold than another anthracyclines, eg. doxorubicin. The conjugate contains about 10% THP/polymer (w/w), and exhibits about 40 kDa. *In vivo* evaluation of antitumor activity in experimental tumors revealed excellent delivery to primary and metastatic tumors, and remarkable antitumor activity was found below toxicity level. P-THP is tolerated more than 7-10 times of free THP equivalent in mice. We conclude superiority of P-THP is attributed to three points in regard to tumor selectivity: EPR-effect, tumor pH for drug-release and drug-uptake by transporter. Having these data in hand we applied P-THP to various human cancer patients, mostly from hospice with stage IV cancers, or inoperable and / or refused conventional chemotherapy, and asked present treatment. The dose of P-THP ranged 50 to 100 mg iv once, free-THP-equivalent per week to 4 wks. Patients received multiple iv infusions. Patch-tape of isosorbide-dinitrate for NO release or ACE-inhibitor (such as verapamil) was used to overcome tumor embolism. After iv-infusion prostate cancer became normal with PSA value in 3/4 pts in 4 wks, and 1 pt showed stabilization. Ovarian cancer pt (2/2) showed great improvement in CA19-9 and CA125 after 2-3 iv-infusion. Metastatic cancer in the bone, lung and lymph nodes were cleared. No toxicity was revealed in blood-counts, liver, kidney and neuronal-functions; no appetite-loss, no hair-loss were seen.

Biography

Hiroshi Maeda is a World renowned expert in macromolecular therapeutics. He created the World first polymeric-conjugate drug, SMANCS, approved for treatment of hepatoma in Japan. Consequently, he discovered the concept of EPR effect of macromolecular-drugs, ubiquitous mechanism for solid tumor selective targeting of polymeric drugs. He received MS, University of California, Davis, Fulbright student, PhD, MD, Tohoku University. He has published more than 450 papers in reputed journals. He was awarded Lifetime-Achievement-Award at Royal-Pharmaceutical-Society, Princess-Takamatsu-Award in Cancer Research, Tomizo-Yoshida-Award, highest award of Japan-Cancer-Assoc., and also selected as most cited influential scientist in pharmacology by Thomson Reuters 2014, and H-index of 89.

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