Evaluation of In-111 DTPA-paclitaxel scintigraphy to predict response on murine tumors to paclitaxel

Tomio Inoue,***** Chun Li,** David J. Yang,* Tetsuya Higuchi,***** Noboru Oriuchi,*****

Dongfang Yu,* Luka Milas,*** Nancy Hunter,*** Sidney Wallace,**

E. Edmund Kim* and Donald A. Podoloff*

Departments of *Nuclear Medicine, **Diagnostic Radiology, and ***Experimental Radiotherapy,
The University of Texas, M.D. Anderson Cancer Center, Houston, USA

****Department of Nuclear Medicine, Gunma University School of Medicine, Japan

Our goal was to determine whether scintigraphy with 111In-DTPA-paclitaxel could predict the response to chemotherapy with paclitaxel. Methods: Ovarian carcinoma (OCA 1), mammary carcinoma (MCA-4), fibrosarcoma (FSA) and squamous cell carcinoma (SCC VII) were inoculated into the thighs of female C3Hf/Kam mice. Mice bearing 8 mm tumors were treated with paclitaxel (40 mg/kg). The growth delay, which was defined as the time in days for tumors in the treated groups to grow from 8 to 12 mm in diameter minus the time in days for tumors in the untreated control group to reach the same size, was measured to determine the effect of paclitaxel on the tumors. Sequential scintigraphy in mice bearing 10 to 14 mm tumors was conducted at 5, 30, 60, 120, 240 min and 24 hrs postinjection of ¹¹¹In-DTPA-paclitaxel (3.7MBq) or ¹¹¹In-DTPA as a control tracer. The tumor uptakes (% injection dose/pixel) were determined. Results: The growth delay of OCA 1, MCA-4, FSA and SCC VII tumors was 13.6, 4.0, -0.02 and -0.28 days, respectively. In other words, OCa 1 and MCA-4 were paclitaxel-sensitive tumors, whereas FSA and SCC VII were paclitaxelresistant tumors. The tumor uptakes at 24 hrs postinjection of In-111 DTPA paclitaxel of OCA 1, MCA-4, FSA and SCC VII were 1.0×10^{-3} , 1.6×10^{-3} , 2.2×10^{-3} and 9.0×10^{-3} % injection dose/ pixel, respectively. There was no correlation between the response to chemotherapy with paclitaxel and the tumor uptakes of ¹¹¹In-DTPA-paclitaxel. Conclusions: Scintigraphy with ¹¹¹In-DTPApaclitaxel could not predict the response to paclitaxel chemotherapy. Although there was significant accumulation of the paclitaxel in the tumor cells, additional mechanisms must be operative for the agent to be effective against the neoplasm. 111In-DTPA-paclitaxel activity is apparently different from that of paclitaxel with Cremophor.

Key words: In-111 DTPA-paclitaxel, paclitaxel, chemotherapy