

Efficacy of repeated injections of CLR 131 (I-131-CLR1404) in a MES SA/Dx5 athymic nude mouse model.

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Abstract Disclosures

Background:

CLR 131 is a novel radioiodinated therapeutic that exploits the selective uptake and retention of phospholipid ethers (PLEs) by malignant cells. Uterine sarcoma (MES SA/Dx5) cells express high levels of P-gp and are known to be a doxorubicin resistant cell line. The cells exhibit a marked cross resistance to several chemotherapy drugs including vinblastine, Taxol®, vincristine, etc. This study evaluates the effect of repeated injections of CLR 131 in MES SA/Dx5 tumor bearing mice and evaluate the ability of CLR 131 to overcome resistance caused by over-expression of the P-gp Multi Drug Resistance (MDR) 'pump'.

Methods:

The MES SA/Dx5 cell line (human uterine sarcoma) was purchased from American Type Culture Collection (Rockville, MD) and maintained in McCoy's 5a media supplemented with 10% fetal bovine serum. Female athymic nude mice (CrI: NU-Foxn1nu); approximately 4-5 weeks of age and between 16-18 g (Charles River, Portage, MI) were injected subcutaneously with 2×10^6 viable cells (in $\sim 100 \mu\text{L}$ Dulbecco's PBS) into the right flank. The study was initiated when tumor size had reached a pre-determined size (approximately $50\text{-}150 \text{ mm}^3$). The mice were given potassium iodide at a concentration of 0.1% in their drinking water to block possible free iodide in the drug formulation. Doses of $\sim 130 \mu\text{Ci}$ and $\sim 145 \mu\text{Ci}$ of CLR 131 were given at Day 0 and Day 7 (N = 6 in treatment group, N = 5 in control group). A single control dose of $\sim 130 \mu\text{Ci}$ of I-127-CLR1404 was given via tail vein injection on Day 0.

Results:

Tumor growth of the treatment group was significantly inhibited. The control group showed exponential growth throughout the study, increasing in volume by an average 21 fold from baseline to day 22 (all control mice died day 23). This compared with a 6 fold increase from baseline in the treatment group.

Conclusions:

The results of the study indicated that multiple injections of CLR 131 on human uterine sarcoma (MES SA/Dx5) tumor bearing model showed a significant inhibition of tumor growth as well as significant survival benefit. The implication is that in this clinically predictive in vivo model CLR 131 is not susceptible to the MDR “pump” and thus CLR 131 might show clinical efficacy in patients with MDR cancer due to P-gp overexpression.

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