

RADIOACTIVE CISPLATIN IN THE TREATMENT OF CANCER

SPECIFICATION

BACKGROUND OF THE INVENTION

Hepatocellular cancer that is non-resectable has had a median survival of six months when treated. A variety of chemotherapeutic agents have been given intravenously, with less-than-realistic results. During the course of investigations in hepatocellular cancer, we found that intr-arterial cisplatin at 50 mg./m² caused a 50 percent remission in 28 patients; and, recently, in 67 patients, a 50 percent response. Thus, 95 patients have had a 50 percent remission, with median survival extended one year to 46 months depending on the classification of the tumor. In addition to these findings, the median survival rate for the worst group of hematomas (AFP+positive) was one year greater than the six months reported from the other therapeutic regimens.

In order to discern why intra-arterial cisplatin was superior to intravenous, we created 195^m cisplatin, and studied the same patient intravenously and intra-arterially. When the drug was given intravenously, less than five percent deposited in the tumor. When the drug was given intra-arterially, 35 to 40 percent of the drug deposited in the tumor, as witnessed by scintigraphic scans. The cisplatin that binds on the hepatoma apparently stays there for a persistent period of time and interrupts DNA metabolism. The use of intravenous cisplatin has had less than a five-percent response rate, and the arterial route is 50 percent or greater.

Having studied the diagnostic distribution of 195^m cisplatin, one realized that the possibility of treating with a radioactive cisplatin exists.

We propose a Phase 1 dose escalation in which 10 mCi of radioactivity, approximately 10 mg of the drug, are substituted for the cold in the infusion of the liver. The dose would be escalated as long as there is no significant hematologic toxicity. The maximum dose we presently give of 50 mg/m² on an



average person would be about 70 to 75 mg. The procedure would take the $^{195\text{m}}$ cisplatin and substitute it for the cold, and the patient would get both the cold cisplatin and the radioactive cisplatin. Cisplatin is also a radiation sensitizer; and, as much, the drug should amplify the therapeutic results from the radiolabeling.

The benefit to the patient would be that the non-radioactive form and the radioactive form would still behave as the drug cisplatin, since it is created radioactive by neutron bombardment and not by chemistry alteration or linkage.

Cisplatin has been used diagnostically in a variety of tumors where its direct infusion is part of the pharmacokinetics. Therapy with $^{195\text{m}}$ cisplatin would have us in hematoma, bladder and brain tumors, but has never been proposed for this use.

A dosage range of approximately 10mCi to 75 mCi or more, depending upon the size of the tumor, may be given in accordance with this invention for all types of solid tumor cancers and not limited to hematomas.

Without further elaboration, the foregoing so fully illustrates my invention that others may adapt and use the invention accordingly.

CLAIMS

1. Use of a composition comprising radioactive cisplatin for the manufacture of a drug for treating cancer.
2. Use according to claim 1 characterized in that the amount of cisplatin is about 10mCi to about 75 mCi.
3. Use according to claim 1 characterized in that the cisplatin is administered intra-arterially.
4. Use according to claim 1 characterized in that the cisplatin is $^{195\text{m}}$ cisplatin.
5. Use of a composition comprising radioactive cisplatin for interrupting DNA metabolism in a cell by administering a therapeutically effective amount of radioactive cisplatin.