



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP130547

Project Title:  
Pharmacokinetics and Pharmacogenomics of 13-cis-retinoic acid in  
treatment outcome of COG Phase III neuroblastoma trials

Award Mechanism:  
Individual Investigator

Principal Investigator:  
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Entity:  
Texas Tech University Health Sciences Center

### Lay Summary:

A drug derived from vitamin A called 13-cis-retinoic acid (isotretinoin or Accutane) is being used to treat the pediatric cancer neuroblastoma. Laboratory studies showed that isotretinoin can change cancer cells to non-growing, non-cancerous cells. Thus, isotretinoin was tested in neuroblastoma patients, and it was found that more patients treated with isotretinoin survived at 5 years after the treatment compared with patients who did not receive isotretinoin. After the study, all neuroblastoma patients receive isotretinoin once the tumor became small after chemotherapy. We have been measuring isotretinoin levels in the blood of most neuroblastoma patients who were treated with the drug in the USA. We found that some patients have very low levels of drug, perhaps because of genetic factors in patients cause some to handle the drug differently in the body. We think that patients with low blood levels will not benefit from the drug, and one reason is that some patients have genetic makeup that affect the way the isotretinoin is handled by the body (metabolism), causing low drug levels in some patients. It is not known which genetic factors affect blood levels of isotretinoin in cancer patients. The purpose of this study is to find out which genetic factors affect blood levels of the drug, and whether patients with those genetic factors have lower isotretinoin blood levels and a less-favorable outcome from therapy. This project will study approximately 800 neuroblastoma patients who are enrolled in large nationwide Children's Oncology Group clinical studies of isotretinoin for the genetic markers, the blood levels of the drug, and survival after treatment. This is the first and largest pediatric study to evaluate the effect of blood levels of isotretinoin and the genetic markers associated with it. The ultimate goal of this study is to optimize the dosing of isotretinoin in patients based on either drug levels measured in the laboratory and their genetic information.