

A Phase II Relapse Prevention Trial of DFMO as a Single Agent in Patients with High Risk Neuroblastoma in Remission

High risk neuroblastoma remains a challenge in pediatric oncology. While most patients are able to attain remission, almost 50% will relapse. Once relapsed, there is currently no curative treatment for these children and relapse is inevitable. As such, new therapeutic approaches are needed to prevent the children from relapsing, allowing them to survive. Relapsed patients who are able to obtain a second remission are not eligible for relapse therapy since they have no evidence of disease and yet they are likely to relapse within 6 months-1year. This study creates a clinical trial for these patients to **prevent the relapse** as our approach to improve outcome in these patients.

These more aggressive forms of NB respond poorly to hormonal and chemotherapeutic approaches, and therefore, there is a great need for antineoplastic agents with novel mechanisms of action. The MYCN protein up-regulates *ornithine decarboxylase (ODC)*, a gene encoding for the ODC enzyme that is pivotal in polyamine biosynthesis. High polyamine content and elevated ODC activities are commonly found in many tumors including neuroblastoma. Therefore, suppression of polyamines in cancer cells is an effective means to reduce tumor cell proliferation. Specific polyamine inhibitors such as DFMO have been evaluated in adult clinical cancer trials (patients on drug for 2 years safely) and shown to prevent formation of polyps and colon cancer. The NMTRC is completing a Phase I study of DFMO in children with neuroblastoma showing safety and tolerability in our patients (www.nmtrc.org, <http://clinicaltrials.gov/ct2/show/NCT01059071?term=dfmo&rank=4>). The NMTRC has agreement from the manufacturer to supply drug for this trial.

GOAL: ODC/polyamines are critical in cancer growth and therefore present a therapeutic target for the treatment and prevention of recurrence of NB. This study will focus on the use of DFMO in high risk neuroblastoma patients that are in remission as a strategy to prevent recurrence and improve survival.