

MCC Clinical Trial Padres Pedal the Cause Fall 2020



A National Phase I Study of Cabozantinib in Combination with 13-*cis*-Retinoic Acid in Children with Relapsed or Refractory Solid Tumors

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Scientific Abstract:

Children with high-risk and relapsed solid tumors have poor outcomes, and novel therapies are needed. Pediatric solid tumors often demonstrate aberrant receptor tyrosine kinase expression and activity, and these kinases therefore represent potential therapeutic targets. Cabozantinib is a small molecule kinase inhibitor with activity against many tumor types, and we have demonstrated that cabozantinib is effective in preclinical models of pediatric solid tumors and has synergistic efficacy when combined with 13-*cis*-retinoic acid. However, the safety and efficacy of the combination of cabozantinib with 13-*cis*-retinoic acid are unknown, and plasma and tumor biomarkers of responses to cabozantinib are not known.

We believe that cabozantinib and 13-*cis*-retinoic acid will be safe and effective in children with relapsed and refractory solid tumors and that levels of cytokines in patient plasma and the activity of signaling pathways in patient tumors will be associated with responses. Our goals are to test the combination of cabozantinib with 13-*cis*-retinoic acid in a national phase I clinical trial for children with relapsed and refractory solid tumors and to evaluate patient plasma and tumor samples to identify biomarkers and signaling pathways that correlate with responses to cabozantinib therapy. These studies will provide important information about the safety and efficacy of a novel therapeutic combination in children with solid tumors and identify biomarkers and signaling pathways associated with treatment responses and will provide support for a novel synergistic treatment combination with the potential to improve the survival rates of children with all forms of cancer.

Lay Abstract:

Children with high-risk and recurrent solid tumors have extremely poor outcomes despite aggressive therapy, and new treatments are desperately needed. Growth factor receptors are proteins on the surfaces of cancer cells that generate signals leading to cancer cell growth and spread, and these receptors therefore represent potential targets for new treatments for many pediatric solid tumors. Cabozantinib is an inhibitor of several key growth factor receptors and kills pediatric solid tumor cells, and the effectiveness of cabozantinib is increased when combined with 13-*cis*-retinoic acid. However, the safety and efficacy of the combination of cabozantinib with 13-*cis*-retinoic acid in children with solid tumors are unknown. We believe that cabozantinib and 13-*cis*-retinoic acid will be safe and effective in children with relapsed and refractory solid tumors and that children will have altered levels of specific proteins in their blood and tumor cells after cabozantinib treatment. We will test the combination of cabozantinib and 13-*cis*-retinoic acid in a national multi-institutional phase I clinical trial for children with relapsed and refractory solid tumors, including brain tumors, and we will also evaluate the levels of proteins in patient blood and tumor samples to determine their association with responses to treatment. The results from this proposed research will provide important information to evaluate a unique treatment combination that could improve the chances of survival in children with all forms of cancer.