

# Proof-of-concept study using dinutuximab and activated natural killer cells leads to a clinical trial

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Neuroblastoma, a disease of immature nerve cells, is the most common solid tumor cancer occurring in children. About 700 new cases are diagnosed in the U.S. each year with approximately half of these children developing high-risk disease, which has a 40 to 50 percent chance of survival.

In 2015, the Food and Drug Administration approved a monoclonal antibody called dinutuximab for treatment of [high-risk neuroblastoma](#). The approval followed a ground-breaking study, led by the Children's Oncology Group and published in the *New England Journal of Medicine*. This pivotal trial halted enrollment earlier than planned because the therapy showed significant improvement in survival over the standard treatment.

"Although dinutuximab is a game-changing treatment in the battle against neuroblastoma, the fact remains—children are still dying from this [disease](#)," said Eugene S. Kim, MD, surgical oncologist at Children's Hospital Los Angeles.

A team, led by Kim, designed basic research studies that would go beyond using tumor-shrinkage as a marker of efficacy and instead focus on recurrent disease and overall survival. The team's approach was to create a model system that more faithfully replicates the patient experience.

Patients with neuroblastoma undergo surgery to remove their tumor and then have subsequent therapy. Children with resistant or [recurrent disease](#) initially improve but then their tumor returns, and they succumb to the disease. For this study, the investigators mimicked the treatment protocol and developed a new, clinically relevant model for studying metastatic disease.

After mice developed neuroblastoma, the tumors were surgically removed but later, metastatic disease recurred in all animals in the study. The mice were then treated with dinutuximab along with activated human natural killer (NK) cells, which are a "supercharged" subset of [white blood cells](#), which actively target and kill cancer cells.

"Not only did we see tumor shrinkage, we saw a reduction in [metastatic disease](#) and a significant increase in survival," said Kim, who is also an associate professor of Surgery at the Keck School of Medicine of USC. Results of the study were recently published in *Clinical Cancer Research*.

The findings were sufficiently compelling that they provided proof-of-concept for a clinical trial at CHLA, which will be enrolling patients in the near future. The study, which will incorporate the use of activated [natural killer cells](#) with dinutuximab therapy in patients, is led by Araz Marachelian, MD, director of the [neuroblastoma](#) program at CHLA and medical director of the New Approaches to Neuroblastoma Therapy (NANT) Consortium.

**More information:** Wesley E. Barry et al, Activated Natural Killer Cells in Combination with Anti-GD2 Antibody Dinutuximab Improve Survival of Mice after Surgical Resection of Primary Neuroblastoma, *Clinical Cancer Research* (2018). [DOI: 10.1158/1078-0432.CCR-18-1317](#)

Provided by Children's Hospital Los Angeles

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