

February 12, 2016

According to a new study by Dr. Mitch Elkind and colleagues, now published online in [Circulation](#), arterial ischemic stroke (AIS) affects at least 2.4 per 100,000 U.S. children every year, and those who survive childhood AIS often face permanent neurological deficits. Established risk factors and symptoms of AIS in adults are rarely present in children, thus, a better understanding of the acute triggers of childhood AIS, and how they relate to chronic risk factors, is necessary to help guide strategies for prevention of stroke in children. There have been several studies to suggest that childhood infections, including varicella zoster virus (VZV), are associated with an increased risk of AIS. In the present Vascular effects of Infection in Pediatric Stroke (VIPs) study, Dr. Elkind and an international team of epidemiological investigators provide “serological evidence that recent, but not past, herpesvirus infection is associated with increased risk of AIS among children.” Acute herpes simplex virus (HSV) infection was the most common, present in 40% of AIS cases. Because herpesvirus infections are treatable with antivirals like acyclovir, this evidence may have important implications for stroke prevention therapies. An [accompanying editorial](#) noted that “while it may not yet be timely to start prolonged treatment with acyclovir, it certainly is timely to pursue further translational studies of this intriguing association between herpesvirus infection and AIS.”

[Recent work](#) by Drs. Yazmín Oda, Fabio Iwamoto, and Teri Kreisl, along with Dr. Howard Fine (Weill Cornell) and colleagues, examined the potential clinical benefit of dual anti-angiogenic therapy—combination enzastaurin and bevacizumab—for recurrent, malignant gliomas. Now published online in [CNS Oncology](#), Oda et al. conducted a similar phase II trial to assess the safety and efficacy of combination tandutinib (a small molecule selective inhibitor of Type III receptor tyrosine kinases, specifically FLT3, c-Kit and PDGFR β) and standard bevacizumab. In keeping with their previous work, the investigators hypothesized that the non-overlapping spectrums of toxicities and different mechanisms of antiangiogenesis in these two treatments would lead to additive inhibition of vascular proliferation and improved anti-glioma efficacy in glioblastomas. Results of this most recent phase II trial showed no clear benefit from adding tandutinib to standard bevacizumab for recurrent glioblastomas, while tandutinib resulted in a severe myasthenic-like muscle weakness with electromyography proven neuromuscular junction pathology in ~10% of treated patients. Looking forward, Dr. Oda expects to serve as principal investigator for other therapeutic trials as well as translational non therapeutic studies for primary and metastatic CNS tumors.

This week, Arturo “Arturito” Estopinan, Jr. (*pictured right*) celebrated his 5th birthday, a major milestone for this child who has a severe myopathy due to thymidine kinase 2 (TK2) mutations. Each year, we look forward to providing an update on Arturito and, thanks to the remarkable care and ongoing fundraising campaign maintained by the Estopinan family, along with efforts by a family in Spain (as well as MDA and NIH grant support), we have more good news to report. Drs. Catarina Garone, Carlos Lopez, and Michio Hirano have demonstrated efficacy of deoxynucleotide and deoxynucleoside therapies in a Tk2 mouse model. Under a compassionate-use protocol, Arturito has been receiving these treatments for three years, during which he has grown bigger and stronger. Over the last year, Arturito regained the ability to stand briefly, with support, and used his hands to play with toys! With the technology transfer office, [Columbia Technology Ventures](#), we are developing a strategy for advancing this promising therapy. Stay tuned!



Important Lectures Next Week:

There will be no Grand Rounds on Friday, February 19 due to the Residency In-service Training Examination scheduled for that date. Grand Rounds will resume, as usual, on Friday, February 26, at 1:15 pm, in the NI Auditorium.

Enjoy the long weekend!

Richard Mayeux, MD, MSc