TransportNPC

Perspectives on the TransportNPC Trial

Lise Lund Kjems, MD, PhD

Dear Niemann-Pick C Community,

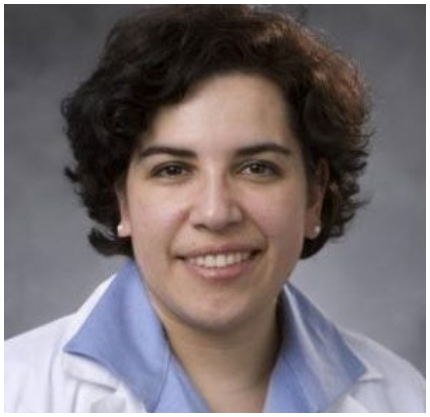
In my first few months leading the clinical development effort for TransportNPC™, our Phase 3 program for NPC, I have received several questions about clinical research in general. People have asked me to describe the steps involved and how members of the NPC community can get involved. To respond to some of these important questions, we have invited Dr. Loren Peña, clinical geneticist at the Department of Pediatrics at Cincinnati Children's Hospital, to share her insights. I hope you find it helpful – let me know!

As we reflect on developments related to NPC in the past 12 months, we have seen both challenges and reasons for hope. Our goal at Cyclo is to work to address these challenges while bringing new opportunities for hope to patients and caregivers. We are working relentlessly with our clinical trial sites to advance the TransportNPC trial as quickly as possible. And, thanks to you and so many other patients and families who work with us, every day we advance our understanding of NPC through our clinical programs and discussions with caregivers and medical experts. Please accept our sincere gratitude for sharing your journeys with NPC with us and enabling us to better understand how this disease affects your lives.

We send you our best wishes for the New Year. May you be surrounded by the support of family and friends, and with the knowledge that there are people around the world who are dedicated to bringing more hope to this deserving community.

Best wishes,

Lise Lund Kjems, MD, PhD
Chief Medical Officer
Cyclo Therapeutics



Loren Peña, MD, PhD

Dr. Loren Peña is a clinical geneticist and associate professor in the department of pediatrics at Cincinnati Children's Hospital. She is a specialist in the treatment of Niemann-Pick disease and other rare genetic diseases and has extensive experience in clinical research.

Understanding Clinical Trials

Q: Can you describe the process for clinical research to develop treatments for NPC?

Clinical research starts with what we understand about the biology of the disorder and any data that exists and supports the use of a particular agent for the disorder. In the case of NPC, the initial work had to do with finding drug candidates that restored cholesterol transport from the lysosome (a sub-compartment in cells) to the cell surface. Once there is a candidate, we need to understand if it shows promising activity in model organisms such as mice, rats and non-human primates, as well as the safety profile of the drug, and a range of potential dosages for use in humans. When we have that information, we can start to design a plan for testing the investigational drug in humans. This planning of course requires a dialogue with the Food and Drug Administration in the USA, or a regulatory agency in the relevant country/continent, and agreement with the regulatory agency on the investigational plan. In the case of candidate treatments that are approved for other indications, we have safety data for use in humans, which is helpful in those conversations with regulatory agencies as we make a plan for testing the investigational drug for NPC.

Q: Can you talk a bit about what is unique or especially challenging about doing clinical research in NPC?

NPC is a rare disorder, and as such there is a limited pool of eligible participants for clinical research. When we develop a protocol for a clinical trial, we need to keep in mind endpoints for the study and eligibility criteria. The endpoints may be neurological, gastrointestinal, or functional. Eligibility may be partially restricted to the safety profile of the candidate drug. When we are testing different drugs in different studies, the pool of prospective participants shrinks and, as exciting as having multiple candidate drugs may be, this also restricts the bandwidth of a clinical trial. This is a challenge and a unique situation for rare disorders. It also challenges us as a community to think creatively about how we can design a clinical trial that utilizes biomarkers and surrogate endpoints that can serve as proxies for clinical outcomes.

Q: Can you talk a bit about the symptoms of adult-onset NPC and what patients and families should look for? How does adult-onset NPC differ from onset in infancy or childhood?

NPC is a mysterious disorder in that multiple presentations are possible across the age span. In adults, the symptoms may overlap with psychiatric symptoms, hence NPC may be under-diagnosed in adults. However, there are other adult presentations such as abnormal postures, problems with balance, and unusual eye movements that may trigger the appropriate investigations.

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Q: What are some steps that patients or caregivers can take to support clinical research?

I say that information is power. I recommend finding out what studies are available, what the criteria for eligibility are, and the safety profile for the drug that is being tested. Study teams are available to review the trial with interested parties, and requesting this type of information does not obligate the family to participate. Even participation in a non-interventional study, such as a natural history study, can be highly valuable, as a longitudinal understanding of the course of a disorder can inform clinical trial endpoints. Natural history studies can take decades to complete and offer highly valuable information to the rare disease community. Every bit of participation helps.

Q: Are there any steps that the research community can take?

Nowadays, engagement with family and patient groups is very important, as we are all vested stakeholders in this rare disease space. Eliciting input from patients and caretakers in terms of priorities for treatments is beneficial. Communicating with patients and caretakers about opportunities for participation in clinical research opportunities is also key.