



The FDA needs to be more flexible in assessing treatments for rare diseases, like the one that seemed to help my son

By Karen Quandt

Sept. 7, 2022

Maria Fabrizio for STAT

Every time I read about clinical trials testing possible treatments for rare diseases, I think of my son, Ty, whose brief but successful foray into such trials highlights their value and their devastating limitations.

Ty was born in Pocatello, Idaho, in October 1996 with green eyes, a big personality, a great sense of humor, and — as we finally learned eight years later — a rare and fatal disease called Niemann-Pick type C.

He appeared to be healthy at birth, and hit all of his first developmental milestones of walking and talking and growing. Yet we realized that he had trouble moving his eyes upward, and had to move his whole head to look up. Then his fine motor skills and balance began to lag, and he had difficulty learning. An enlarged spleen complicated the picture. Ty was eventually diagnosed with Niemann-Pick type C.

Meet us in DC this September 15th for conversation and a cocktail hour on how to align science and policy to bring treatments to the patients who need them.

This condition interferes with the body's ability to transport cholesterol and other fats into cells. Large amounts of them accumulate in the liver, spleen, and brain. This metabolic disorder leads to a series of neurological problems that are ultimately fatal.

With his diagnosis established, Ty's neurologist treated his neurological symptoms. We also turned to pulmonologists, physical therapists, occupational therapists, special education teachers, and multiple caregivers to help give Ty the care he needed.

Despite this attention and work, Ty's function continued to decline, though he never lost his sense of humor. One day as he floated in the bathtub, he called out, "Look Mom, I'm Titanic!"

With help from the Make-A-Wish Foundation, Ty got to meet Joe, a gorilla living in Georgia. Ty was awed by Joe's size and strength. Joe seemed to enjoy the attention and even took celery from Ty, who handed it to him through the bars of Joe's enclosure.



Ty holding a mouse engineered to have Niemann-Pick type C, the rare disease he was born with *Courtesy Karen Quandt*

His favorite movie was "A Christmas Carol" because, as he once told me, Tiny Tim did not die.

By the time Ty was 19 years old, he could talk but walked only with assistance and needed to be tube fed because he had difficulty swallowing. Niemann-Pick type C causes dementia, which made conversation difficult and caused learning disabilities. He was also having multiple seizures every day, and so needed around-the-clock assistance.

We had heard about an experimental drug called VTS-270 (adrabetadex) being developed by Vtesse to treat Niemann-Pick type C. The drug binds cholesterol at a cellular level. We were able to enroll Ty in a clinical trial of the drug in February 2016.

The earlier someone starts a therapy for a neurodegenerative disease like Niemann-Pick type C, the better the results might be. Ty was getting VTS-270 late in the disease process, so we weren't sure if it would help him. But we enrolled him anyway because, even if it didn't help him, it might help get the drug approved by the Food and Drug Administration so other children and their parents wouldn't have to face this rare disease without a treatment to fight it.

Every two weeks, we made the 7-hour trip from our home outside of Seattle to Chicago to see Elizabeth Berry-Kravis, a physician at Rush University Hospital, who gave Ty an infusion of VTS-270 via lumbar puncture so the drug could cross the blood-brain barrier and treat the cells in the brain as well as those in his body.

As part of the trial, Ty was given neurological tests every two months to see how his nervous system was reacting to the medicine. One of these was a nine-hole peg test to check his fine motor coordination. Ty had to put each of the nine little pegs into their holes with his left hand, and then repeat the process with his right hand. At the beginning of the trial, Ty couldn't put any pegs into their holes. But after six months of biweekly doses of VTS-270, he was able to put all nine pegs in all nine holes with both his left hand and right hand.

Ty was delighted that his hands were doing what his mind was telling them to do. I believed I was witnessing the reversal of a neurodegenerative disease, and cried as I watched him place the pegs.

After 16 months on the medication, Ty was able to stand up from a sitting position on his own and walk a few steps by himself, something he had not been able to do for years. He was feeling better and his mood had improved. We were hearing similar stories from other families who had children in the VTS-270 trial.

Ty died three months later, in September 2017, of aspiration pneumonia, triggered by one of the seizures he routinely experienced. He was 19 months into the trial and three weeks shy of his 21st birthday.

Drug trials for common conditions like diabetes and heart failure can include thousands of participants; their size makes it easier to achieve better randomization and see statistical significance of the drug's efficacy. Trials are much more difficult for rare diseases. The VTS-270 trial included just [56 children and young adults](#)⁷, some in the U.S. and others around the world, which limited the interpretation of the results.

A review of the evidence in late 2020 [showed no difference in progression](#)⁸ between the participants treated with VTS-270 and those given placebo. As Berry-Kravis told me, that lack of difference was likely due to a problem with the trial, not the drug — the control patients' conditions did not worsen due to problems with unequal randomization, which can happen in small trials and those involving variable diseases, and because the trial did not last long enough to see definitive progression in the patients enrolled.

So far, the FDA has declined to look at long-term outcomes with VTS-270 that have been based on comparisons to a natural history study and [within-patient comparisons](#)⁹. The drug, now being [developed by Mandos Health](#)¹⁰, is being given to people with Niemann-Pick type C as part of the company's [Expanded Access Program](#)¹¹.

A paradigm shift is needed in the way the FDA assesses and approves drugs for rare diseases, which are held to the same standards and requirements as those for common diseases. The FDA is not following the [mandate](#)

[from Congress](#)¹³ to look at other clinical trial models, including natural history studies, in rare diseases. This creates an impossible barrier to approval.

Cost also contributes to this barrier.

Developing any new medicine is a costly undertaking. Companies aren't in this business for public good — shareholders expect profits. Setting the price of a drug that several hundred people will use in a year is far different than setting the price for one that will be taken by millions of people. The cost of rare disease drugs could threaten the U.S. health care system.

There are 7,000 or so rare diseases affecting 25 million to 30 million

Americans. The average drug approved for a rare disease [costs \\$118,820 per year](#)¹⁴. If a single drug were approved for 10% of rare diseases, the total cost would exceed \$350 billion annually, more than 10% of the total amount the U.S. spends on health care.

The FDA is [currently prohibited](#)¹⁵ from considering cost or value in its decision making, which needs to change. The FDA and federal payers, including Medicare, must be allowed to consider drug costs and outcomes, and this process should factor into federal investment in drug discovery.

Congress needs to work for these changes and fix the broken drug approval process so these medicines can be approved to treat rare diseases.

Karen Quandt is a registered nurse and advocate for people with Niemann- Pick type C.

Links

1. <https://www.parsintl.com/publication/stat/>
2. <https://www.statnews.com/stat-events>
3. <https://www.statnews.com/privacy/>
4. <https://www.statnews.com/wp-content/uploads/2022/09/Ty-with-NPC-mouse.jpeg>
5. <https://www.statnews.com/signup/>
6. <https://www.statnews.com/2022/07/22/moonshot-warp-speed-for-rare-diseases/>
7. <https://mallinckrodt.gcs-web.com/static-files/e0712994-a013-4658-b8be-0a3bc4da0c5b#page=6>
8. <https://parseghianfund.nd.edu/2021/01/20/adrabetadex-update-from-mallinckrodt-jan-2021/>
9. <https://pubmed.ncbi.nlm.nih.gov/28803710/>
10. <https://www.statnews.com/wp-content/uploads/2021/05/mallinckrodt-sale-mandos.pdf>
11. https://mandoshealth.com/communications/September_16_2021
12. <https://www.statnews.com/2021/11/10/sequencing-whole-genomes-helps-diagnose-more-rare-diseases/>
13. <https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/21st-century-cures-act>
14. <https://hbr.org/2017/04/the-cost-of-drugs-for-rare-diseases-is-threatening-the-u-s-health-care-system>
15. <https://www.drugs.com/fda-approval-process.html>
16. <https://www.statnews.com/2022/09/07/the-fda-needs-to-be-more-flexible-in-assessing-treatments-for-rare-diseases-like-the-one-that-seemed-to-help-my-son/>mailto:kquandt9@gmail.com
17. <https://www.statnews.com/topic/advocacy/>
18. <https://www.statnews.com/topic/rare-disease/>
19. <https://www.statnews.com/topic/research/>

Karen Quandt is a registered nurse and advocate for people with Niemann-Pick type C.

About the Author Karen Quandt

kquandt9@gmail.com 16

 Add a Comment

Create a display name to comment This name will appear with your comment

Links

1. <https://www.parsintl.com/publication/stat/>
2. <https://www.statnews.com/stat-events>
3. <https://www.statnews.com/privacy/>
4. <https://www.statnews.com/wp-content/uploads/2022/09/Ty-with-NPC-mouse.jpeg>
5. <https://www.statnews.com/signup/>
6. <https://www.statnews.com/2022/07/22/moonshot-warp-speed-for-rare-diseases/>
7. <https://mallinckrodt.gcs-web.com/static-files/e0712994-a013-4658-b8be-0a3bc4da0c5b#page=6>
8. <https://parseghianfund.nd.edu/2021/01/20/adrabetadex-update-from-mallinckrodt-jan-2021/>
9. <https://pubmed.ncbi.nlm.nih.gov/28803710/>
10. <https://www.statnews.com/wp-content/uploads/2021/05/mallinckrodt-sale-mandos.pdf>
11. https://mandoshealth.com/communications/September_16_2021
12. <https://www.statnews.com/2021/11/10/sequencing-whole-genomes-helps-diagnose-more-rare-diseases/>
13. <https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/21st-century-cures-act>
14. <https://hbr.org/2017/04/the-cost-of-drugs-for-rare-diseases-is-threatening-the-u-s-health-care-system>
15. <https://www.drugs.com/fda-approval-process.html>
16. <https://www.statnews.com/2022/09/07/the-fda-needs-to-be-more-flexible-in-assessing-treatments-for-rare-diseases-like-the-one-that-seemed-to-help-my-son/mailto:kquandt9@gmail.com>

17. <https://www.statnews.com/topic/advocacy/>
18. <https://www.statnews.com/topic/rare-disease/>
19. <https://www.statnews.com/topic/research/>