Question: Could you please comment on n-of-1 trials and how a clinician might do one?

Answer: CNF's 2021 Symposium at CNS focused on shortening the diagnostic odyssey. The presentation by Dr. Christelle Moufawad El Achkar discussed n-of-1 trials in detail. You can view her slides and her answers to the Q&A at childneurologyfoundation.org/diagnostic-odyssey

Question: Families who raise funds for specific research initiatives generally have an expectation that their child will have access to the intervention, perhaps ahead of / instead of another child. The trial has to be designed to answer the scientific question - not to ensure a specific child is eligible. How to navigate this? This is especially relevant as the number of gene tx trials increases – the industry will not fund them all - and a child may "age out" of eligibility while funds are being raised.

Answer: This is mostly about clear communication and transparency from the beginning. Families need to know that unless it is an N=1 trial, the goal is to design the study that is most likely to benefit the most people with the condition which may mean their child does not qualify. Having open communication with the advocacy groups or fundraisers from the beginning about the design of the trial and the expectations is important. When a trial is designed contrary to what the caregivers expected, being clear about the reasoning for those changes is necessary.

The hope of therapeutic advancement often comes at a cost for legacy families (those whose children are past the therapeutic window or those who have died). For some, participating gives purpose to their pain and continues their child's legacy to benefit others. This article speaks to the DMD community -- how families who advocated FOR YEARS never benefitted personally from it and lost their children. A bittersweet, unique form of grief.

Question: If a medication is approved in Europe or other non-US location but fails to get approved in US what is the most appropriate way to continue these therapies?

Answer: This would have to be done under a compassionate use IND in the US, provided the company is open to such a program.

Question: Paperwork for compassionate use after trial is really time-consuming – do you have any suggestions?

Answer:The main efficiency that can be possible is if the manufacturer will agree to a multi-patient program, to reduce the paperwork per patient. This still will not make it seamless, but certainly will reduce the totality of the burden.

Question: Please discuss the following scenario: A trial has ended with no evidence for efficacy, yet some participant families are convinced their child is better after receiving the study drug. The drug is not available commercially. How do you best support that family and their needs?

Answer: You likely would not convince a parent that the benefit is a placebo effect (and as a clinician, you may also believe that it benefited a specific patient, even if the trial didn't generally show promise).
I would start by understanding why there was no evidence of efficacy. Was efficacy seen in some, but not enough due to the small sample size to reach significance – at least supporting that the family's perception may be valid? Then, how much of a positive impact is the child experiencing from the treatment? If both favor continuing med, consider approaching the company for compassionate use of the product (similar to what we've done for triheptanoin for GLUT1.) If the company is not willing to offer compassionate use, you will need to evaluate other options. The real answer will vary depending on what other options for treatment (or other trials) exist for such a patient. But the reality is that at some point (even if you initially get compassionate use access), such a patient will probably lose access. It is important to begin discussing alternatives and backup plans, even while pursuing compassionate use.

Question: For a multi-year, placebo-controlled trial with no new information to share, what frequency and how do you recommend speaking to advocacy/patients?

Answer: It needs to be decided in collaboration with the community represented on the appropriate communication cadence with participants. There's always SOMETHING to communicate -- enrollment, other related research, relevant regulatory updates, etc.