

PFDD Voice of the Patient Report Appendix  
Additional materials available at [www.cdkl5.com/PFDD](http://www.cdkl5.com/PFDD)

## CDKL5 Deficiency Disorder PFDD Post-Meeting Survey CDD



**IFCR**

**International Foundation  
for CDKL5 Research**



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Tackling CDKL5 Deficiency

**This document presents information on the CDKL5 Deficiency survey. It includes an explanation of the survey rationale and the survey questions, as well as the 36 responses in full, though identifying features such as emails and names have been omitted (though spelling and punctuation have not been edited).**

### **Intro**

We are extremely grateful to all the community for their participation in CDKL5 deficiency disorder (CDD) Patient-Focused Drug Development meeting. Your testimonies will be invaluable in developing the Voice of the Patient Report. Please visit <https://www.cdkl5.com/pfdd/> if you wish to view the webcast or learn more about the meeting.

After some reflection, we thought it would be in our children’s best interest to conduct a short post-meeting survey with some additional questions designed to help FDA reviewers understand what risks associated with a new treatment would the caregivers of an individual with CDD be willing to contemplate or accept in exchange for the treatment outcomes (or benefits) that would be most important to them?

\*Note, some of the introductory questions cover some of the same topics discussed at the meeting. Your responses to these questions need not be lengthy—they are repeated here merely to provide context to your answers about the treatment decisions you would be likely to make for a treatment that may be effective, or partially effective for your child’s symptoms. These questions are very difficult to think about, but your opinions could shape the direction of therapeutic research, and whether potential therapeutic options are approved for use or considered not worth pursuing.

### **Survey Questions:**

- 1) Describe how you participated in the November 1 meeting:
  - a) In Person
  - b) Webcast (live)
  - c) Webcast (recorded)
  - d) I have not watched the webcast
  - e) Other
  
- 2) What is the age of the family member living with CDKL5 Deficiency Disorder (CDD)?
  
- 3) Please tell us about the top 1-3 most burdensome CDD symptoms your child has and how they impact the child’s activities in daily life and overall quality of life. Have any of your child’s symptoms improved or worsened over time? If so, how? If so, please give details.
  
- 4) What are you currently doing to manage your child’s major symptoms? (Examples may include prescription medicines, over-the-counter products, and other therapies such as physical therapy).
  
- 5) How well does your/your child's current treatment regimen manage the most significant symptoms that you listed earlier? What do you consider to be the most significant downsides to your child's current treatments, and how do they affect your daily life? (Examples of downsides may include bothersome side effects, interacts with other medications, time devoted to treatment, etc.)
  
- 6) Short of a cure for your child’s CDD, what specifically would you look for in an ideal treatment for CDD? This can include, but is not limited to, improving certain symptoms, enabling certain abilities or

activities in daily life, slowing or stopping future losses, extending lifespan, avoiding certain downsides or safety risks of treatments? What factors do/will you take into account when making decisions about using a therapy or treatment?

7) What types of side effects would you be willing to risk in exchange for a treatment that improves one or some of the symptoms that matter most to you and your child? What if that treatment only affects some symptoms but does not reduce seizures? Note: the following side effects are examples to consider, this is not a multiple-choice question. Please provide your own perspective. (Common side effects such as nausea, vomiting, loss of appetite, weight gain, headaches, back pain, fatigue, etc.? Increased risks infections as a result of treatment? A small risk of a severe life-threatening reaction or serious side effects to the heart, liver, or kidney that may affect normal organ functioning and therefore require immediate medical attention? A treatment that may result in possible serious comorbidities such as cardiovascular disease, kidney disease, diabetes, weight gain, etc., for the rest of their lives?)

8) What would you be willing to risk for a treatment that cures or leads to major improvement in all/most the major symptoms of CDD? Would you consider giving your child a treatment that could significantly improve neurocognitive development or the ability to communicate if there was a very small risk of death? What if there is a risk of it shortening your child's lifespan later in their adult years? What risks would you not be willing to take?

9) Has your child ever been in a clinical trial for drug for CDD or its symptoms? Would you enter such a trial if you had the opportunity? If your child was in a clinical trial, can you describe your experience?

10) Which of the following factors would influence your decision to participate in a clinical trial? Select TOP 4.

- a) How the treatment might improve my child's health
- b) Whether my child needs to stop some of his/her current treatment
- c) Whether my child might get placebo ("sugar pill")
- d) Promise to receive open label therapy at the end of the study
- e) Reputation of the study site principal investigator (doctor)
- f) Nearness of the study site / travel
- g) Concern over risks of common side effects of treatment (loss of appetite, tiredness,
- h) nausea)
- i) Concern over risks of serious side effects (cardiac or liver issues)
- j) The way the treatment is administered (orally, IV, injection into spinal cord)
- k) Concern over commitments to participate (hospitalization, doctor visits, blood draws)
- l) Length of trial
- m) Other:

11) Do you have anything else you would like to say about a possible treatment?

## Responses:

(Note, not all respondents were native English speakers. Spelling and punctuation have not been corrected. However, names have been removed.)

### Respondent 1

- 1) I have not watched the webcast
- 2) 35
- 3) Drug resistant seizures, central sleep apnea
- 4) Prescription medication
- 5) Poor seizure control . Unpredictable apnea episodes. Requires 24/7 care.
- 6) Seizure control. Management of apnea episodes.
- 7) Fatigue, weight gain, possible effects on organs.
- 8) At this stage of her life neurocognitive development is not as important as it once was. Lifespan and quality of life is more important.
- 9) Vigabatrin trial to control seizures. Initial adverse reaction with increased seizures on too high dose. Not sure I'd put her through another trial. She has been through too much in her life.
- 10) b, e, g, h
- 11)

### Respondent 2

- 1) In Person
- 2) 12
- 3) Lack of effective communication, hypotonia, and bowel irregularities. [Her] lack of communication prevents her from being able to tell us what she needs and when, her hypotonia prevents her from being able to progress in her ADL skills including self feeding, toilet training, and mobility, her GI irregularity causes pain, decreased appetite, increased seizure activity and prevents her from being able to participate in social activities. [Her] hypotonia has worsened since she was a toddler. She was able to stand and cruise and had an emerging pincer grasp at 18 months but lost these skills and has never regained them.
- 4) PT, OT, Speech therapy, music therapy, prescription antiepileptic medication, prune juice, state CBD product, bilateral AFO, speech generating device with nuzage technology, stander and gait trainer.
- 5) [Her] treatment regimen is not as effective as we would like as she has difficulty using the speech generating device due to poor head and neck control. The prune juice while better at controlling her GI symptoms than medication has been she still has alternating constipation and diarrhea.
- 6) Improved muscle tone and control would be the best treatment for us as it would improve overall quality of life. The biggest factor to consider about using treatments for us is side effects of medications and interactions with current treatments
- 7) Nausea vomiting diarrhea small risk of life threatening disease.
- 8) Possibilities of developing future comorbidities for example a small risk for developing contractures or certain types of cancer
- 9) She has not been on clinical trials due to accessibility to trial sites. We would consider enrolling in a trial depending on potential effects
- 10) d, f, h
- 11) Symptomatic treatment while good for short term is not what I would look for as this is a global disease and requires global treatment.

**Respondent 3**

- 1) Webcast (Recorded)
- 2) 12
- 3) Seizures; unpredictability and uncontrollable. Not mobile; this makes EVERY aspect of our daily lives more difficult to have to do literally everything; he cannot do one thing for himself at all. As he gets bigger we leave the house less and less because it's too difficult and or there are not public places that have appropriate changing area for anyone larger than a baby.  
Sleep; the sleep is inconsistent and more bad than good....  
Vision also had to put its up there with sleep.
- 4) Seizure meds that have so far been unsuccessful. Pt OT Vision therapies....only helps by maybe slowing the regression?
- 5) They are unsuccessful in helping 100%. Nothing has every been 100%. We are only treating symptoms though. Not the problem
- 6) More time and money put into treating the problem NOT the symptoms of it!
- 7) Cannot answer this but we have stayed away from certain types of treatments for our son because the side effects are not worth the risking over the symptom it's meant to treat
- 8) I mean I guess that's a risk for every surgery? These questions are way to general to answer.
- 9) Yes; it worked well for 2-3 years and slowly the seizure activity crept back up. I would try another...depending
- 10) b, c, e, f, g, h
- 11) Please put more focus towards fixing the problem and not so much h the symptoms!

**Respondent 4**

- 1) In Person
- 2) 3.5
- 3) Please see my speech from Panel 1. Seizures, Respiratory Health/Low Tone, CVI
- 4) AEDs, therapies, recently began enrolling in a clinical trial for new AED
- 5) Not well. My son continues to have daily seizures and other health issues. He is severely impaired with no head control.
- 6) Improvement in tone and respiratory health would make a tremendous impact.
- 7) To be honest, unless a treatment is developed that improves my son's neurological health I believe his life will be considerably shortened. I would be willing to take considerable risk for an improvement.
- 8) Again, if my son doesn't get a treatment for CDD he will likely die prematurely. I would be willing to take considerable risk.
- 9) We have just begun the process of enrolling in the Arcade trial. We have had only one study visit and have not begun the drug. I would consider entering a clinical trial if the benefit outweighed the risk.
- 10) a, c, f, h
- 11) In my mind, a disease-modifying treatment would mean that the neurological symptoms of CDD would alleviate for my son. I envision his tone would normalize and he would be able to support his own head. I envision he would start to develop functional vision. I envision he would have no more seizures. I envision he could regain his ability to eat by mouth. It would be life changing.

**Respondent 5**

- 1) I have not watched the webcast
- 2) 15
- 3) Chronic insomnia, Seizures, Constipation
- 4) Nothing works for the insomnia or seizures (but on Phenobarbital) and on Resotran for the constipation.

- 5) No management for sleep issues. Phenobarbital minimally manages the seizures but her dosage is too high and she's uncoordinated and sleepy in the day due to lack of sleep and high dose Pheno. The Resotran works very well.
- 6) An ideal treatment for my daughter would be better seizure control and reduction in postictal phase. A medication that will help my daughter to sleep. And something that will help her have a BM on a regular basis. When making a decision on a therapy or treatment I look for the least amount of side effect.
- 7) I am not prepared to accept any of those side effects except a little weight gain.
- 8) I don't know.
- 9) No.
- 10) a, d, e, f, g, h, i, k
- 11) While I'm waiting for cures that are safe with minimal side effects. I am open and willing to try treatments that can improve symptoms.

### **Respondent 6**

- 1) I have not watched the webcast
- 2) 3
- 3) seizures, dysphagia, respiratory infections
- 4) anticonvulsivant therapies, g-tube, physical therapies
- 5) anticonvulsivants are the major problem, almost all of them had a different side effect in our daughter
- 6) stopping seizures with possibility of enabling activities in daily life, as walking and talking a few sentences; less hospitalizations
- 7) facing her condition nowadays, common side effects do not look a problem; weight gain would be a plus for her, in fact; maybe risk of kidney disease or cardiac arrhythmias leading to sudden death would be of concern to us
- 8) yes, no doubt, we are willing to take this risk
- 9) no, never
- 10) a, d, e, h
- 11) we have hope we can overcome this devastating disease.

### **Respondent 7**

- 1) Webcast (Recorded)
- 2) 4
- 3) 1. Seizures. They change constantly but are worse now than originally. 2. Developmental Delay. She has the same developmental and cognitive functions now as she did at 3 months old. 4. Hand movement. ITs like she doesn't have hands. If she's could grasp and support herself she could be sitting/playing independently which we very much want done her.
- 4) Prescription medication, Keto, clinical trial participation, Physio, hippotherapy, hydrotherapy.
- 5) We are effectively stagnant. There seem to be no improvements to her developmental delay/hand movement. And her seizures seem to exist outside of how we treat her. They beat to their own drum and nothing seems to help. The biggest downside is that we spend so much time making her bottles and preparing her supplements for Keto and it's doesn't seem to help her.
- 6) We are looking to improve her quality of life. For our daughter seizures are paramount to improving that and by eliminating them, we have better prospects for reaching other goals. After seizures developmental delays would be next, including speech. To not be able to communicate with our daughter is difficult and devastating.

7) I guess it would depend what it was. To gain a skill at this point would be worth a risk. She cannot sit or stand, walk or talk. She has seizures everyday multiple times a day. Any gain would be appreciated at this point, seizures or not. As long as the risk is manageable and doesn't take away from her overall quality of life. So essentially, the risk has to be worth the gain.

8) I'm not sure to be honest. I think it is unfair that we are even faced with such questions. What other parent has to weigh these things. To risk shortening her life for more function I would say yes but that seems like playing god to some extent. We know how lucky we are to have her with us when so many families have lost children. At the same time it seems selfish to not want more for her.

9) Yes we participated in the ganaxalone trial. Sadly, the drug had adverse effects for our daughter however it was a good experience and we contributed to research so not a total failure. We would absolutely try another trial again in the future.

10) a, b, g, h

11) At the end of the day the question should be difficult to answer but we are open to anything that will improve the quality of life for our daughter.

### **Respondent 8**

1) Webcast (Recorded)

2) 3

3) Seizures, respiratory issues, low tone. Two months ago, he was in the hospital for 2 weeks for rhinovirus. Since then, he has had constant respiratory issues, low tone, and feeding issues.

4) Seizure meds, Zantac, vitamin c, miralax, physical therapy, occupational therapy, and speech therapy

5) Side effects of the seizure meds and time!

6) I really want him to be healthy first and foremost. Improved respiratory function, tone, and eating ability.

7) I would be willing to take some risk since I'm afraid I'm losing my son already.

8) I would be willing to risk those things, since I'm not sure how long my son will continue to live.

9) Yes, we are in the Marigold study in the double blind portion. We have not benefitted much from it at this point.

10) a, b, d, f

11) We are desperate for something at this point!

### **Respondent 9**

1) In Person

2) 11

3) Seizures, vision, cognition

4) Epidiolex and tranxene for sleep, therapy, school, horseback riding.

5) Epidiolex has been good.

6) Seizures and cognition

7) Not sure what risks I would take because I do accept her for who she is

8) Hard to answer at this time

9) Epidiolex at NYU-- best decision/ treatment we have had thus far

10) b, c, g, j

11)

**Respondent 10**

- 1) I have not watched the webcast
- 2) 12
- 3) Seizures, no hand use, no self-service. This symptoms disturb daily life and he cannot be independent. Seizures are controlled.
- 4) Music therapy, AED, occupational therapy.
- 5) There was no significant improvement, Seizures are now controlled by AED.
- 6) For me seizures are main problems, improving/enabling certain abilities: for example communication, self-service, for him to be activer.
- 7) loss of appetite, weight gain, loss, fatigue. Nothing associated with pain.
- 8) In case of improving all the symptoms, enabling communication skills I will accept treatment with a very small risk of death.
- 9) My child has never been in a clinical trial for drug, I will enter without hesitation.
- 10) a, e, f, h
- 11)

**Respondent 11**

- 1) I have not watched the webcast
- 2) 30
- 3) Seizures, hypotonic , reflux and difficulty swallowing. [She] has a GJ tube , is non-verbal, requires wheelchair and is incontinent.
- 4) Anti-convulsants medication, Ativan, GJ tube, wheelchair, hospital bed, OT, PT and full time Care.
- 5) Sleepy, tired and unable to participate in many activities.
- 6) Preserving life vs quality of life will definitely be a balancing act. I would definitely love to see [she] more alert and responsive without increasing the risk of more seizures.
- 7) This is a very tough question as [she] is non-verbal and we must make all decisions for her. I am not willing for her to be in any kind of pain in exchange for less seizures. We have lived through some very rough times where [she] moaned for hours on end. We have also been in the hospital because her seizures could not be controlled.
- 8) [She] is 30 and lived well beyond what we were told her life expectancy was. A “small” risk would be acceptable to me.
- 9) No. As [She] is an adult, she has not Bennet eligible for a clinical trial.
- 10) a, e, f, h
- 11) Please, please include older people living with CDD.

**Respondent 12**

- 1) I have not watched the webcast
- 2) 14
- 3) Seizures, developmental delay, minimal communication
- 4) prescription medicine, AED and consultation of neurologist.
- 5) AED can partial decrease an amount of seizures.
- 6) Improvement of mental status, enabling verbal communication and stopping seizures.
- 7) gain of weight, loss of appetite, fatigue.
- 8) both options are acceptable for me.
- 9) No she has never been in a clinical trial. will enter such trial without hesitation.
- 10)
- 11)



**Respondent 13**

1) Webcast (live)

2) 11

3) Respiratory issues due to aspiration, sleep issues, and seizures. They've become worse as she gets older. Her first documented seizure did not occur until she was 8. She was fairly healthy until then except for GI and sleeping problems.

4) Rx medications and physical therapies.

5) Sleep is still erratic. She still wakes up or stays awake all night long and power naps in the morning. Therapies had to be stopped and due to her sporadic naps, they're infrequent at school. She hurts herself at night if someone's not there to stop her. She scraped her entire foot on the wall all night long without making a sound. We didn't realize it until we saw the dried blood on the wall. Her seizures are getting more intense we've run out of medications to try. They might also be causing her respiratory issues. It's so hard to pinpoint what is causing her sleep, lung, and other issues. Whether it's her brain or her medications. Plus if we make the wrong choice, will it make things worse?

6) We want a better quality of life for her. Sometimes, I think we haven't seen her real personality due to the seizures, her medications, and the pain she must feel. The biggest factor I consider is if the risk is worth the payoff.

7) We've discovered that every treatment always seems to have a significant side effect that affects her. Every new therapy, medication, and treatment we take into consideration her health at that point in time. If her GI issues are manageable we take a risk by giving a medication that increases GI problems, if it will help her more problematic seizure control. So we take each option and weigh the benefits and consequences depending on how she's doing on that day.

8) Yes to all. I would trade a few years of her life or take that very small risk of death if it means a cure or a very large improvement in her quality of life. We're already taking risks by giving her medications that can significantly and probably do affect her lifespan negatively.

9) No. I tried to get her in a trial near our home. However, the team did not get back to me for months and finally replied a few days after she started a medication that excluded her from the trial. When I found out they were now accepting patients on that drug, I contacted them back but they did not even know the change had been approved. They contacted me again to say they were ready months later but she is having numerous respiratory issues so we decided that giving her a trial medication is not in her best interest at this point.

10) a, b, d, e, h, i

11)

**Respondent 14**

1) I have not watched the webcast

2) 9

3) Seizures, lungs infects

4) Cbd oil, bromide, valproat

5) 24 hours intensive care at home, seizures 10 a day

6) Stop seizures

7) Don't know

8) No risk

9) No

10) a

11)

### **Respondent 15**

- 1) I have not watched the webcast
- 2) 6
- 3) Our girl has epilepsy and a global delay. her biggest problem is the „normal“ speech. she can walk, talk a little bit and is autonome in a lot of things, she is interested in a lot of things and is developing quite well all over the time. She is social, has little friends,...
- 4) Epilepsy: completely stabilised since 4 years: Keppra, Sabril, Ketodiet. Integrationclass, therapies: ortophonnie, ergotherapie, physio. a healthy, very strict and regular lifestyle. (sleep, overstimulation,...)
- 5) Everything works in global absolut amazing. it takes a lot of time to manage everything, our girl can't eat spontany due to regime. Everything has to be calculated and prepared. That's the most difficult thing for us to manage.
- 6) We don't like to change to much, we want to give time to everything and listen to our intuition. Our girl's treatment didn't changed over the past years. we want for our girl happiness and quality in life. if there would exist something to activate speech more we would be happy or if there would exist something like a ketopill.
- 7) Nothing at all. we have a perfect treatment for our girl and aren't willing to change anything.
- 8) Nothing at all
- 9) no
- 8) What would you be willing to risk for a treatment that cures or leads to a
- 10) a, b, g, h
- 11) We don't want that our girl is considered as a someone you can use for a trial. she has her deficits and her problems, but is doing quite well, she develops well, is a happy, social girl, interested in a lot of things. we don't want to risk all this for a trial. we accept her as she is. She is stabilised in epilepsy. for us she is just perfect as she is.

### **Respondent 16**

- 1) I have not watched the webcast
- 2) 3
- 3) 1. Non-verbal
  2. Unconsolable crying (pain related? Also got worse after her second birthday)
  3. Seizures (got worse compared to the first 2 years)
- 4) - physical therapy
  - stander
  - pain meds
  - movicol
  - cbd-oil
  - diazepam
- 5) It's ok at the moment. We don't try for seizure freedom. As long it's only a couple a week.
- 6) Quality of life over quantity of life! Would love for her to become more „social“. If she could communicate with us that would be great!
- 7) Our philosophy is less is sometimes more! I wouldn't want to experiment to much with her. Anything that brings her pain or takes away her personality I wouldn't want to try. Also eating is the one thing she does really well - side effects like nausea or vomiting are a no go! If there was a med which could help her communicate with us, maybe I would risk some side effects listed above.
- 8) Yes I think If there ever was a treatment like that I would risk shortening her life span. I would love to get to know her and for her to enjoy life even if it means a shorter life.
- 9) No she has never been in a trial. And I don't think we would be up to it.

- 10) a, c, f, g, j
- 11)

**Respondent 17**

- 1) In Person
- 2) 4
- 3) Physical disabilities, intellectual disabilities, vision and hearing impairments
- 4) Multiple prescription AED medications, PT, OT, Speech Therapy, MNRI - reflex integration, Ketogenic Diet, Macro-nutrient supplements, SCL, medical daycare
- 5) Yes, all of his treatments impact all of our family members daily life. skin issues, TIME, lack of flexibility in our schedule/day, 1 parent unable to work leaving serious financial issues, need to make choices for him that exclude choices/options for other family members
- 6) In an ideal treatment, we would like increased physical ability, increased intellectual cognition and increased neurological processing for vision and hearing.
- 7) We are willing to risk no reduction in seizures for improvement in other symptoms, kidney and liver effects, slow weight gain and growth, fatigue, skin irritations/eczema, frequent dr visits and blood draws
- 8) Yes, we would consider all of these risks. we would be willing to give him a better life, that may be shorter due to treatment risks
- 9) No he has not ever been in a clinical trial. Yes, we would enter one, we are considering it at this time.
- 10) a, c, e, h
- 11) Any options for treatment are good options for CDKL5 families to consider. We need providers working on options and committed and interested in providing us options.

**Respondent 18**

- 1) I have not watched the webcast
- 2) 12
- 3) Epilepsy disability to use hands disability to speak
- 4) Physical therapy
- 5) Epilepsy without medication has improved
- 6) Na
- 7) None
- 8) Nothing
- 9) Maybe
- 10) a, g, h, i, j

**Respondent 19**

- 1) I have not watched the webcast
- 2) 6
- 3) paroxysm, developmental delay,
- 4) 3 time per day she recives Levetiracetam and Orifiril
- 5) Actually ist ok, she has only a few of paroxysm
- 6) Important for us is too recive help from the state, interms of a helping Person and regular money
- 7) In consideration of the aspect, that she is aactually more or less stabel we would´n go for additional risks
- 8) no risk
- 9) no we don´t have participate
- 10) a, d, f, i

**Respondent 20**

1) Webcast (Recorded)

2) 12

3) 1. Gastrointestinal gas/rectal prolapse/chronic constipation - these impact everyday living by limiting movement and daily activities, causing pain and discomfort

2. Lack of meaningful communication - she cannot tell us what the problem is when she is unwell or feeling pain, we can only ever guess and eliminate options by trial and error

3. Lack of independence

4) 1. Paediatric stool softeners, manually reducing the rectal prolapse when it occurs, making sure [she] gets to move and stretch and be upright regularly to promote gut motility. Using a dairy and practically gluten free diet.

2. Take guesses at what is causing her pain/ discomfort

3. Feed her hand over hand when possible, get her to walk independently as much as possible, promote standing/moving as much as possible. Accessing PT, OT when they are rarely available (serious lack of resourcing in Ireland currently, therapies are practically non existent)

5) We haven't found a treatment for excessive intestinal gas, we have tried all treatments that have been offered/available without meaningful success. Using lactose free diet is very limiting as products are few and far in between - availability of lactose free products in Ireland is not good.

Her seizures are daily, so we do not have seizure control. Side effects of multiple drugs simultaneously have caused her cognitive delay, her gums and teeth are in a fearful state, some AEDs get her very agitated, some lethargic and some have caused loss of muscle control, fuzziness, dizziness etc., etc., When introducing new AEDs the trial and error approach is slow and bothersome as she cannot tell us how she is feeling. Getting up to an effective dose can often take weeks and initially there are almost always unwanted side effects before her body adjusts to the new chemicals. And sometimes we end up spending weeks in "torturing" her with a new drug that ultimately doesn't work for her or suit her, just to wean it right back off again.

6) The invasiveness of a treatment is always a factor, is it a medication taken orally/intravenously/ does the treatment require surgery or some type of procedure. The less invasive, the lower the threshold for willingness to trial something new out. The more that is known about possible negative side effects, the better.

The accessibility of treatment - can it be accessed locally through family doctor or do we need to travel to a hospital consultant. The closer the better as traveling is bothersome with her.

Better management of the gastrointestinal problems we have. I am 100% certain that intestinal gas triggers seizures. So if we could get the gas under control, I believe it would have a positive impact on her seizure management also.

Way of communication with her, which may need restoration/development of her cognitive abilities.

This would most likely also help with steps towards some independence, like feeding herself.

7) Not getting direct seizure reduction is not a must for us. So if a treatment helps with let's say gastrointestinal problems, I wouldn't expect it to directly work on seizures. Seizures are not the only problematic symptom with CDD.

The common side effects such as nausea, dizziness, loss of appetite if they were temporary.

8) Considering all surgery carried a small risk of death, that probably is unavoidable. If a treatment would considerably cure her from her problems and help her with her cognition and development and with that improve her quality of life, I would probably consider it even if it meant shortening of her life span in her later years.

I would not consider anything with a risk of incapacitating her further.

9) She hasn't been part of a trial because there hasn't been one near enough for us to access. I would enter a trial if one was to go to Ireland.

10) a, d, f, i

11)

### **Respondent 21**

1) Webcast (Recorded)

2) 5

3) Her frustration of the lack of communication. Seizures. Sleep issues.

4) Prescription seizure medication. Prescription sleep and behavior medication. Therapies.

5) Minimal efficacy on seizures. Sleep has worsened since we started, she screams at night instead of awake and happy.

6) Improvement of CDD symptoms such as sleep and seizures. Help in gaining ability in use of hands, use of communication or language skills, ambulatory. Willing to take certain risks in therapy and treatment.

7) The examples of side effects listed are similar if not the same side effects listed with the drugs that CDD children and adults currently have to take just to manage their symptoms with minimal if not any change in the symptoms whether it's their seizures, their sleep, their GI issues, etc. Seizures are difficult to deal with but the possibility of gaining basic life function that many CDD children live without is far more "valuable" to us parents to give our children that possibility in life. Yes, we are willing to take those same risks.

8) Death would be a risk we would not be comfortable taking.

9) Never been involved in a trial. We would love to enter one.

10) a, d, e, h

11)

### **Respondent 22**

1) Webcast (live)

2) 4

3) 1. GI (worsened-on J feeds and TPN) 2. Seizures (ebb and flow-never had honeymoon, never ideal, always occurring) 3. No communication-CVI too poor to use Tobii, attempted PODD system but still unable to use accurately with her.

4) Medications, Various bandaids to whatever is occurring (IE: zometa infusion for osteoporosis, mega doses of seizures balanced so there is some quality of life, TPN to assist with GI pain and take away the burden to her system for feeds).

5) TPN has alleviated the pain and allowed her to gain 10lbs in a year...however she now has a port and has a risk of a central line infection. Seizure medications have never done anything the VNS has helped some, however she still has seizures all the time. There is nothing that has been able to assist us successfully with communication and I am an SLP, so it really is sad.

6) Allowing her to be a functioning member of society. I could handle the seizures if she were able to develop skills and actually meet basic milestones and be an active member of our family. We wish she could tell us what is hurting her or bothering her and what she would like us to do to aid in her comfort. I will never allow her to be a full-fledged guinea pig and participate in a trial with unknown side effects that could lead to death. I am hesitant to participate in gene therapy or the sort due to the above reason. There needs to be a line between treating our children like lab rats and the search for a cure. Some things are honestly not worth the "potential".

7) No life threatening side effects or potential harm to major organs are worth a medication potential-to me that defeats the goal of the drug in the first place. Small side effects if they do not pose a significant negative impact on quality of life can be dealt with-ideally no side effects are worth a potential if they

do not significantly advance another area that is seriously suffering. For example, if she is having an anti-seizure medication and has no seizures but is debilitated from a side effect of the medication-not worth it. If the side effect does not impact her in a way that makes the benefit of no seizures worth it, then fantastic and doable.

Comorbidities are also out for me as well-unless again we are talking a significantly improved quality of life that decreased her length of life than it would/could be considered. If you said there was a drug that could cure all of CDKL5 BUT the tradeoff would be a shortened life-I would take that trade. BUT it would have to be a guarantee that she wouldn't suffer at all.

8) See above answer. If you said there was a drug that could cure all of CDKL5 BUT the tradeoff would be a shortened life-I would take that trade. BUT it would have to be a guarantee that she wouldn't suffer at all.

9) No. Considered but ultimately the potential was not worth the small chance it might help. We have tried enough medications and failed to not feel it necessary to play this game when other children with cdkl5 have not all sung its praises.

10) a, c, e, h

11) I think there needs to be research for a potential cure, but I think it also needs to be said that you cannot mess with genetics in terms of making an apple out of an orange. When a gene like CDKL5 is impacted in such a way to cause the severity it does to some of our children, it cannot be treated as if a cure is on the horizon. A cure is NOT going to make our current 4 year old typical ever, and I feel it a disservice to insinuate such a potential. I also feel like at times the fact that our children are children and not pieces of science gets muddled. While I am all for eradicating the impact of CDKL5, that is not possible currently and I appreciate the need to help other children in the future, but the selfish mom in me says, if it isn't going to help our daughter now and in her lifetime, I do not feel the need to subject her to a series of trials that might wreak unnecessary and irrevocable damage.

### **Respondent 23**

1) In Person

2) 5

3) 1) Global Developmental Delay including no walking, talking or purposeful hand use.

2) Cortical Visual Impairment.

3) Epilepsy.

4) Therapies including Physical, Occupational, Speech, Vision. And 3 AEDs.

5) Small slow improvements from the therapies, or at least preventing decline.

Side effects from AEDs including dulling personality.

6) Enhancing cognitive including "awareness" and social interaction/basic communication (even if non-verbal).

7) Of course all would like to avoid serious permanent side effects. Risk of short term side effects more acceptable if chance of a real "cure", i.e. disease-modifying treatment.

8) Too many questions! Yes, yes and yes. But good safety profile would need to be established in pre-clinical questions and other diseases in clinic with similar approach (for example gene therapy).

9) Yes. Yes. Good experience-great PI and trial site. Protocol not burdensome.

10) a, d, e, h

11) What we are waiting for is disease-modifying treatments that can really address the underlying disease so we can have improved quality of life for our child including basic communication and social interaction. Not just better epilepsy drugs.

**Respondent 24**

- 1) In Person
- 2) 5
- 3) Lack of Communication, Lack of Mobility and Severe Developmental Delay. Have not improved and requires us to constantly provide one-on-one care to our child which has become more and more difficult as she grows and gains weight.
- 4) Various Anti-epileptics, daily therapies - Occupational, Physical, Speech, Feeding, Vision
- 5) Requires Time, Side effects from Medication, High Costs.
- 6) I would love for my child to engage with me, gain some independence, be able to stand, take a few steps, communicate basic needs and attend to her surrounding. Safety is my key decision marker.
- 7) I would accept some temporary common side effects but nothing that might risk her life.
- 8) Not willing to take a risk that will shorten her life or lead to death
- 9) Yes on the Marigold Treatment. Was smooth but definitely a commitment.
- 10) a, h

**Respondent 25**

- 1) I have not watched the webcast
- 2) 23
- 3) Seizures , crying spells , non verbal . All 3 combined make looking after my daughter a tough job from day one as u feel as a mother u should b able to comfort & protect ur child . As the yrs have passed I feel that the seizures have lessened not due to any drug & the other effects of CDD have just been part of our life & we have just had to organise & sacrifice a lot of our everyday family life to deal with them .
- 4) We have decided the seizures r as stable as will ever get them & have stopped trying to get our daughter seizure free . Constipation we deal with prescription drugs & crying spells r dealt with by home comforts , music , sensory lights & some pain management.
- 5) At present we feel it's the only thing we have to manage the effects, as we have no input from any other professional , we feel we miss out on a lot of family time as we revolve around [her] & her state of mind / health .
- 6) What I would give to find out the reason why my daughter going thru spells of crying for days at a time , as to what I would take as a "cure " & how that "cure would come about I can't answer that question until it is giving to me .
- 7) I would have weigh up the options as will the "cure " affect my daughter worse than the symptom it's supposed to be treating. My daughter is a healthy girl so I wouldn't be sacrificing damage to other parts of her body ie heart , kidneys ,liver , but I would probably take slight side effects if improved the symptom.
- 8) Sorry wouldn't b risking my child's life for any treatment .
- 9) Never been on a trial & don't think we would be a candidate for one.
- 10) a, f, i, k
- 11)

**Respondent 26**

- 1) I have not watched the webcast
- 2) 2
- 3) 1. no head control- if he could sit better, he could be motivated to see more. if he could be motivated to see more, he would be motivated to interact with his world more, and others would be more motivated to interact with him as well. this has improved ever so slightly over time. 2. does anyone ever say teething? he spits up and is very upset when the teething is bad.

i think its obvious why spitting up is bad for our kiddos (aspiration etc). this has improved relatively over time and soon he will have all his teeth! and 3. hospital admissions due to respiratory illness.

4) Vision/physical/occupational/speech/feeding therapy. anti-epileptic drugs (2) and diet (keto).

He sees about 7 medical specialists. we have lots of equipment (supportive chairs, stander, wheelchair, bath, pulmonary equipment, feeding tube equipment).

5) 1. head control - not well. we do a lot of therapy and he still can't hold up his head. the hard thing is timing with the therapy- sometimes he's not feeling his strongest/most motivated during scheduled therapy sessions 2. teething- we try to control with pain meds/ anxiety meds so we control the pain/dysregulation somewhat but not completely. we worry about giving tylenol bc of the liver (he takes a lot of medication) but we have to give it if the advil isn't doing the trick 3. we recently got some pulmonary equipment to use daily to try to avoid the hospital in the future...but no word yet on whether its working, as he hasn't caught a cold since we started the regimen

6) Getting him stronger, vision improving. i certainly am not cool with major safety risks of treatments.

7) This is quite a pointed question. If it TRULY helped him build strength so that he could hold his head up or avoid severe respiratory infections I would consider some other risks. What a difficult question to answer- especially with no short-term promise of a drug that will seriously improve our kids. Us parents already struggle making daily decisions for our kids that can't communicate. I would be inclined to think more deeply about an answer if I had a narrowed down list of terrible hypotheticals.

8) If the treatment was really that promising, I would risk crazy things happening as long as the risk was VERY SMALL.

9) Not yet. I would if there is a promising trial at a time we need to consider a new drug.

10) a, c, d, h

11) I applaud your efforts to consider families' perspectives. I dream of a treatment for CDKL5 every day. Thank you for helping our kiddos!!

### **Respondent 27**

1) Webcast (Recorded)

2) 11

3) Seizures, sensory processing issues, anxiety/hyperventilating . We haven't had seizures in 3 months. It's been years since we've gone this long .

4) Seizure meds, OT, PT and speech therapy

5) Therapies can be very time consuming.

6) Seizure freedom, Decreased anxiety, improve purposeful hand movements, increased eye contact.

7) Weight gain, fatigue. Any type of improvement is worth the risk.

8) Not willing to try it if death risk is involved.

9) My daughter participated in the Epidiolex trial back in 2016 and did not work. No seizure improvement was noted, However no negative side effects either. Yes I would enroll on a clinical trial that would improve symptoms if given the opportunity.

10) a, b, g, h

11)

### **Respondent 28**

1) Webcast (Recorded)

2) 9

3) Feeding. She stopped eating at 8 months and has to be tube fed. She doesn't get to enjoy foods of any kind. Symptoms have not changed.

4) Physical therapy because she has virtually no fine motor skills and limited gross motor. She can be assisted to sitting. But she's a weeble wobble. She cannot stand, walk, and has no functional use of her



hands. She has absent speech and has been in and out of therapy for speech and eating her whole life. She's been on at least 14 different AEDs in her life. No impact. Keto permanently reduced frequency by close to 75%, but had no impact on severity.

She's been on and off melatonin. It briefly gave her less seizures. But they returned. She's on two daily AEDs Banzel and zonisimide. Her rescue is klonopin. She takes lactulose daily.

5) Nothing we have done improves her quality of life with the exception of the ketogenic diet. No therapy or meds help her function better be it eating or getting around for herself. It's disheartening.

6) I'd like her to be able to communicate. We have no idea how she feels or what she needs! It's been a 9 year guessing game.

7) At this point I'm less concerned with the seizures. The seizure meds she's been on have pretty bad potential side effects and yet she still takes them. Mild to moderate symptoms I can handle. Potentially life threatening or comorbidities would give me serious pause. If the treatment is worse than the disease that's a no for me.

8) A shorter life span bothers me less than a lifetime like she is now.

9) No. Tried to get into epilodex. But they were only taking dravet kids.

10) c, d, h, i

11) We've been waiting for this opportunity for 9 years. Please help our kiddos improve the quality of life!

### **Respondent 29**

1) Webcast (live)

2) 21

3) Epilepsy - during the first 13 years of her life, our daughter had at least one nocturnal tonic clinic seizure each week. This has improved dramatically as she has not had a tonic-clinic seizure in over 8 years and rarely has absence seizures (a couple each year).

Developmental delay - our daughter functions at a high level compared to most CDD diagnosed children but is unable to do most basic tasks (hygiene, food preparation, etc.) and requires 24/7 care. She continues to learn and her abilities continue to slowly improve with time and repetition.

Physical development issues - our daughter has a poor gait and kyphosis. These have hampered her ability to easily move but she can walk significant distances (a couple miles).

These continue to worsen with time but we continue exercise on a daily basis.

4) Prescription epilepsy medication, walking, hippo, behavior and music therapies

5) Her current symptoms are well managed with her treatments. The downside is mostly reduced energy level associated with epilepsy medication but she functions well overall. Time spent to make her life better is considerable and does reduce 'our' time but that is what we choose to do.

6) Anything that will eliminate the seizure threat and increase her cognitive abilities more is most welcomed. We would also like to see an elimination of any losses (Parkinson's-like symptoms can occur with increased age).

7) Our situation is somewhat unique due to our daughter's overall good health and quality of life. We are not willing to take any risks that could result in risk of life or comorbidities occurring.

8) Again, our situation is unique so we are not willing to take any risks for a treatment at this time.

9) Our daughter has not participated in any clinical trials. Depending on the possible outcomes to improve her life, we may want to participate in the future.

10) a, c, e, h

11) Not at this time

**Respondent 30**

- 1) In Person
- 2) 25
- 3) Seizures, non-verbal, GI issues
- 4) Medications for seizures and GI
- 5) Refractory epilepsy, side effects
- 6) Daily living
- 7) No
- 8) She must be comfortable
- 9) No
- 10) a, b, d, e, f, g, h, i, j, k
- 11)

**Respondent 31**

- 1) Webcast (live)
- 2) 2.2
- 3) Not to mention, never having seizure control and taking too many medications. Now the way that affects life the thing that shakes you most is knowing that with each seizure it loses something!
- 4) [She] Has already gone through a wide range of medicines, is currently using Depakene, Canabidiol, keppra and Topiramate. Do therapies from Tuesday to Friday, such as: Medek, pediasuit, bobath, occupational therapy, speech therapy and visual stimulation.
- 5) My daughter has been on medication since she was twenty days old, it is frustrating never to see an improvement in the condition what affects her most is the insomnia that sometimes stays up to 2 days awake
- 6) To cure my daughter would be capable of any act if it did not endanger her life.
- 7) I can't imagine a concrete answer, but I think it would be worth a try, because I wouldn't want to have that doubt forever
- 8) If you are already at risk of death, you probably would not want to do
- 9) I would rather participate, but I have never been to one before.
- 10) a, b, e, g, h
- 11) Can this treatment be performed in Brazil?

**Respondent 32**

- 1) In Person
- 2) 16
- 3) 1 - Global Developmental Delay and her inability to walk and talk or communicate.  
2 - Intractable Seizures  
3 - Digestive Health for example constipation
- 4) prescription medicines for seizures  
PT, OT, Speech and Visual Therapy  
Miralax and Vitamins  
AFOs and Back brace for Scoliosis
- 5) The medicines are ineffective  
The therapies are beneficial  
The time consumed by daily care is the biggest downside.
- 6) Improved Communication and mental cognition would be our ideal result from a future treatment.  
Moderate level of risk would be tolerated for treatment

- 7) We would probably accept a high level of risk in order to improve our daughter's condition in hopes of finding a cure.
- 8) Yes - we would be willing to try a treatment to improve cognitive development and communication with a very small risk of death.
- 9) Yes - Ganaxolone  
Slight improvement in seizure and GI symptoms without too much additional downside. Some additional doctor appts as well as documentation.
- 10) a, e, h, j
- 11) We feel the focus should be on gene, enzyme and protein therapies in order to cure the condition.

### **Respondent 33**

- 1) In Person
- 2) 14
- 3 Communication/cognition, GI dysmotility, seizures
- 4) All of the above - captured in initial survey
- 5) REVISIT
- 6) Reducing anxiety and behaviors that I suspect stem from lack of communication. Improved motor planning so she is better able to participate in ADLs (such as self-feeding, dressing, toileting - to give you further detail - being able to pull her pants up/down would be a huge help, even if she still needed assistance with peri-care). Reflux/constipation control would also be a worthy trial. I do not trust that seizures will be controlled without a disease modifying treatment so I am much more skeptical and critical of enrollment in trials that only address this aspect.
- 7) REVISIT
- 8) We have always prioritized quality of life over quantity of life in treatment considerations however, risks that might cause undue suffering would be weighed heavily. Our risk consideration might also depend on the current state of her health when the study option presented.
- 9) Yes. My child participated in an open label phase 2 study and continues to be in the extension phase of the study. I don't have to travel far and the benefits of the study have outweighed the burden of participation.
- 10) a, f, h, i
- 11) Will update REVISIT fields

### **Respondent 34**

- 1) Webcast (Recorded)
- 2) 1
- 3) Delayed / Lack of Motor Skills/ Function  
Seizures: Causes tiredness and irritability that impact her daily routine  
Visual Impairment: Unable to focus on objects and lack of sustained gaze / interest. Makes it hard to work on motor skills when she can't see something that interests her.  
All symptoms have improved in some kind of capacity. Seizures went from five to eight a day to now averaging currently 1 / week. Vision has gone from zero focus to now sustaining a gaze up to fifteen seconds on objects and faces. Motor skills: Learned to roll both ways, Head control has improved over time, Able to sit with assistance for long period of time.
- 4) Keto Diet, Keppra, Vitamin D, Poly Citra K, Physical / Occupational therapy,
- 5) She has better seizure control and physical abilities have improved during current treatment regimen. Keto diet is hard on parents, it's difficult to find good tasting foods on her ratio. Medication administrations can be a burden while trying to enjoy activities.
- 6) Medication that would control seizures without impacting motor and visual abilities.

Treatments to help with fine and gross motor skills.

7) weight gain. Sure, I would take any improvement in her ability to function in daily activities.

8) I am not willing to take even a small risk of death for treatment. I would however consider treatment that has a risk of shortening her lifespan in adult years.

9) No, Yes, but I would have to know more about a trial before entering her into one.

10) a, b, h, i

11) No

### **Respondent 35**

1) Webcast (Recorded)

2) 4

3) 1) Uncontrolled seizures;

2) Low muscle tone, so cannot cough well, nor sit up, nor stand;

3) Cortical Visual Impairment.

Muscle tone was better but not great, got worse last year, and is getting better again now that we changed medication and stopped modified Atkins diet.

4) Px meds, CBD, PT, OT, Speech Therapy, monitored at night for SUDEP, fed thickened fluids with care by mouth to prevent aspiration,

5) Epilepsy is still uncontrolled and she still has 1-2 painful seizures per day, and 3-5 smaller ones. She is getting a stronger cough to prevent aspiration, but cannot speak, nor grab objects, nor sit up but is progressing. She seems to be gaining visual acuity. I quit my job as a research coordinator to care for her and her neuro-typical brother.

6) reduce or stop seizures, improve muscle tone, improve mental development and visual capacity

7) We would not risk side effects that noticeably reduced her quality of life below baseline, caused serious comorbidities, or impacted longevity.

8) We would consider a treatment that significantly improved neurocognitive dev or the ability to communicate if there was a very small risk of death. We would probably not consider a treatment that shortened lifespan and instead wait in hope that a better treatment was developed later without affecting lifespan.

9) No. We did not because we live outside the US and the travel requirements were too onerous and there was a 50% chance we were given placebo.

10) a, c, d, f,

11) We would weigh new treatments that had permanent negative impact against the likelihood that better treatments are developed later, to try to minimize permanent damage for short-term gain.

### **Respondent 36**

1) In Person

2) 5

3) Lack of communication, significant developmental delays and GI issues

4) Prescription medications, the ketogenic diet (and associated dietary supplementation), over the counter GI medications. Speech, physical, occupational and vision therapy as well as aquatherapy and hippotherapy

5) Not very well - my child is still having several seizures a day. The diet is time consuming and the side effects of all the drugs that we give her are sedating.

6) Something that would allow for communication and greater developmental growth. I could deal with the seizures if we could treat the rest of it.

7) I would be open to the "common" rather benign side effects listed in the example. Of course, if it worked she would be able to communicate to me how those were effecting her daily life and she could have a say in treatment. Right now, the drugs we give her list all these side effects but I have no idea if she is experiencing them. Any risk greater would need to be considered on a one on one basis with her doctors.

8) Yes - I would consider it. Without concrete data in front of me it is difficult to say if we would do it, but we would at least consider it. My child is pretty significantly affected by CDKL5 and her lifespan is not guaranteed.

9) She has. We would consider it again, but cautiously. The drug in question did not end up working for her once we bridged into open label. So for us, it ended up being a waste of time where we on placebo for the blinded portion. It was definitely a learning experience, but I will think twice before doing it again.

10) a, c, e, h

11)