

Evaluating the Patient Experience with CD55 Deficiency with Hyperactivation of Complement, Angiopathic Thrombosis, and Protein-Losing Enteropathy (CHAPLE) Disease: A Deadly Ultra-Rare Pediatric Disease

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Conflict of interest

- > The research study described in this presentation was funded by Regeneron Pharmaceuticals (Tarrytown, NY).
- > Leighann Litcher-Kelly, Sarah Ollis, and Andrew Yaworsky are employees of Adelphi Values, LLC (Boston, MA). Adelphi Values received funding from Regeneron to support the research activities described in this presentation.
- > Jessica Jalbert and Olivier Harari are employees of Regeneron Pharmaceuticals, Inc.
- > Hagit Baris Feldman is an employee at Tel Aviv University, and a member of the scientific advisory board for this clinical program and received funding from Regeneron for her consulting time.
- > Ahmet Ozen is an employee at Marmara University, which received funding from Regeneron for his consulting time.

Background

- > CD55 deficiency with **H**yper-activation, **A**ngiopathic thrombosis, and **P**rotein **L**osing **E**nteropathy (**CHAPLE**) or CD55-deficient PLE
 - Newly identified condition, first described in 2017 with no approved treatment^{1,2}
 - Ultra-rare orphan (<100 patients worldwide^{3,4})
 - Autosomal recessive disease with loss of function mutations in *CD55 gene* characterized by:
 - Edema;
 - Severe GI manifestations; and
 - Thromboembolic complications.
 - Many children do not survive into adulthood

¹Ozen et al. 2017. *NEJM*

²Kurolap et al. 2017. *NEJM*

³Regeneron. 2023. [Pozeлимab \(C5 Antibody\) BLA for Treatment of Children and Adults with Ultra-rare CHAPLE Disease](#)

⁴Ozen et al. 2021. *Nat Immunol*

Background

- > Regeneron is conducting a Phase 2/3 clinical trial of pozelimab for the treatment of CHAPLE (Clinical Trial: NCT04209634)⁵
 - Treating clinicians provided information about the ***signs, symptoms, and impacts*** of CHAPLE to support planning for the clinical trial

- > Within-trial interviews were included in the clinical trial protocol to:
 - Provide confirmation of the clinical outcome assessment (COA) measurement strategy
 - Document the most bothersome sign or symptom for each patient
 - Understand the broader patient experience (signs, symptoms, health-related quality of life [HRQoL] impacts)
 - *The focus of this presentation is on the latter*

Methods

- > 60-minute interviews were conducted at Screening and Week 24 with all trial patients and/or their caregivers (N=10) by trained interviewers using a semi-structured interview guide
 - Open-ended questions about the signs/symptoms and impacts of CHAPLE were used to capture the participants' own ways of describing their experiences
 - For patients <8 years old, the caregiver was targeted to be the primary or sole interview respondent
 - For patients ≥ 8 years old, the patient was targeted to be the primary respondent during the interviews (with input from their caregiver, if needed)
- > Most bothersome sign/symptom was elicited from a list of signs and symptoms of CHAPLE identified by treating clinicians as the most common signs and symptoms of CHAPLE:
 - Abdominal pain, Facial edema/swelling, Peripheral edema/swelling, Diarrhea, Nausea, Vomiting
- > All interviews were audio-recorded, transcribed verbatim, translated to US English, coded and analyzed using Atlas.TI

Results

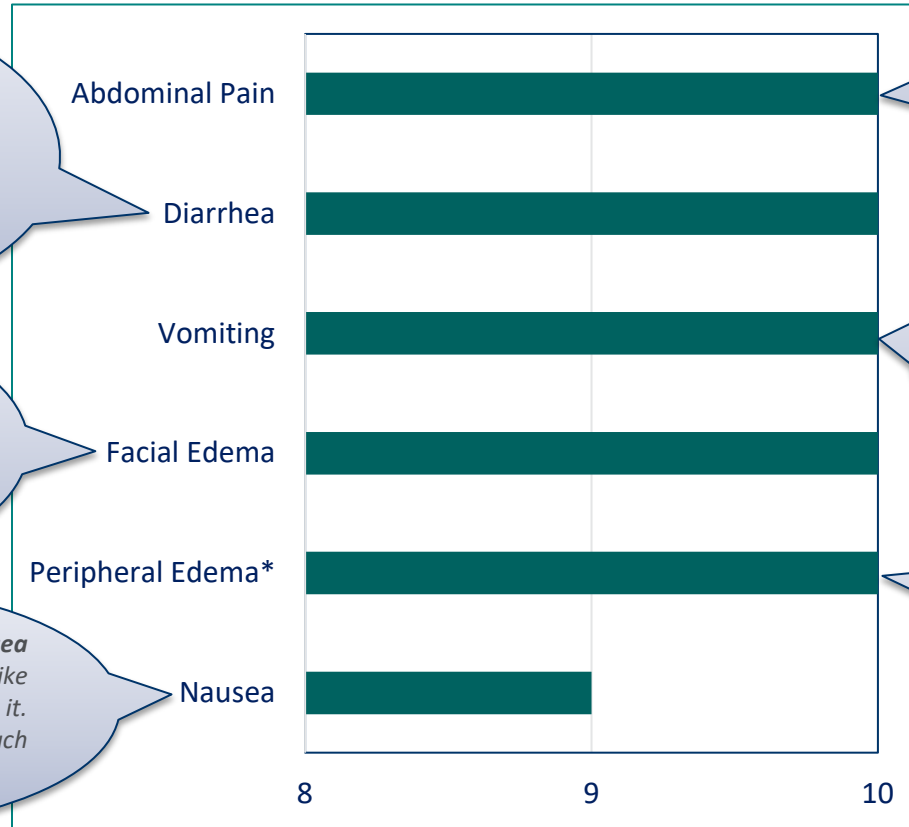
Characteristic	Total (N=10) n (%)
Interview respondents at screening interview	
Patient only	1 (10.0%)
Caregiver only	4 (40.0%)*
Patient/caregiver dyad	5 (50.0%)*
Age (years)	
Median (range)	8.5 (3–19)
Mean (SD)	9.3 (4.9)
Breakdown of patients by age	
<8 years of age	4 (40.0%)
≥8 years of age	6 (60.0%)
Sex	
Female	6 (60.0%)
Male	4 (40.0%)
Country of origin	
Bolivia	1 (10.0%)
Syria	2 (20.0%)
Thailand	2 (20.0%)
Türkiye	5 (50.0%)

*To note, there was one more dyad at the Week 24 interviews (i.e., patient only [n=1, 10.0%]; caregiver only [n=3, 30.0%]; dyad [n=6, 60.0%])

Results: Signs and Symptoms

- > A total of 31 signs and symptoms were reported during the interviews
- > At screening, $\geq 90\%$ of patients experienced abdominal pain, diarrhea, facial edema/swelling, vomiting, peripheral edema/swelling, and nausea
 - Other signs and symptoms experienced by more than two patients included fever (n=4), bowel incontinence (n=3), and headaches (n=3)
- > Most bothersome signs/symptoms:
 - Abdominal pain (9/10)
 - Facial edema/swelling (1/10)
- > Most important sign/symptom to improve with treatment:
 - Abdominal pain (7/10)
 - Facial edema/swelling (2/10)

Results: Core signs and symptoms



CAREGIVER: She gets pain and contraction, she understands it and then she runs to the toilet right away.... **Sometimes it does not stop at all and I take her to the hospital....** once per month due to **diarrhea**

CAREGIVER: Swelling of the **face** and eyes and **edema** started...it was like as if she **had bee sting** and the eyes were completely swollen nose and face

PATIENT: Sometimes I get **nausea** first but I don't throw up... I feel like throwing up but don't actually do it. Then my stomach aches, so much pain, and only then I throw up.

PATIENT: If my **abdominal pain** is severe, I even cannot get up. I **literally cannot get up** if I do not have someone next to me to take my arm and help me in getting up

CAREGIVER: ...Sometimes there's pain and **vomiting** too. It's not just one episode of vomiting – it's like a **vomiting marathon**, like vomiting until the insides are completely empty.

PATIENT: ...it is usually very significant in my **hands** and face.... When I have **edema**, I say I will definitely get sick

*n=9 participants reported peripheral edema at screening, however n=10 reported at Week 24 (the additional patient confirmed they did experience this sign before treatment)

Results

- > A total of 64 HRQoL impacts across 11 domains were reported during the interviews
 - Activities of daily living (ADL) and physical impact domains included the most impact concepts

- > Impacts reported most frequently:

- Restricted diet (n=10, 100.0%)
- Sleep disruptions (n=10, 100.0%)
- Missing school (n=9, 90.0%)
- Difficulty engaging in play activities (n=8, 80.0%)

PATIENT: *I can't sleep well; those nights when I'm in pain I don't sleep at all; it hurts all the time; last night I was lying there from 10 pm until 1:30am... I was crying*

CAREGIVER: *She cannot play, she walks around and cries. She cries all the time. Sometimes she gets upset and pulls her hair....*

CAREGIVER: *When socializing, she can't eat what other people are eating...It's like she's not like other children who can live in society. ...when other people's children go out to eat, they don't need to do anything, but our kid can't eat like everyone else's kids. She can only sit and watch....*

CAREGIVER: *She misses school very often. In a week, she barely goes to school... Even when it's the semester break, she'll have to go back to school to take make-up exams because she hasn't taken them yet.*

Conclusion

- > Patients with CHAPLE disease experience a core set of six signs/symptoms with the most critical aspect being abdominal pain, suggesting a relatively homogeneous experience of disease

- > Overall, given the ultra-rare condition, the within-trial interviews provided vital information about the broad patient experience of CHAPLE

Acknowledgments

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Back-up slides

Full patient-centric conceptual model

CHAPLE sign, symptom, and impact conceptual model



*Concepts that were reported by patients/caregivers and were also discussed by KOLs are in **blue text**; KOLs reported that abdominal pain, vomiting, diarrhea, and frequent bowel movements may be the most important to evaluate from the patient perspective while patients/caregivers reported that abdominal pain and facial edema/swelling are the most important signs/symptoms to improve; these signs/symptoms have been bolded for emphasis

Results: Caregiver descriptions of symptoms

Symptom	Caregiver Description
Abdominal Pain	<ul style="list-style-type: none">• Described pain behaviors, such as crying and holding one’s belly, while abdominal pain occurs• Reported seeing and feeling contractions on the child’s stomach
Nausea	<ul style="list-style-type: none">• Described the patient communicating their feeling of nausea or wanting to vomit.• Reported observing the patient being nauseous with sounds (“she makes sounds like ughhh and that is how I understand it.”), facial expressions, or actions (“She makes a sour face, you know. Sometimes she would try to vomit even though she did not eat anything”)

Core s/s description reported by patient and/or caregiver at screening and exemplary quotes

Abdominal pain (n=10, 100.0%)

- Described by patients and caregivers as hurting, aching, tightness, straining, and/or cramping in the stomach and/or abdomen
- Caregivers describe pain behaviors, such as crying and holding one's belly, while abdominal pain occurs

Exemplary quotes

PATIENT: If my abdominal pain is severe, I even cannot get up. I literally cannot get up if I do not have someone next to me to take my arm and help me in getting up. I started experiencing this more often for a few years, three, even four years. Previously, I was able to handle it somehow when I had pain, good or bad, but for a couple of years at least, the situation is not like that. It started to be severer and make me feel more exhausted. After I have abdominal pain, I feel drowsy. That day is literally wasted. It is very rare that I can continue my day.

CAREGIVER: Stomach pain – first, her stomach will swell, like she is bloated. It gets round and hard, so we can feel her stomach and that its contracted. We can feel it. Then, she'll have a twisting pain, and she'll cry out – like, it's very painful. If there's a full score, I'd give it the full score.

Core s/s and description reported by patient and/or caregiver at screening and exemplary quotes

Diarrhea (n=10, 100.0%)

- Described by patients as a bowel movement with a watery or soft consistency, which may be accompanied by abdominal pain, urgency, and/or frequent need to go. Reported bowel movement colors varied (e.g., orange, brown, yellow), and one patient attributed the symptom as a contributor to feelings of weakness.
- Caregivers describe watery, liquid, or soft stool

Exemplary quotes

PATIENT: INTERVIEWER: OK. And what was the main reason why you went to the doctor's? **PATIENT:** Lots of diarrhea, vomiting and, finally, I started having stomachaches. I got very dehydrated and they took me (to the hospital) and hooked me to a saline drip, painkillers and sent me back home. At [REDACTED] all they did was give me a saline drip and painkillers, and they would send me back home. They didn't prescribe any treatment.... **INTERVIEWER:** First, let's talk about the symptoms you have due to your disease. You told me that it started with diarrhea. **PATIENT:** Diarrhea, vomiting, stomachache. Those were the three main symptoms I had; I didn't get – Sometimes I had a fever, but rarely. When I was vomiting a lot or having diarrhea, I felt weak.

CAREGIVER: **INTERVIEWER:** How often does she get diarrhea? How many times per month? How many times per week? Let's understand that first and then we can go into details. **CAREGIVER:** Sometimes it lasts 3 days or 4 days per week.... Diarrhea has never stopped on its own. If I give her potatoes. Sometimes it does not stop at all and I take her to the hospital. **INTERVIEWER:** Does she get an IV line at the hospital? **CAREGIVER:** Yes. I mean, here is the thing. Even though I give her potatoes, it is not resolved completely, it just softens. Sometimes, I give her yoghurt. **INTERVIEWER:** Do they have to go to hospital? **CAREGIVER:** She definitely goes once per month due to diarrhea....**INTERVIEWER:** Okay. How bad is diarrhea? **CAREGIVER:** [SPEAKING ARABIC] That is 9 as well, because her whole body shakes after she gets up from the toilet seat.

Core s/s and description reported by patient and/or caregiver at screening and exemplary quotes

Facial edema/swelling (n=10, 100.0%)

- Described by patients as the face and/or eyelids becoming swollen, causing pain (similar to a bee sting)
- Caregivers describe the face, areas around the eye or eyelids, forehead, cheeks, and/or nose becoming swollen (due to fluid retention); also associated this with pain (similar to a bee sting)

Exemplary quotes

PATIENT: INTERVIEWER: You said you had stomach ache; what else did you experience? **PATIENT:** Swelling in the face.... **INTERVIEWER:** Yes, you said swelling in the eyes and face; I am asking about that. How much pain did you have? **PATIENT:** The pain was as if I had bee sting.... The swelling was too much here.

CAREGIVER: INTERVIEWER: Let's talk about your child's stomach and eyes again, how bad do you think the swelling in the eye is for your child? **CAREGIVER:** Ten. **INTERVIEWER:** Why? **CAREGIVER:** He could not see anything. He could not open his eye. I mean, his eyes were excessively swollen. He could not open his eyes either. Therefore, he could not see anything.

Core s/s and description reported by patient and/or caregiver at screening and exemplary quotes

Vomiting (n=10, 100.0%)

- Described by patients as throwing up stomach fluids due to abdominal pain, nausea, physical activity, and/or eating food/drinking

Exemplary quotes

PATIENT: INTERVIEWER: Vomiting, now, how does vomiting make you feel? What can you tell? How does it happen? PATIENT: I mean it causes exhaustion. I do not know if anything diminishes. Because vomiting is sometimes excessive. INTERVIEWER: How is it? How much? PATIENT: I mean, I feel like nothing is left in my stomach. I get it; we feel like that when we are hungry. I literally feel like that. I sometimes drink some water and throw it up after one-two minute(s). It happens like that. I mean, it is a bit challenging in that aspect.

CAREGIVER: For example, children eat something once every hour, I try to make her eat once every 3 hours. I mean, she is not a child who eats non-stop. I mean, as she is vomiting all the time now, her muscle development is – I had to give her formula all the time from the hospital.

Core s/s and description reported by patient and/or caregiver at screening and exemplary quotes

Nausea (n=9, 90.0%)

- Described by patients and caregivers as feeling the urge to vomit or feeling sick, which can occur with vomiting and stomach/abdominal pain
- Caregivers described the patient communicating their feeling of nausea or wanting to vomit. Caregivers also reported observing the patient being nauseous with sounds (“she makes sounds like ughhh and that is how I understand it.”), facial expressions, or actions (“She makes a sour face, you know. Sometimes she would try to vomit even though she did not eat anything”).

Exemplary quotes

PATIENT: When I play with the ball or go out and run, I have nausea and sometimes I have heartache. Therefore, I stop and I felt like that before. I do not want to vomit.

CAREGIVER: INTERVIEWER: What is the second symptom that she develops after stomach ache?Does she get nausea? CAREGIVER: Yes. INTERVIEWER: Alright, does she vomit when she gets nausea? CAREGIVER: She vomits every time she feels nauseous. INTERVIEWER: ... How does she understand that the child gets nausea? Does the child tell her or does she realize it? CAREGIVER: No, she tells me herself. Or she makes sounds like ughhh and that is how I understand it. Sometimes, she cannot wait to tell me. INTERVIEWER: Does she run to the bathroom immediately? CAREGIVER: Sometimes I don't see her at all, she just throws up, I mean she lets it out. INTERVIEWER: Alright, did the child tell her or explain now or in the past how nausea or vomiting made her feel? CAREGIVER: She says, Mom, I feel relieved when I throw up. INTERVIEWER: So does she actually throw up to feel relieved? CAREGIVER: Yes.

Core s/s and description reported by patient and/or caregiver at screening and exemplary quotes

Peripheral edema/swelling (n=9, 90.0%)*

- Described by patients and caregivers as fluid retention, or fluid in the body (e.g., hands, feet, legs, arms, etc.) that leads to swelling; can also cause pain

Exemplary quotes

PATIENT: INTERVIEWER: Okay, swelling in the face. I asked about your life, I'm sorry. We did not ask about the swelling in your arms and legs. How many points? **PATIENT:** Seven. **INTERVIEWER:** Seven. Why did you give seven points; tell me about it as well? **PATIENT:** Because I feel uncomfortable when my feet and my hands become swollen. I feel uncomfortable.

CAREGIVER: INTERVIEWER: How long would it last? Swelling in the hands-feet? **CAREGIVER:** It lasts for 1-2 days, then it goes away. But it continues in the eyes.... **INTERVIEWER:** How long does this swelling last? Doesn't it go away until she takes the medicine or otherwise? **CAREGIVER:** It gets resolved after she takes the medicine, 2-3 days before she takes the medicine, this Solaris as I said, her swelling and loss of appetite complaints start again. Vomiting starts.

*n=9 participants reported peripheral edema at screening, however n=10 reported at Week 24 (the additional patient confirmed they did experience this sign before treatment)