Lived Experiences of Patients Treated With Lonvoguran Ziclumeran, a One-Time CRISPR Treatment for Hereditary Angioedema

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First report of a qualitative study describing the voice of patients who received an in vivo CRISPR gene editing therapy

- Lonvoguran ziclumeran (lonvo-z) was designed as a one-time treatment to permanently inactivate the *KLKB1* gene and reduce kallikrein production to treat hereditary angioedema due to C1 inhibitor deficiency / dysfunction (HAE-C1INH)[1,2]
- This study was conducted to understand patient experiences before and after a one-time IV infusion of lonvo-z in an outpatient setting in the Phase 1/2 trial

Research Questions	Evaluation Domains
• How do patients describe living with HAE before versus after receiving lonvo-z?	• Impact of HAE on patients' ability to live their life • Perceived control of HAE with treatment
• What characteristics contribute to the perception of an optimal HAE therapy? • Do patients consider lonvo-z to be an optimal HAE therapy?	• Patient-defined characteristics of an optimal HAE therapy

Methods

- In this standalone, cross-sectional, non-interventional study, in-depth telephone or video-conference interviews were conducted with patients by a trained qualitative interviewer in each patient's native language
- Eligible patients completed the Phase 1/2 study (NCT05120830), were enrolled in the long-term follow-up (LTFU) study (NCT06262399), and received at least a 50 mg dose of lonvo-z during the Phase 1/2 study
- A qualitative thematic analysis approach was used to analyze the patient interviews conducted Jan - May 2026 using a codebook developed in MAXQDA
  - Frequencies represent the number of patients reporting each theme, whether spontaneously or following interviewer probing. Patients may have reported multiple themes for a single interview question and are not mutually exclusive
- Phase 1/2 and LTFU study data were summarized using descriptive statistics

Results: Interviews were conducted with 23 patients across 4 countries

- Median (range) time since lonvo-z infusion was 2.4 (1.1 – 4.2) years
- Prior to entering the Phase 1/2 study, patients reported having a mean (SD) monthly attack rate of 2.4 (2.7) attacks per month

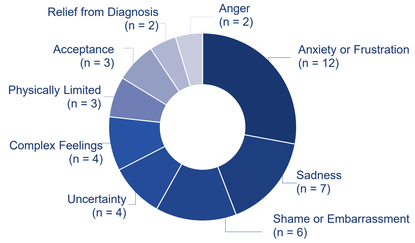
Table 1. Patient Characteristics

Characteristic	N = 23
Age at Phase 1/2 study enrolment, median (range), years	51 (18 – 76)
Sex, Female, n (%)	12 (52%)
Race, White, n (%)	22 (96%)
Country, n (%)	
New Zealand	8 (35%)
Netherlands	7 (30%)
United Kingdom	5 (22%)
Germany	3 (13%)
Monthly attack rate prior to Phase 1/2 study, mean (SD)	2.4 (2.7)
On-study monthly attack rate, mean (SD)	0.1 (0.1)
Time since lonvo-z infusion, median (range), years	2.4 (1.1 – 4.2)

Before lonvo-z, patients described living with HAE as being associated with negative emotions, disruptive to their lives, and physically impactful

Figure 1: Life with HAE Before Lonvo-z

A. Feelings Living with HAE Before Lonvo-z (N = 21)



Interview Probe: How did you feel about living with HAE before you joined the clinical trial?
Themes above are represented for those reported by more than 1 patient and only for the sample of patients asked the specific probe during interviews (n = 21 / 23)

B. Representative Quotes from Patients Reflecting on Life Before Lonvo-z

"A lot of things maybe that affected me, that people would go and do activities, and I'd be like, I'm not coming but I'd **never be brave enough** *to say why."* — *Female, 32Y, 1.9 attacks/month pre-lonvo-z*

"There's just so much **when you don't know anything different, it just feels normal** *because you don't know what it's like not to have the condition…"* — *Male, 51Y, 1.2 attacks/month pre-lonvo-z*

"I would say that it was more difficult. And that I **needed to be more careful with my body** *because I might get an attack at almost any time."* — *Male, 18Y, 1.2 attacks/month pre-lonvo-z*

*"***You're constantly thinking, am I gonna wake up ill today?** *Am I gonna open my eyes this morning and my feet are gonna be swollen overnight?"* — *Female, 32Y, 1.9 attacks/month pre-lonvo-z*

"I always felt some **anxiety about whether I would always be able to have access to my medication**… *really, really frightened if it wasn't going to be available."* — *Female, 73Y, 1.9 attacks/month pre-lonvo-z*

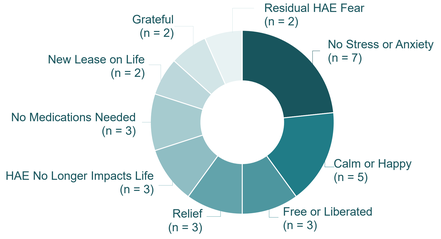
"I had to **take medication every day** *anyway, so then [I thought about HAE] definitely…"* — *Male, 49Y, 1.9 attacks/month pre-lonvo-z*

Interview Probe: How did you feel about living with HAE before you joined the clinical trial? How much did you think about your HAE on a regular basis before you joined the clinical trial?

After lonvo-z, patients described living with HAE without worry, with positive emotions, and without HAE impacting their lives

Figure 2: Life with HAE After Lonvo-z

A. Feelings Living with HAE After Lonvo-z (N = 21)



Interview Probe: How do you feel about living with HAE now after receiving NTLA-2002?
Themes above are represented for those reported by more than 1 patient and only for the sample of patients asked the specific probe during interviews (n = 21 / 23)

B. Representative Quotes from Patients Reflecting on Life After Lonvo-z

"I no longer need to make choices on the basis of HAE, but purely on the basis of what I want for myself… I just **don't need to take HAE into account** *anymore."* — *Male, 34Y, 2.2 attacks/month pre-lonvo-z*

"There is still simply nevertheless the fear about the throat - that the throat will swell up again. **This fear is sometimes overpowering.**" — *Male, 31Y, 0.9 attacks/month pre-lonvo-z*

"To be fair, in my head now, I don't even, **I don't even feel like a person that's living with HAE.**" — *Male, 53Y, 1.9 attacks/month pre-lonvo-z*

*"***It's just gone.** *I just, yeah, I just. It's really weird but I feel like I've never been ill."* — *Female, 32Y, 1.9 attacks/month pre-lonvo-z*

*"***I no longer have to take medication.** *That is actually the biggest change and I am really very happy about that."* — *Male, 49Y, 1.9 attacks/month pre-lonvo-z*

"Yes, so **it's still in the back of the mind,** *yes. And is it very strong? I think it depends on the situation."* — *Female, 50Y, 2.5 attacks/month pre-lonvo-z*

Interview Probe: How do you feel about living with HAE now after receiving NTLA-2002? How did you define "well-controlled" before you joined the clinical trial?

After lonvo-z, patients reported positive changes in key areas of everyday life impacted by HAE

- Prior to lonvo-z, all patients (23/23, 100%) reported at least one negative impact on their life due to HAE:
  - Most commonly education/work impairment (20/23, 87%) and emotional impairment (18/23, 78%), including stress, anxiety, depression, and feelings of inferiority, impaired travel (17/23, 74%), relationships (15/23, 65%), physical impacts (13/23, 57%), hobbies or recreation (12/23, 52%), and need for medical care (12/23, 52%)
- Following lonvo-z, all patients (23/23, 100%) reported at least one positive change or improvement in areas that were previously negatively impacted by HAE:
  - The greatest improvements were in emotional wellbeing (16/23; 70%), work/education (15/23; 65%), and ability to travel and physical function (10/23; 44%)

Interview Probes: How did HAE affect your life before you joined the clinical trial? Has anything changed about how you live your life since receiving NTLA-2002?
Themes above are represented for those reported by 10 or more patients and only for the sample of patients asked the specific probe during interviews (n = 23 / 23)

All patients described HAE as well-controlled after lonvo-z, compared to 48% before lonvo-z

Before Lonvo-z	After Lonvo-z
48% of patients reported HAE as well-controlled	**100%** of patients reported HAE as well-controlled
"Well-controlled" defined by patients as • Fewer or less severe attacks compared to previous experience • Symptoms remaining manageable • Medication working when needed • Daily life continuing despite HAE	*"Well-controlled" defined by patients as* • No attacks or symptoms • Little or nothing perceived as left to control • Less ongoing treatment burden • HAE being less prominent in daily life

- Most patients (86%) changed their definition of "well-controlled" after lonvo-z
- Before lonvo-z, 74% of patients (17/23) thought about HAE all of the time because of fear of attacks, reminders of taking or having access to medications, and thinking about family members with HAE
- After lonvo-z, 35% of patients (8/23) never/rarely thought about their own HAE, and 52% of patients (12/23) only when reminded by others, attending clinical trial study visits, or when thinking about family members with HAE

Interview Probes: Do you feel your HAE was well-controlled before you joined the clinical trial? How did you define "well-controlled" before you joined the clinical trial? How much did you think about your HAE on a regular basis before you joined the clinical trial? Do you think your HAE is well-controlled after receiving NTLA-2002? Has your definition of well-controlled changed? How? How much do you think about HAE on a regular basis now after receiving NTLA-2002? Themes above are represented for those reported by more than 1 patient and only for the sample of patients asked the specific probe during interviews (n = 23 / 23)

Most patients (96%, 22/23) felt that lonvo-z was an optimal therapy

- Patients thought lonvo-z was an optimal therapy for various reasons: effective for treating HAE, one-time therapy, and no need for further preventive treatment

Figure 3: Responses to the Prompt: "Is lonvo-z an optimal HAE therapy?" (N = 23)



Representative Quotes for Reasons For Whether Lonvo-z is an Optimal HAE Therapy

Yes (83%)	Yes, if durable (13%)	No (4%)
"I've tried many drugs for HAE…. and there is no comparison." – Female, 32Y, 1.9 attacks/month pre-lonvo-z *Well, I feel like it's the new gold standard… There's nothing else that comes close to that sort of response." – Female, 41Y, 1.2 attacks/month pre-lonvo-z*	*"I think the gene therapy is very effective… the best form of therapy I have had to date. I am very keen to find out what it might look like in the far future, because it is not sure that it will work for ever." – Male, 18Y, 1.2 attacks/month pre-lonvo-z*	*"I think it's almost optimal… I think [I] still get those prodromal symptoms sometimes. I mean, that's being super picky.[…] But, you know, if you didn't have any of those early symptoms of HAE. even though, for me, […] it just goes away." – Female, 27Y, 4.4 attacks/month pre-lonvo-z*

Interview Probes: Is lonvo-z an optimal HAE therapy? Why?
Themes above are represented for those reported by more than 1 patient and only for the sample of patients asked the specific probe during interviews (n = 23 / 23)

Conclusions

- These findings support the meaningful patient-relevant benefits of lonvo-z beyond clinical endpoints
- Prior to lonvo-z, HAE imposed a substantial and pervasive burden, and following lonvo-z, patients reported a marked shift in how they experienced HAE
- Post-lonvo-z treatment, emotional and functional outcomes were predominantly positive
- After receiving lonvo-z, patients described a significant life shift to a life free from attacks, medication dependence, and constant thoughts of HAE, leading them to redefine "well-controlled"
- Given that patients described lonvo-z as an effective, one-time treatment for their HAE, the majority of patients considered it to be an optimal HAE therapy

This presentation includes data for an investigational product not yet approved by regulatory authorities

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REFERENCES:

1. Longhurst HJ, et al. N Engl J Med. 2024;390(5):432-441.
2. Cohn DM, et al. N Engl J Med. 2025;392(5): 458-467.

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