Mixed-Methods Study Assessing the Impact of C3 Inhibition on the Emotional and Physical Burden of Living with Paroxysmal Nocturnal Hemoglobinuria

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OBJECTIVE

Characterize the emotional and physical burden of illness of PNH and assess the real-world impact of pegcetacoplan in addressing this disease burden and improving the patient experience.

CONCLUSIONS

- Study participants reported improvement in daily life quality measures such as reduction in fatigue and stress and increases in ability to conduct daily activities compared to their time on C5-inihibitors.
- Patients treated with pegcetacoplan described a general return to normalcy and experienced more symptom free days compared to their experience on C5-inhibitors.

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Context

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired hematologic condition associated with significant morbidity, mortality, and impact on health-related quality of life (HRQoL)[1]
- C5-inhibitors (C5is) (i.e., eculizumab and ravulizumab) are commonly used to treat PNH as the first therapies available for PNH in addition to blood transfusions
- Pegcetacoplan was approved in the US and EU in 2021 as the first targeted complement component C3 inhibitor[2,3]

Design

- This mixed-methods study enrolled consenting adults with PNH (> 21 years old) in the US for 60-minute Telephone Depth Interviews (TDIs)
- Patients are currently receiving pegcetacoplan treatment for PNH for ≥ 3 months
- Patients were recruited by a specialist patient recruitment agency using a multi-model approach including convenience sampling of internal panels and a patient flyer; the study received exempt status from the Advarra IRB in the US because patient-identifying information was blinded

Patient Demographics

Patients with PNH (N=15), previously treated with a C5i, were interviewed:

40 Years Median age (range 24 – 77)

53% female | **47%** male

Prior Therapy: Soliris, Ultomiris, Both (10)

22.1 Months Average time on prior C5i (range 1 – 48 months)

5.6 Months pegcetacoplan experience (range 3 – 10 months)

Results

Life with PNH at Diagnosis

- Given the rarity and non-specific symptoms of PNH, correct diagnosis is often delayed, leading to disease progression and development of severe, debilitating symptoms

Life with PNH on C5is

- Patients (n=6) described life with PNH while on C5is as "tolerable, average, and bearable," while n=9 patients recalled that life was "exhausting, frustrating, and a struggle," due to the inadequate control of their PNH symptoms, continued transfusion dependence, and burdensome C5i administration

Life with PNH on Pegcetacoplan

- Most patients felt that pegcetacoplan has addressed residual treatment goals, including reduced transfusion frequency and improved quality of life
- Increased energy and optimism best describe how patients felt on pegcetacoplan compared to how they felt on C5is

"I was just exhausted. It wasn't just a mental thing. It was that my whole body just couldn't move, it was awful."

"You're just constantly tired, washed out, listless, fatigued. You can never get enough sleep. Something like walking up a flight of stairs will make you feel like you just ran a marathon"

"[It was] a progression of starting to feel ill and having a general malaise, to eventually not being able to do much but barely leave my bedroom, get perhaps a little bit of food, use the facilities, and then go straight back to my bed. That's how bad it got."

"One gets very tired of having to go every two weeks to a clinic and sit for hours with a needle in your arms"

"Needing a blood transfusion every couple of months isn't a very good quality of life, in my opinion."

"The biweekly infusions were really kind of killing us. I didn't have my license at the time, so my mother had to constantly drive me every two weeks"

"After a year or two on Ultomiris, I had the conversation with my doctor, asking him "am I ever going to get better?" And he said not really… we just don't want you to get worse."

"It has basically given me a new life. Within 2 weeks of starting, I had normal haptoglobin and normal LDH levels… Then within a month and a half, I had normal hemoglobin, which I have not had since I was a teenager."

"On my good days, I think, this is what a 'normal' person must feel like"

"I can get a lot more accomplished at home, I can walk regularly with my friends… I'm just living and feeling like a person again."

"It just doesn't feel like anything is wrong, I guess. If I had to put it anyway, I just feel fine. It's hard to compare to anything else because I haven't really felt this normal in forever... I'm able to do what I need to do without too much trouble, and I don't feel overly exhausted at the end of the day."

Voice of the Patient – how patients feel on the therapy



On pegcetacoplan, I feel ___



Thanks to pegcetacoplan, I can now do___

Most Bothersome Symptom

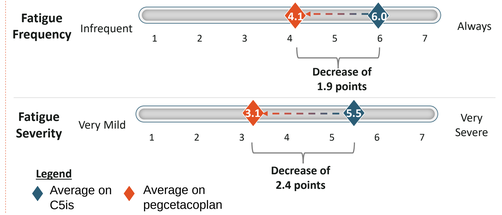
- Most bothersome symptom (MBS) is described as the symptom with the largest impact on daily lives
- Most patients reported fatigue as their MBS (n=13 / 15), n=1 patient's MBS was difficulty concentrating, and another did not report an MBS
- Fatigue was described as a hindrance to patients' ability to exercise, work, and carry out daily tasks
- This reduced physical ability, including the ability to walk up a flight of stairs or play with their children, negatively impacted their HRQoL and made patients feel that normal life had been lost

- I should have more energy to get out of bed in the morning and go up and down stairs
- Volunteering in my community has come to an end as I'm barely able to take care of my own family now and myself.
- I feel when you're tired you can miss anything – you can overlook anything
- I always had to cancel a lot of plans because that day would come, and I would [not feel well]. So, I never even made plans because I just felt like I was always disappointing people



Pegcetacoplan Impact on Fatigue

- Average frequency and severity of fatigue while on pegcetacoplan decreased (-1.9 points and -2.4 points on a 7-point Likert scale, where 1 is "infrequent" or "very mild" and 7 is "always" or "very severe") compared to time on C5is



Symptom-Free Days

Patients describe feeling a brief sense of normalcy and relief during their symptom-free days compared to days they are focused on disease symptoms

6.4 days on average per month were symptom free while on **C5is**

13.1 days on average per month were symptom free while on **pegcetacoplan**



I can go up the stairs without getting winded. I can take care of my girls. I can play outside. I can do all those things that used to make me too tired.

I've been able to walk a couple times a week regularly with one of my friends and go like four miles. Whereas I'd be lucky if I could do a mile and a half before.

Abbreviations: C5is,C5-inhibitors; EU, European Union; HRQoL, Health-Related Quality of Life; IRB, Institutional Review Board; MBS, Most Bothersome Symptom; PNH, Paroxysmal Nocturnal Hemoglobinuria; TDI, Telephone Depth Interview; US, United States