December 12, 2019

Comment on

HAEGARDA (C1 Esterase Inhibitor Subcutaneous - Human) for the prevention of swelling and/or painful attacks in adults and adolescents with hereditary angioedema (HAE).

To: **Canadian Blood Services**

From: **HAE CANADA**

Contents

About HAE Canada (HAEC)

HAE Canada (www.haecanada.net) is committed to creating awareness about HAE and other related angioedema, to help speed the diagnosis of patients, and to enable them to become champions for their own quality of life. We equip patients, caregivers, family members and health care providers with the information, tools and resources they need to ensure that those with HAE and other related angioedema can live healthy and productive lives.

Purpose of Report

The purpose of this report is to provide Canadian Blood Services with patient perspectives on the experience of living with hereditary angioedema. Further, this report aims to identify health outcomes and issues that are important to patients and their caregivers, and to characterize the current hardship that is experienced by patients due to unmet need, gaps in therapy, or restrictions on access to therapy. And, this report will specifically address patient experience with HAEGARDA.

Information Gathering

In 2019, HAE Canada has conducted two online surveys, of patients and caregivers to assess the challenges patients and caregivers face as a result of hereditary angioedema. We sought also to gain insight into their experience and expectation with therapies used to treat hereditary angioedema, in particular the treatments (Takhzyro) (lanadelumab) and HAEGARDA (C1 Esterase Inhibitor Subcutaneous – Human).

The first survey was conducted on June 2, 2019 to June 11, 2019

A total of 73 Type 1 and 2 HAE patients and caregivers responded to the survey. Seventy-three (73) Canadians responded. Sixty-eight (68) (92%) were individuals living with hereditary angioedema, and 6 (8%) were caregivers. The survey contained the use of free-form commentary, scoring options and limited closed questions. A total of 8 survey respondents indicated that they had used (or are using) lanadelumab (Takhzyro) to treat their hereditary angioedema. Follow-up telephone interviews, using an interview guide, were conducted with four (4) patients who are currently using lanadelumab. This report reflects the results of the survey and patient interviews, as well as insights HAE Canada has garnered from more than a decade of experience in patient support and advocacy related to hereditary angioedema, and previously gathered data from our membership which is outlined in our National Report Card.

The second survey was conducted from November 28 - December 4, 2019

A total of seventeen (17) Type 1 and 2 HAE patients and caregivers responded to the survey. 17 (100%) were individuals living with hereditary angioedema. The survey contained the use of free-form commentary, scoring options and limited closed questions. A total of 3 survey respondents indicated that they had used HAEGARDA (C1 Esterase Inhibitor Subcutaneous – Human) to treat their hereditary angioedema. Follow-up telephone interviews, using an interview guide, were conducted with 2 patients who had experience with HAEGARDA. This report reflects the results of these surveys and patient interviews, as well as insights HAE Canada has garnered from more than a decade of experience in patient support and advocacy related to hereditary angioedema, and previously gathered data from our membership which is outlined in our National Report Card.

Disease Experience

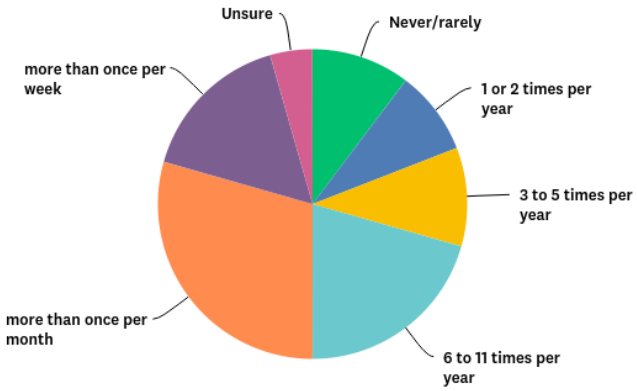
Hereditary angioedema (HAE) is a severely debilitating and life-threatening disease. It manifests as unpredictable, recurrent/intermittent edema attacks in different parts of the body including the gastrointestinal tract, upper respiratory tract, extremities and face. Gastrointestinal (GI) attacks are common in HAE, with severe abdominal pain and other GI symptoms. Untreated laryngeal attacks may result in asphyxiation and death. Swelling in other body parts can also significantly interfere with patients' daily pursuits, resulting in severely impaired quality of life.

Patients may still be affected by HAE even after the physical symptoms of an attack abate. For many, the expectation of HAE attacks imposes harsh limits on activities and plans. Due to the unpredictable nature of the disease, many patients experience high levels of distress and anxiety in everyday life, often attributed to: restricted or disrupted social life, anxiety due to fear of future attacks, the concern of HAE being passed to their children, and disruption/interference in educational and career pursuits. Many patients report that they do not pursue higher education due to HAE, and that they deliberately elect to not seek out certain jobs, and job advancements, due to expected recurrent edema attacks.

Frequency of Attacks

In our June 2019 recent survey, we asked patients and caregivers:

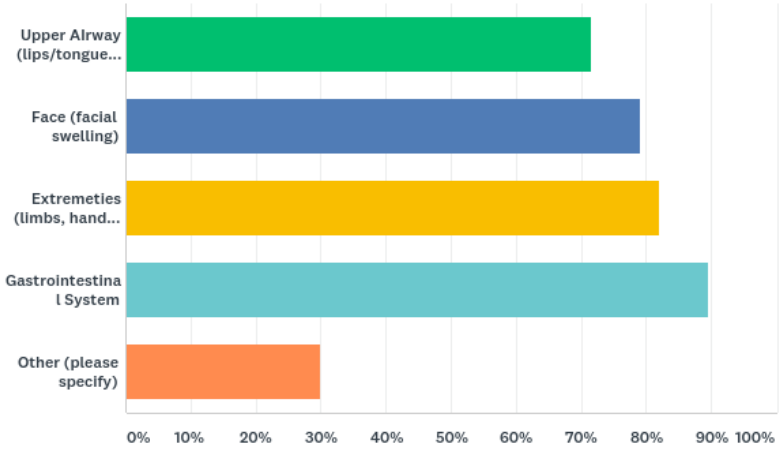
Q8 How frequently do you (or the person you care for) experience attacks?



ANSWER CHOICES	RESPONSES
Never/rarely	10.29% (n=7)
1 or 2 times per year	8.82% (n=6)
3 to 5 times per year	10.29% (n=7)
6 to 11 times per year	20.59% (n=14)
more than once per month	29.41% (n=20)
more than once per week	16.18% (n=11)
Unsure	4.41% (n=3)
TOTAL	**n=68**

Location on Body of Attacks

Q11 On what part of the body have you experienced attacks? (check all that apply)



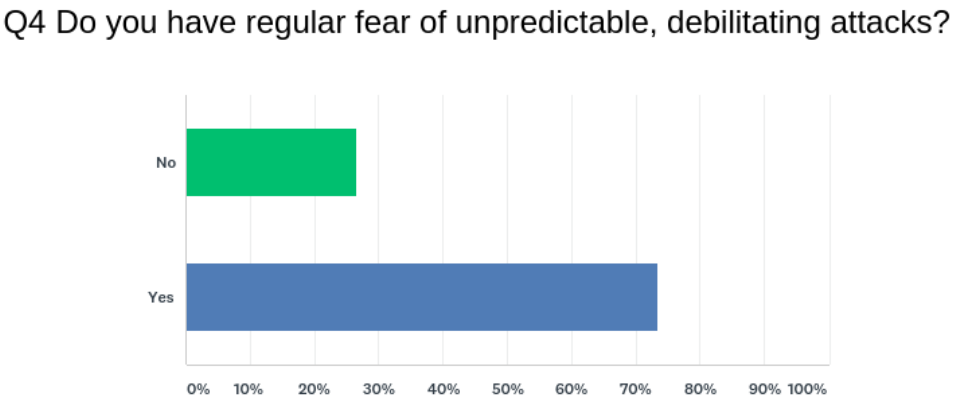
Answer Choices	Responses
Gastrointestinal System	89.6% (n=60)
Extremities (limbs, hands, feet)	82.1% (n=55)
Face (facial swelling)	79.1% (n=53)
Upper Airway (lips/tongue, throat/larynx)	71.6% (n=48)
Other (see free-form commentary below*)	29.9% (n=20)
TOTAL	**n=68**

*Patients had an option to add other body sites to the question: On what part of the body have you experienced attacks. 20 individuals added body locations on which they experienced attacks as follows:

Body Location	Response
Genitals/groin	17
Posterior	2
Breasts	1
Sinus cavity	1
Lungs	1
Back/shoulders	2
Joints	1
Full body	1

Fear of Attacks and Psychosocial Impacts

We also asked:



Sixty-eight (68) patients responded to the question.

74% (n=50) of patients report having fear of unpredictable, debilitating attacks.

We asked those 50 patients: ***If "Yes", how strongly would you rate your fear?*** *("Mild", "Moderate" or "Severe")*.

30% (n=15)	report their fear as being	"Mild".
62% (n=31)	report their fear as being	"Moderate"
8% (n=4)	report their fear as being	"Severe"

We further asked these patients: ***Does your fear of attacks lead to any of the following symptoms/behaviours/feelings****? Please check all that apply*

Answer Choices	**Answered** (n=49)
Generalized Anxiety	63% (n=31)
Desire for control over your HAE swells and treatment plans	59% (n=29)
Flashbacks to other times when difficulties occurred administering medications for swells of any kind	49% (n=24)
Sense of powerlessness	41% (n=20)
Mistrust of health care systems and/or treating professionals on your medical team	35% (n=17)
Extreme emotional reactions such as irritability, sadness, or complete terror	33% (n=16)
Difficulty focusing on the present situation due to fears of past HAE swells and/or treatments	28.5% (n=14)
Panic Attacks	8% (n=4)

We asked: ***How has hereditary angioedema affected you psychologically/emotionally?***

Patients said:

"I nearly died from a laryngeal HAE attack which has profoundly changed all levels of my life"

-"when i was undiagnosed I experienced a lot of pain (abdominal attacks) and with no diagnosis -- no one believed me"
-"depending on the location of the attack I have not wanted to go out in public"
-"Unrelenting source of stress."
-"Chronic anxiety over the unpredictability of this disease."
-"Depression, anxiety, feature of future attacks, embarrassment and shame"

Hereditary Angioedema Impacts on Patient Lives and Day-to-day Activities

We asked: *On a scale of 1 - 5* ***please rate how Hereditary Angioedema impacts or limits your life and day-to-day activities****. 1 is "not at all" and 5 is "significant impact".*

We had 6 categories as follows: Ability to Travel, Ability to Exercise, Ability to Work, Financial Situation, Ability to Spend time with Family and Friends, and Ability to Conduct Household Chores.

Ability to Travel

1. Rate how Hereditary Angioedema impacts your ***Ability to Travel*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
10pts (15%)	20pts (30%)	11pts (17%)	6pts (9%)	15pts (23%)	4pts (6%)	**2.94**

Impact on Ability to Exercise

2. Rate how Hereditary Angioedema impacts your ***Ability to Exercise*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
18pts (27%)	13pts (20%)	9pts (14%)	11pts (17%)	13pts (20%)	2pts (3%)	**2.81**

Impact on Ability to Work

3. Rate how Hereditary Angioedema impacts your ***Ability to Work*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
14pts (21%)	16pts (24%)	10pts (15%)	8pts (12%)	12pts (18%)	**6pts (9%)**	**2.80**

Impact on Financial Situation

4. Rate how Hereditary Angioedema impacts your ***Financial Situation*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
26pts (39%)	16pts (24%)	3pts (4.5%)	9pts (14%)	8pts (12%)	4pts (6%)	**2.31**

Impact on Ability to spend time with family and friends

5. Rate how Hereditary Angioedema impacts your ***Ability to spend time with family and friends*** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
23pts (35%)	18pts (27%)	14pts (21%)	6pts (9%)	4pts (6%)	1pt (1.5%)	**2.23**

Impact on Ability to Conduct Household Chores

6. Rate how Hereditary Angioedema impacts your **Ability to Conduct Household Chores** *N=66*						
1 (not at all)	2	3	4	5 (significant impact)	N/A	Weighted Average (WA)
24pts (36%)	18pts (27%)	12pts (18%)	5pts (8%)	5pts (8%)	2pts (3%)	**2.20**

Patients had an option to add free-form commentary to the question re: **impacts on day-to-day activities**. These are a selection of their comments:

> -*"… From the ages of 20-50 I had attacks weekly and it did affect my life adversely. A preventative medicine would have been fantastic when I was younger*."
>
> -*"For the last 3 years I have been given C1 Esteres 1500 injections by a health nurse, weekly. This has made a huge difference to me. There is rarely a flare up since this method has taken place. Prior to this I would have a flare up at least every 3 days."* 6/7/2019 11:17 AM
>
> -*"The veil of anxiety coloured my life every day."*. 6/6/2019 2:31 PM

We also sought more detail on the financial impacts of HAE, and asked: ***How has hereditary angioedema impacted you financially?*** *(n=65)*

- ***61.54%*** *(n=40) reported HAE caused them to miss time at work or be less productive at work*
- ***21.54%*** *(n=14) reported HAE required them to spend out-of-pocket for medical care*
- ***9.23%*** *(n=6) reported that HAE has prevented them from securing a job*
- ***6.15%*** *(n=4) reported hereditary angioedema has impeded their ability to advance in the workplace*

Some patients expounded:

> -*"Reluctant to advance further due to fear of additional work stressors having a negative impact on my health"*
> -*"Retired now but it was very challenging to meet the demands of work before I stopped."*
> -*"My inability to pay for the medication while being a student has left me on welfare"*
> -*"Caused me to be absent from my job"*

Conclusion

The impact of Hereditary angioedema (HAE) goes well beyond its immediate debilitating and life-threatening manifestations. The majority of our recently surveyed patients/caregivers report having regular fear of unpredictable attacks. These patients experience generalized anxiety and stress along with many other emotional and cognitive impacts. HAE also interferes with patients' daily activities, with the disease having substantial negative impact on many patient's ability to work, travel, exercise, do household chores, and socialize with family and friends. HAE inhibits many patients' ability to pursue higher education or job advancements, and negatively affects their personal finances due to sub-optimal employment, interference with employment and costs due to treatment for HAE.

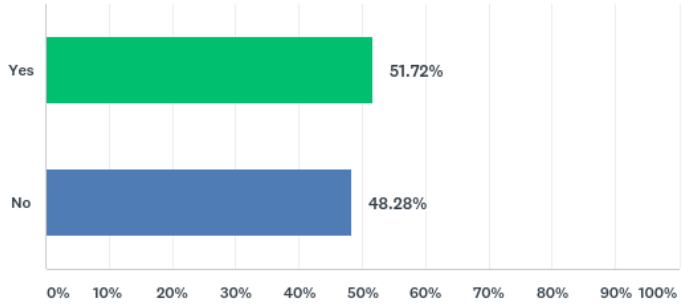
Experiences With Currently Available Treatments

Recognizing the burden to patients associated with HAE, including the ever present risk of experiencing a life-threatening laryngeal attack, improved preventative treatments are urgently needed. Further, IV treatments have the effect of requiring patients to expend much time traveling to treatment, and undergoing treatment; especially if they have difficulty doing home infusions. Many patients experience, or worry about damage to their veins. Drugs that are for the treatment of acute HAE attacks - that require venous access - pose a serious problem to patients as their ability precisely and safely self-administer the drug is naturally compromised by the fact that they are having an attack.

These barriers amount to amplified risk, and consequently increased fear and anxiety among HAE patients – severely compromising their quality-of-life. HAE patients urgently require improved prophylactic treatments, such as those injected subcutaneously, and therefore easier to administer at home.

We asked:

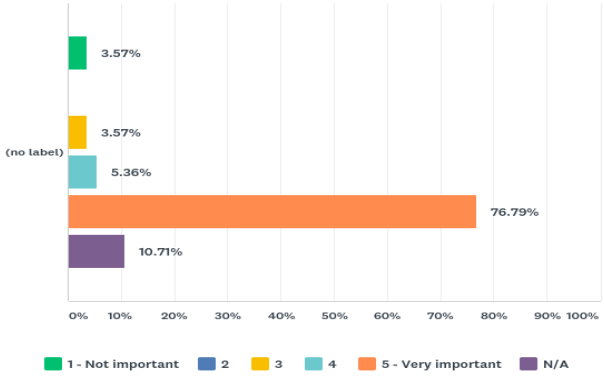
Q19 Have you and/or your physician made a choice of drug(s) based on mode of delivery (i.e. IV, subcutaneous etc.)?



30pts (52%) had made a choice of drug based on its method of administration.

We also asked:

Q18 Please rate on a scale of 1 – 5 how important it was for you and your physician to be able to make a choice of drug(s) based upon each different drug's known side effects? 1 is "not important" and 5 is "very important".



Over 82% of respondents to this questions rated the importance of treatment choice based upon each different drug's known side effects as **5**-*very important* (77%) or **4**-*somewhat important* (5%).

Patients had an option to add free-form commentary to the question re: *choice based on side effects*. Here is a selection of their comments:

-"There is no choice as of now. If i had a choice I would choose a sub-Q option 100%"

-"still waiting for subcutaneous rather than doing an iv twice a week."

-"...Administering this IV at home was impossible without assistance so it required attendance at the emergency department. …. subcutaneous injection is easy to administer. Lanadelumab has dramatically reduced my attack frequency and is also easy to administer."

-"Because of very poor veins and IV drugs going interstitial - we decided that I participate in a Subcutaneous drug trial which i am doing now."

-"At first it was IV but my veins could not take it anymore. I had too change for subcutaneous. I have to give myself the treatment more often."

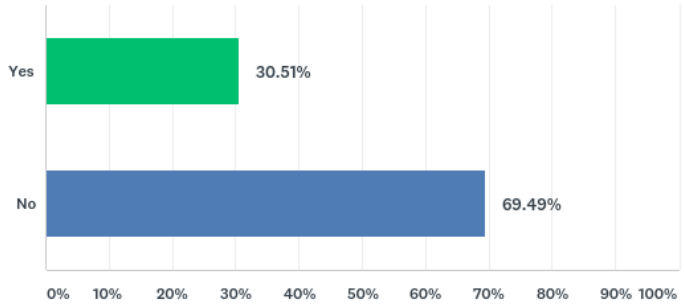
-"Would like subcutaneous treatment will discuss with Dr at next visit"

-"Giving IVs to yourself can be difficult without any assist and I don't want to hurt my veins for future use."

Difficulty Accessing Treatment

We asked:

Q20 Have you and/or your physician experienced any challenges or hardships in accessing therapy for your Hereditary Angioedema? (These may be related to cost, length of wait time, distance to travel).



Fifty-nine (59) pts responded to the question. 18pts (30.5%) reported having challenges in accessing therapy, and 41pts (69.5%) did not.

Patients had an option to add free-form commentary to the question re: challenges accessing therapy. Select comments:

-"Length of wait time to get diagnosis (63 years)!!!"

-"travel time is 45 minutes to a hospital"

-"Drug shortages"

-"Long hospital wait times before in home therapy"

-"cost is unbearable and wait time can sometimes be lengthy"

-"Costs as I'm currently a student and the medication will only be covered under Ontario works insurance"

Conclusion

Many patients find the treatment schedule for current treatments to be onerous, and disrupting. They also find administering IV treatments at home to be difficult and uncomfortable with some patients reporting damage to their veins, or concern about damage to their veins after years of treatment. Further, it is evident that a sizeable number of patients do not have any choice of treatment, or are not aware there is a choice.

Expectations for New Treatments

Patients continue to seek treatments that better control attacks while offering greater convenience and ease of use. Treatments that eliminate or substantially reduce attacks compared to existing treatments are of critical importance to patients as each edema attack can be severely debilitating and in many cases life-threatening. Greater control of attacks would also ameliorate the ever present anxiety and fear many patients experience due to unpredictable attacks, and reduce the negative impact on a patient's ability to work, pursue education, travel, exercise, do household chores, and socialize with family and friends.

We asked: ***If you were to consider taking a new therapy for your hereditary angioedema please rate the following on a scale of 1 - 5. 1 is "not important" and 5 is "extremely important".*** We had 5 categories as follows: 1) Improved management/reduction in attacks of edema (swelling), 2) No direct cost to user/patient, 3) Option to administer prophylactically before known triggers, 4) Easier mode of delivery as a subcutaneous option, and 5) A more convenient dosing interval/less frequent dosing.

1. Improved management/reduction in attacks of edema

Improved management/reduction in attacks of edema (swelling) *n=57*						
1 (not important)	2	3	4	5 (extremely important)	N/A	Weighted Average (WA)
1pt (1.75%)	0pts (0%)	2pts (3.5%)	7pts (12.3%)	47pts (82.5%)	**0pts (0%)**	**4.74**

2. No direct cost to user/patient

No direct cost to user/patient *n=58*						
1 (not important)	2	3	4	5 (extremely important)	N/A	Weighted Average (WA)
2pts (3.5%)	1pt (1.7%)	1pt (1.7%)	2pts (3.5%)	52pts (90%)	**0pt (0%)**	**4.74**

3. Option to administer prophylactically before known triggers

Option to administer prophylactically before known triggers (eg. traveling, dental procedures etc.) *n=56*						
1 (not important)	2	3	4	5 (extremely important)	N/A	Weighted Average (WA)
1pt (1.8%)	1pt (1.8%)	2pts (3.6%)	7pts (12.5%)	44pts (78.6%)	**1pt (1.8%)**	**4.67**

4. Easier mode of delivery

1. Easier mode of delivery as a subcutaneous option *(vs. IV) n=58*						
1 (not important)	2	3	4	5 (extremely important)	N/A	Weighted Average (WA)
2pts (3.5%)	1pt (1.7%)	3pts (5%)	7pts (12%)	44pts (76%)	**1pts (1.7%)**	**4.58**

5. A more convenient dosing interval/less frequent dosing

2. A more convenient dosing interval/less frequent dosing *n=58*						
1 (not important)	2	3	4	5 (extremely important)	N/A	Weighted Average (WA)
5pts (8.6%)	2pts (3.5%)	5pts (8.6%)	8pts (13.8%)	38pts (65.5%)	**0pts (0%)**	**4.24**

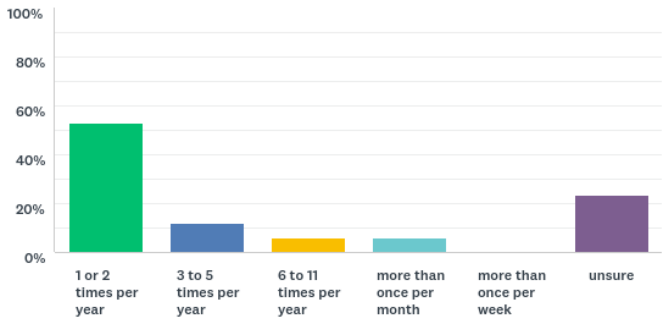
Treating On-demand is Not Keeping Patients Well

Patients with HAE continue to report that existing on-demand therapies are not meeting their needs.

Emergency Medical Care

In our November 2019 survey we asked patients:

Q4 How frequently have you (or the person you care for) had to seek emergency medical care and/or been hospitalized due to an attack?



17 patients provided their responses. These patients, despite use of available *on-demand* therapy to treat their attacks have had to continue to seek emergency medical care, and suffer disease-related impacts on their quality-of-life. Wider availability of prophylactic treatments for HAE will greatly improve the lives of those with HAE, and reduce the continued need to rely on emergency medical care.

Treatments that Prevent Attacks are Desperately Needed

HAE Canada acknowledges that some patients are using existing "on-demand" treatment for HAE as prophylaxis. In 2017 HAE Canada conducted a national survey to better understand product use, symptoms and needs of Canadians who live with HAE. We asked patients specifically about their use of C1 esterase inhibitor (Berinert), asking them to describe their use as i) On-demand, ii) Chronic Prophylaxis only or iii) Chronic Prophylaxis + on-demand.

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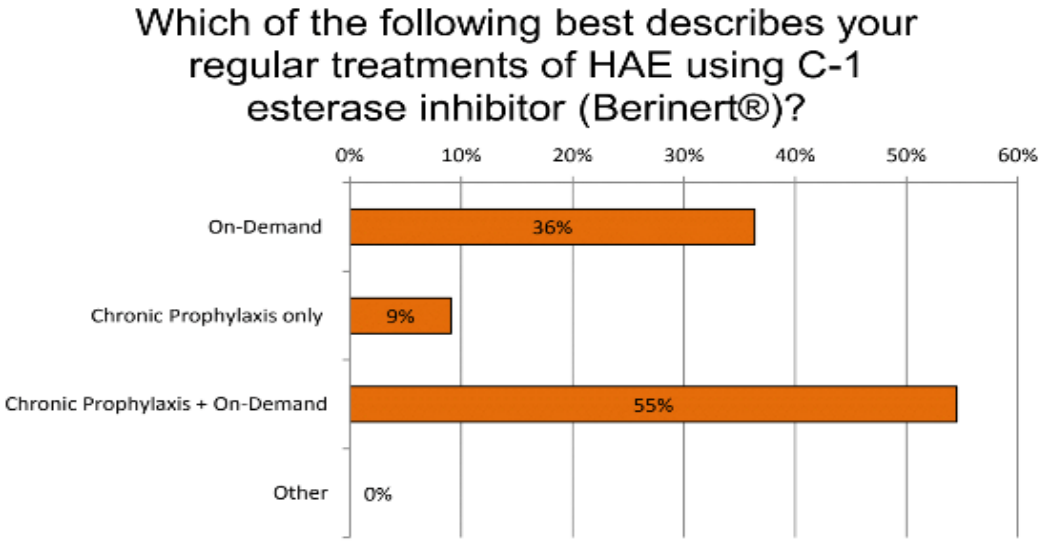

N=55

Patients are desperately seeking treatments that prevent attacks and keep them healthy and functional, and many are using existing therapies to achieve this. In our November 2019 survey, patients provided

many personal insights as to why treatments that prevent attacks are critically needed:

-My son who is 13 has HAE and 99% of his attacks are in his throat so having access to this treatment (to prevent attacks) in the future is going to allow him to live a normal full life without being a "frequent flyer" in Emerg or worse… 12/4/2019 2:29 AM

-I had a major HAE attack in January 2019 where my airway was completely swollen shut. I ended up in ICU and the hospital for 3 weeks. This year has been an intense year of recovery and healing. I continue to experience swellings a few times a month and take Berinert as a treatment. This works effectively but it is a response to an episode rather than a prophylaxis which helps to prevent future attacks. Treatments like HAEGARDA would improve the quality of my life and give the gift of less stress and more freedom. 12/4/2019 5:53 AM

- I am intrigued by the prospect of gaining access to HARGARDA. I am hopeful that such a treatment would give control and freedom back to me as a patient with HAE. 12/4/2019 5:53 AM

- I have not yet tried this therapy but am interested in learning more about it. Thank you. 12/1/2019 10:30 PM

-Having regular SC infusions has stopped the up and down swings that I had before when I treated acute attacks; even if I treated the acute attack right away, I still had the downswing of fatigue, low mood, irritability, and pain that came before the attack and then had the recovery period after the attack which could be as long as 72 hours depending on how fast the attack progressed. When I was having weekly attacks there was a lot of days that i did not feel my optimal self. Once I started SC infusions twice weekly I realized what normal felt like. I had got so used to suffering the prodrome before the attack, then the attack, and then the recovery period that I had forgotten what it was like not to live that way… 12/4/2019 2:29 AM

- I would be interested in learning more about this medication 12/1/2019 10:30 PM

- I used to have abdominal attacks a few times a month and would have to go to ER…My daughters and grand kid have HAE. Hopefully new therapies will help everyone 12/2/2019 3:42 PM

Conclusion

Of critical importance to patients are therapies with improved efficacy in preventing attacks. Additionally patients are seeking treatments that provide an easier mode of delivery (vs IV), and have no direct cost to the patients. Patients are also seeking treatments that have fewer side effects, and can be administered prophylactically before known triggers such as traveling or dental procedures.

Experience with HAEGARDA

In Canada, patient experience with HAEGARDA is limited to patients that took part in the COMPACT trial. Of the patients who underwent randomization, 79 completed the trial. These 79 patients were from ten countries: Australia, Czechia, Hungary, Israel, Italy, Romania, Spain, United Kingdom, United States and Canada. In Canada, the few patients that took part in the COMPACT study did so across 5 sites, with three sites in Ontario, one in Quebec and one in Alberta.

HAE Canada, in our survey conducted from November 28 - December 4, 2019, sought to reach patients with HAEGARDA experience through a combination of emailing our membership, and through appeals to the COMPACT investigators to share our the HAE Canada survey link with their patients who were on the COMPACT trial. Three (3) patients with HAEGARDA experience responded to that survey. Two of those three patients also took part in a follow-up in-person interview.

The survey contained the use of free-form commentary, scoring options and limited closed questions. And, as mentioned above, follow-up telephone interviews were conducted with two (2) patients who had experience with HAEGARDA.

The insights and experiences from these patients are detailed below.

Effectiveness of HAEGARDA

Ranking of Effectiveness

We asked these three patients: Based on personal experience with HAEGARDA, how would you rate its effectiveness in prevention of attacks of hereditary angioedema? 1 is "not effective" and 5 is "extremely effective".

All three patients selected "***5- Extremely Effective"***.

Reduction of Attacks

We asked these three patients: *How has the frequency of your HAE attacks changed since starting HAEGARDA?*

Patients had following answer choices:

Not at all (0%)

Reduced somewhat (1-25%)

Reduced noticeably (26-50%)

Reduced significantly (51%-75%)

Reduced enormously (more than 76%)

Two (2) patients selected "*Reduced significantly (51%-75%)*", and one (1) patient selected "*Reduced enormously (more than 76%)*"

Side Effects

We asked these three (3) patients: ***Based on your personal experience with HAEGARDA, how would you rate its side effects?*** (1 is "completely intolerable" and 5 is "very tolerable").
All three patients selected ***"5- very tolerable***".

We also asked: ***What are the side effects that you have experienced with HAEGARDA?*** (1 is "completely intolerable" and 5 is "very tolerable").

Patients had following answer choices:

Headache

Injection site reaction (bruising, skin inflammation, pain, hives, itching, hardening of skin tissue, hemorrhage)

Upper Respiratory-tract infection or cold

Dizziness

Fatigue

Back pain

One patient (Pt.#1) indicated only two applicable side effects: "Headache", which TO rated as "4-Tolerable" and "Injection site reaction" which TO rated as: "5-Very Tolerable"

One patient (Pt.#2) indicated that, with respect to HAEGARDA, all listed side effects were ""5-Very Tolerable"

One patient (Pt#3) not answer the question on the survey, but provided input in a live interview as follows:

[redacted]: "*The only noticeable side effect was Injection site reaction, which was very tolerable. There were no other reactions or side effects I experienced as a result of using this treatment."*

Comparative Tolerability

We asked these patients: *Based on your personal experience with HAEGARDA, how does it compare in terms of side effects to the other therapies you have taken to treat your hereditary angioedema? Rate on a scale of 1 - 5. 1 is "much harder to tolerate" and 5 is "much easier to tolerate". Patients were given a list of the following treatments with which to compare with HAEGARDA:*

Cinryze C1 Inhibitor (human)

Takhzyro (lanadelumab)

Berinert C1 Estrase Inhibitor (Human)

Firazyr (icatibant injection)

One patient (Pt.#2) only had one other treatment with which to compare to HAEGARDA. That treatment was *Berinert*. AP found that HAEGARDA was "***5 - Much easier to tolerate***" than *Berinert*.

One patient (Pt.#1) had two other treatments with which to compare with HAEGARDA. Those treatments were: *Berinert* and *Firazyr*. TO found that HAEGARDA was "***5 - Much easier to tolerate***" than both *Berinert and Firazyr*.

One patient (Pt.#3) did not answer this question on the survey, but provided input in a live interview as follows:

Pt.#3: "*HAEGARDA, is very tolerable, and the only side effect that I can remember is that I would get a bit of redness and stinging at injection site. But, this would only last a minute or two just around the time of injection, and really only noticeable when injecting in a new site. After 2 minutes the stinging would disappear. When I would inject at a previously used site, the redness/stinging would be less noticeable. When I was taking Takhzyro, the burning/stinging sensation was more noticeable*."

Quality of Life

We asked these three (3) patients: *On a scale of 1-5 how would you rate your quality of life while taking HAEGARDA?* (1 is "low/seriously impacted", and 5 is "high/normal living").

All three patients reported that their quality of life, while on HAEGARDA was "***5 - high/normal living"***

Patient Commentary

We asked patients: *Is there anything else about (HAEGARDA) that you would like us to know and include?*

Pt.#1: *I still had breakthrough attacks about once every couple of months with the 40 unit per kg dose but since going up to the 60 unit per kg dose I have had no attacks at all. Having regular SC infusions has stopped the up and down swings that I had before when I treated acute attacks; even if I treated the acute attack right away, I still had the downswing of fatigue, low mood, irritability, and pain that came before the attack and then had the recovery period after the attack which could be as long as 72 hours depending on how fast the attack progressed. When I was having weekly attacks there was a lot of days that i did not feel my optimal self. Once I started SC infusions twice weekly I realized what normal felt like. I had got so used to suffering the prodrome before the attack, then the attack, and then the recovery period that I had forgotten what it was like not to live that way. My attacks started at age 19 and became progressively more severe and frequent until i started SC C1 infusion in 2014 at age 44.*

Pt.#3*: I had more frequent attacks when I was on Takhzyro than when I was on HAEGARDA. Once on HAEGARDA I had very few attacks where I needed a rescue. While some people did better on Takhzyro than others, HAEGARDA worked better for me. I felt better on the HAEGARDA trial. I didn't feel the fatigue on the HAEGARDA trial like I did on Takhzyro. That is why we need treatment options, because not every patients responds to each treatment in the same way. HAE patients require treatment options. Many patients need to keep our veins for emergencies. In my case, I have much vein scarring from frequent IVs. Many other patients have scarring,, or veins which roll or collapse. This is why we need options with subcutaneous mode of delivery.*

We asked patients: *How has HAEGARDA changed, or how is it expected to change, your long-term health and well-being?*

Pt.#1: *Having regular SC infusions has stopped the up and down swings that I had before when I treated acute attacks; even if I treated the acute attack right away, I still had the downswing of fatigue, low mood, irritability, and pain that came before the attack and then had the recovery period after the attack which could be as long as 72 hours depending on how fast the attack progressed. When I was having weekly attacks there was a lot of days that i did not feel my optimal self. Once I started SC infusions with HAEGARDA twice weekly I realized what normal felt like. I had got so used to suffering the prodrome before the attack, then the attack, and then the recovery period that I had forgotten what it was like not to live that way. My attacks started at age 19 and became progressively more severe and frequent until i started SC C1 infusion in 2014 at age 44.*

During the period of 2014 to 2018 I worked full time in the ICU as an RN and went to school part time while also looking after my kids. I frequently worked 16 to 18 days in a row between my paying job and clinical hours for school with many of those days being 12 hour shifts. I graduated from the [redacted] *University Masters in Nursing/Primary Care Nurse Practitioner Program in 2018 as the graduate with the highest academic average. I could not have done that if I was having HAE attacks all the time. In fact, I had started my Masters in 2008 at* [redacted] *and had to drop out because I was sick with HAE attacks constantly. At that time there was no treatment for HAE except off-label*

danazol which I was allergic to. If I had not had access to replacement C1 and other HAE treatments I would never have been able to complete my Masters in Nursing.

We also asked: *Can you tell us about your story and why access to HAEGARDA and future therapies are so important to you?*

Pt.#1: *My son who is 13 has HAE and 99% of his attacks are in his throat so having access to this treatment (HAEGARDA) in the future is going to allow him to live a normal full life without being a "frequent flyer" in Emerg or worse.*

We currently treat his acute attacks with C1 inhibitor IV which we have available for him at home.

I work in health care and know the shortage there is for so many drugs in the market today. Without more than one treatment option patients run the risk of not having treatment when they need it .

Conclusion

HAE patients require a variety of treatment options to address a range of unmet needs including: improvement in prevention of attacks, improvement in the acute management of HAE, and more convenient methods/modalities of self-administration (vs. IV). Different treatment options are vital to ensure patients have options when they are faced with drug shortages, with both oral and injectable treatments; which is currently a reality and potentially will continue to be in the future. HAEGARDA is an extremely important addition to treatment options for HAE, and will greatly improve quality-of-life for many patients. Patients with experience with this treatment report better, and in many cases complete, control of attacks. Patients also report greatly improved quality of life afforded through much reduced attack-fearing anxiety, easier mode of treatment administration, and reduced dosing frequency. HAEGARDA is a superior drug treatment that affords patients desperately needed efficacy, while reducing the burden of disease related to treatment modality.

Financial Impact on Public Payers

HAE Canada would like to remind Canadian Blood Services that newly available improved treatment options for HAE should not be regarded only as a “cost” to public payers, but rather as an investment that we believe can deliver significant benefit to the health system.

In the COMPACT study, among patients with hereditary angioedema, a twice-weekly administration of HAEGARDA showed a median reduction in the attack rate, relative to placebo, of 89% with 40 IU and 95% with 60. This treatment effect was associated with an overall reduced need for rescue medication.

HAE patients are high users of the institutional care in our health care system. HAE attacks frequently result in emergency room (ER) visits and hospitalizations in the Intensive Care Unit (ICU). Further, HAE patients often have to rely on ambulance/EMT services to transport them to the hospital in the event of an attack. ER visits, ICU admissions and paramedic/emergency medical services are among the top drivers of health care costs in our health care system. .

Critically, HAE patients remain high users of the health care institutional care because treating on-demand is not keeping patients well.

As CBS, along with the Canadian Agency for Drugs and Technology in Health (CADTH) conduct an economic analysis of HAE treatments, including C1-INH products, to assess system challenges, treatment costs, patient access, utilization and sustainability, we urge you to also consider the cost offsets that these new innovative therapies afford our health system.

HAE Canada is prepared to partner with CBS to assess the financial impacts of current and emerging HAE treatments in the areas of costs and cost offsets to public payers across our health care system. HAE Canada has extensive reach to a highly-engaged patient population from across Canada to enable such research.