

VOICE OF THE PATIENT REPORT

Hypereosinophilic Syndromes



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This publication is a summary report developed by a patient advocacy organization as a result of an externally-led patient-focused drug development meeting, and reflects the host organization's account of the perspectives of patients and caregivers who participated in the meeting.

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Table of Contents

Introduction	3
Hypereosinophilic Syndromes Overview	4
Conference Overview	7
Report Overview and Key Themes	8
Topic 1: Patient Perspectives on Impact of Daily Life	9
Topic 2: Patient Perspectives on Current Therapies	13
Topic 3: Patient Perspectives on Ideal Treatments	15
Conclusion	17
Appendix	18
Appendix 1: Conference Agenda and Discussion Questions	18
Appendix 2: Patient Panel Participants	20
Appendix 3: Conference Polling Questions	22
Appendix 4: Results of Conference Polling Questions	25
Appendix 5: Patient Perspective Captured Through Apfed.org	31
Appendix 6: Incorporating Patient Perspective into Benefit-Risk Assessment for HES	37

Introduction

This is a summary report resulting from the Hypereosinophilic Syndromes Patient Education and Drug Development Conference on March 23, 2018 in Rockville, MD, organized and hosted by the American Partnership for Eosinophilic Disorder (APFED). Founded in 2001, APFED is a 501c3 nonprofit advocacy organization whose mission to passionately embrace, support, and improve the lives of patients and families affected by eosinophil-associated diseases through education and awareness, research, support, and advocacy.

This report reflects the perspectives of patients and caregivers who participated in the conference. It offered a unique opportunity to learn about treatments and research advances for hypereosinophilic syndromes (HES), and to share perspectives with the U.S. Food and Drug Administration (FDA) and other key stakeholders about the impact HES has on patients who have these conditions and their families, as well as learn about patient views on current treatment approaches to HES. Dynamic sessions and question and answer opportunities allowed all those who participated in-person and by live webcast to learn and share knowledge.

The conference was financially supported by APFED's education partner Knopp Biosciences which offset costs related to hosting this conference. APFED worked independently on conference planning, content, speakers and panelist identification, and development of this report.

The Voice of the Patient: Hypereosinophilic Syndromes Report Contributors

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Hypereosinophilic Syndromes Overview

Hypereosinophilic syndromes (HES) is the umbrella term for a group of rare disorders in which high numbers of eosinophils are found in the blood and affected organs for prolonged periods. In the vast majority of cases, the cause of the cell proliferation is unknown.

The continuous presence of high numbers of eosinophils in blood with infiltration of organs, causes inflammation and progressive damage.¹ HES can affect any organ in the body, including the heart, skin, lungs, gastrointestinal tract, liver, spleen and eyes.^{2,3}

HES is debilitating and can be fatal. It is a disease that is chronic, symptomatic, and can greatly impact the individual's quality of life and be associated with greater healthcare utilization.

The cause of HES is not known. While both men and women may be affected by HES, the disease is more commonly seen in males ages 20-50. While it is more commonly diagnosed in adulthood, it has also been diagnosed in children. HES is a rare disease, with U.S. prevalence estimates ranging widely, from 1,000-20,000 people affected. Approximately 13 years ago, the European Medicines Agency estimated the prevalence of HES to be 1.5 per 100,000 people,⁴ which extrapolates to about 8,000 in the EU, 5,000 in the U.S., and 2,000 in Japan.

To date, there are three known subtypes of HES:

- *Myeloproliferative HES (M-HES)*: Accounts for an estimated 15% of all HES cases. This subtype is most frequently associated with a genetic deletion causing the chromosomal rearrangement the PDGFRA and FIP1L1 genes, resulting in the clonal proliferation of eosinophils and chronic eosinophilic leukemia⁵.
- *Lymphocytic HES (L-HES)*: Accounts for an additional 15% of all HES prevalence. This subtype is associated with a proliferation of clonal T cells that drive eosinophil proliferation and activation.
- *Idiopathic HES (I-HES)*: Approximately 70% of estimated prevalence is considered idiopathic. This subtype does not have a defined etiology and is not associated with a known chromosomal or clonal abnormality.⁶

Diagnostic criteria for HES include:

1. Peripheral blood eosinophilia (high numbers of eosinophils in the blood) more than 1,500 eosinophils/ μ L, for at least six months' duration.
2. End-organ (e.g., heart, lungs, GI tract, brain, skin) involvement with eosinophil tissue infiltration (invasion) and injury.
3. Exclusion of known other causes for the eosinophilia, such as parasitic infections and certain bone marrow and blood diseases.

Tests are used to diagnose HES and exclude other causes of eosinophilia include a complete blood cell count with eosinophil count, blood samples for liver and kidney function, and blood tests for Vitamin B12 and tryptase. Molecular and flow cytometric tests are used to support the diagnosis of myeloproliferative or lymphocytic HES. A bone

marrow biopsy is recommended in patients suspected of having HES. Other tests may also be performed, such as echocardiography to look at the function of the heart and a chest CT to examine the lungs.

The disease may be diagnosed and monitored by a team of physicians, including hematology, allergist/immunology, pulmonology, and/or cardiology specialists.

Patients with HES suffer significant morbidity, delays in diagnosis, increases in healthcare utilization, and have limited treatments options.

Current Therapies

To date, there are limited therapeutic options for HES. Current standard of care in treating both idiopathic and lymphocytic HES involves chronic, off-label use of corticosteroids. Treatment goals of HES include decreasing blood eosinophil numbers, preventing organ damage, and slowing disease progression. Treatments vary based on organs involved and disease severity, as well as on the presence of other medical problems a patient may have.

These therapies may include:

- Corticosteroids (i.e., prednisone) suppress inflammation and decrease eosinophil number. Corticosteroids can be effective for controlling eosinophil numbers in blood and tissue. Most L-HES and I-HES patients can be maintained on oral corticosteroids for long periods of time with fairly good success in suppressing eosinophils. However, the chronic use of oral corticosteroids is associated with serious side effects, including osteoporosis, glucose intolerance and diabetes, dyslipidemia, hypertension, atherosclerosis, cardiovascular disease, cataracts and glaucoma, infections, adrenal insufficiency, and avascular necrosis.⁷ The risk of serious side effects increases with greater dose and duration of corticosteroid exposure, and is apparent at doses greater than 10 mg/day.
- Interferon alpha (IFN- α), has been shown to be effective in suppressing eosinophil counts and HES-related symptoms, but its use is limited due to side effects of therapy. Upon the initiation of therapy most patients experience influenza-like symptoms such as fever, chills, muscle aches, headaches, and joint pain. Other side effects of IFN- α are low blood counts and elevated liver enzymes that require careful monitoring. These side effects usually lessen over time, but other toxicities can manifest themselves in various forms after long-term therapy. In one multicenter retrospective study in HES, IFN- α was discontinued in 87% of patients started on the drug, mainly due to side effects (50%) and lack of efficacy (36%).⁸
- Anti-neoplastic agents (chemotherapy), particularly the agents hydroxyurea, methotrexate, etoposide, cyclophosphamide, vincristine, and cladribine, provide an alternative approach to therapy of advanced cases of HES. They are potent medications that kill cells that grow the fastest (eosinophils in HES), but may potentially have harmful side effects and are reserved only for more severe cases. Hydroxyurea was discontinued in 77% of HES patients, mainly due to lack of efficacy (47%) and side effects (43%).⁸

- Imatinib mesylate (Gleevec) is a tyrosine kinase inhibitor for controlling malignant cell growth. Eosinophils in the 10-20% of patients with M-HES have a genetic abnormality of eosinophils involving a tyrosine kinase that is responsible for their HES. Genetic testing for this abnormality is usually part of an HES evaluation and helps to determine if this drug is best first therapy. Imatinib is the only drug with an FDA-approved label for use in HES. Imatinib treatment typically lowers eosinophil counts to the normal range and is an effective treatment for M-HES. In other forms of HES, Gleevec has not been shown to be effective.

For patients who are refractory to conventional therapies, off-label use of monoclonal antibody therapy is sometimes considered. Mepolizumab, reslizumab and benralizumab are drugs approved for eosinophilic asthma. Both work by targeting interleukin-5 or its receptor, the major eosinophil active cytokine. Alemtuzumab (CAMPATH) is approved for use in B-cell chronic lymphocytic leukemia but has shown some activity as a salvage therapy in HES.

References

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Conference Overview

APFED's Hypereosinophilic Syndromes Patient Education and Drug Development Conference offered participants the unique opportunity to learn from medical experts who presented lay-friendly lectures about diagnostic and treatment approaches to hypereosinophilic syndromes (HES), and for patients to share the impact HES and its treatment has on them and their families, as well as their views on current treatment approaches.

The facilitated discussions focused on three topics: (1) patient perspectives on impact of disease on daily life, (2) current treatment options and side effects, and (3) patient perspectives on ideal treatments. The questions discussed are presented in Appendix 1.

For each topic, a panel of patients (Appendix 2) shared comments to begin the discussion. Panel comments were followed by inviting comments from other patients and caregivers in the audience. APFED's President, Dr. Wendy Book, facilitated the discussion. Participants who joined the conference via the live webcast (virtual participants) were invited to contribute comments throughout the discussion.

Attendees

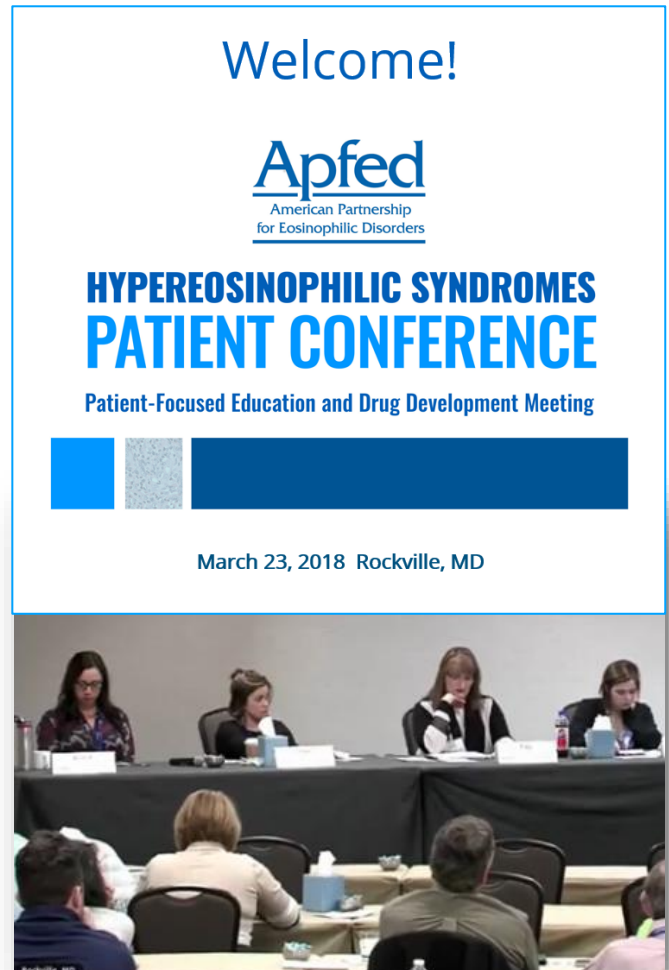
More than 50 people attended the conference in-person and more than 50 additional people attended the conference virtually.

The in-person attendees included:

- Approximately 29 HES patients and caregivers
- Approximately 4 representatives of the FDA
- Approximately 14 industry representatives
- Approximately 5 APFED staff/consultant, and volunteers

Both in-person and virtual participants were periodically invited to respond to polling questions (Appendix 3), which provided a sense of the demographic makeup of participants (see Appendix 4, Q1-4) and how many participants shared perspectives. An audience response system (ARS) was used to conduct the polling questions. More than 50 patients and caregivers answered the questions. To supplement the input gathered at the conference, APFED invited patients and caregivers who were unable to attend the conference to submit information about their experiences through a form on apfed.org. Four people completed the questionnaire (see Appendix 5).

Conference materials, including the archived webcast and transcripts are available on APFED's website at <https://apfed.org/events/2018-hes-pc/>.



Report Overview and Key Themes

The report is divided into three sections based on the three patient perspective discussion sessions at the conference (Impact of Disease on Daily Life, Current Therapies, and Ideal Treatments) and includes an appendix.

This report summarizes the input provided by meeting participants. To the extent possible, the terminology used in this report reflects the words used by the participants. This report is not meant to be representative in any way of the views and experiences of any specific group of individuals or entities. There may be symptoms, impacts, treatments, or other aspects of HES that are not included in the report. Comments made during the conference and submitted online to APFED through apfed.org covered a range of other important topics.

- Patients who have been diagnosed with hypereosinophilic syndromes report that symptoms and side effect of therapies have negatively impacted work, social/leisure/recreational activities, and personal relationships.
- Patients report a myriad of symptoms of HES; most commonly cited symptoms include lung/heart (e.g., shortness of breath, cough, wheezing, or chest pain), skin (e.g., itchiness, rash, swelling, angioedema), fatigue, muscle or joint pain, gastrointestinal (e.g., lack of appetite, pain, nausea, vomiting, diarrhea), and neurological (e.g., numbness/tingling, neuropathy/pain, muscle weakness, “brain fog”/poor memory).
- Of all symptoms a patient had ever experienced, they reported fatigue or tiredness, coughing, wheezing, or shortness of breath, and brain fog or poor memory had the most bothersome impact on their daily lives.
- Patients reported depression, anxiety or worry, difficulty concentrating, limitations on work or school, and sleep problems to be the most bothersome impacts of HES symptoms.

Discussion Topic 1: Patient Perspectives on Impact of Daily Life

The first discussion topic focused on patients' perspectives on the impact of HES on their daily life. The discussion topics can be found in Appendix 1.

Four patient panelists (Appendix 2) provided comments to begin the dialogue. They included:

- Shelly Parks: 27 years old, diagnosed one year ago
- Tina Singer: 45 years old, diagnosed more than 20 years ago
- Lorien Hall: 36 years old, diagnosed 27 years ago
- Amber Felts: 39 years old, diagnosed three years ago

The panelists shared their experiences with HES and its impact on their daily lives, including detailed descriptions of their symptoms and their journey through diagnosis and treatment. Their comments highlighted daily challenges with pain and fatigue. The contributions from in-person and virtual attendees mirrored that of the panelists and provided further insight. More specifics about the symptoms and impact of HES on daily life are described below.

Perspectives on most significant symptoms

Skin, liver, and heart symptoms are common for HES patients. The ARS responses to live polling of the panelists and attendees confirmed this through questions about the patient's most common and most troublesome symptoms (see Appendix 4, Q5-7).

The Audience Response System (ARS) responses revealed the following:

- **Most common symptoms** (see Appendix 4, Q5 and 6): lung/heart (e.g., shortness of breath, cough, wheezing, or chest pain), skin (e.g., itchiness, rash, swelling, angioedema), fatigue, muscle or joint pain, gastrointestinal (e.g., lack of appetite, pain, nausea, vomiting, diarrhea), and neurological (e.g., numbness/tingling, neuropathy/pain, muscle weakness, "brain fog"/poor memory)
- **Most bothersome symptoms** (see Appendix 4, Q7): fatigue or tiredness, coughing, wheezing, or shortness of breath, brain fog or poor memory

Commentary from panelists and participants reinforced the challenges with pain (e.g., muscles, joints), gastrointestinal symptoms (e.g., pain, vomiting), and neurologic issues (e.g., fainting, nausea, migraines). Patients also commented on the challenges of getting an accurate diagnosis.



One of the panelists described the onset of her symptoms by saying “I was suddenly struck with asthma as we were visiting high elevations.” Another shared that “My journey started when I was admitted to the hospital several times for uncontrollable vomiting” and later she experienced “heart failure seven times.” Another panelist experienced “extreme swelling, rash and boils that covered most of my body.”

The nature and severity of the symptoms varies widely among patients and can even vary within the course of an individual’s life. Because the symptoms of HES are also common in many other medical problems, HES is difficult to diagnose, and the diagnosis is often delayed.

Overall impact of HES on daily life

Participants described the physical, social, and emotional impact that HES has had on their lives. The ARS responses revealed the most bothersome impacts of their symptoms (see Appendix 4, Q8) to be: depression, anxiety, or worry; difficulty concentrating or staying focused; sleep problems; insomnia; limitations on work or school. The discussion touched on these areas with comments such as the following:

Not participating as fully in activities they enjoy. Participants discussed the impact HES has on their ability to do specific activities that are important to them. A common theme among the comments were physical activities such as exercise. “Before I became ill I was an exercise enthusiast,” shares one panelist. “The gym was my stress relief, my place to go to let everything go. Unfortunately, my HES has limited all activities in the gym. There are days where I am unable to take my dog for a walk because either the pain is so bad or I am running back and forth to the bathroom so much that I don't think I'll be able to make it for an entire walk. Extracurricular activities have been completely limited by my disease.”

“I was also really active before I was diagnosed,” agreed another panelist. “I went from working out four or five days a week to zero. I went from being really active to totally not active. Then obviously with that comes the weight gain, and you start to feel pretty terrible about yourself.”

“The symptoms and fatigue of HES prohibit me from doing what is important to me. Sometimes I am not able to do what I want to do because of exhaustion and pain such as attending family outings, events and day to day life activities. I feel like my days have been shortened so to the fatigue, chronic pain and systematic symptoms.”
HES Patient

Caring for self or family. Participants shared the difficulties they experience in both caring for themselves and their families. One participant had been living in California and commented, “We came back to Virginia so my mother could help me with my son and the many things I could no longer do for myself.” Another participant shared that she could “no longer exercise or lead an active lifestyle.” Furthermore, another participant contributed that “There are days where I am unable to take my dog for a walk because the pain is so bad.”

The challenges that people with HES have with their care have also led to some difficult decisions. An audience member – a patient with HES – shared that due to her lack of energy and the memory loss/brain fog she was experiencing, she could no longer fully support her daughters at home. “We’ve made the decision this year that both of my older girls will be at boarding school for probably the rest of high school.”

The participants described their lives before HES as quite active and indicated that they wished they could be active again. One participant shared, "...the things that I really wish that I could do is go bike-riding with my boys. I can't do that physically. Too much energy exertion. Even going to a theme park with my family, walking through the park I would have to sit down, and then I'd just have to go to sleep. There are days that if I push myself too hard than I'm out for 15 to 20 hours of sleeping, just getting tired all the time."

Job and school performance. Participants shared that the pain and fatigue they experience also impact their ability to concentrate, which impacts their work/school performance and their ability to work and attend school. One participant noted that she hasn't been able to work for nearly two years, and "at age 27, I spend most of my time at doctor's appointments, in and out of the hospital, and consistently fighting to live a healthier life."

"HES has affected both my work life and my school life...I actually missed graduation because I was in the hospital...Since I became ill, I have been out of work."
HES Patient

One parent of a HES patient shared, "This has impacted our family tremendously. [My daughter] has missed a great deal of school over the past few years. I have my own business. Fortunately, I have employees, but at 53, I am essentially semi-retired so that I can become the primary caregiver for her...Endless doctor visits and treatments and so forth. Certainly a significant impact in cost as well."



Emotional and social impacts. There are numerous emotional and social impacts of HES that participants shared including depression, anxiety, and worry. One participant shared that “At 22, I told my parents no one deserves to live like this.” She went on to comment that “my life is a constant battle of benefit versus risk.”

Several participants expressed concern about the long-term prognosis of HES, and their own mortality.

One participant shared, “the biggest fear that I have is that I will not be able to have a family or children to care for.” Another said, “I’ve definitely had a lot of days thinking about my own funeral.” Yet another participant commented, “I force myself to get out of bed every single day. I know that when I decide to stop being active that my illness will take over. I refuse to give in to my illness and allow my illness to determine my death. I will fight it until my last breath.”

One HES patient who was not in attendance at the meeting, but responded to a questionnaire posted on apfed.org wrote, “My concerns looking to the future for HES is the severity of the illness and the impacts.”

“I am worried about long term prognosis. At this point I am able to control my disease with a small dose of Prednisone every other day. I am concerned about disease progression and alternate treatments.”
HES Patient

Topic 2: Patient Perspectives on Current Therapies

The second discussion topic focused on patients' perspectives on current therapies used to treat HES. The discussion topics can be found in Appendix 1.

The four patient panelists (Appendix 2) provided comments to begin the dialogue.

When treating HES, the goal is to reduce the eosinophils in the blood, prevent organ damage, and slow disease progression. The treatments vary based on the organs involved, disease severity, and other medical issues. They may include:

- Corticosteroids (e.g., prednisone)
- Interferon alpha (IFN- α) injections
- Cyclosporine
- Anti-neoplastic agents or chemotherapy
- Imatinib mesylate
- Monoclonal antibody therapy

A variety of the treatments listed above were discussed by the panelists and participants. The discussion included perspectives on the benefits and downsides to these treatments. The panelists and participant perspectives are summarized below.

The majority of ARS respondents indicated they or the patient they care for are currently using or have used oral corticosteroids to treat HES, which is currently the standard of care for HES. Nearly 30 percent of the ARS respondents indicated they have had to stop an HES treatment due to side effects. (See Appendix 4, Q9-11.)

Perspectives on current treatments for HES

The focus of the discussion on current treatments for HES captured how the patients felt about current treatments available for HES. Several participants expressed concerns about if their treatment was actually helping them.

The positive feedback on the currently available treatments included:

Increased energy. Comments repeatedly focused on how that the treatments, particularly steroids, increased the patients' energy levels. One participant commented that "the only thing I liked about it was it gave me more energy." Another commented, "It increases my energy. Makes me feel way better."

Once a week treatment. Those that are taking or have taken treatments by injection commented that they appreciate the once a week treatment. One participant commented, "The best thing about methotrexate is that it's once a week. I don't have to worry about it daily."

The feedback on the downsides of the treatments included:

Pain and fatigue. Rather than helping with their fatigue and pain, many participants commented that the treatments make it worse. One participant commented that it “Doesn’t help my chronic fatigue or the pain.” Some participants commented that the treatments make their pain worse. One participant commented “The day I get the shot, I try not to plan anything else.”

Another participant shared, “When I was complaining about the pain, numerous doctors accused me of being a narcotic-seeker just simply looking for the narcotics.”

Weight gain. Multiple participants commented negatively about gaining weight as a result of taking steroids. “Looking at yourself in the mirror and not seeing the same person any more is a really big deal,” one HES patient said.

“I only had steroids as an option. I starved myself sometimes to cope with the abnormal type of weight gain.”
HES Patient

Mental impact. Multiple participants commented on the mental impact they experienced from taking steroids. One participant shared, “The steroids make you so just on edge, going so fast that you’ll say things faster than you can even think and you’re emotional.” Another participant described the mood swings she experienced while taking steroids as “going between the Incredible Hulk and Sylvia Plath in the same day.”

Long-term effect. Multiple participants shared their concerns about the long-term effect of steroids which is associated with serious side effects such as adrenal insufficiency, avascular necrosis, osteoporosis, infections, and stunted growth. This was well summarized by the comment of one participant when they said, “The concerns I have about steroids would be the long-term effect on the body, the bone loss, the damage to the adrenal glands, which was one of the reasons I fought so hard to get off of it and find another option.”

Current treatments impact on relationships with others

The treatments not only have an impact on the patients themselves, they also have an impact on the patient’s relationships with others. Two participants’ comments summarized the feedback:

- “It almost feels like my life has stopped and everybody else has just continued to grow, and to move on, and to get married, and do all these things that at age 27, I feel like I should be doing, too.”
- “I got to the point where I just don’t have a social life. I have my kids, I have my husband, my family, and I have my animals.”

Topic 3: Patient Perspectives on Ideal Treatments

The third discussion topic focused on patients' perspectives on ideal treatments. The discussion topics can be found in Appendix 1.

Four patient panelists (Appendix 2) provided comments to begin the dialogue.

Participants were asked to identify specific attributes they would look for in an ideal treatment for their HES. A range of perspectives was provided and are summarized below.

In the live polling that was conducted, ARS respondents indicated the following benefits were the most important when considering a new treatment for HES:

- less depression, anxiety, or worry
- decreases long-term end organ damage
- improved concentration and focus

These were closely followed by:

- improves HES symptoms, and
- enables greater participation/involvement in social activities

The answer choice of a treatment being “convenient to take” garnered the fewest responses.

Perspectives on ideal treatments

There are a variety of aspects of treatments that the participants would like to see improved. They want a treatment to better manage their symptoms, to decrease the eosinophils in their organs and/or blood in order to slow the disease progression, to be more affordable and available, and they want to know that there are not long-term negative effects to using the treatment.

“An ideal treatment for HES would be a less invasive method. One that is not too harsh on the body and works to help stabilize the illness.”
HES Patient

One participant shared, “I have come to realize that managing my symptoms is more realistic than finding a cure.” Another participant shared, “I would like to see help with chronic fatigue, and then find a way to have the eosinophils in the blood match the eosinophils in the organs so doctors can better treat the patient's organ damage before it gets to the point of having to remove the organ.” And another participant commented, “I'd also like to add an ideal treatment would be something that we also know how it may affect us in the future.”

The discussion about ideal treatments also raised points about a desire for medical professionals to have more awareness and knowledge of HES.

The questionnaire posted to apfed.org included an open text field area for HES patients to share what they considered to be a meaningful improvement a HES treatment could offer. This question captured additional perspective, such as “less muscle fatigue”, “a therapy that had few side effects”, and that injections on a monthly basis would be reasonable.

Selecting new treatments: benefits vs. risks

When deciding to take or not to take a new treatment, the participants shared the desire to analyze the benefits and the risks both short- and long-term, particularly regarding side effects. One participant shared, “I do a benefits and risk analysis to see if the benefits for this drug will outweigh even some of the side effects that I may have from it, and if long term, if this is a drug that will keep me healthy longer than what I'm on now, it's definitely a risk that I would take.” The group agreed that risk benefit analysis may be different for each person depending on their current challenges and the side effects that they personally experience. This was summarized by one participant who shared, “It depends on the position you're in and what the risk/reward would be.”

“The factors and information on the potential benefits of treatments that I take into account when deciding on a course of treatment is one, how will it stabilize my HES, how will it affect me today and later? What will it do to my body now and in the future?”
HES Patient

Participants also expressed that the effectiveness of treatments play a role in their decision-making process. One participant commented, “Another thing I look at with new drugs is effectiveness because I would like to know is it an 80% chance that I'll see results, I'll see improvement, or is it a 30% chance because even if it has less side effects, I don't know if I'd be willing to jump on this new bandwagon and try this medication if it's not more likely to work.”

Another HES patient responding through the questionnaire posted to apfed.org shared perspective about factors or information on the potential benefits of treatments taken into account when deciding on a course of treatment. She wrote, “Long-term effectiveness; convenience is also important with a corporate job with high demands and time constraints.” She also noted there were limited effective treatment options.

“I think it depends on where you are with the condition. If I were in a position where I had tried everything, and I was suffering and not able to function, then I would consider something that was risky if I felt like I didn't have any other options left, and especially with all...we get blood tests constantly, we have our hearts checked, we have our organs checked. So, if I knew I was going to be monitored enough to catch something like that, then I would be willing to risk it a little bit if I was in that position.”
HES Patient

“I look at the quality of life,” answered a HES patient when asked about how she weighs the potential benefits of a treatment versus common side effects. “Basically, if I found a treatment that would give me more energy and allow me to do more things, but I would get a case of nausea and maybe in the morning and the evening, I feel like I can handle it, I would definitely take the benefit of having that energy and a better quality of life, and able to do more things because at this point, I don't do a lot of things, a lot of anything, except for teach. I would definitely look towards the benefit of having more energy and sacrificing maybe feeling sick once in a while just so I could have a little more energy during the day.”

Conclusion

APFED's Hypereosinophilic Syndromes Patient Education and Drug Development Conference emphasized the need for more effective treatments for HES with fewer side-effects, both short-term and long-term.

The conference enabled clinicians, researchers, pharmaceutical developers, members of FDA, and other stakeholders the unique opportunity to hear directly from HES patients and to better appreciate their physical and emotional impacts related to living with these diseases.

Presentations by renowned HES researchers and clinicians provided unique insights into the complex issues faced in developing better treatments for HES.

We are grateful to the HES patients, caregivers, researchers, and clinicians who participated. It was clear that there is a desire to advocate for current and future HES patients.

Conference materials, including the archived webcast and transcripts are available on APFED's website at <https://apfed.org/events/2018-hes-pc/>.

Appendix

Appendix 1: Conference Agenda and Discussion Questions

Hyper eosinophilic Syndromes (HES) Patient Conference

Patient Focused Drug Development Meeting

Friday, March 23, 2018

Hilton Washington DC/Rockville Hotel & Executive Meeting Center
Roosevelt and Madison Rooms | 1750 Rockville Pike, Rockville, MD

Time	Sessions	Speakers
7:30 AM	Check in and Breakfast	
8:30 AM	Conference Opening and Welcome Remarks, Speaker Intro	Dr. Wendy Book <i>APFED President</i>
8:35 AM	Patient-Centered Therapies: The Role of the Patient in Drug Development	Dr. Calman Prussin Dr. Dawn Phillips
8:45 AM	Hyper eosinophilic Syndromes, Then and Now: Perspective Piece	Dr. Gerald Gleich
9:05 AM	Introduction of panelists, panelist remarks Patient Perspectives on Impact of Disease on Daily Life	Patient panel
10:35 AM	Break	
10:50 AM	Patient Perspectives on Current Therapies	Patient panel
12:00 PM	Current Treatment Options and Side Effects (with Q&A)	Dr. Paneez Khoury
12:20 PM	Lunch	
1:20 PM	Patient Perspectives on Ideal Treatments	Patient panel
2:20 PM	Pediatric vs Adult HES + Q&A	Dr. Patricia Fulkerson
2:40 PM	HES Research Update + Q&A	Dr. Amy Klion
3:05 PM	Connecting with Resources and Support: For Patients and Providers	Mary Jo Strobel <i>APFED Executive Director</i>
3:15 PM	Closing Remarks	Dr. Wendy Book <i>APFED President</i>

Discussion Questions

The following is a framework for the discussion topics to be addressed in the panelist panels. Conference attendees will be invited to participate in the discussion, along with the panelists.

Discussion Segment #1: Patient Perspectives on Impact of Disease on Daily Life

1. How does HES affect your abilities at work or school?
2. Are there specific activities that are important to you but that you cannot do at all, or as fully, because of HES?
3. What worries you most about your condition?
4. Do you feel your condition changed over time, since diagnosis? If so, how?
5. Do you consider your HES to be well-managed today? What does “well-managed” mean for you specifically?
6. Do you feel HES has impacted your relationships with others? If so, how? Or if you are a family member or friend of someone with HES, how would you describe the impact of HES on you?
7. What are your concerns about your HES in the future?

Discussion Segment #2: Patient Perspectives on Current Therapies

1. Regarding treatments that you are currently using, what do you like about it? What don't you like about it?
 - o What are the most significant downsides to your current treatments?
 - o What concerns, if any, do you have about your current treatments?
 - o How well do you feel it controls your symptoms?
When you answer, please include which treatment your answer is related to.
2. Do your treatments impact daily life? If so, how?
3. Steroids, such as prednisone, are commonly used to treat HES. If steroids are part of your treatment:
 - o What do you like about steroids?
 - o What do you not like about steroids?
 - o What concerns, if any, do you have about steroids?

Discussion Segment #3: Patient Perspectives on Ideal Treatments

1. Aside from a complete cure, what meaningful improvement would an ideal treatment for HES provide?
2. What factors or information on the potential benefits of treatments do you take into account when deciding on a course of treatment?
3. How do you weigh the potential benefits of a treatment versus any *common* side effects such as headache or nausea?
4. How do you weigh the potential benefits of a treatment versus any *less common* side effects such as serious risks to liver or kidney damage?

Appendix 2: Patient Panel Participants

Patients with HES participated in the conference as panelists. They shared their experiences with HES during each of the discussion segments.

Shelly Parks

Shelly is a 27-year-old who was diagnosed with idiopathic HES in 2017. Before she became ill, she described herself as a “strong, hardworking and outgoing individual.” When she wasn’t working or at school earning her second master’s degree, she could be found in the gym competing in CrossFit competitions, or with her boyfriend or friends, or cheering on her favorite sports team. As her symptoms worsened, doing these became almost impossible. Shelly saw a number of specialists over the course of a year and received several misdiagnoses before she was diagnosed with HES. Since her diagnosis, her team of doctors have worked to get her disease under control, trying several therapies, all of which have not proved effective. Her disease progression has caused damage to her gastrointestinal tract, lungs, and she suffers from short-term memory loss.



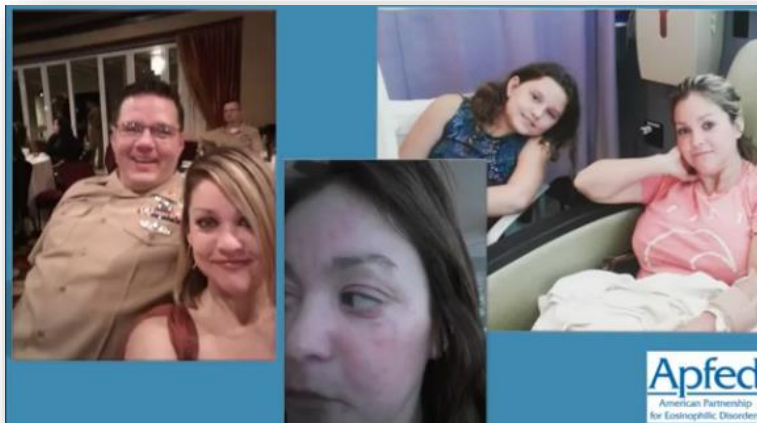
Tina Singer

Tina is 45 years old and lives with her husband and two teenage sons. She owns a dance studio in Stafford, VA. She began her journey with HES over 20 years ago after being admitted to the hospital several times for uncontrollable vomiting. She had several digestive problems affecting her intestines, peripheral neuropathy in her legs, brain lesions, occipital neuralgia, high protein levels in her spinal fluid, moderate leakage in her mitral valve and tricuspid valve with thickening of the valve walls of her heart. Over time, she was misdiagnosed with different conditions including irritable bowel syndrome, eosinophilic gastroenteritis, and Lupus. Today, Tina’s blood eosinophils remain low, but her organs continue to have large amounts of eosinophils in them.



Lorien Hall

Lorien was diagnosed at the age of 9 and described her symptoms as extreme swelling, rash and boils that covered most of her body. Her doctor prescribed high doses of steroids. She also participated in experimental trials and was prescribed chemotherapy treatments and high doses of antihistamines which were not effective. As a young adult, Lorien began a trial with mepolizumab and eventually received the medication under Compassionate Use. A new doctor working with Lorien diagnosed her with a specific subset of HES -- Lymphocytic Hypereosinophilic Syndrome -- and prescribed cyclosporine with the mepolizumab, which Lorien credits with changing her life for the better. Lorien moved from the West Coast to the East and is experiencing difficulty in accessing mepolizumab. She is currently traveling back and forth to California to receive the treatment that helps her.



Amber Felts

Amber is 39 years old whose journey with HES began three years ago after she was suddenly struck with asthma symptoms while visiting high elevations. Not having had asthma in over 20 years, accompanied by a cough she had developed, she sought urgent care and was prescribed antibiotics and inhalers. While the inhalers helped, her symptoms persisted and expanded, and she continued to seek care. She was diagnosed with allergies and her symptoms continued to worsen. After collapsing at home and having a battery of test performed at the hospital, she was diagnosed with HES. After finding APFED, Amber was able to connect with other patients and learn of other treatments, which she discussed with her doctors. She soon started mepolizumab which enabled her to get off prednisone and stabilize her eosinophil counts and has been able to return to an active lifestyle.



Appendix 3: Conference Polling Questions

The following questions were posed to in-person and virtual participants at various points throughout the March 23, 2018 HES Patient Conference. Participation in the polling questions was voluntary. The results were used as a discussion aid only and should not be considered scientific data. Please see Appendix 4 for polling results.

Demographics

1. Are you a patient with HES or a caregiver of a person with HES?
 - a. I have HES
 - b. I am a caregiver of a person with HES
 - c. None of the above

2. Where do you live?
 - a. Within the Washington, DC metropolitan area (including the Virginia and Maryland suburbs)
 - b. Outside the Washington, DC metropolitan area.

3. Please share your age (or age of patient)
 - a. Less than 18
 - b. 18–29
 - c. 30–39
 - d. 40–49
 - e. 50–59
 - f. 60 or greater

4. Do you identify as:
 - a. Male
 - b. Female

Questions for Discussion Segment #1: Patient Perspectives on Impact of Disease on Daily Life

5. What type of HES symptoms do you currently have? Check all areas that apply
 - a. Skin: itch, rash, hives, angioedema (swelling), ulcers/sores, or pain/sensitivity
 - b. Lung/heart: shortness of breath, cough, wheezing, or chest pain
 - c. Gastrointestinal: lack of appetite, pain, nausea, vomiting, diarrhea
 - d. Neurological: numbness/tingling, neuropathy/pain, muscle weakness, “brain fog”/poor memory
 - e. Fatigue
 - f. Muscle or joint pain
 - g. Other, not noted above

6. What type of HES symptoms have you ever had? Check all areas that apply
 - a. Skin: itch, rash, hives, angioedema (swelling), ulcers/sores, or pain/sensitivity
 - b. Lung/heart: shortness of breath, cough, wheezing, or chest pain
 - c. Gastrointestinal: lack of appetite, pain, nausea, vomiting, diarrhea
 - d. Neurological: numbness/tingling, neuropathy/pain, muscle weakness, “brain fog”/poor memory

- e. Fatigue
 - f. Muscle or joint pain
 - g. Other, not noted above
7. Of all of symptoms that you have experienced with HES, which **THREE** would you consider having the most bothersome impact on your daily life? You can choose up to three.
- a. Itch
 - b. Rash or hives
 - c. Angioedema/swelling
 - d. Ulcers/sores
 - e. Coughing, wheezing, or shortness of breath
 - f. Decreased appetite
 - g. Nausea, diarrhea, or vomiting
 - h. Numbness or tingling
 - i. Brain fog or poor memory
 - j. Muscle weakness
 - k. Fatigue or tiredness
 - l. Pain
8. What do you find to be the most bothersome impacts of your HES symptoms on your daily life? Please choose up to **THREE**.
- a. Limitations on work or school
 - b. Limitations on social activities with friends, sports, and hobbies
 - c. Difficulty concentrating or staying focused
 - d. Sleep problems, insomnia
 - e. Impact on relationships, social isolation, hard to meet people
 - f. Impact on sexual intimacy, family planning
 - g. Emotional impacts (such as self-esteem)
 - h. Depression, anxiety, or worry
 - i. Financial worries, paying for medical care
 - j. Other impacts not mentioned

Questions for Discussion Segment #2: Patient Perspectives on Current Therapies

9. Have you ever used any of the following drug therapies to treat your HES? Check ALL that apply.
- a. Oral corticosteroids: prednisone, methylprednisolone/Medrol®, budesonide/Entocort®
 - b. Hydroxyurea/Hydrea®
 - c. Interferon-alpha
 - d. Anti-IL-5/R drugs: mepolizumab/Nucala®, reslizumab/Cinqair®, or benralizumab/Fasenra®
 - e. Imatinib/Gleevec®
 - f. Other chemotherapy: cyclophosphamide/Cytoxan®, Campath®
 - g. Natural, complementary, or alternative medicines
10. Are you currently using any of the following drug therapies to treat your HES? Check ALL that apply.
- a. Oral corticosteroids: prednisone, methylprednisolone/Medrol®, budesonide/Entocort®

- b. Hydroxyurea/Hydra®
 - c. Interferon-alpha
 - d. Anti-IL-5/R drugs: mepolizumab/Nucala®, reslizumab/Cinqair®, or benralizumab/Fasenra®
 - e. Imatinib/Gleevec®
 - f. Other chemotherapy: cyclophosphamide/Cytoxan®, Campath®
 - g. Natural, complementary, or alternative medicines
11. Have you ever had to stop treatment with any HES medication due to side effects?
- a. No. I continue to use my HES medications and I have not experienced side effects
 - b. No. I continue to use my HES medications, despite experiencing side effects
 - c. Yes. I stopped my HES medications due to side effects

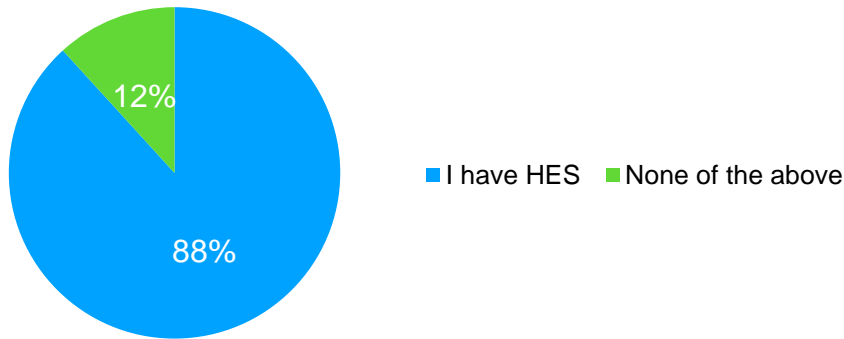
Question for Discussion Segment #3: Patient Perspectives on Ideal Treatments

12. When considering a new treatment for HES, which of the following benefits would you consider to be the most important? Choose up to THREE.
- a. Improves HES symptoms
 - b. Decreases fatigue
 - c. Lowers eosinophil count
 - d. Lowers corticosteroid dose
 - e. Decreases long-term end organ damage
 - f. Has few or no side effects
 - g. Convenient to take

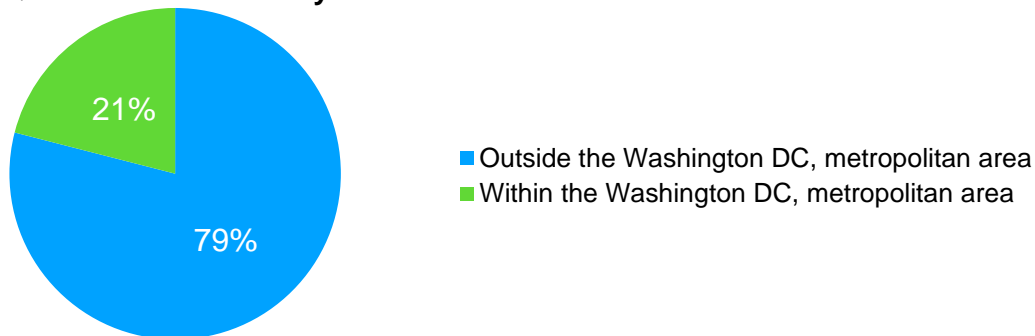
Appendix 4: Results of Conference Polling Questions

The following are results of questions posed to in-person and virtual participants at various points through the March 23, 2019 conference. Participation in the polling questions was voluntary. The results were used as a discussion aid and to help gain a better understanding of the full impact of the disease and should not be considered scientific data.

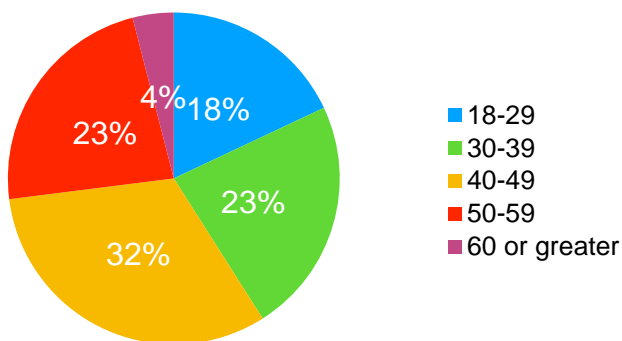
Question 1: What is your relationship to HES?



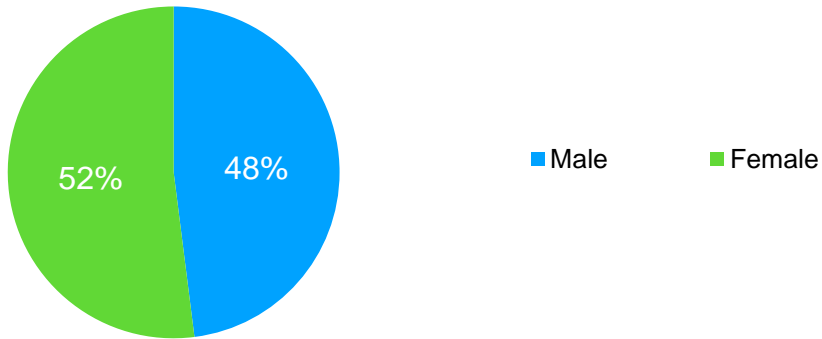
Question 2: Where do you live?



Question 3: Please share your age (or age of patient).

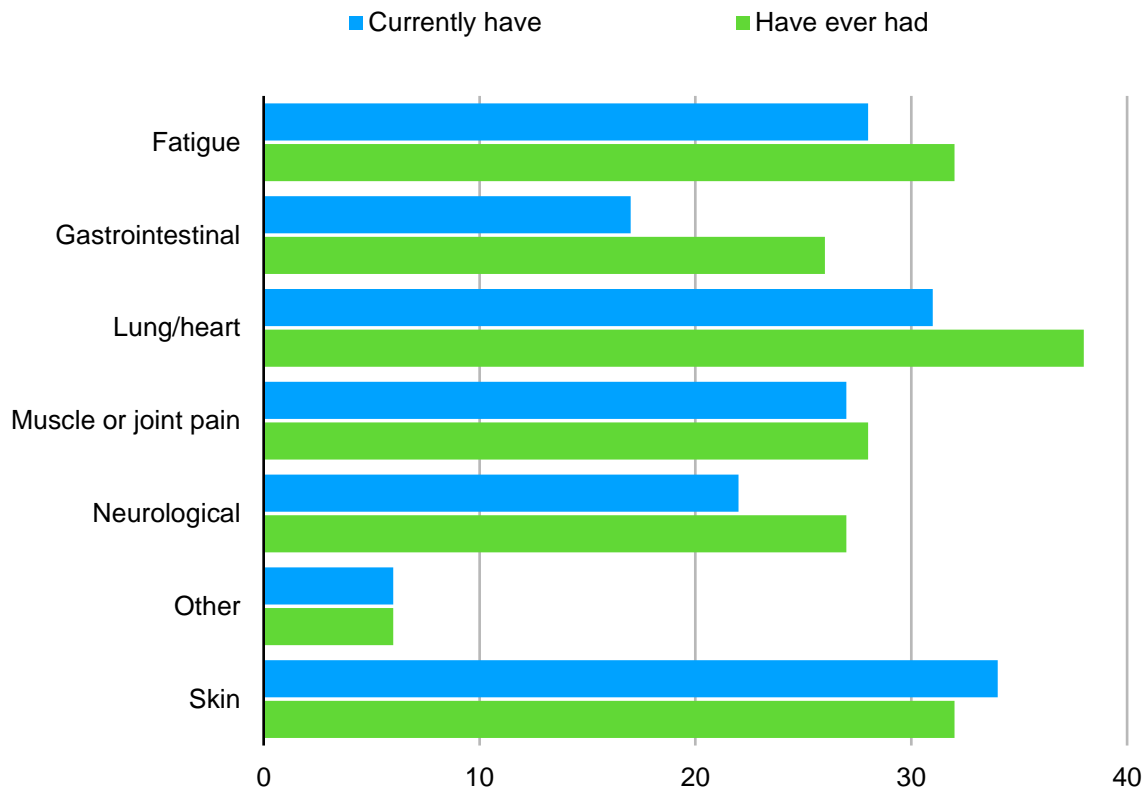


Question 4: Do you identify as:

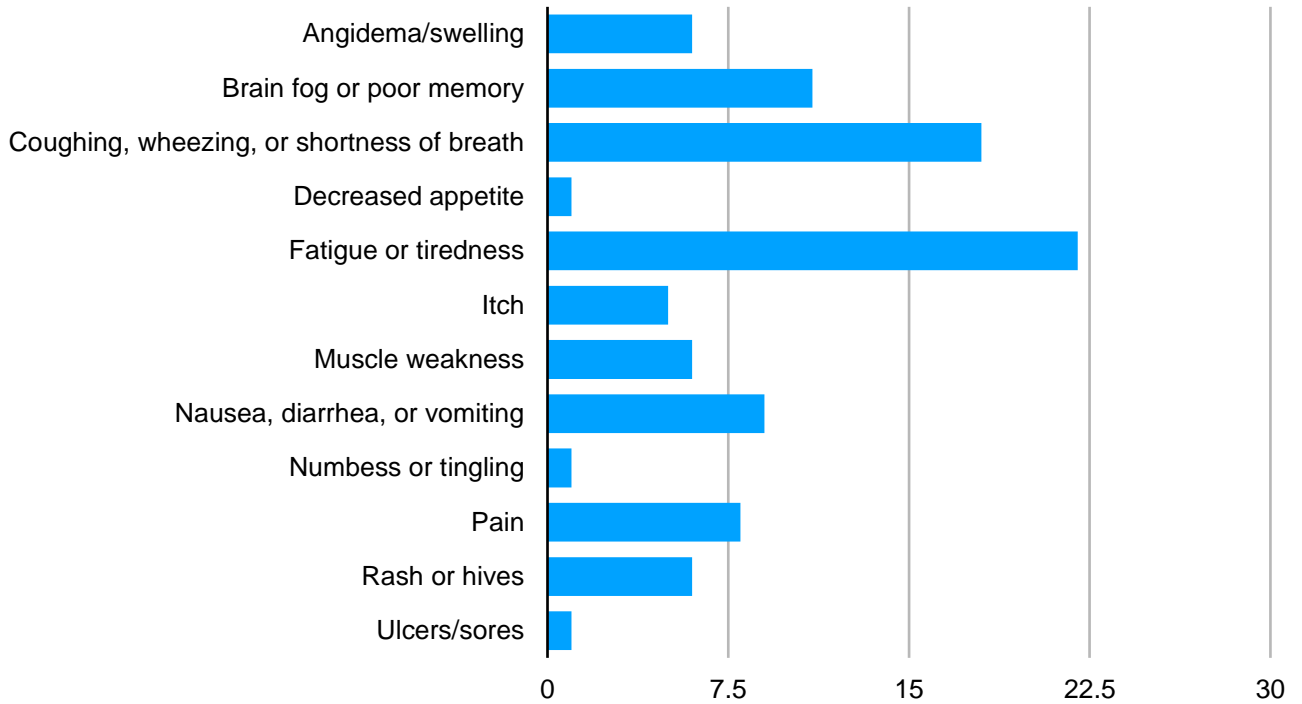


Question 5: What type of HES symptoms do you currently have? Check all areas that apply.

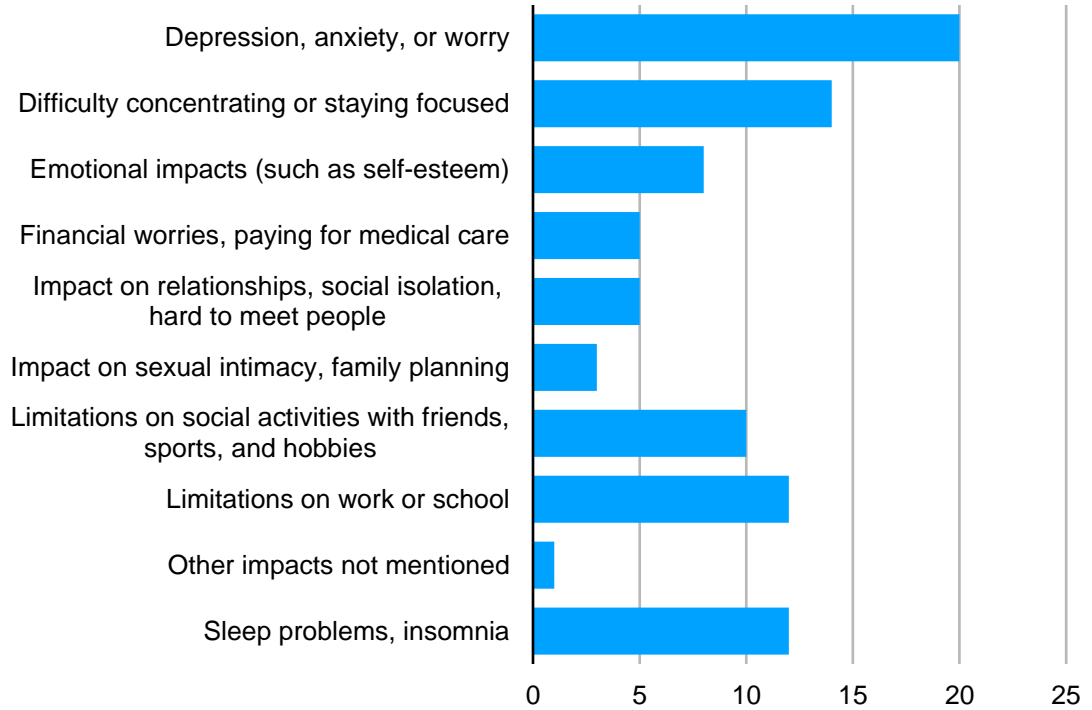
Question 6: What type of HES symptoms have you ever had? Check all areas that apply.



Question 7: Of all of symptoms that you have experienced with HES, which THREE would you consider having the most bothersome impact on your daily life? You can choose up to three.

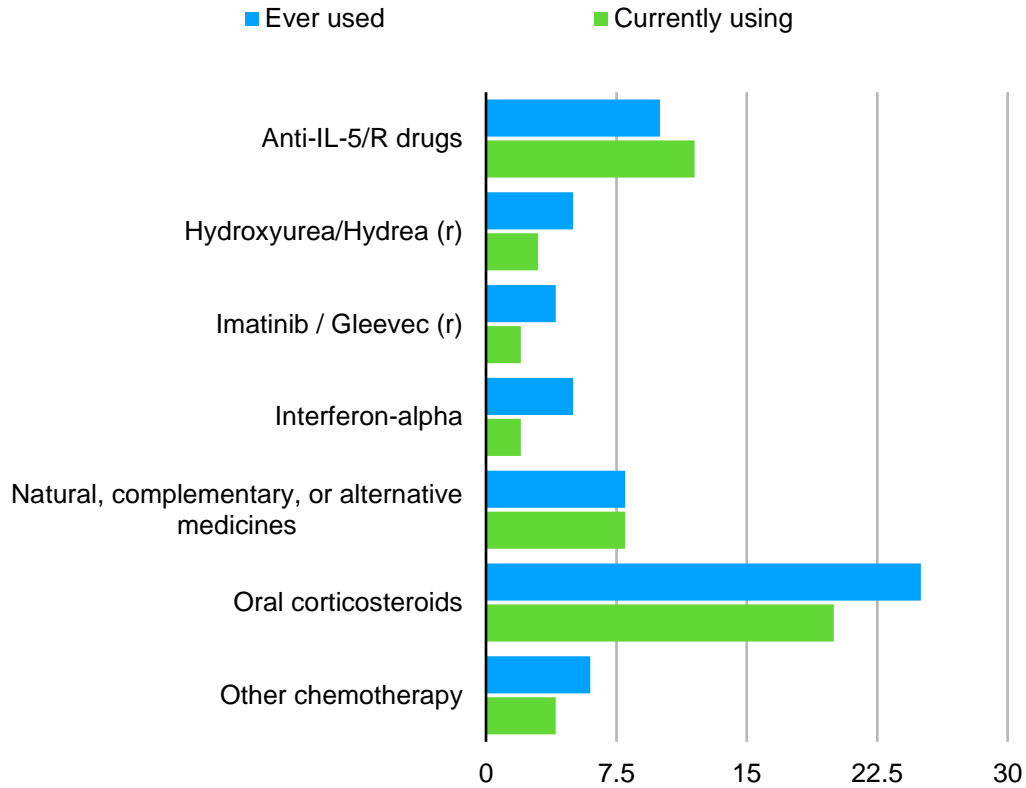


Question 8: What do you find to be the most bothersome impacts of your HES symptoms on your daily life? Please choose up to THREE.

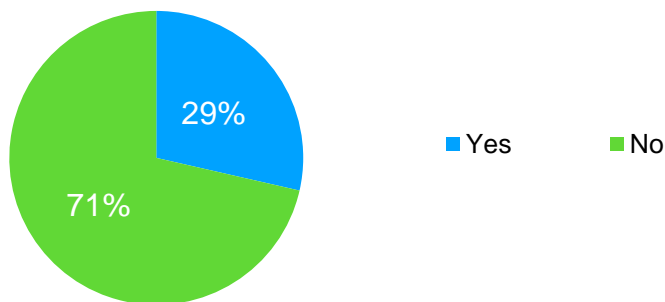


Question 9: Have you ever used any of the following drug therapies to treat your HES? Check ALL that apply.

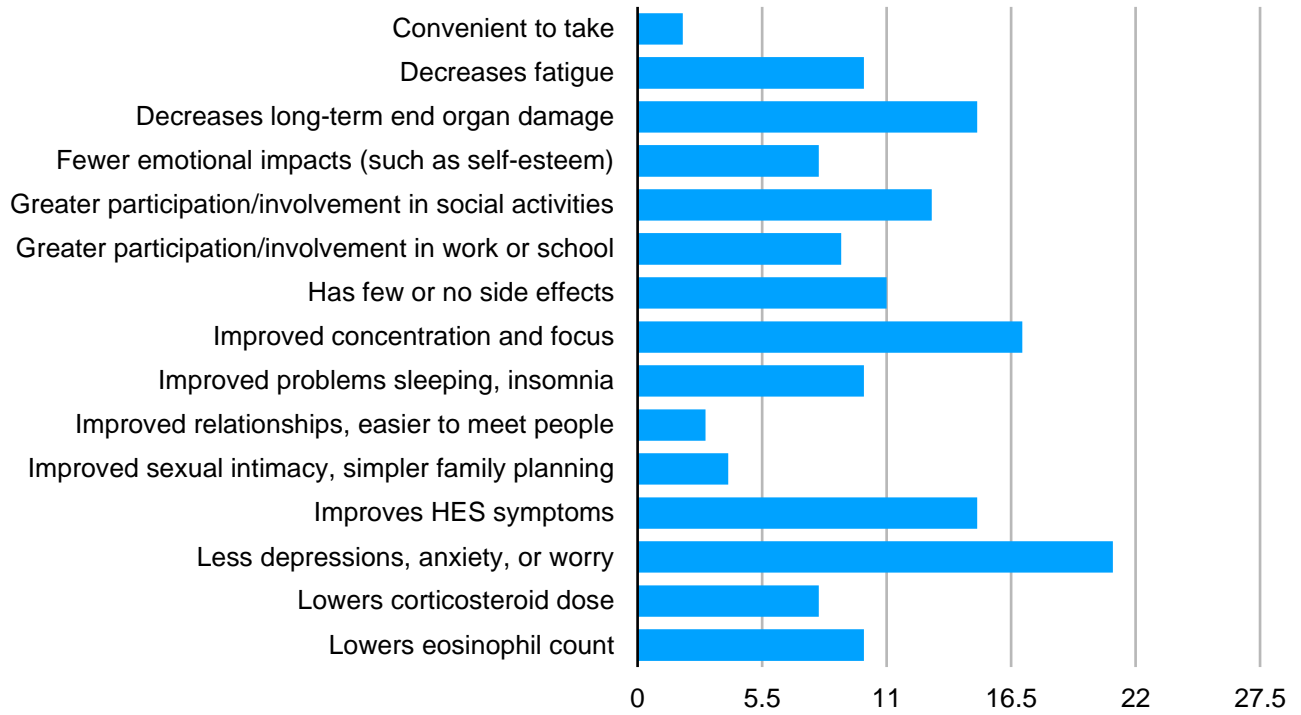
Question 10: Are you currently using any of the following drug therapies to treat your HES? Check ALL that apply.



Question 11: Have you ever had to stop treatment with any HES medication due to side effects?



Question 12: When considering a new treatment for HES, which of the following benefits would you consider to be the most important? Choose up to THREE.



Appendix 5: Patient Perspective Captured Through Form on Apfed.org Website

Patient 1: Male, Jacksonville, FL, age not disclosed

Patient 2: Female, Scottsdale, AZ, age 56

Patient 3: Female, Westport, MA, age 52

Patient 4: Female, Springdale, AR, age 35

How does HES affect your abilities at work or school?

Patient 1: No significant effects on work, other than sometimes tired.

Patient 2: I am able to work with no problems. However, my condition includes Vasculitis and because of that I have had 2 MI's. And when my HES flares up, it can include vasculitis induced problems as they seem to flare hand in hand.

Patient 3: HES has affected my abilities in the work force over the years. During the intensified setbacks of the illness it has resulted in two medical leaves, absentees and has resulted in me going a little over part time to maintain my quality of life.

Patient 4: I have fatigue like other HES patients but with GI involvement I also suffer from regular nausea, abdominal pain, vomiting, constipation or diarrhea, and difficulty swallowing. The symptoms sometimes increase anxiety and irritability or decrease concentration at work. I avoid group meals and cafeteria settings because of the difficulty swallowing and likelihood for food impaction.

Are there specific activities that are important to you but that you cannot do at all, or as fully, because of HES?

Patient 1: Can no longer participate in active events, such as tennis, jogging, swimming

Patient 2: Because of the HES/Vasculitis having caused 2 MI's I am limited in the intensity of the exercise I do.

Patient 3: The symptoms and fatigue of HES do prohibit me from doing what is important to me. Sometimes I am not able to do what I want to do because of exhaustion and pain such as attending family outings, events and day to day life activities. I feel like my days have been shortened so to the fatigue, chronic pain and systematic symptoms.

Patient 4: Group or cafeteria meals due to difficulty swallowing and likelihood for food impaction; unable to participate in sports or athletic activities

What worries you most about your condition?

Patient 1: Original HES symptoms were severe lung congestion and sinus problems, lasting from 2009-2014. More recent problems caused by HES are muscle fatigue and lack of blood circulation, preventing me from playing tennis or other continuous exertion activities: muscles seem to build up lactic acid, near instant fatigue symptoms. I continue to have sinus congestion and cough, intermittent lung problems.

Patient 2: I am worried about long term prognosis. At this point I am able to control my disease with a small dose of Prednisone every other day. I am concerned about disease progression and alternate treatments.

Patient 3: What worries me most about my condition is the unknown. Living day by day and not knowing what the day holds for my illness. The onset of Eosinophilic Pneumonia and other affects add to the worries of my condition. Not knowing the stability of the illness and where it could take me. Which is why more research needs to be cultivated in order to find out more about the disease, better treatment plans and the overarching goal a cure!

Patient 4: Continuing permanent, irreversible damage; losing more function

Do you feel your condition changed over time, since diagnosis? If so, how?

Patient 1: Yes, original HES symptoms were severe lung congestion and sinus problems. More recent problems caused by HES are muscle fatigue and lack of blood circulation, near instant fatigue symptoms. I continue to have sinus congestion and cough, intermittent lung problems.

Patient 2: My condition is much better than when I was initially diagnosed. I was very sick and on chemo and large doses of prednisone for years until I got a better diagnosis and a better understanding of the disease. To this end, I have discovered that I have a lot of food allergies and when I eat certain foods it tends to make my HES flare up. Most significantly are dairy and wheat. If I avoid those two food groups my EOS blood count actually stays lower.

Patient 3: The condition does seem to change over time. Some days are better than other and seeing that when first diagnosed it was my lungs in particular that are impaired. Currently, I have been experiencing more digestive issues than usual and eye problems. My belief is that they could be connected.

Patient 4: Yes, difficulty swallowing and weight loss has increased; I believe intestinal absorption has decreased

Do you consider your HES to be well-managed today? What does “well-managed” mean for you specifically?

Patient 1: Stabilized. I don't seem to be getting worse, but I am not getting better either.

Patient 2: Yes, I feel I am well managed. In that my EOS count stays within an acceptable range (for me). I have found the best way to control my disease is through diet management. If I eat properly I can avoid flare ups and can keep my prednisone dose below 5mg every other day.

Patient 3: My HES seems to be stable today. Well-managed is hard to define because it is different for everyone and you never know what the next day or hour holds. One day you are stable (well-managed) the next day your levels could be elevated. Well-managed to me means being able to stabilize the illness. I have far less strength my body has taken a toll.

Patient 4: Yes, because of benralizumab treatment; I still have symptoms but at a more manageable frequency

Do you feel HES has impacted your relationships with others? If so, how? Or if you are a family member or friend of someone with HES, how would you describe the impact of HES on you?

Patient 1: Cough and sleeping problems sometimes keep me from sleeping in the same room as my wife.

Patient 2: I feel that my HES has impacted my relationships with others. I had several men break up with me when I was single when they learned of my disease. My husband today is wonderful and tries to support me in my dietary restrictions. I know my father worries about my long-term outcome, but he supports me in my day to day life. Actually, my friends and family are all very supportive. However, it is so long between really bad flare ups, that I think they forget that I have HES and just treat me like me.

Patient 3: HES has impacted my relationships with others seeing that only a select few understand the illness. Most people do not understand my fatigue or pain level. They feel as if there is nothing wrong or often forget that in order to manage my illness there are precautions and daily life scheduling that I have to take into consideration. They feel that if you go into work or school today that you are fine and can keep on going.

Patient 4: Yes, eating occasions and athletic differences are notable. I can't physically participate in athletic activities and share those experiences with my husband and friends. I am underweight and have difficulty eating which people who do not know my condition may make assumptions regarding the reasons why.

What are your concerns about your HES in the future?

Patient 1: I want to get better, not just continue to live with it.

Patient 2: I would love to be on a medication that was not Prednisone. But, I am on a super low dose, so, for now it's ok. I worry that the disease my progress. I worry that, when I "cheat" and eat the wrong foods for a period that I am killing myself because I have seen how it affects my EOS numbers. I would love to know that I can live as long as anyone else even though I live with HES

Patient 3: My concerns looking to the future for HES is the severity of the illness and the impacts. We don't know what the future holds and there is so little published on HES that more needs to be discovered to help researchers find a cure and better methods of treatment. The lack of awareness also needs to be addressed in order to help doctors and others to understand the disease more. Not many doctors are aware of this case and often mistreat patients.

Patient 4: Continuing permanent, irreversible damage; losing more function

Regarding treatments that you are currently using, what do you like about it? What don't you like about it? What are the most significant downsides to your current treatments? What concerns, if any, do you have about your current treatments? How well do you feel it controls your symptoms? When you answer, please include which treatment your answer is related to.

Patient 1: I take 20mg of Methotrexate per week, Prolia injection every 6 months for bone density, 5mg of prednisone and 1mg of folic acid daily, plus calcium, vitamin B-12 and D-3

Patient 2: I currently take 5mg prednisone every other day. I can live with this. When I flare up, I take higher doses until I get the flare under control. I don't like some of the long term potential side effects from Prednisone use. However, since it works I am ok with the therapy. The only significant downside for me is weight gain.

Patient 3: Currently when my levels are elevated my doctor prescribes me prednisone. I feel that it controls my symptoms adequately and is seen as a quick fix, but not something I can take over time.

Patient 4: Benralizumab - effective with 0 eosinophils, symptoms are improved, injection, downside is not yet FDA-approved for HES
Advair, Zyrtec, Singulair, Flonase - control asthma and some allergy-related symptoms
Flovent - swallowed to improve swallowing
Protonix - aid gastroenteritis control
Zofran, Phenergan - control severe nausea or vomiting
Lunesta - cannot sleep without Lunesta

Do your treatments impact daily life? If so, how?

Patient 1: Cannot maintain previous active lifestyle, very limited alcohol intake, more fatigue.

Patient 2: No.

Patient 3: My treatments can impact daily life, when on prednisone it depletes your bone density and can lead to cataracts.

Patient 4: Numerous medications to manage and pack for travel
Timing of Flovent/oral budesonide (i.e. not within 30min of eating/drinking)
Benralizumab administered at NIH in MD

Steroids, such as prednisone, are the most commonly used treatment for HES. If you use steroids, what do you like and/or not like about them? What concerns, if any, do you have about steroids?

Patient 1: I take 5mg of prednisone per day. I have tried reducing the dosage, but when I do I develop a worse cough and lung congestion.

Patient 2: I don't like the long term potential side effects like bone density loss, glucose metabolism issues, cataracts. However, having been on Prednisone for 20+ years I do not have those things. I definitely do not like taking higher doses when I flare because it makes me moody, irritable, and fat!

Patient 3: The steroids are what I use when my levels get too high. The only good thing is that it brings down my levels to a more stabilized number. However, the downside is the effects. Prednisone

does a number on your body and I feel there are other substitutions that need to be found that can replace this steroid. I am concerned about how the steroid may work now but lead me to other health complications in the future. The unknown is a huge worry.

Patient 4: I previously took prednisone which was ineffective in managing my disease and symptoms

Aside from a complete cure, what meaningful improvement would an ideal treatment for HES provide?

Patient 1: Less muscle fatigue and lung/sinus congestion.

Patient 2: Few side effects with no flares!

Patient 3: An ideal treatment for HES would be a less invasive method. One that is not too harsh on the body and works to help stabilize the illness, leading us to be able to manage our HES and furthermore lead to a cure!

Patient 4: Benralizumab injections on a monthly frequency are reasonable

What factors or information on the potential benefits of treatments do you take into account when deciding on a course of treatment?

Patient 1: There are few to no doctors in Jacksonville who are familiar with HES. NIH does not like to prescribe medicines, so I actually have few choices of treatments. I have an appointment with a new doctor, recommended by my GP, who he says he met at a conference and discussed HES and she actually had some knowledge and interest. She is a pulmonary and oncology doctor, and I have an appointment on May 1.

Patient 2: Side effects, long term adverse events, possible short term adverse events.

Patient 3: The factors and information on the potential benefits of treatments that I take into account when deciding on a course of treatment is one, how will it stabilize my HES, how will it affect me today and later? What will it do to my body now and in the future?

Patient 4: Long-term effectiveness; convenience is also important with a corporate job with high demands and time constraints; limited effective treatment options

How do you weigh the potential benefits of a treatment versus any common side effects such as headache or nausea?

Patient 1: I have not suffered significant nausea since I stopped taking Alendronate Sodium for my bones. I have not had headaches caused by my medicines.

Patient 2: since Prednisone seems to manage my disease at such a low dose, I am not willing to feel lousy to try another drug. I don't want head aches or nausea or mood changes in order to be on another drug.

Patient 3: Although, the benefits greatly outweigh the common side effects which are mild compared to what HES patients cope with on a daily basis, I do experience headaches and nausea with the disease, in addition to, antibiotics (for dealing with other side illnesses) and other treatments.

Patient 4: Assess long-term benefits; I was on interferon alfa-2B for six years and dealt with the side effects knowing it was better in the long run than long-term, uncontrolled disease; limited effective treatment options

How do you weigh the potential benefits of a treatment versus any less common side effects such as serious risks to liver or kidney damage?

Patient 1: I am aware that methotrexate can cause liver damage, hence reduced alcohol consumption (2-3 beers/week).

Patient 2: I would consider it detrimental to taking a specific treatment if the outcome could lead to kidney or liver damage.

Patient 3: This is a tough question seeing that the benefit would be to help save my levels from getting into the danger zone; however, the difficult situation is what will happen if I develop liver or kidney damage, which can lead a patient to worry on what they should do. The weighing in is a back and forth issues that needs to be addressed.

Patient 4: Assess likelihood of side effects and long-term value of treatment v. no treatment; limited effective treatment options

Appendix 6: Incorporating Patient Perspective into Benefit-Risk Assessment for HES

The input provided by patients through the Hypereosinophilic Syndromes Patient Education and Drug Development Conference will inform our understanding of the Analysis of Condition and Current Treatment Options for this disease.

The FDA has developed a plan for a structured approach to benefit-risk assessment in regulatory decision making, calling for assessment of certain factors for each potential therapeutic under consideration for approval: Therapeutic Context, Consisting of Analysis of Condition and Current Treatment Options; Benefit; Risk; and Risk Management.

The input gathered by APFED at the Hypereosinophilic Syndromes Patient Education and Drug Development Conference and the related web-form is compiled in this report and can be used to guide such a framework for HES patients.

Below is an example of the Therapeutic Context section. This is a sample framework of how the data from this report may be incorporated into a benefit-risk assessment framework for HES drugs under review.

Decision Factor	Evidence and Uncertainties	Conclusions and Reasons
<p>Analysis of Condition</p>	<ul style="list-style-type: none"> - Hypereosinophilic syndromes (HES) is the umbrella term for a group of rare disorders in which high numbers of eosinophils are found in the blood and affected organs for prolonged periods. In the vast majority of cases, the cause of the cell proliferation is unknown. -The continuous presence of high numbers of eosinophils in blood, infiltrating specific tissues, cause inflammation and progressive organ damage. HES can affect any organ in the body, including the heart, skin, lungs, gastrointestinal tract, liver, spleen and eyes. -HES is debilitating and can be fatal. It is a disease that is chronic, symptomatic, and 	<ul style="list-style-type: none"> -HES can be a severe, debilitating, and potentially fatal disease that can affect multiple organ systems. -Lung, heart, and skin involvement is commonly reported among HES patients. -HES symptoms and side effects of current treatment can severely impact quality of life. - Nearly all patients with HES are affected in some way by the symptoms of the disease or side effect of their current treatment. -Patients noted that stress/anxiety/worry, difficulty focusing, and emotional impact such as self-esteem

Decision Factor	Evidence and Uncertainties	Conclusions and Reasons
<p>Current Treatment Options</p>	<p>can greatly impact the quality of life for and healthcare utilization of the patient.</p> <p>-HES symptoms and side effects can severely and negatively impact quality of life.</p>	<p>were the most bothersome impacts of HES symptoms.</p> <p>- Patients reported that HES impacts their ability to attend school, work, and raise a family.</p>
	<p>- There is no cure for HES. Scientific literature offers treatment algorithms used by medical experts, however, there currently are no official consensus guidelines on HES diagnostics and management.</p> <p>- The drugs most commonly used to treat HES include oral corticosteroids, followed by Anti IL-5/R drugs. Steroids are associated with serious side effects such as adrenal insufficiency, avascular necrosis, osteoporosis, infections, and stunted growth.</p>	<p>-HES is a chronic and lifelong condition. Symptoms of HES are currently treated as they arise.</p> <p>- Patients express a need for therapy options, noting concern about side effects, long term use, and effectiveness of oral corticosteroids.</p> <p>-As of 2019, there are no FDA-approved treatments indicated for the treatment of HES, which is a chronic and potentially life-threatening disease.</p>