CMEology

HAE – Hereditary Angioedema

Interview with “12”

May 6, 2024

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CMEology

Interview with 12 – Hereditary Angioedema

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QUESTION: The focus of this interview is really to talk to practicing clinicians about hereditary angioedema and how they apply what is getting written in the research, in the literature, to what they're doing in practice; and then, also to get your opinions about how HAE is treated in practice as well. So first question: what is your personal experience evaluating the HAE literature in terms of its implications for clinical practice? So for example, how do you approach evaluating the HAE literature; what are you looking for; what sorts of questions are you going to the literature with?

12: The treatments we have currently are so effective and far more convenient than they were a few years ago. So when I'm looking at the literature, I'm looking at, first of all, often, by the way, the pharmaceutical industry, we're a private group, so we have pharmaceutical reps who are still not banned from the office, whereas the university folks have banned them completely. So they're often in with stuff ahead of time, and so, I'll hear from the pharmaceutical industry individuals. I also do some work on making questions for medical students and things like that, and we have a large group of individuals, some of which are very top HAE specialists, so they have 50, 60, 70 patients on the medicine, so they usually will bring up topics first [phonetic] in articles.

And then third, sometimes the QuadAI [phonetic] or the college will have CE courses or sometimes some main certification where they'll have latest HAE guidelines as one of the topics you can pick to maintain your certification or get CE credits, and that doesn't even get into the Medscapes. So then, I'm looking at the articles and almost always, I want to look at, does it look like it's more effective? Now, nobody will do a head-to-head trial with these products, so the best you can do is take the data and look at how they did compared to placebo and assess how many attacks they had, what the attack reduction was.

So then you have to recall what you've got for, going back to Cinryze which was the first one we had, and then start going, how effective was Cinryze compared to, for example, Danocrine or danazol, Danocrine is the branding, the attenuated androgens, and then I break it down and start looking and say, you know, now we've got, since that time, we have gotten Haegarda, Takhzyro, Orladeyo, and so forth, in terms of prophylactic treatments.

So I'm going to look to see, hey, what's the attack rate on those? How does this new product compare to those others? And then, the more important things are what is the convenience factor and the safety factors that would lead me to prescribe this new one over the old and existing treatments because many patients are now treated.

When it comes to the rescue medications, it's a little different: you're looking at time to resolution and tolerability. I don't think you're going to exceed too much. I can't advance attack ratio, or I should say not the attack ratio but their time to resolution, but I do look at it to determine, is this better tolerated by the patient; were there less side effects, particularly local side effects which is the major complaint. And then, we have the Holy Grail, which is the oral rescue medicine if there is one because there still are needlephobics out there.

QUESTION: Sure, of course. When considering the implications of the HAE research on clinical care, is there any particular format of research results that is more influential to you than another? So for example, abstract, poster presentation, academic detailing, UpToDate or another type of database, journal publications: what do you see as being the most influential format for you?

12: I often will go to the abstract, but I really don't like abstracts that are just released. The Fellows have, somebody has to, somebody is trying to publish or perish, so a lot of those abstracts that never hit a major publication [unintelligible] yes. I mean, I could just see the trainee standing there in front of their poster at

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Pharma rep detailing/MLs

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CME

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Prof society updates or tests
CME

Commented [4]: Codes (1908-1909)
CME

Commented [5]: Codes (2762-2847)
Superiority of efficacy

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Safety

Commented [7]: Codes (3168-3182)
Adverse effects

the meeting; I mean, nobody, you know, when they speak about champagne [phonetic] years ago, people would attend the poster session, but I really like to see it published in a major journal.

QUESTION: Sure, yes. As a former, I'm a [redacted] and I worked at a [redacted], if that gives you any clue?

12: Yes.

QUESTION: Anyway, I have been the Fellow who sat there, stood there in front of a poster, and boy, that experience certainly taught me a little bit about how abstract results get translated or not into actual publications. So yes, good experience. How about other sessions at a big meeting for HAE?

12: You know, I have been very absent in going to any of the meetings recently. After Covid, even before then, my life got so busy. Everything is online now. You can pick-and-choose what you want, and I've always, I believe if I roll back time decades and we diagnose things, I would have probably been that ADHD kid. So I have a tremendous flight of ideas. When I was in seventh, eighth grade, if you sent me over to the library, I would get stuck on the bookshelf on something completely unrelated. So focus is difficult for me, so that's where the internet is, I would be a child of the internet if I was born when we had the internet and computers. I would have loved that going off and Googling everything.

So that's what I do: I look for, I will search all the time; I'll do a lit search. I'll pull up, I'll go to Google Scholar, and sometimes Medscape will prompt my, or one of those ones will come up, I'll get an email and then I'll say, boy, this looks interesting, and then I will go to the original article and then start pulling it up and looking for novel factors. Right now, we're working with Factor XIIa a lot, and whether that's going to be some form of the Holy Grail for the type III or normal C4 folks is unresolved right now. And then, we've got the new agents directed in various cycles in the kallikrein cycle.

QUESTION: Okay. So it sounds like Google Scholar, Medscape, or some of the online sources that you might go to, is there anything else that you use in terms of an online source?

12: Epocrates. Looks like they got in trouble though because they lost their CE license for [phonetic] clicking the link and the article would pop up, and then, all of a sudden, they'd tell you [unintelligible] CE credits. But they were a good source up until recently. I liked their sources because they would take you right to very salient articles that you needed on HAE, but I've used them; and like I said, the college and the Academy, everything is online now. Even the maintenance of certification courses are online and they have, now they've made them a little more user-friendly. They're nice because you're maintaining your certification, you're not going through the same cycle, and you're able to sort through what the experts think are the most relevant articles in any given area.

QUESTION: Okay. So it sounds like even if you're going to an online source, one of the things you're keying into is where is the actual paper that I could look at?

12: That is correct.

QUESTION: Yes, okay, so not just taking it at face value, expert discussion, someone else's opinion, but wanting to see the original publication, make some judgments for yourself by looking at the data.

12: And what I'll do is I'll print in PDF there or I'll use Adobe, and then I will save the file, the article, the original article to a file, like I have an HAE file, whatever different groups of topics that I'm needing. And so, when the time comes, I could pull up the article again and don't have to go to Google Search as much.

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Journal reputation

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QUOTE

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Expert opinion/Up To Date/Google/Medscape

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Expert opinion/Up To Date/Google/Medscape

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QUOTE

QUESTION: Okay, got it. So what factors are most important to you in the process of interpreting the HAE literature and applying it to clinical care? So for example, interactions with colleagues, anything that you would want to change about your skill level or knowledge base when it come to interpreting the literature.

12: Well, interaction with colleagues is a problem, that's the problem with a large private practice: the only colleagues you have is your medical associates. And years ago, we had medical students and Fellows and things like that, but that's really gone by the wayside after Covid. But I mean, there used to be a time when you got dinner presentations and things like that. I mean, giving my age away, basically, they rarely have them and with all the restrictions, it was no spouses, no friends. I remember you had kids there; you could bring your children.

QUESTION: [Laughter] Yes, yes.

12: And they're not going to have alcohol, they're not going to have anything, and it's like, come to the timeshare meeting but you're not going to get the Disney tickets. I mean, nobody is going to go to one of those. And then, not only that, the topics, the lecturers are terrible because they have this pharma-lawyer presentation, so those are not a good source anymore. So the sources I've told you so far, which were the online sources and the links to major lectures, are the most important ones.

QUESTION: And the dinner meetings that you're talking about that have the kind of pharma-lawyer, those are non-CME?

12: Well, they're non-CME, and even when they had them, like sometimes the companies would sponsor the local allergy society, but they started getting really, I don't want to go withou[redacted]an, I have very little time and n[redacted]ut I mean, nobody wants to take time out of their busy day to go get a free meal. For a CE course that you, and I've got more than enough CE, I mean, I'm swimming in CE, and I'm going there for the event and to socialize, but if you're going to sit there and I've got to guess whether they're, you know, [redacted]ut whether this company has this rule or that rule, I'm just not going to go. I'm there for the social and having a meal and relaxing; I am not there, I can get CE in other ways.

QUESTION: Sure, of course. All right: can you describe any barriers to incorporating research findings in HAE into clinical practice that you've experienced? So examples: patient-related barriers, healthcare provider-related barriers, practice-related barriers, or institutional barriers, things that prevent the incorporation of research findings into practice for HAE.

12: Well, fortunately, I don't have the institutional barriers; that's one advantage to being private. I don't have anybody or [phonetic] some recent graduate from some Masters of Health association walking in, 26 years old, telling me what to do about a patient. So that's one thing about being private: I don't have that nonmedical influence that even the universities now have. So I just do what I want to do, but then, I run into the insurance industry barriers that we always get to deal with. And as I say, with the HAE patient, provided they're young and healthy, and we've got some complicated ones that have more than one thing going on, but the young and healthy ones, the typical 24-, 25-year-old comes in and Mom's got it, Uncle Bob's got it, those types of things, those you spend about five minutes seeing them, assessing the condition; another 20 minutes talking to them about the condition and how it affects their life; that's provided they haven't moved from another state and already been under somebody else's care, in which case they don't want to hear all that again, they just want their meds.

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Collegiality

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Institutional barriers

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QUOTE
Institutional barriers

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Insurance/Prior authorization

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Clinician time constraints
Insurance/Prior authorization

And then, the big hassle comes about when I have to pull resources. I have dedicated employees that have to come in, so they're getting an hourly salary and then they have to get these things prior auth'd, so then, you get into the situation, which company is easier to deal with? And I could tell you, our phone nurses, if I mention certain companies for biologics and I'm not talking about HAE in particular, I'm talking about any of these biologics, one of them will roll her eyes and she'll crack your knuckles; she jokes about it but it is a major hassle at getting them approved. And so, there is that inclination to just let things, if they are on a med, you just leave them alone.

QUESTION: I see.

12: Don't rock the boat, I mean, because it costs money to switch drugs, a lot of money [phonetic].

[INAUDIBLE]

QUESTION: So it sound like of the barriers that you've encountered, dealing with insurance issues has really been an issue; and having done a number of interviews with people now, I can say you're not alone. And certainly, for HAE and also for asthma, biologics are tremendously useful, but there is a hurdle to jump through that we didn't have to necessarily deal with with other therapies, and it is a big time-suck for everybody, and money, right? Like you said, you've got to hire staff to come in and deal with these things, or it takes staff away from doing other things like answering other patient calls, et cetera.

12: It does. It's a lot of hassle and it's going to be billed at some point, ready to bill indirectly, but someday, they're going to get a prior auth fee. And I know the private doctors, a few of them dermatologists in the area that are doing various techniques, like they have a $350.00 prior auth fee or they charge by the hour, as opposed to sometimes they put a nurse practitioner or PA who sit there with a telescreen, and while they're sitting there on hold waiting for the biologic company to come on, the insurance company is getting billed for that visit and they're talking to the patient, and now it's an hour visit while they're waiting on hold.

QUESTION: Interesting, sure.

12: So you're seeing a lot of that. We're too busy to do that. We're down to [redacted] doctors. We were a [redacted]octor group, and to be honest with you, there is nobody, the number of people in our specialty is half of what it was just ten years ago in the [redacted] phonetic] area. And they're just closing; nobody is replacing them. People are dying and there is nobody to replace them.

QUESTION: Yes. What do you think introduction of evidence-based practices, why do you think it might be delayed in HAE?

12: Oh, it just takes, we've done this with urticaria, we've done this with asthma, there's always this lag-time while the insurance company is using whatever they had a meeting three years ago on, and just continues. This is where [phonetic] they'll have a prior auth for a generic medicine that's like $10.00, and there's this big prior auth hassle, and I just give them, I say, well, this is generic, why are they doing this, and I just hand them a [redacted] and say, go buy it; I'm not going through this prior auth hassle for $20 bucks with [unintelligible]. So they are decades behind some of them, and some of them are a few years behind, and I would say nobody is current within the last year or two.

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QUOTE

QUESTION: Yes, okay. How do you think some of these delays might be overcome? Sounds like insurance companies could be a little bit quicker to get on the ball as far as evidence and what things could actually do for patients. Is there anything else that you do or your practice does in terms of getting over some of the barriers to introducing evidence-based care? Anything around education, for example?

12: You mean education for the patient or education for the—

QUESTION: Well, yes, the patient or for your staff or for your colleagues?

12: It's not even education, the only thing that I've done is, like I said, that's where, and this goes back to a business course, Organizational Behavior, one of the problems you find is people just don't care anymore in medicine. I mean, this is across the board: I mean, the medical care, the technology has gotten better but the medical care gets worse every year. The younger physicians, honestly, most of them done care, or they've been replaced by nurses and PAs who just don't care. Nobody peels the onion back.

Commented [19]: Codes (15887-16099)
QUOTE

So what I am forced to do is, and I shouldn't be doing this, but I have a whole portfolio of files of articles and guidelines because when that question comes up on the phone, the first thing I do, you have the physician reviewer, or it's usually not a physician anymore, and if it is, it's a 90-year-old retired pathologist, but you just send them a bunch of articles and then it gets approved. I mean, I highlight little things in there because I know what the barrier is going to be, and they say, well, they've got a normal C4, or they've got [inaudible], and then you have to send them an article showing that the C4 is low in some cases.

The other one I got from one of our [redacted] programs is we had an HAE patient, she's type II, all of her relatives are, but she has a [redacted] which you see in that, and she happened to have a low C1q. So automatically, they denied her coverage because that particular plan was insisting that she was not a type II; she was an acquired and they don't cover that. So I had to zap off a bunch of articles explaining that you can get a positive [redacted] thyroiditis, and with autoimmunity in general, you can get a low C1q.

So it's a challenge. So you have to keep all these articles ready to go and fire them off. And sometimes the companies will even give me an article source, so I can get it there. I don't know if they're allowed, you know, wink-wink [phonetic] what I'm supposed to do with it, but I'll keep it on file.

QUESTION: So is that generally something, I mean, it sounds like you're quite knowledgeable about the field, is it effective when you send an article or a guideline set to an insurer, do they respond to that?

12: Oh, yes. If you can get a hold of a pharmacist or a physician or a nurse, no matter which field it is with a biologic, they get on the phone and often it's a primary care doctor if it is a physician, and they start stumbling, they don't want to read the article, either, they don't have time, and we just memorize some lines from it, they say 'uncle' [phonetic].

QUESTION: Okay, got it. And HAE is a complex field and it's not something that people are used to dealing with, obviously, especially if your background is primary care; this is something you've probably seen once, if ever, in your entire career.

12: And I've gotten one turned down by the proctologist; I kid you not [phonetic]. I mean, we call them proctologists; they're colorectal surgeons. But he was a retired colorectal, because I saw his thing: I'm a retired colorectal surgeon. And it was funny: the denial letter was from a colorectal surgeon. This is kind of almost funny: I can see the attachment between GI, and I was thinking, well, maybe this was somebody at the university that was researching HAE when it was [unintelligible] back in the 1980s and 1990s and retired and wanted to do something in retirement and just did HAE; but no, it wasn't. He had no clue what HAE was; he was just a straightforward colorectal surgeon.

QUESTION: Colorectal surgeon, right. What's been your experience in identifying patients with HAE who would benefit from long-term prophylaxis? Any challenges there? Anything that helped you identify those patients?

12: Those are the most challenging. Some of the challenges are bizarre. I have one gentleman who, he thinks he is the guardian of the insurance companies' treasury, and now Medicare's treasury. He was on, I think the old Winstrol and then more recently danazol, so he's been on androgens or attenuated androgens since the 1970s; he's developed a peliosis hepatis and he just looks like crap, and I'm always afraid he's going to bleed into one of the sinusoids. But he is insisting upon androgens, and I'm trying to get him on Takhzyro. Orladeyo wasn't well-tolerated and that's understandable, but I think he's back on androgens again. I think he thinks it's inexcusable. He looks at the prices of these things and their impact on the healthcare system, and he gets upset and he says, no no, I'm not spending that on myself. He feels he's doing something for vanity by not feeding the beast, the pharmaceutical beast.

And so, I've got ones who are just lazy, they're borrowing pills off somebody, or they're Medicare and it's just too much of a hassle to get the assistance programs. And so, I've got a decent number of people still taking danazol. They even use it for rescue.

QUESTION: It sounds like the patients are resistant to changing or—

12: Oh, yes.

QUESTION: —entertaining the idea of a new treatment then. Yes, okay.

12: Yes. I will tell you the HAE crowd is [unintelligible] amongst our clientele compared to the asthmatics.

QUESTION: Really?

12: Yes, yes, they're very different than any other field. I think it's because they're a rare disease and it's hereditary, so they have relatives and they get online and they talk and they call them on the phone and they borrow pills and they do all types of crazy stuff. They borrow their Firazyr and it's just [inaudible].

QUESTION: Hmm, wow, okay. Yes, I can say having taken care of a lot of asthmatics in my day that there certainly are asthma patient groups, but as far as sharing meds with each other, that's not something I've really ever come across.

(Overlapping Voices)

QUESTION: Other than, 'could I borrow your albuterol?'

12: I've seen borrowing albuterol, yes—

QUESTION: Yes.

12: —but other than that, no, I've never seen anybody take their Fasenra [unintelligible].

QUESTION: Right, exactly.

12: I've had some crazy stuff, and I've heard from other people where one person will be taking Takhzyro and then another family member, they're taking it once a month and they're splitting the dose. I mean, it's just crazy stuff. It works monthly: you know, you can get—

(Overlapping Voices)

QUESTION: Very interesting. How do you gather and assess information about the impact of HAE on patient work, school, social, family life? And can you say a little bit about how that process goes for you in the office?

12: That's if they volunteer that information, but sadly, there's really not enough time for that. I mean, most of the time is spent explaining, you know, they come in and tell me about it, they'll do that, but they rarely do. Most of these people have had this disease or their family has had it and it's their first attack; you just don't get much of a history on that. It's a certain patient type that would tell you that. But most of the time, you're spent explaining to them stuff about use, so how to use the injector, how to do this, how to do that, how to get it. So it's a shame where 5% of the visit is spent on medical and the other 90% or 95% is spent on administrative things for the patient to understand.

QUESTION: Yes, sure. Are you aware that there are some validated tools and questionnaires for looking at health-related quality of life in HAE?

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HRQOL self assessment instruments

12: Yes. We never use them, I mean mostly, and no private practice does. Their research, I mean, I'm sure somebody out there, OCD [phonetic], that does it, but they're like the validated eczema score or asthma scores that you get, I mean, all those things. I can remember everybody was doing the ACT [phonetic]. Really nobody, payers don't pay for it; it's a hassle; the patients don't want to do it; and it's that and $4 will get you a coffee at Starbucks.

QUESTION: So how do you engage patients in treatment decision-making regarding long-term prevention or reduction of HAE attacks?

12: That's where a lot of the explanation is: rather than playing with validated tools, I'm going to explain to them, okay, if you want to stay danazol, here's what you need to know. If you're at 50 mg, I'm not too worried, but if you're taking 400 mg a day to control your HAE, I want some liver enzymes and that's the hard part about it. With any drug that needs monitoring, it's like herding cats to get them to show up and get their, once-a-year, I always do an ultrasound. If you go on this drug, you need to report back to me and let me know what's going on, and just going over the side effects. Orladeyo has got the gastric side effects and companies downplay it, but it's real. Takhzyro has the ouch factor; I haven't seen too many serious side effects other than it's a shot. Haegarda: very good product but nobody wants to do subcutaneous infusions twice a week. And Cinryze has got even more issues there. Berinert: nobody is using that anymore except for hospitals. I mean, there's IV access; same thing with Ruconest. So they all have their downsides. Right now, the leaders are Orladeyo and Takhzyro because of convenience, not efficacy.

QUESTION: Okay, got it. Anything that you feel makes the process go more smoothly with patients when you're trying to engage them in decision-making about prophylaxis?

12: Well, I don't do the laryngeal scare tactic that some seem to be pushing all the time. I don't really do that unless they have had laryngeal attacks. I do make them aware that that can occur. I try to emphasize that, particularly with prophylaxis as opposed to rescue alone, I say it gives you some freedom to travel; I say you don't have to worry about having to use your Takhzyro on an airplane. It's kind of like a controller medicine. I used to do, if we roll back the clock 25 years, 30 years, we were talking about using

your Flovent or your Advair when it came out to keep you from using your albuterol at the water park because a lot of patients, they would be glued to that. I don't know if you have seen the commercial with the dinosaur albuterol inhaler; he's hauling the dinosaur with him everywhere. I think it's Airsupra's commercial.

So that's the same tactic: by taking your medicines, especially with Takhzyro, it's nice because they can take a shot before they leave and they don't have to carry a little bottle. Well, the older patients are already carrying a bottle of pills, but the young people, they don't want to carry Orladeyo with them even on the plane or wherever they're going, if they're going t[redacted]wo; they'll bring the Firazyr if you get them to. I like to try to emphasize, you've got to bring this with you, or security won't take it, and all that kind of stuff.

QUESTION: Yes, it can be difficult especially with international travel for sure, absolutely. How do you choose medications for long-term prevention or reduction of HAE attacks? Anything that you prioritize in terms of different factors? And what helps you decide between different agents? We've talked a little bit about this just now, but anything else that you want to add on that?

12: Yes. The two things to me right now: I can't get anybody interested in Haegarda anymore. Haegarda to me is something, it's got better efficacy data than just about anybody, but nobody wants to do that. So it comes down to convenience and right now, the market leaders, like I said, are Orladeyo and Takhzyro; and if they're needlephobic or they don't like to use injections, I think they're not going to use injections, Orladeyo is the way to go. I explain to them that it may cause some gastric issues early on: if it does, then I drop it down to 110 mg, but I don't honestly think the 110 mg works as well.

Commented [21]: Codes (26951-27064)
Pt time constraints

And if they're a noncompliant patient, Takhzyro is a much better product because they're going every two weeks. And some of them, I've had one HAE patient, he's now extended to the three months, and then he decided he was going to try to do four or five months, and at that point, it stopped [phonetic] working. And I'll be honest with you, he was only on the three-month dosing interval for a relatively brief period, and it's a monoclonal, so if you use the half-lives, your steady state is anywhere from 9-15 weeks, and the same is occurring when you're coming off. So it stands to reason about 2-3 months is the max you can extend it.

QUESTION: All right. So it really comes down to mode of administration; patient acceptance; patient adherence issues; and then, like you said, getting over that hurdle of how much trouble does the patient want to go through to actually try to change medications if they are being treated with an older med, for example, like danazol.

12: Exactly. Same reason I've stopped taking clinical trials in HAE. I stopped a number of years ago. After the drugs became available, it just got ridiculously impossible to get anybody that was willing to get on them [phonetic].

QUESTION: Yes, okay. You did not do the CME activity on HAE, is that correct? You were not contacted because you had participated in a CME activity on HAE?

12: Not that I know of, no.

QUESTION: Not that you know of, okay; that's all I need to know.

12: Not that I know of.

QUESTION: Yes, that's fine; that's totally fine. So clinical guidelines, you mentioned, they can be one way that research gets translated into clinical practice, and it sounds like you have used clinical guidelines when you've had to go to the table with an insurer for prior auth and other reasons. Can you describe your awareness of clinical guidelines? And then, how are you using them when it comes to patient care in the exam room?

Commented [22]: Codes (29390-29511) Guidelines

12: I don't, to be honest with you, and this goes to all of the drugs for eczema, I pay very little attention to guidelines. I've been to guideline meetings, and they're just a bunch of malarkey. They'll say a [unintelligible] by a committee, and that's exactly what they are, but I find them useful as a whole when I am going to confront an insurer. I think that almost always, I'm following the guidelines without even reading the guidelines. So you'll have things like how many months, how many attacks, and then it changes in two years. If you have one laryngeal attack guidelines, I mean, guidelines are, I think, things that the insurance industry and the malpractice people use to attack physicians because they didn't follow DVT prophylaxis guidelines.

So really, so much commonsense comes into play that I pay very little attention to that. Almost all of my patients that are showing up having attacks, they get put on, everybody gets a rescue medicine, everybody if they're true HAE, and if it works. Now, with the type IIIs, they're another question altogether because it's a lot of hassle to get them on medicine, and if I'm not really convinced this is bradykinin-mediated, I'm not going to put them Firazyr. But for everybody with a true low C4, whether it's acquired type I and type II, or even a type III that has the low C4 even though their C1 inhibitor and C1q are normal, those I can see the mechanism, so they're going to get a rescue medicine which right now really is Firazyr, Sajazir, or the generic.

With the prophylaxis, that's going to come down to how is this affecting your life? Have you had a laryngeal attack? They can have their first laryngeal attack out of the blue, and then, I will try to convince them all to be on something if I can.

QUESTION: Okay. So looking at the frequency and severity of attacks, making judgments based on your own clinical experience, not necessarily what's written in the guidelines, and it does sound like you've been fortunate enough to have some insight into how guidelines and consensus statements, as they are sometimes called, how those actually get written, published, disseminated, et cetera, so there is probably value to that for sure. Is there anything else that comes to mind while we're talking that you think I should know about HAE, anything that came up that was surprising to you? Anything that you feel people like yourself in practice should know about HAE, what's currently out there in terms of options for therapy?

12: I think doing these, believe it or not, while doing clinical trials was great for me, I mean, I'm not doing HAE anymore but I'm doing asthma, got a lot of them, and going to [inaudible] meetings was a wonderful education. Unfortunately, with Covid, they have now gone all Zoom, and so, nobody is really mentally with it at the Zoom conference; they sign in and they do the investigator meeting. The investigator meetings used to be very educational in the past.

But even sometimes, the surveys, the industry-driven things like you're doing today helps bring to mind what's on the horizon. Some marketing company will have you evaluate various different urticaria drugs or asthma drugs, and then tell you that this is the mechanism of action, what do you think of the product, and that's very educational in itself because you get to look at the different, what's coming up on the horizon, what's going to be out in the next 3-5 years as opposed to what's out right now. So by the time it gets on the market, your brain is already primed, yes, they've already heard about blocking Factor XIIa and all that, different mechanisms of controlling HAE.

QUESTION: Okay. Well, those are all the questions that I have for you today, Doctor. Is there anything else that you want to ask me or anything else that you feel we need to do before we conclude?

12: No.

[IRRELEVANT MATERIAL OMITTED]

QUESTION: You should be receiving your gift card in a timely fashion. If you do not for some reason, please contact [redacted] who is the person who set up the interview.

[IRRELEVANT MATERIAL OMITTED]

[END 12 5.6.24.M4A]