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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Addressing the Unique Needs of Women with Migraine

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Addressing the Unique Needs of Women with Migraine” was presented during Omnia Education’s Women’s Health 2021: Beyond the Annual Visit.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Goadsby:
Welcome to Omnia Education, Women's Health 2021: Beyond the Annual Visit. Thank you for joining us today. I’m Peter Goadsby, and today we'll be addressing the unique needs of women with migraine. I'll be taking a closer look at the diagnosis of headache and migraine, focusing on how acute and preventive strategies have evolved, and how the lines have been defined, and, most recently how they blurred. My colleague, Dr. Kate Mullin, will focus on the new treatment medications and on their safety. So let's get started.

Our objectives today are to identify the signs and symptoms of migraine needed to make an accurate and timely diagnosis, to discuss the safety and efficacy data for current therapeutic options for migraine prevention and acute treatment, and to describe strategies for women diagnosed with migraine at various different stages of their life.

In this, slide, what I'm showing you are my disclosures; there's a range of them. Importantly, I've underlined and bolded all of those that potentially have an interest in the area that we're discussing, and I hope that you see what we're going to present today will be fair balanced.

Migraine is one of the primary headache disorders. The International Classification of Headache Disorders, as I'm showing you here, it's a 211-page romping good bedtime read. It's available on the International Headache Society's website. It divides headache disorders into secondary ones, those that are caused, so to speak, where you get headache from an injury, from an infection, homeostatic changes, or headache that's where headache is the problem. And migraine is listed as number one in the ICHD because it's the commonest cause of disabling headache in the world and, indeed, the commonest cause of disability due to a neurologic disorder, and particularly in the under 50s. The other forms of headache, we won't be going into – they're there for your attention.

Now I want to do this with a case because it's quite illustrative, I think, of what we do and what's changing. So a female, 38 years, who started having headache at about the age of 12. Unsurprisingly, this was around the time that she started to menstruate. And she got used to it; it came and went, became more troublesome in the 7 or so years before I first saw her. And so by the time I first saw her, she was having headache on 22 days a month with 10 bad days. And I often find that a useful way to characterize things are somewhat to add up all their days, make sure that if they say 22 it means they have 8 great days, and then tell you about the severe days, which will usually be less, and then try and characterize the severe days. It’s a very useful way of focusing down on the problem.

Now migraine is very common in the community, as I said. And on this slide what I'm showing is the epidemiology and the burden. So when you look at the one-year prevalence of migraines in who's had it in the last year, you see that at peak, about 1 in 3 adult females have migraine – contrast, at peak about 10% of males in any year. It affects women particularly from when they start to menstruate through to the time they have menopause, when you’ll see that the number plummets.

And then when you look at the burden, the years lost to migraine, you can see it dwarfs – there's a data from *Lancet Neurology* from the Global Burden of Disease – it dwarfs tension-type headache because migraine at its core is a disabling form of primary headache disorder.

Now, in the next slide, what I'm illustrating is the impact, you might say, in general practice and in neurology practice. It gives you some idea of why it is that neurologists get interested in or anyone should be interested in migraine. On one side, I've got the Landmark study, and it was a landmark. Patients who'd come along to their primary care physician in the US who said that headache was their problem were given a diary. They were sent away. They filled out the diary and then experts, whatever you think of that terminology, looked at the diary blindly, and assigned diagnoses. 75% of patients coming to see a primary care physician in the US fulfilled ICHD criteria for migraine, and another 18%. So in total, nearly 92% of patients who are coming along with headache problem have migraine. It's the commonest reason to turn up. Why? Disability. And then of course, it's the commonest thing that turns up to neurology, at least in the US, some UK data, I should say, 20%, more or less, of patients who are coming along to neurology. And in general, neurology, it's more – it tends to be migraine and dizziness, and the other things, epilepsy, MS, movement disorders, often particularly in academic practice, will get taken off by the various super-specialty people. So headache and dizziness tends to really win the day when it comes to the general practice.

So if we then go back to the case and ask the questions – and it's important to ask on the bad days, get the person to focus down and say, "Tell me, let's talk about your really bad days." Why don't we sit here with a canonical, so to speak, ICHD symptoms that make up the diagnosis that's used by, for example, regulatory bodies when, medication to study, a person had one-sided pain, it was throbbing, they sometimes say pounding, sometimes they say stabbing. And what they mean is regular stabbing. And you must ask them about the cadence of the stabbing. Because if the cadence of stabbing is regular, they're just describing pounding; they're not describing anything else. In particular, they're not describing trigeminal neuralgia. The pain of this person was made worse with movement; 90% of migraineurs will happily agree to that. They also had nausea, light and sound sensitivity – photophobia and phonophobia. Now for added value, they were sensitive to the touch during headache, cranial allodynia, pain with a non-painful stimulus. They had no dizziness and they had no visual disturbance, no aura symptoms. They did have cranial autonomic symptoms. These are quite common; three-quarters of patients will have them if you ask. Some tearing, and she had some periorbital – around the eye – edema. Many will have some nasal symptoms or even some blockage in the ear. And you can imagine how that ends up with ENT folks when actually they're cranial autonomic symptoms of migraine. She also had neck discomfort, concentration problems – patients will often say a brain fog. She would yawn, feel tired, as in fatigued, and have mood change. I've listed them here as premonitory-like symptoms because most of them start in the premonitory phase, and many of them continue into the headache phase. They can be very disabling. And certainly, the brain fog can really change a person's ability to interact with the world. In the postdrome, after the headache settles down, often we don't ask but we should, they can spend up to a day feeling weary, like their batteries are drained or they have concentration problems. All of these are all disabling symptoms of migraine. And getting a full history will help you a lot in connecting with the patient and also understanding what their burden is.

So on the next slide, I just lined up her symptoms with the rulebook, so to speak. She's got criteria fulfilling all of these. Her attacks last several hours, in fact a day. They're unilateral, they're pulsating, severe, aggravated with physical activity. So I've underlined all of those, ticked the box. She has nausea, photophobia, and phonophobia, tick the box, and there's not a better diagnosis. And while that system seems a bit clunky, as you can see, you could pull it out of the history and, at the same time, really start to build a relationship with the patient around what they're doing.

Now on the next slide, I've contrasted that with tension-type headaches. It's throbbing; it's not non-throbbing. There's an affective movement; shouldn't be with tension-type headache. She's got nausea, photophobia, and phonophobia. You don't get any of those with tension-type headaches. Tension-type headache is just pain without any features. It's generally not disabling. Every person I've ever spoken to who's come to see me about it are curious about it. But their lives are not ruined or stopped by it. And I think that's quite important.

And then on the next slide, let's get a little bit more history. It's got hypercholesterolemia, her mother had headache with a menstrual period. She was never diagnosed as migraine, but headache with the menstrual period, entirely likely to be migraines. Nonsmoker, 3 children, owns a small business – industrious – 81 kilos, a tad on the outside, normal examination, and a normal brain MRI. And again, looking at the attacks, which we said on the right side there. She ticks the family history. And she, in fact, also had menstrual worsening of the headache, which is a really big red flag. But women very often get used to the idea that that's normal. Well, it is normal if you've got migraine. So it's a very high-value question to ask.

Now on the next slide, I'm just setting this out again in a diagram that you keep in follow-up, a pathway. You take people who've got featureful headache, meaning that throbbing, one-sided, light/sound sensitivity, movement, and then you ask yourself the question,

“How many do they have? How many headache days?” Well, you ask them the question. Do they have 15 or more or less? Because if they got 15 or more, you're going to end up calling it chronic migraine. And if they got less, we're going to call it episodic migraine. And that's the first differential place. And then – because it's important for therapy. And then you might, if they've got aura, migraine with aura, or they haven’t, migraine without aura.

Now, the important thing as you're going down this is just to ask about analgesic use. Many patients will be taking an analgesic on every day they've got a headache. Why would they not? They're trying to function. And so what you're trying to do is assess the number, not in a judgy way, but in a way to understand what the burden is, to point out that that could be making things worse, and to point out that as you engage in therapy, you want to be de-escalating their analgesic use. And typically, we describe medication overuse at about 10 days per month. I tend to use that term rather than medication overuse headache because, A, there's no clear evidence that in this individual it’s creating headache, and B, it's just simply a statement of fact, and it encourages people to think a little bit about what they're doing.

So then if we just go back to the next slide, a bigger picture of what's going on. It gets complex, but it's a building block of things. Now, the attacks, the premonitory phase, she had craving – she had food cravings, and she also had cranial autonomic symptoms; we noticed that. She had canonical IHS symptoms, and she had a postdrome of tiredness and weariness. She got 15 days or more of headache, a family history. And she got some of these triggers that I mentioned that sometimes can lead people to over associate with some of the trigger things.

Now misdiagnosis things are quite interesting. I've listed some of those on the right side of the slide. So cranial autonomic symptoms like eye watering or redness, nasal symptoms, oral fullness, they very often lead to sinusitis. Back up. Ask about light sensitivity, ask about sound sensitivity; that's not part of sinusitis. Ask about migraine symptoms; you'll be very rewarded for doing it. Food cravings. Sweet and savory foods very often lead to people thinking that they've got a food trigger. They seek out something sweet, they seek out something savory, they end up with a headache, not because it's triggering anything, because it’s a premonitory symptom. Their mood – they've got mood problems. That happens with migraine. The aminergic systems in the brain are associated with that. You don't have to run immediately to a diagnosis that they have depression. It’s worthwhile asking of the association with the attack. And then one of the big misdiagnoses, I think, are people who’ve got frequent headache are very often just thought of as having tension-type headache just because they have a lot of headache. There's nothing stopping a migraineur suffering every day of their life. Counting the numbers doesn't help you with that. But asking all these questions does. Gives the patient some faith in what you're doing, starts to build a therapeutic relationship, which could be very important as you discuss therapies. So I'm going to hand over to Kate to discuss the new treatment options that we have.

Dr. Mullin:
That’s great. Thank you, Peter. My name is Dr. Kate Mullin. I'm going to be discussing, as Peter mentioned, the new migraine treatment options. In my presentation, we're going to build upon Peter’s discussion by taking a critical look at the standard of care and then shifting paradigms based on our current understanding of acute and preventive strategies. We're going to focus on how new migraine treatments provide patients and providers with more choices that can be modified according to patient's needs. As our toolkit expands, patients now have a better ability to control their migraines, and we can work with them to ensure that their needs are optimally addressed. So just real quick, I'm going to take you through my disclosures, so just some speaking and some consulting.

Okay, so I thought it was important to discuss the previous standard of care before we get into the new medications. And the reason for that is because really, essentially for my entire career until about 3 years ago, this was all we had. It was really stagnant for decades. So we did our best to work with what we had.

So in terms of prevention, and when we think about using prevention in a headache patient, we think about their burden of disability. So really, that comes down to the frequency of their migraines. And for most part, if someone has 4 or more migraine headache days in a month, that's when I have that conversation. There are some rare examples where I'll do it if it's even less, but 4 is usually my minimum.

And if you look at our different categories of the medications we use for prevention of migraine, you'll see that migraine headaches isn't listed. And the reason for that is because we sort of fell into our preventative migraine medications by accident in a lot of ways a long, long time ago. So you’ll see antidepressants, blood pressure medications, seizure medications, and then sort of a catchall of some other medications that are used in other fields of medicine.

Antidepressants, we primarily were using the tricyclics, so nortriptyline and amitriptyline, as well as venlafaxine. Blood pressure medications, so primarily propranolol was used, other beta-blockers, nadolol, timolol, metoprolol also fairly popular. A little less commonly used, calcium channel blockers like verapamil, candesartan, or lisinopril, which is an ARB and an ACE, respectively. We then oftentimes will use seizure medications. So divalproex is a really great medication; however, it's really poorly tolerated. So I do my

best in my career to really use that as a last-ditch effort. Topiramate, however, I actually – until recently, I used very often. It's relatively effective and well tolerated at certain dosages. Gabapentin, very well tolerated, oftentimes not very effective, unfortunately. And then some other medications that we reach to. Again, not first line but not that far off, memantine, different methylergonovine derivatives, and then onabotulinumtoxinA, otherwise known as Botox.

So as Peter said, we look at migraine in terms of 2 different categories. Chronic or episodic. As of now, Botox is only FDA-approved for chronic migraine, so 15 or more days of headache a month, 8 of which classify as migraine. So that's the only caveat to that. Everything else we use both for chronic and episodic migraine patients.

Every patient who has ever had a migraine in their life should have an acute medication offered to them. And I can't emphasize that enough. So the top of the line that we've used for decades are the triptans. Triptans are migraine-specific. They do vasoconstrict, so there are some contraindications to prescribing triptans to certain patients. Anyone with a cardiovascular risk factor. So by that, I mean uncontrolled hypertension, a history of a TIA or an MI. You don't want to further potentially compromise their vasculature. Sumatriptan or Imitrex are the oldest, the most well known. They do come with a potential building of side effects, so they can all give you some tachycardia, racing heartbeat, they can make you feel flush, they can make your chest or your jaw muscles feel tight, which for patients can sometimes be disconcerting and they have to be walked through the potential triptan effects before they take it because you might scare them off of the entire category of medications if you don't have that conversation. They have been tweaked along the way. You can see now there's many other triptans. Some have longer half-lives, some have different ways of taking them. So some are nasal sprays; some are injectable. So you can really tailor that to your patient's needs, again, unless they have cardiovascular risk factors or they don't tolerate the triptans.

Nonsteroidals generally always have some sort of a role in a migraine. Generally, we try not to use them first. Triptans are most effective when taken early. So I always try to get my patients to start there, or at least I used to until our new medications came to the market. And then if that didn't work or if the headache was breaking through, I'd have them what we call rescue with a nonsteroidal, so something like naproxen or ibuprofen because there is a lot of inflammation especially the longer a headache lasts.

Muscle relaxers do have a role. I personally like to use them. Let's say a patient took a triptan in the morning but then they're going to bed, and they're feeling it sort of build up again. They don't want to take another triptan, but they feel like if they go to bed and don't do something, it'll be there in the morning. I recommend muscle relaxer in that case. Or if they haven't had a migraine yet, but they go to bed feeling tense or stressed and they're worried if they stay tight overnight that they'll develop a morning headache, then I recommend to take a muscle relaxer then. Muscle relaxers as a side effect can be sedating. So that is why, for the most part, I recommend them be close or at bedtime. Some of them more so than others. I can usually get away with low-dose cyclobenzaprine without too much sedation. But tizanidine tends to be pretty sedating for most patients.

And ergot derivatives. So much like the triptans, ergots do affect the vasculature. So you do have to be cautious in which patients you prescribe them to. But there are now two DHA nasal sprays that tend to be pretty effective in patients when taken early. They're a nice option, although for the most part, I think mostly headache doctors are the ones that have familiarity with the ergot derivatives.

So maybe it was clear when I was discussing what we used to have for our prevention and acutes that there's obviously some problems with our old medications. For the most part for prevention, none of them were disease-specific. So like we said, the beta-blockers, the tricyclics, the anti-seizure medications, none of those were anti-migraine medications. And because of that, they tended to be a little bit hard to tolerate. We were getting sedation with antidepressants, even though we weren't necessarily treating depression or sleeplessness. Because of that, we go up very slowly and carefully on the oral medications. And patients would lose patience with the titration schedule. It would sometimes take up to a month, let's say, to get to an effective dose. So during that month when the patient may or may not be experiencing some side effects, they're not even at a dose yet where they're necessarily going to see any benefit. So there's lots of compliance issues with the old medications. We would find patients at their 3-month follow-up saying that they stopped the medication a month in because they didn't feel any better and they weren't tolerating it.

The acute medications. So inefficacy, obviously, if your medicine that you're taking to stop your headache does not stop your headache, you're probably going to look for something else. And recurrence. So a lot of our acute medications are short acting, and migraines are not. As you heard from the diagnosis, migraines can be days long. So sometimes an acute medication that's in and out of your body and 6 to 8 hours, when that medicine runs its course your headache's going to perk back up. And that's a big problem with the triptans, especially because then if you reach for another triptan, and then you do that for 2, 3 days at a time, you can fall into what's called medication overuse or rebound headache, where now the acute medication that you're taking to make yourself feel better might actually be making your headache worse.

Tolerability. So while the triptans, sumatriptan in particular, are very effective, they are sometimes rough around the edges and patients sometimes avoid taking them or they postpone or prolong taking them because of the way they make them feel. Sometimes it's that

tightness in the chest that makes them uncomfortable. Sometimes they feel just a little bit loopy, and they don't necessarily want to drive or take care of their kids. So they hold off and they wait and take it later. The problem with that, as I said, is that triptans are most effective when taken early. So now we have patients with a good tool kit, but they're hesitant to take it and when they finally do reach for their tool kit reach for their triptan, they've missed that therapeutic window. And then again, the contraindications. So anyone that's got any vascular compromise, you're not going to prescribe them a triptan. And that was, you know, as our patient population ages, that category of patients becomes larger and larger. And our hands were tied for a long time with what to give them for their acute medications.

So on my next slide I get to talk about the new acute medications that sort of filled in all those gaps and answered all those questions. So the first one is the ditans. So triptans are 5-HT1B and D serotonin receptor agonists. The ditans are 5-HT1F serotonin receptor agonists. The 5-HT1B and D seems to play the role in the vasoconstriction. So what Reyvow, which is the new ditan or lasmiditan was able to do was to get the efficacy of the triptans without the vasoconstriction. Hence, say for patients with cardiovascular risk factors. It was approved in October of 2019 by the FDA. There are multiple dosing options, so you can start low and go up slowly if you choose. But just a big caveat to the ditans. So these medications definitely penetrate your central nervous system [CNS]. That's how it works. That's where migraine, you know, begins from. However, it was found that when you penetrate the CNS, there's a potential for alteration of awareness, sort of loss of insight. So there is a driving restriction with the ditans. You cannot drive and you need to counsel your patients very clearly, and if there's a question, get it in writing, for 8 hours after taking Reyvow, or lasmiditan. Again, it's not necessarily a sleepiness. So even if you feel like you'd be well enough or awake enough to drive, there is an 8-hour limit of taking this medication before getting behind a wheel.

Gepants. So again, an entirely new category of acute medication. That's been a long time coming. So this has nothing to do with serotonin receptor agonists. So you may have heard about CGRP. It's sort of all the rage in the headache community in the past couple years, which is great. CGRP is a neuropeptide that we all have circulating, that plays a role in sort of the inflammatory cascade that then leads to migraine, and what the gepants do as – they're CGRP small molecule receptor antagonists. And what that means is that these medicines find the CGRP receptor and they bind to it so that when CGRP comes along to trigger or worsen a headache, these medications are there already and it can't trigger that inflammatory cascade. So we have two of these medications that are considered acute. Ubrelvy, or ubrogepant, is one of them that was approved in December 2019 by the FDA. Again, different dosages. So 50- or 100-milligram pills. You can take up to 200 milligrams in 24 hours. So that does give patients some flexibility. If they want to start low, they know they can take a second dose as long as they don't get to that 200 milligrams. Patients do like that flexibility. Nurtec, or rimegepant, is another acute gepant. It was approved just a month later in January of 2020. This is a one-dose 75-milligram ODT, oral dissolving tablet, so you put it under your tongue and it literally disappears. This is a one and done so you can't take a second Nurtec, but in the clinical trials 85% of the patients didn't need to so that helps patients feel secure that the one dose will be enough. So entirely new category of medications, no issues with cardiovascular risk factors. So far in clinical practice very little issues with tolerability. So it's been really great to have these in our tool kit. So finally something where we looked at the science behind migraine, in this case CGRP, and we said, "Okay, what happens if we manipulate this pathway?" And lo and behold, we came up with really great medications that help our patients prevent their headaches.

So CGRP monoclonal antibodies, sort of the same idea as we talked about the gepants, they find either CGRP or its receptor and bind to them so that that bond cannot be made and that cascade cannot initiate. So we have 3 that are subcutaneous that are either self-administered or administered with a nurse if the patient's not comfortable. But generally one of the flexibilities of this medication is that it can be given at home. Galcanezumab, fremanezumab, and erenumab. And then the fourth one, eptinezumab, is actually a quarterly infusion that you would need to give in an infusion center of sorts, but again, it's only once every 3 months. These, like I said, are migraine-specific, which makes them sort of much less messy in terms of side effects. Convenient, so taking a daily pill is really hard for most of my patients. My patients, you know, these are young, healthy, busy moms, women, students, and it's amazing how hard it is for them to remember. I mean once a day is hard, twice a day is nearly impossible. So once a month, they can usually pull off. They're very well tolerated. So the number one side effect in all of the injectables is what's called an injection site reaction. Sort of a catchall, could be redness, could be bruising, could be even something like a hive. Most of them are mild to moderate and don't make the patients discontinue the medication.

I have lots of patients – so anxiety and depression are comorbid with migraine. We do oftentimes see them in our migraine patients. So they are on antidepressants. SSRIs. And they're also usually of childbearing age. So birth control. Two big categories of medication that we want to make sure are safe when taken together with these preventions and there are no issues, no overlaps, or interactions.

And then gepants, so we just talked about, right, how the gepants are this great new acute migraine therapy, but we have two now, gepants, that work for prevention. So Nurtec might look familiar to you. So rimegepant, that's a medication that was approved for the acute therapy, that 75-milligram oral dissolving tablet, when taken every other day was also FDA approved now for a prevention. So now doctors can sort of play with that Nurtec, or rimegepant. It's the only medication that's got that dual indication for both acute and prevention, depending on how you want to take it, what your headache burden is, and what you and your doctor decide would be best for you. But a really neat thing to play with in terms of your tool kit.

And then Qulipta, which is brand new, FDA-approved in just September of this year. Atogepant, this is a once-a-day medication with different dosages. So 10, 30, or 60 milligrams given once a day, again to prevent your headaches or reduce your frequency to reduce your migraine burden. Again, the gepants are migraine-specific because they work on that CGRP. There's no needles. So for patients, some of them are very attracted to idea of just one needle once a month. And some, you go to break out via your model and they say, "Absolutely not. I don't want the needle. What else do you have?" As I said with Nurtec, there is some flexibility. Some patients are hesitant to go full ahead into a preventive, so sometimes it's sort of a nice way to ease them in. The half-life is shorter, and especially, you know, in women of childbearing age or women that are starting to think about family planning, because the gepants are shorter, you can stop them and start your family planning sooner as opposed to the monoclonals, where you really have to wait a couple of months, really 5 to 6 months, before you start your family planning if you're on, a monoclonal. Something to think about. And also very well tolerated. Maybe a little bit of nausea, but for the most part, my patients have found these medicines very easy to take, which is refreshing compared to the triptans which are always sort of difficult to convince patients to take.

Finally, we have devices. So people have really gone full head into the device industry, which I think is great because they're generally incredibly safe and usually well tolerated. And again, women of childbearing age, you don't have to worry about things being absorbed systemically, passed on to a baby. So Cefaly device is the little Wonder Woman-looking device. That is an electronic trigeminal nerve stimulator. That's approved both for prevention and for acute therapy so you do it routinely to prevent and then you do it as needed when a headache comes on. GammaCore is a noninvasive vagal nerve stimulator. You see that man, and your vagus nerve runs really the length of your core but up into your neck. Again, both for prevention when used routinely, and then if you have a headache and you're near device, you can use it then to abort your headache. And then finally Nerivio, which is a peripheral nerve stimulator. That goes on your arm. Acutely when you get a headache, you use an Nerivio to see if you can abort the headache that way. So that one doesn't have a preventative indication.

So there really has been a plethora of new medications, new devices. Our tool kits have expanded considerably in the last couple of years, like I said. And thinking about Dr. Goadsby's case presentation, you know, so 38-year-old mom, I would have to say – and, Dr. Goadsby, tell me if you feel differently – but I think that I probably would have, maybe 5 years ago, put her on Topamax, topiramate, given her rizatriptan, had her keep the diary. I can tell you now that my plan would be incredibly different. I'd probably put her on a monoclonal, maybe give her a gepant, maybe give her a triptan, too, to have options because they can be taken together. And then my plan would be entirely different if she hadn't already been the mother of 3 and still had family planning in the future. What do you think, Dr. Goadsby?

Dr. Goadsby:
Yeah, you're quite right. I mean it's a very individual thing, isn't it? That's why some of the nuances are in the history, because it really does come down to the individual. You can give general rules, but if you don't pay attention to all the detail, you'll kind of miss the signposting for the best way to go. My first go-to in this lady's situation – I can tell you that she'd already had amitriptyline and already had propranolol and had not much effect and predictable side effects with the amitriptyline, dry mouth and sleepiness. With the propranolol some postural dizziness and exercise limitation. She was getting to a stage in life where she wanted to be careful with herself when exercising, so that was, in retrospect, not a very great idea. I use candesartan quite a lot because I find it better tolerated than topiramate. So there's no cognitive issues with candesartan. Topiramate, there are many, many ways a person can say nothing when they've come back on topiramate because of the word-finding problems. And sometimes, you know, they'll do quite well from a headache perspective, but they'll barely be able to explain that to you because of the word-finding problem. So I tend to use candesartan, because once-daily dosing, no weight gain, no cognitive things. You get the dizziness, but nothing is perfect.

And I agree with you. Now what I tend to do is try and give people a choice. So I would say that there's a tablet, there are devices, and there are injections. Let them sort of think about the buckets, the monoclonal injections, the devices that, as you describe them, and then tablets, candesartan, whatever they've not had. And now, as you say, rimegepant and atogepant.

I like the idea of the person telling me what they want. Because I think if they tell you what they want, and you give them what they want, that if someone buys into their therapy and says, "I want to go down that road," you don't have such compliance problems with that because that's what they want to do. You could spend a lot of time exploring with people why they want something in particular, but

they'll know why.

And it's usually sensible in their world. I try to give them buckets, and tell me which bucket you want to play in. If you want to play in the monoclonal bucket, okay, there's 4 of those. You can give them by injection once a month, once every 3 months, you know, the way you said it. If you want to play stimulate, you can play it. So I think our job – I see my job as to know as much as possible. And then the job of the patient is to kind of decide what they want to do. And I'll facilitate what they want to do, and I think it's good for compliance.

Dr. Mullin:
Yeah, I agree. And also a little bit more of placebo, you know. If they're convinced something's going to work and then you give them something else, they think they're much less likely to have a benefit than if you give them what they think is going to work.

Dr. Goadsby:
I think to be fair also that these medicines that we're looking at, whether you look at whichever the monoclonals or any of the current treatments, they're not spectacularly different. You look at the 4 monoclonals, the response rates are more or less the same. The adverse event problems are more or less the same because, as you said, the target has fidelity. So there's – the placebos wander around, so the clinical trials look like they're a bit different, but I don't pay much attention to that, really. I actually think that you'd expect it to be similar, and they're more similar than they are different. So you want to kind of listen to the subtleties of what is going to happen. And indeed, the response rates with, like, candesartan are about the same as the response rates with topiramate or the response rate for propranolol, and not much different to the response rate for the monoclonal.

The big deal is tolerability. I mean, it's spectacular when – one of the things that's funny about the monoclonals, I think in my practice, is they've kind of cut a whole section of the conversation out. My prescribing habit used to be to describe what side effects I could offer you and then let the person tell me which side effect they don't want. You know, do you want to be sleepy? Do you want to put on weight? Do you want to sound stupid? Or do you want to have trouble with exercise tolerance? Tell me which one really irritates you; we'll get rid of those. And instead of having these long discussions about side effects now, it's almost an embarrassing discussion where you say, well, you know, you sort of drag out for maybe 10% or so of people might, or 15% might get some bowel problems on one of them, on a monoclonal or with rimegepant or arogepant given orally, 1 in 50 people might get a little bit of mild nausea. You're really struggling to have anything to say. And I'll often say to people, I'd say it's difficult me for because I've got not much to say. These are really quite good, which is quite a different conversation to the conversations we've been having for a long time. It's quite amazing. It's really something folks should try, you know, and see what you think.

Dr. Mullin:
Yeah, it's very refreshing to have these new conversations with patients because we're finally talking about the science of migraine, and I can finally say, "This is how it works," not, "Well, we think maybe it shares a receptor on the pain pathway," but it used to be a lot of hand waving.

Dr. Goadsby:
And of course, you make a very good point around reproduction. We're effectively talking about the reproductive years, whether we're talking about the effects of menstruation, any potential interaction with oral contraceptive. Are we talking about pregnancy? Those factors are terribly important that one needs to bear in mind when you're thinking about prescribing. And again, the gepants do quite well on that scale with really not any troublesome interactions, and as you say, 5 half-lives of a drug with a half-life of 10 hours, well, that's not very long.

Dr. Mullin:
Right. I mean, I think that if she was 38 years old and planning on freezing her eggs, that's what I would do instead of the monoclonal.

Dr. Goadsby:
Yeah, well with 5 half-lives multiplied by 10, that's about 2 days. People could just restrain themselves for 2 or 3 days, and then it's not much more than that. But asking them to restrain themselves for 5 months, that's a different prospect altogether, as you point out.

Dr. Mullin:
Right. That's right. That's why it matters to find out about your family planning from your patients. Because 38, you never know these days.

Dr. Goadsby:
And the trouble with family planning is it's not always as planned as you'd like it to be.

Dr. Mullin:
No.

Dr. Goadsby:
You know, humans are very efficient at reproduction and not always as efficient at the planning of it. So while we're sort of joking about it, I mean, it's really been a serious discussion, and I think you must have had it over the years –

Dr. Mullin:
No, absolutely.

Dr. Goadsby:
– with people who are on a preventive or on something and all of a sudden, "Oh God, I'm pregnant." You get the call.

Dr. Mullin:
Yep.

Dr. Goadsby:
And then 6 weeks in or 7 weeks in or something like that, it's quite troublesome.

Dr. Mullin:
No matter how many times I've said to them once you and your partner decide that it's time to take the next step, I want to be the next phone call, I'm still not the next phone call. And sometimes it was an accident, you know, like you said, sometimes it wasn't planned. And then it's just a matter of washing them out as fast as we can.

Dr. Goadsby:
I don't mind them talking to their relatives first, but I'd like to be in the first tranche of things. And we mustn't forget for chronic migraine, of course, botulinum toxin remains still a not unreasonable treatment. I mean, it's 31 injections every 3 months. But I think I appreciate it more, how useful some patients have found botulinum toxin, with COVID when we had to stop doing it.

Dr. Mullin:
Yep.

Dr. Goadsby:
And there's a core of people who came out of that saying, you know, really every other idea, thank you very much for trying, but can we just go back to the injections of botulinum? COVID was a real, unblinded, open-label, real-world test of whether it's really useful or not. And I was impressed by the patients who were absolutely very unhappy during COVID times. Understanding the problem, of course, but unhappy that we couldn't do the injections.

Dr. Mullin:
I mean, that's actually how patients and I figure out if they're still benefiting from it. As I say, instead of 12 weeks, do 16 and see how you feel. And I usually get a phone call at 14 being like, "I need it." So yeah, it was a necessary torture, but a lesson learned for all those patients that they do in fact need it.

Dr. Goadsby:
So I think we've covered quite a few things. And I hope that those watching or listening get something out of it. And I can assure you that migraine's a happy place to be. You have to look at the faces of people who are interested in migraine, look at Dr. Mullin, look at myself; we're not unhappy people because we've got all these new things that we can do. So it's a time to take an interest.

Dr. Mullin:
Absolutely.

Dr. Goadsby:
Get a decent history and look at what the options are.

So on behalf of the Omnia Education team, let me thank you for joining us. And thanks, Dr. Mullin, and for you for taking an interest on this presentation regarding migraine and treatment choices for women. Thank you and goodbye.

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