Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/lowering-burden-to-raise-adherence-optimizing-prophylaxis-for-hemophilia-a/15518/

Released: 07/20/2023
Valid until: 07/19/2024
Time needed to complete: 30 minutes

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

Lowering Burden to Raise Adherence: Optimizing Prophylaxis for Hemophilia A

Announcer Introduction:
Welcome to CME on ReachMD.

This activity, titled " *Lowering Burden to Raise Adherence: Optimizing Prophylaxis for Hemophilia A* " is brought to you by AXIS Medical Education and is supported by an educational grant from Sanofi.

Before starting this activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Young:
Hello, my name is Guy Young. I'm the Director of the Hemostasis and Thrombosis Center at Children's Hospital, Los Angeles, and a Professor of Pediatrics at the Keck School of Medicine at the University of Southern California in Los Angeles. We're going to be talking about optimizing prophylaxis for hemophilia A.

So why don't we get started?

First of all, you should be familiar with the World Federation of Hemophilia Guidelines for the Management of Hemophilia 3rd Edition. It was published in 2020, but certainly is still current today. As you can see, it is 158 pages long so a lot to read there. The good thing for you is we're not going to review all 158 pages, because if you're sitting in front of a computer like this person, that's probably how you'll end up well before we get to the 158th page.

I do want to review a few key points though, of the new WFH guidelines. So here's some of the modifications. There are some sections added, and there were some sections removed, particularly on transfusion-transmitted infections, as that is really no longer an issue in hemophilia anymore.

The emphasis though, in the guidelines, or one of the main new emphases is prophylaxis. And basically, some of the new language is that it says all patients with severe hemophilia A and B should be on prophylaxis sufficient to prevent bleeds at all times. That is definitely new. It does mention that countries that have less access to factor can use less intensive regimens. And then when prophylaxis is not available, at the very least, on-demand treatment must be available.

It also says early initiation of prophylaxis is recommended with clotting factor concentrates or other agents prior to the onset of joint bleeding or by age 3. So again, prophylaxis is really intended to be for all patients and to start early, before the age of 3, and that would be what we call primary prophylaxis. All forms of prophylaxis are superior to episodic therapy. So that could be plasma derived, factor VIII or factor IX, recombinant forms, either standard half-life, extended half-life, or also emicizumab.

Now I do want to show you a little bit of data what could be our concern with the lack of prophylaxis. So here is the Joint Outcome Study that randomized patients, pediatric patients, to prophylaxis versus on-demand regimens. And what you see here is the MRI and radiographic score, as well as joint bleeding and total bleeding, comparing the group that was randomized to prophylaxis in red, and on-demand in blue. And when you look at the Y axis, for the radiology part on the left, it says patients with no joint damage, and you can see the vast majority, well over 90%, had no joint damage either MRI or radiographically for those on prophylaxis. For those on demand,

© 2023 ReachMD

it's only 55% that had no joint damage on MRI, and 81% on x-ray. And if we look at the number of bleeds per year in the histogram on the right, clearly you can see that prophylaxis is a lot less compared to on-demand. And so this study really proved finally that was published 15 years ago now, 16 years ago, that prophylaxis is really the only way to really prevent bleeding and the long-term joint damage that goes with it.

Okay, more importantly as we look forward to patients as they continue with prophylaxis, one of the important other outcomes of this study was the long-term version, which is called the Joint Outcome Study-Continuation. Here, we're looking at patients, not just from the Joint Outcome Study at entry and exit, but also further down the line. So let me walk you through this. Here's the joint MRI score. And here's the joint physical exam score. We're going to focus on the treatment group that is in blue, early prophylaxis. And if we look at the timeline, so there's the events, and here's the ages. So we start with the Joint Outcome Study that I just showed you. Early prophylaxis, these patients started prophylaxis around 1.5 years of age, they had an exit MRI when they were 6. And then for the JOS-C, the continuation, they re-entered this portion of the trial at the age of 13.8 years, you can see roughly 14 and exited at 18. And what I want to emphasize is that even the group on early prophylaxis in blue, that their mean joint MRI score gets worse over the years from 1 to 18, as does their joint health score, as you can see here.

And so while prophylaxis was proven to be more effective than on-demand, what we've learned from the Joint Outcome Continuation Study is that prophylaxis with factor, even started early, as you can see in this group in the blue bar, with effective and intensive and appropriate dosing or prophylaxis, a joint disease still develops. And this suggests to us that we do need to improve on our treatments in order to prevent long-term joint damage.

So that brings us to this next section where I want to talk about nonfactor therapies and focusing on factor-mimetics and rebalancing therapies in hemophilia A. And again, the unmet need, as I just showed you, is that with factor prophylaxis, even started early in life, as you saw in the previous slide, joint disease does still seem to develop. And that's likely due to the trough levels that are aimed at about 1% in that study with the factors that were available at the time that we're not allowing for higher, longer control of bleeding and prevention of subclinical bleeding and managing with higher factor levels. So this is where the unmet need is.

So nonfactor therapies, what are these in general? Well, first of all, they're all given subcutaneously. So that's a big advantage. And most of them are given less, perhaps even much less frequently than factor. They are, based on the clinical trial data, and we will review some of that, more effective at preventing bleeding than factors therapy, and therefore they may be more effective at preventing joint disease. I mean, after all, if they're more effective at preventing bleeding, if they provide sort of higher hemostatic protection, they likely are also preventing the subclinical bleeding that goes along into making for long-term joint damage.

So what are nonfactor therapies? I break them down into two categories, factor VIII mimetics, and rebalancing agents. So let's take a look at the coagulation cascade. This is my version of it. And let's take a look at the mechanism of action of these newer agents. So in green, I have what are replacement therapies, so literally factor replacement. In blue, are substitution therapies or mimetics, of which we only have factor VIII mimetics currently. And then in red is the rebalancing agents. And keep in mind that all the dash lines mean inhibits.

So for replacement therapy, we do have a new replacement therapy, and we will discuss that in a bit. And that's called efanesoctocog alfa. And it is factor VIII replacement therapy with a novel mechanism and a longer half-life than any of the products that had been on the market up until now. For the substitution therapies, emicizumab, this has been on the market in the U.S. now for more than 5 years. But there are others that are being developed that are going to consider potentially enhancing the, the properties of emicizumab. In other words, increasing the benefits compared to emicizumab. One is called Mim8 and one it's called NXT007. And these are both now in human clinical trials.

As far as rebalancing agents, fitusiran inhibits anti-thrombin, concizumab, marstacimab, and MG1113, inhibit tissue factor pathway inhibitor. Fitusiran, concizumab, and marstacimab are in phase 3 clinical trials. And then there's SerpinPC, which inhibits activated protein C, that just started phase 3 clinical trials. Inhibitors for the protein S system are also in development, but not yet in human trials. And then of course, there's gene therapy approved now in the U.S. for both factor VIII and factor IX.

Let's talk more about factor VIII mimetics. What do we mean by mimetic? So I like to use analogies. So here's your steak that you can find in the grocery store. And what will be a mimetic? Well, something that basically is similar to and meant to mimic a steak, in this case, a plant-based burger. But what's interesting to me is you see here it says new meatier taste. So the point is that mimetics are always trying to be more like the real thing. And it's the same thing with the factor VIII mimetics, we're trying to get them to be more and more like the real factor VIII replacement, if you will.

So here, mimetics work, factor VIII here, the activated form, its job is to bring factor IXa and factor X into the proper alignment. So it's a cofactor. The mimetics are bispecific antibodies that essentially perform the same function. They bring factor IXa and X into the proper

© 2023 ReachMD

alignment to generate factor Xa.

Here's some of the properties of these mimetics. So emicizumab, of course, is already FDA approved. It is given subcutaneously either once a week, every 2 weeks or every 4 weeks, that's following 4 weekly loading doses. It is now the most commonly prescribed medication for prophylaxis in hemophilia A in the United States. And has also been used extensively around the world. Mim8 in a phase 3 clinical trial. The dosage in the trials was every week or every month, although my understanding is they're going to also start in every-2-week dosing regimen. NXT007 just had its phase 1 data presented for the first time. And for both of these, the preclinical studies show increased thrombin generation so they're more potent in other words to emicizumab. And how that will translate in the clinic remains to be seen.

So let's talk about emicizumab since we have so much data. So the pivotal trials were the HAVEN trials, HAVEN, 1, 2, 3, and 4. This included patients above and below 12 with and without inhibitors. And the bottom line is if we look in this box, as far as ABR and treated bleeds, I'm not going to read each box, but suffice it to say, it was shown to be very effective at preventing bleeding and including very effective at preventing bleeding when compared to the best other therapy these patients had, be it bypassing agents for the inhibitor patients, or factor VIII replacement for the HAVEN 3 trial.

Here's another way of looking at it. This is the percent of patients with zero bleeds across the HAVEN pivotal trials. And you can see that the majority of the patients had zero bleeds during the trial. And particularly the pediatric inhibitor patients had a very high degree of zero bleeds.

And then looking long-term. So this is the pooled analysis looking at HAVEN – the HAVEN 1 through 4 trials over a longer period of time. The bars below, we have 24-week increments of time, going out as much as 3 to 4 years. And you can see that the bleed rates, the longer you stay on emicizumab, the bleed rates continue to go down. And the percent of patients does continue to go up, seems to plateau around at 3%. That's a high percentage of patients with zero bleeds.

The additional emicizumab trials that were not part of the pivotal series include HAVEN 6 and 7, as well as the STASEY study, not going to spend a lot of time on these. I'll suffice it to say that HAVEN 6 was specifically designed for patients with mild or moderate hemophilia A. Those patients were excluded from the HAVEN 1 through 4 trials I showed you. And the bottom line is the bleed rates were exceptionally good here as well, similar to what was seen in HAVEN 1 through 4. This allowed for the expansion of the label, which in Europe did not include patients with severe hemophilia A. In the U.S., we've always had the label that included all types of hemophilia A.

The next one is HAVEN 7. This is a study looking at infants with severe hemophilia A. So these patients had to be enrolled before they were 12 months of age. And this is an ongoing trial. Although interim results confirmed that emicizumab was safe in this age group and also as effective as all the other trials and having very, very low bleed rates in this young infant group.

And then the STASEY trial, a long-term safety trial, basically demonstrated the safety of emicizumab in a long-term window and basically show that beyond the thromboembolic events that were seen initially in HAVEN 1, but no other significant major safety issues were identified.

Let's talk about rebalancing agents. So what do I mean by rebalancing? Well, the hemostatic system typically is in a balance. A balance of procoagulant proteins like the factors and coagulation inhibitors, as you see listed here, anti-thrombin, tissue factor pathway inhibitor, protein C and S. If we're missing a procoagulant protein, we have a bleeding disorder, and you see pictures there of patients with bleeding. If we have a imbalance where we lose anti-thrombin, or protein C or protein S, we end up with a thrombotic disorder. So what rebalancing means is if we're missing factor VIII or factor IX and at the same time we pharmacologically induce a deficiency in anti-thrombin, or it could be TFPI, or protein C or protein S, that in theory, could allow us to restore the hemostatic balance. So it's a way to treat hemophilia without replacing or substituting for factor VIII or factor IX. And that's the idea behind these. And that's why we call them rebalancing agents because their goal is essentially rebalance the amount, if you will, of procoagulants and coagulation inhibitors.

So why should we even be thinking about these drugs? Well, here's a list of the pros and cons. First of all, the pro is that because these are not factor replacements they are factor substitutes, this same medication can be effective in all types of hemophilia - Hemophilia A or B, and with or without inhibitors. So all hemophilia patients could get these drugs and it could be effective for them as opposed to factor which would be specific for hemophilia A, as well as the factor VIII mimetics, which are specific to factor VIII deficiency. They have several mechanisms of action. And so for different types of patients, one mechanism of action may make more sense than others. They've been shown to be efficacious, mostly safe, they're all administered subcutaneously. And they do have the potential to treat other bleeding disorders, which is not the subject of today's talk, but we may see trials using these drugs and bleeding disorders beyond hemophilia.

The downside is that, it's a novel mechanism of action. So people have to learn and understand the other part of the coagulation cascade. And maybe not everybody learned the details of tissue factor pathway inhibitor when they went to medical school, as it's a

© 2023 ReachMD

relatively newer identified protein. Therapeutic drug monitoring with dose adjustments will be required, at least for some of these rebalancing agents. And there have been safety concerns, particularly with thrombosis. And there's a lack of an antidote for most of these.

So the question really becomes can we get the balance right? Because if we don't have the balance right, and it's tilted in this direction, we may not have thrombosis, but we could have poor bleed control. But if we push things too far the other way, we may get excellent bleed control, but end up with too many thrombotic events. So the idea is trying to get the balance perfectly right.

So in this table are the rebalancing agents that I've mentioned in that previous figure. We have an anti anti-thrombin small interfering RNA called fitusiran. Anti-tissue factor pathway inhibitor monoclonal antibodies concizumab and marstacimab. And the anti-activated protein C serpin, called SerpinPC. You can see they're all subcutaneous. The dosing regimens vary quite a bit though. Concizumab is subcutaneous daily, so every day; whereas, fitusiran is subcutaneous every other month, or for some patients every month; and marstacimab is weekly; and SerpinPC is more similar to emicizumab with a variety of dosing regimens. There have been thrombotic complications noted with fitusiran and with concizumab. Those have led to new dosing regimens that then require targeting of the anti-thrombin level or the concizumab level. And that's where the therapeutic drug monitoring comes in. There have not been thrombotic events reported with marstacimab so far, as far as I know. SerpinPC was specifically designed to improve hemostasis without increasing the risk for thrombosis. Now so far, there's only phase 1 data in a relatively small number of patients. So I think we really need the clinical trials to see if, you know, that specific design really does bear out in the clinical trials.

So fitusiran was studied in three large phase 3 trials, called the ATLAS series, ATLAS-INH for inhibitor patients, ATLAS-A/B, which was for non-inhibitor patients with hemophilia A or B, and ATLAS-PPX, which was for patients with hemophilia A or B with or without inhibitors, but who came into the trial already on prophylaxis. Whereas ATLAS-INH and A/B included on-demand patients and had a randomization where the on-demand patients stayed on demand for period of time. On the bottom you can see that there's been quite a lot of fanfare with these. The ATLAS-INH trial was presented as an ASH plenary presentation. So keep in mind that's only 1 out of 1,000 abstracts that ASH gets a plenary. The ATLAS-A/B was presented as a late breaker at ASH, also a highly sought after spot. And the late breaker at ISTH for ATLAS-PPX. So really quite a lot of prestige has gone into these abstracts.

So let's take a look on the lumping all of these together here. What you're going to see is the ABR, the median ABR, and you're going to have on the left side, the previous treatment. So in this case, we have bypassing agent on demand for ATLAS-INH, factor replacement on demand for ATLAS-A/B, and ATLAS-PPX, those patients, remember, came in on prophylaxis. So it's factor of bypassing agent prophylaxis. And if you look at the median ABR for fitusiran with this higher dose that was initially started, the doses are a bit different now, but you see that the medians are 0 for all of them. So a dramatic reduction in bleeding across all three trials, including those who came in already on some form of prophylaxis.

Let's take a look at concizumab. This is the clinical trial groups that you see here. Basically, phase 1, 2, and 3, looking at patients with hemophilia A and B with and without inhibitors. I won't get into all the details of the different trials. But we have some early data. So here you can see the Explorer 7 trial. This is for patients with inhibitors. And when patients were on no prophylaxis, you see a bleeding rate of about 10; whereas on concizumab, the median ABR as 0. So similar to what we saw with the ATLAS-INH trial for fitusiran and then on the right side, you're looking at the mean ABR. So the mean was 12, whereas the mean ABR on concizumab was 1.7. So again, significant reduction in bleeding compared to on-demand but also overall really low bleed rates comparable to what we're seeing with fitusiran.

With marstacimab we only have phase 1/2 data, so I'll caution you here that we're still waiting for the phase 3 data. Uh, but at least in sort of the early phase of this trial, you see two different dosing regimens, one, the loading dose one without. but the bottom line is the bleed rates also are very low. As you can see, that median and median ABR is the mean and medians are comparable to what you saw with concizumab and with fitusiran. But again, this is phase 2 data in a relatively small group of patients. Whereas what I showed you with fitusiran and concizumab, was phase 3 in much larger sample size.

So another way to think about these novel agents that I just went over is thinking about them by administrations per year. So factor replacement could be 52 to 283 I.V. infusions per year depending on the type of factor. Emicizumab or Mim8 are 13 to 52 subcutaneous injections a year. See, fitusiran has the lowest treatment burden. Concizumab is daily, so it's a lot of subcutaneous injections. But the advantage there is there is also a rapid washout. So for patients that might be at risk for thrombosis or need to have surgeries, there could be some benefit in some patients to have this rapid washout.

Now, moving on, I do want to talk about even newer factor replacement therapy that we haven't gotten to yet, which is efanesoctocog alfa. This was recently licensed in the United States for all patients with hemophilia A, for both prevention of bleeding, treatment of bleeding, and surgical prophylaxis. So this is a recombinant coagulation factory VIII FC von Willebrand factor XTEN fusion protein. So I'll explain what that is in a moment. And it's really a new class of factor VIII replacement because it goes well beyond the half-life that

© 2023 ReachMD

the current extended half-life products allow. And in fact, here's the mechanism of action you see on the left. So the design includes the factor VIII part which is in purple, as well as the FC fusion protein, so that's already a factor VIII molecule that's on the market. But what was done here is that it was recognized that the main impediment to extending the half-life of factor VIII beyond what we have already with EHLs is that they bind to von Willebrand factor. And factor VIII, once it's bound von Willebrand factor, will leave the circulation along with von Willebrand factor with the half-life of von Willebrand factor. And so the half-life of von Willebrand factor is about 1.5 times the half-life of factor VIII. And so that's why the EHLs only prolong the half-life about 1.5-fold or to about 18 hours. So that's why in brown here you see the D'D3 domain, which is there to decouple factor VIII from VWF, in other words, prevent this molecule from binding to von Willebrand factor. And this way, the half-life potentially could be prolonged even longer than the half-life of von Willebrand factor. And finally, in green is the XTEN moiety that is added to two parts, and XTEN is basically a large polypeptide, which functions sort of like PEG, you're probably familiar with PEG, to make the protein larger, and to help prevent clearance. So the combination of the FC fusion, the D'D3 decoupling from VWF, and the XTEN, has led to this product having a very long half-life. So if you look on the right, you can see the PK curve.

And so in particular, if you look at day 4 you still have a factor VIII level with efanesoctocog alfa of around 40% versus down around 2 or 3% for the extended half-life factor VIII. And it's not even measured for the standard half-life of factor VIII. So the half-life was three- to four-fold longer getting it out to about 45 to 50 hours. The dosing is 50 units per kilo once a week. And it's the same dose to treat bleeding episodes when they occur. And this is now FDA approve in all ages of patients with hemophilia A, it doesn't specify mild, moderate, or severe either. So you can use it for any hemophilia A patient including those who are on-demand if you want to use this for their on-demand control of bleeding.

So the trials included the XTEND-1, XTEND-Kids, and the XTEND-ed trial, which is the long-term extension. I won't read all the details here, XTEND-1 was 12 and older XTEND-Kids was less than 12. But these patients who are less than 12 are not previously untreated patients that are heavily previously treated patients. So we don't expect to see inhibitors in this group of patients.

In the XTEND-1 trial, if you look at the results, so these patients came into the trial, or this group here in this figure is on pre-study prophylaxis, so they are on factor VIII prophylaxis. And you see their ABR was about 3. Whereas with efanesoctocog alfa, it was 0.7. So going from one type of factor VIII prophylaxis to efanesoctocog alfa resulted in a substantial reduction in bleeding. And that's not surprising, given the high factor VIII levels that you have throughout the week.

In the XTEND-Kids trial, again just recently published the ISTH Congress, so we don't have a lot of data to show you. Suffice it to say that bleeding rates were very low with a median ABR of 0, and the mean of 0.89. So similar to the adolescent trial and adult trial on XTEND-1. Also, there were no safety events in either trials in terms of development of anti-drug antibodies or inhibitors. So it looks like it's really quite a safe option.

So with all these options you know, what are we going to do? What do we need to know? And really, how do we choose? So I want to talk a little about shared decision-making. So here's an acronym for shared decision-making – seek your patient's participation, right? So you want your patients to participate in the decision-making, help them explore the different options, you're going to have to talk to them about all these different options. Explain to them what these are, explain the pros and cons of each of these new drugs as they come out, and then determine and allow them to compare those options. Assess your patient's values and preferences. Some patients may value more, the least intrusive on their life, they might want the least treatment burden, others might want the highest possible efficacy. So that's something you have to discuss with your patients. And then you can reach a decision and then go forward with that decision. And then importantly, evaluate that decision. And don't be afraid to make changes if the results are not as you like.

So other ways to think about different types of patients, of course, there's the standard adult and pediatric, heme A, heme B, the different severities and inhibitor positive or negative. But beyond that, we have other ways of breaking down our patients. We have those who have good venous access or poor venous access. So those with poor venous access, obviously, a subcutaneous drug would be better. Good or bad adherence. Some are not risk averse to try new things. Others are very risk averse. What about lifestyle? Does somebody have a higher-risk job? Or are they very active or somebody sedentary? And what about age? Are they older? Are they younger? Are they older than 58? So as we get to the older group, we may have more risk for thrombosis and also cardiovascular risk factors and individual patient values. Do they want high efficacy or low treatment burden?

So I have these algorithms. I'll walk you through some of these now. So let's say you have a hemophilia A patient who's older than 18 and he does not have a history of an inhibitor. And he does not have good venous access or good adherence, but not risk averse, that could be a candidate for gene therapy. Somebody who doesn't have good venous access, willing to try something new, they're not risk averse gene therapy might be the best option for them. Now, if they're risk averse, then you'll have to try something a little bit different. Maybe not something as novel as gene therapy. And in that case, the subcutaneous drugs, the mimetics or the rebalancing agents might make sense, because remember, this patient does not have good venous access. If they have good venous access, well, more or

© 2023 ReachMD

less anything is on the table. Any of the factor products, including the new one efanesoctocog alfa, is shortened here for EFA. And of course, they could be interested in gene therapy too, assuming they're not risk averse.

So this is where you'd have to really use the shared decision-making tools I just showed you to come to a decision because you've really got, the way I look at it is, you know, three different factor options, a mimetic, so that's four, a rebalancing age, that's five, and gene therapy. So really like six different options. Now, if there's a history of an inhibitor, and they have good venous access, again, you can use all those tools, there are all those options there using shared decision-making. But if they have a history of an inhibitor, I crossed off gene therapy because they won't be eligible for that. No good venous access, then you're down to the subcutaneous drugs, because again, history of inhibitor, they cannot get gene therapy, at least at this time. So it'd be one of the rebalancing agents, or one of the mimetics. Again, thinking about shared decision-making to get to the best option.

What about children? Well, again, no history of inhibitor, good venous access, well, anything's on the table for them, except gene therapy, because gene therapy is only for those older than 18. So the different factor products, the mimetics, rebalancing agents, and again, shared decision-making, with the parents to make the best choice. They have a history of an inhibitor, and they have good venous access, well, you know, they may or may not be able to get a standard half-life, or extended half-life product, as long as they're inhibitor is tolerized. If you're going to use a rebalancing agent or mimetic, then there's the risk of recurrent inhibitor, if you're not going to use factor VIII continuously. If they don't have good venous access, well, then it doesn't really matter, you're going to be stuck with the subcutaneous agent. And you know, what is the risk for the inhibitor recurring is something we do not know.

If somebody has an active inhibitor, we've have to take gene therapy off the board. And we have to take all the factor products off the board. So what we're left with is the subcutaneous drugs, the mimetics, or the rebalancing agents. And that's what you use for either age. Now, for hemophilia B with an active inhibitor, you can't use emicizumab or Mim8, of course, because those are for hemophilia A, so then you're left with the rebalancing agents.

So what are the questions to ask your patients when you're thinking about the shared decision-making? So what is their definition of well control? How do they feel about their current bleed control? Does it agree with your definition? And if not, you should discuss what really well-controlled bleeding should mean. And keep in mind the first slides I showed you that even with really good prophylaxis, joint disease can happen. So if you don't have really good prophylaxis, then for sure you're in line to develop joint disease over time.

What are their goals and preferences? I mentioned the lifestyles issues that I pointed out earlier. What aspects of treatment are most important to them? Is bleed prevention the only thing that matters? They want the top-line best bleed prevention? Or is ease of administration the only thing that matters? They need something that is easy, simple, less frequent and perhaps subcutaneous. Or is it some sort of combination of, 'I do want really good improvement of my disease burden, but my treatment burden is also important.' So those are things to think about. And you can co-create treatment plans that can improve adherence and reduce bleeding episodes. And as you see, we're going to have more and more options to choose from, that can sort of match a patient who's really interested in full-on bleed prevention doesn't care about the mode - mechanism of delivery of the drug, one who's really looking for the easiest thing to administer, because they really have a hard time administering medication, or some combination. And again, the shared decision-making approach is critical to follow that, and if you're not familiar with that, you really should familiarize yourself with some of that literature.

So what are the steps to improve the outcomes? Well make a treatment plan with the patients or their caregivers and make sure they agree with the treatment plan, right? If there's no buy-in, if you tell them well, you have to do this, or you should do this and they don't buy in, well, they're likely not going to adhere. So if they buy in, that will likely improve their adherence. So again, don't dictate what you think they should do, make the decision together. And then explain health equity to your patients that your view on health equity is you want to have them live a normal life, like their non-hemophilia counterparts or relatives. There are some families where there's one boy with hemophilia, another one without. Well, let's make their lives the same. Let's not make the boy with hemophilia, say, 'Well, you no, you can't do this activity, or, "no, you have to infuse something I.V. 3 times a week.' And that's difficult. Try to make you know, their life as much like a non-hemophilia life as possible. And convince them that it is mostly achievable. I mean, yeah, they can't just not do any treatment. But, you know, if fitusiran, when it gets licensed, for example, if it's every other month subcutaneous, and they want the least intrusion on their life that could be an option. Or if they want gene therapy, and they're eligible, that could be an option. So keep in mind that you should be optimistic. I'm exceptionally optimistic with my patients. Because we're at a point in our journey of hemophilia where we already have emicizumab. We now have efanesoctocog alfa. We have gene therapy for heme A and heme B. I mean, we're getting to a point where we're going to have lots and lots of great options. And there's always going to be a good option for one of the patients. So be optimistic and tell them, 'Yes, you can live a normal life. Yes, you may have a couple of things you might have to do. But if you do those relatively minor intrusive things, you can have a normal life, you can go climb Mount Everest as we saw one of our hemophilia patients do. So yes, you can do anything you want.'

© 2023 ReachMD

Thank you so much for participating in this activity. I hope you learned something, not just about the new medications that we have and the new medications that are coming, But also more importantly about shared decision-making. This is going to become really critical, as we have more and more drugs available, we have to incorporate the patient and the caregiver in our decision-making and in our strategies for improving their hemophilia care. So please do focus on that. Please think about bringing your sense of optimism about the future of hemophilia, even the current status of hemophilia to your patients. And you're definitely going to have great outcomes for your patients if you do that. So thanks again, and take care.

Announcer Close:
This activity was brought to you by AXIS Medical Education and is supported by an educational grant from Sanofi. To receive your free CME credit, be sure to complete the post-test and evaluation at reachmd.com/CME. This is CME on ReachMD. Be Part of the Knowledge.

© 2023 ReachMD