Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/hand-in-hand-walking-patients-through-their-journey-with-a-therapy-for-early-alzheimers-disease-ad/24361/

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Hand-in-Hand: Walking Patients Through Their Journey with a Therapy for Early Alzheimer's Disease (AD)

Chapter 1: Identifying Patients in the Mild Cognitive Impairment and Mild Dementia Stages of Alzheimer's Disease

Narrator:
For clinicians who manage patients with or at risk of developing Alzheimer's disease, we have found ourselves in an exciting treatment era with the traditional FDA approval of LEQEMBI® (lecanemab-irmb).

How can we prepare for LEQEMBI? How do we best prepare ourselves, our practice settings, and our patients and their families for navigating the LEQEMBI journey? Hand-in-hand.

In this video, Dr Gregory Cooper shares his practical perspectives and insights to help HCPs feel more confident identifying appropriate patients, navigating protocols for treatment and monitoring, and simplifying the patient journey.

INDICATION
LEQEMBI is indicated for the treatment of Alzheimer's disease. Treatment with LEQEMBI should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.

IMPORTANT SAFETY INFORMATION

WARNING: AMYLOID-RELATED IMAGING ABNORMALITIES (ARIA)

- **Monoclonal antibodies directed against aggregated forms of amyloid beta, including LEQEMBI, can cause ARIA, characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). Incidence and timing of ARIA vary among treatments. ARIA usually occurs early in treatment and is asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. Serious intracerebral hemorrhages >1 cm, some fatal, have been observed with this class of medications.**
  - **Apolipoprotein E ε4 (ApoE ε4) Homozygotes: Patients who are ApoE ε4 homozygotes (~15% of patients with AD) treated with this class of medications have a higher incidence of ARIA, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results. Prescribers should inform patients that if genotype testing is not performed, they can still be treated with LEQEMBI; however, it cannot be determined if they are ApoE ε4 homozygotes and at higher risk for ARIA.**
- **Consider the benefit of LEQEMBI for the treatment of AD and the potential risk of serious ARIA events when deciding to initiate treatment with LEQEMBI.**

Please see additional Select Safety Information in chapter 6 of this video and accompanying full US Prescribing Information, including Boxed WARNING.

Dr. Cooper:
First things first. We need to identify patients with Alzheimer's disease, or AD, early, in the mild cognitive impairment (MCI) or mild dementia stage of disease. And even more, we need to amplify the conversation around the importance of identifying patents with AD in the MCI and mild dementia stages.

Time is of the essence. Now, we have a therapy that can slow the course of AD for patients in the early MCI or mild dementia stage. If a patient isn't identified until they have moderate dementia, they've missed the opportunity to be an appropriate candidate for LEQEMBI. So, now, a potential cost of “wait and see” is lost opportunity.

Stage of illness is the number one reason that patients referred to me are not eligible for LEQEMBI. We want to change that so that patients aren’t missing their opportunity. MCI due to AD and mild AD dementia are different stages and are critical points for intervention. Intervening early can delay progression.

At my center, about 80% of my patients with possible AD are referred from primary care, and another 10% or so are referred from another neurologist. Often when patients are referred to me, they come in with a diagnosis of MCI or dementia, and that diagnosis is typically accurate. However, it’s always important to confirm the diagnosis because research has shown that about 25% of patients with a diagnosis of AD won’t have amyloid positivity on PET, and about 11% of patients with a dementia diagnosis that is not AD actually do have AD. And, sometimes, patients don’t come in with a diagnosis at all, and we need to complete the necessary workup from scratch.

We identify these patients the old-fashioned way. We get their history, particularly from an informant. The most important component for identifying these patients is the history. Then we do the standard bloodwork and MRI to rule out other causes.

To confirm MCI or mild dementia, I typically use 1 of 2 tests: the Mini-Mental State Exam, or MMSE, or the Montreal Cognitive Assessment, or MoCA. In a perfect world, I would only see people that are so mild that the MMSE doesn't detect the problem. Then I would need the MoCA to confirm some objective evidence for cognitive impairment. These are not the only 2 tests you can use, but regardless of which tool you use in your practice, ideally you want to use an MCI-sensitive neurocognitive assessment tool to confirm MCI or mild dementia.

I believe that we, as a field, do have barriers in identifying MCI due to AD or mild AD dementia early enough. These include getting patients and their family or caregiver to recognize the problem and seek help, and getting primary care physicians to recognize the problem early and take action. So we need to raise that level of suspicion.

Years ago, at another center, I would never see patients until they had moderate- to late-stage dementia because there was just that feeling of, “Well, there’s nothing you can do about it, so why bother?”

The real job we have now, especially with the introduction of anti-amyloid therapies, is to change that mindset and push for early recognition, and that means empowering primary care or finding ways to better identify and evaluate these patients and/or get these patients to specialists earlier.

Chapter 2: Confirming Amyloid β Pathology

Dr. Cooper:
Once patients with MCI or mild dementia are identified, we need to confirm the presence of amyloid beta pathology. In my practice, we use either CSF or PET to do this. With advances in testing, we may use blood-based biomarkers to facilitate identification.

I order the tests and interpret them. Our radiologists conduct CSF under fluoroscopy, so it’s been a pretty smooth process. I have some patients who have an amyloid PET scan that was done as part of a research study, and I am trying to prepare our organization for exploring the potential of doing a lot more amyloid PET scans.

By the time I test for amyloid pathology, I would have already identified patients who are in the appropriate disease stage based on history, initial testing, and assessments. At this point, I’ll have the discussion with the patient and family and say, “You may be a good candidate for this medication. This medication targets and removes an abnormal protein called amyloid beta from the brain, and the clinical data supports this. But to confirm that you’re a candidate for this, we would have to confirm that you have amyloid in the brain. There’s no point in trying to remove something that’s not there.”

I think it makes a lot of sense that LEQEMBI targets protofibrils. We think a lot about plaque, but protofibrils are neurotoxic, and continuously accumulating and causing damage in AD, possibly even after plaques are removed. I don’t actually bring that up with patients, because it's probably getting into the weeds more than most of my patients are interested in, so I stick with, “With LEQEMBI, we’re removing the amyloid beta aggregates.”

With the table set like that, we order the CSF or PET test, and if it comes back positive for amyloid, I tell them, “Okay, we see amyloid. This is consistent with eligibility for this medication.” If the biomarkers don’t show amyloid, I bring them back and say, “Well, I was clearly wrong,” and then we figure out what else is needed.

Chapter 3: Preparing for Treatment with LEQEMBI and Individualizing Risk Assessment for ARIA

Now, we have identified our patients with MCI or mild dementia, and we have confirmed an AD diagnosis by detecting amyloid pathology with CSF or PET.

Here comes the part where we discuss the benefits and risk of treatment with LEQEMBI. I urge clinicians to be honest and straightforward during this conversation, yet empathetic. I want my patients and their families to have all the information.

What I tell people is that this medication is designed to remove amyloid. It does not reverse memory loss or loss of functional abilities, but it does slow progression by 27% on average. For most patients and families, that's all they want to hear. Usually the answer is, "That sounds great! Let's get started."

I make sure they understand that it doesn't stop or reverse the disease. I think you should you deliver this message in an open-ended way. You're constantly asking, "Do you have any questions?" So you're inviting people to ask those questions and develop a deeper understanding.

Now, in terms of patients that I offer this medication to, I would say almost anybody that has an appropriate diagnosis of mild cognitive impairment due to AD or mild AD dementia, with confirmed amyloid pathology. Anticoagulants are not contraindicated in the LEQEMBI Prescribing Information, however the PI does encourage additional caution when considering the administration of anticoagulants or a thrombolytic agent to a patient being treated with LEQEMBI. So in my practice, this is something we consider very carefully.

To me, the ideal patient for LEQEMBI is someone who just has early MCI and has amyloid in the brain. I would add that my ideal patient is otherwise in reasonably good health. If someone has severe heart failure, severe kidney disease, or has a life expectancy of 1 to 2 years, it may not make sense to start them on this medication. And finally, my ideal patient has a good social support network. In our infusion center, we have required that a caregiver be with them during the infusion. You could argue, is that really necessary for the infusion? But I think it is important for them to have that support network for this medication, because there is a lot involved.

So, it's a broad net of people I offer this medication to: appropriate diagnosis of MCI due to AD or mild AD dementia with amyloid pathology confirmed, no other major medical concerns, and a reasonable support network. If we hit those, then I'm comfortable discussing moving forward.

I also tell patients and families that we need a good recent MRI scan, which, in my practice, means within the last 12 months. I'm looking for any reason that they would be at a high risk for bleeding complications. That's usually where I leave the discussion. If they do want more information on the baseline MRI, I'll say, "We're looking to see if there's been evidence of prior stroke or severe vascular disease, or evidence of prior microhemorrhages."

I tell patients that ApoE ε4 genetic testing is not required, but it's very strongly recommended before we initiate treatment with LEQEMBI. The reason it is recommended is that it allows us to give a more precise estimate of their risk of ARIA, which is bleeding or swelling in the brain. It allows us to be more accurate.

In my experience, most people say, "Okay, yes. Let's do the genetic test." I've had a couple of people decline the test. So for these patients, we have gone ahead and started treatment.

When discussing the safety profile of LEQEMBI with patients, I will say, "So, we just talked about what's good about the drug, but it's not a simple drug. It's not a pill I can give you to take every day. It's an infusion, every 2 weeks, so there is a real commitment. There's also a risk of side effects; approximately 1 in 4 (a little over 26% to be exact) will have an infusion reaction, which can include symptoms like feeling achy, or chilled, or feverish. These reactions tend to be mild or moderate in severity, and we can treat ahead of future infusions with medications like acetaminophen or antihistamines."

"What I want to discuss in more depth is ARIA, which stands for amyloid-related imaging abnormalities, but the name is not what's important. What that really means is swelling or bleeding in the brain."

I tell them about 1 out of every 5 patients getting this medication will have some degree of bleeding or swelling in the brain. Most of those people will have no symptoms. But about 3% of people will have symptoms. I'll describe those as including headache, nausea, blurred vision, and confusion. I tell them, "Less than 1% of the time that may be serious enough that you have to go into the hospital. Experts are saying that this can be life-threatening in rare instances. So you need to understand that."

I think that explanation is serious enough, but it's also accurate and balanced enough that I feel like I'm getting the message across. I say, "I know I've given you a lot to think about, and if you already know this is not for you, I won't hassle you about it anymore. If you've already decided that this is what you want, we'll keep going forward." I say that because a lot of people have made the decision before they ever talk to me, and, frankly, I'm pretty sure they're just politely listening to me, hoping I'll hurry up so we can get on with it.

I will also tell patients, “This is a big decision, and I am not trying to push you to make that decision right now. The purpose of today’s visit is for you to get all of that information and ask all the questions you need to so that you and your family can sit down, think about this, and make the right decision for you. I’ve got a folder full of information that that our team has created that I can give you to take home, and if you have questions, call me. If you decide you want to do this, call me.”

The only other thing I say is, “I do not want you to feel pressured to decide. I want you to make the right decision for you, and I will support you in whatever that decision may be. However, I would encourage you to make that decision in a timely basis, because if you come back and see me in 6 months or a year from now and say “I’ve decided I want this medication”, your exam may have changed, and you may not be eligible for it. That’s not going to change tomorrow or next week, but one way or the other, do make that decision in the next few days or weeks because your eligibility may change over time.”

I think people take that very well. I try hard not to make people feel pressured. I also want them to understand there is a there is some sense of urgency.

Chapter 4: Initiation of Treatment (Infusion Process; Setting Expectations)

For LEQEMBI, we have a multidisciplinary team including myself, a nurse navigator, radiology, pharmacy, administration, infusion—people across the institution to develop the protocols that we use for the workup, administration of medication, and then, of course, safety monitoring.

We start with the nurse navigator whose role is only LEQEMBI. She helps oversee the whole process, so she ultimately keeps us in line. She ensures that we’re ordering the safety MRIs when we need to and getting the patient agreement completed. The agreement explains the process and confirms that they have all the information and still want the medication. The agreement also includes coming back for regular MRIs.

Our nurse navigator liaises with our reimbursement specialist and with our infusion team. She is essentially the quarterback that ties all of that together, and then she interfaces with the patient. We go through the process, and then, if everybody is on board, we start scheduling the infusions.

You also must have a partnership with radiology, both from an operations standpoint—the administrators, the techs, the magnets—and the radiologist. We have a great neuroradiology group, so we were able to team with them from the very beginning to prepare them for this. My advice is to motivate your team early to set up this partnership.

We meet as a group every Thursday morning and go over the whole process for our LEQEMBI patients to see what’s working. I think that’s important. We need to be a continuously learning organization. We are always looking for opportunities for improvement.

We are working on creating a document or even a video that illustrates what to expect from the whole process. We want to expand and describe the entire experience—when you show up, who you will see, where you will go, what the infusion center will look and feel like.

It’s important to listen to patient and family feedback, as well. Some asked for help to create a support group for LEQEMBI patients and families. This would be separate from our other Alzheimer’s disease support groups. So we are doing that, and allowing them to feel that sense of community. They can learn from each other, and we can learn from them.

Many of our patients and families have expressed that they are truly excited to be doing something that gives them hope and makes them feel as though they are part of history. They feel like pioneers, helping future generations, and I’m happy for them.

Chapter 5: ARIA Monitoring and Management

I’d like to talk about ARIA monitoring and management—particularly what we, as healthcare providers, should know about it, and how we should communicate with fellow healthcare providers and, of course, patients and their families.

First, what we need to know about ARIA—as neurologists, geriatricians, or other healthcare providers who treat early AD, I think that we should be aware of the incidences from the clinical trial: 21% of patients on LEQEMBI experienced ARIA, and 3% experienced symptomatic ARIA.

We need to have a plan for what to do in the case of symptomatic and serious ARIA. We need to know if people have stroke-like symptoms and present to the emergency room. The ER needs to know to do an MRI in case it is ARIA.

Every neurologist, geriatrician, or other healthcare provider who treats early AD needs to understand that this is a side effect of an anti-

amyloid beta monoclonal antibody like LEQEMBI, and that they might see ARIA. I, personally, would like to be better at reading the films, myself, but also understand the value of working with our highly skilled radiologists, as well.

I also think we need to come up with systems to help figure out how to extend ARIA expertise to rural places. How do we, for example, obtain the MRI locally, but then send the images to urban centers with expertise to get the read? It's not realistic to think that we're going to make everybody an expert. I would like to see us figure out a way to create partnerships where we can help patients in rural areas get convenient access to this medication.

How do we coordinate care across all the team members involved in care for a patient on LEQEMBI? At my center, it's using a combination of tools and over-emphasizing the need for open communication. Don't let something fester. If you have a question, ask it. If you have a concern, address it.

When I communicate with any of my multidisciplinary partners, I'm sure to treat them as equals, as colleagues. I'm asking them for their help in partnership, not telling them. I think when you treat people with respect, and you acknowledge that you're asking for their help, people usually respond to that well.

We invited the radiologists to our group meetings on a couple of occasions. We work with them to explain what we want these safety reports to look like, as well. We don't tell them how to do their job because they know how to do it very well. We simply agree on how to work together.

The radiologist and I have each other's numbers, and generally we just text each other back and forth if we have questions. If we need to do more than that, we get on the phone. Fortunately, our system allows us to look at films together, even though we're in separate hospitals or separate parts of the same campus.

If the infusion center has an issue, they will call here to the office, and we'll handle it. We also have both regular and irregular meetings, so we have a regular cadence with which we're going to connect with each other. The simplest thing to do is arrange a time for everybody to get on a Zoom meeting, and, in 20 minutes, we can figure something out.

I think the ER should be educated to know enough about LEQEMBI and possible adverse events. If a patient has a delayed infusion reaction—we observe them, they go home, and then they have shaking, chills—I think the ER should be trained on these symptoms.

If the ER staff know the patient had an infusion this afternoon, they recognize an infusion reaction, they can potentially give acetaminophen and an antihistamine, and observe for resolution. If they have more severe symptoms—particularly that might be stroke-like or an indication of ARIA—that don't look like an infusion reaction, then proceed immediately to an MRI. I personally have met with ER leadership, presented at group meetings, and worked with the ER administration team to create algorithms for evaluating ARIA.

At my center, we have taken an even more conservative approach. If somebody comes into the ER and they are on LEQEMBI, we will strongly consider an MRI, if indicated. We have instituted something in our electronic medical record so that a big banner comes up letting us know that the patient is taking LEQEMBI. As part of that, I have connected with our stroke and neuro-hospitalist teams and educated our ER teams, as well. We have developed algorithms for ER evaluation and modified our stroke order sets for patients taking LEQEMBI.

The first thing is to know that if you're prescribing a lot of LEQEMBI, ARIA is eventually going to happen. When it does happen, take a deep breath and remember you have a plan. Then, review the MRI and radiology report and speak with the radiologist directly, if necessary. Is it mild, moderate, or severe on the MRI? Make yourself familiar with Table 3 in the Prescribing Information. It lays it all out for both ARIA-E and ARIA-H.

Find out if the patient is having any symptoms. Then, all you have to do is follow the algorithm in Tables 1 and 2 of the Prescribing Information to know what to do. You can have a reasonable amount of confidence based on following that algorithm. You don't have to reinvent the wheel. For example, if ARIA is mild radiographically, and the patient isn't having any symptoms, dosing may be continued.

You must know this is an expected complication, and, most of the time, it's not going to be symptomatic. We can handle this, and we have a protocol in place. "Oh yes, we can continue treatment", or "No, we're going to hold treatment for now, and we're going to follow up with MRI." Or it's severe, but our ER team knows what to do. Lay the framework and be confident that you've done all that work ahead of time, and now all you have to do is talk to the patient and say, "I'm sorry, but we've already planned for this, and here's what we're going to do."

Treatment suspension does happen. When we see ARIA on MRI, first, I'm going to call the patient and make sure they and their loved ones are okay. I say, "I want to know how you're doing." If they are having bad symptoms, I will send them to the ER, but most of the time, it won't be symptomatic.

Then I'm going to say, “Listen. I am sorry, but this is what the MRI shows.” Depending on the severity, I may say, “This is serious, but it's not of a severity that it has to stop our treatment. But now it means we're going to have to monitor more carefully for symptoms, even more than we were, and we're going to have to do a follow up MRI.” They're going to understand that we've already talked about these possibilities before starting treatment. They may not remember the details, but I'm going to reassure them that we prepared for this.

If it's moderate on the MRI, I say, “For your safety, right now, we do have to stop treatment, and we have to monitor this. Maybe we can restart treatment later on. We don't know that answer, but for your own safety, right now, this is just where we are, and I'm very sorry.”

I'm also going to reassure them we have prepared for this, and we are with them every step of the way—“we” meaning the whole team. “This is not what we wanted to have happen, but we're prepared and we are with you.” I want to reassure them that we are taking this seriously. They need to take it seriously too.

I think that’s a perfect point to stop and emphasize that we all need to be prepared. This preparedness will give us all the confidence that our patients deserve. We can take the appropriate steps to identify, treat, support, and counsel appropriate patients, and take them and their families or caregivers through the patient journey with LEQEMBI.

Chapter 6: LEQEMBI Important Safety Information

Dr. Cooper:
Let’s now review the Important Safety Information for LEQEMBI.

Narrator:
INDICATION
LEQEMBI is indicated for the treatment of Alzheimer’s disease. Treatment with LEQEMBI should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.

IMPORTANT SAFETY INFORMATION

WARNING: AMYLOID-RELATED IMAGING ABNORMALITIES (ARIA)

- **Monoclonal antibodies directed against aggregated forms of amyloid beta, including LEQEMBI, can cause ARIA, characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). Incidence and timing of ARIA vary among treatments. ARIA usually occurs early in treatment and is asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. Serious intracerebral hemorrhages >1 cm, some fatal, have been observed with this class of medications.**
  - **Apolipoprotein E ε4 (ApoE ε4) Homozygotes: Patients who are ApoE ε4 homozygotes (~15% of patients with AD) treated with this class of medications have a higher incidence of ARIA, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results. Prescribers should inform patients that if genotype testing is not performed, they can still be treated with LEQEMBI; however, it cannot be determined if they are ApoE ε4 homozygotes and at higher risk for ARIA.**
- **Consider the benefit of LEQEMBI for the treatment of AD and the potential risk of serious ARIA events when deciding to initiate treatment with LEQEMBI.**

CONTRAINDICATION
LEQEMBI is contraindicated in patients with serious hypersensitivity to lecanemab-irmb or to any of the excipients of LEQEMBI. Reactions have included angioedema and anaphylaxis.

WARNINGS AND PRECAUTIONS
AMYLOID-RELATED IMAGING ABNORMALITIES
ARIA-E and ARIA-H can occur together. ARIA-E can be observed on MRI as brain edema or sulcal effusions and ARIA-H as microhemorrhage and superficial siderosis. ARIA can occur spontaneously in patients with AD. ARIA-H generally occurs in association with ARIA-E. Reported ARIA symptoms may include headache, confusion, visual changes, dizziness, nausea, and gait difficulty. Focal neurologic deficits may also occur. Symptoms usually resolve over time.

Incidence of ARIA

Symptomatic ARIA occurred in 3% and serious ARIA symptoms in 0.7% with LEQEMBI. Clinical ARIA symptoms resolved in 79% of patients during the period of observation. ARIA, including asymptomatic radiographic events, was observed: LEQEMBI, 21%; placebo, 9%. ARIA-E was observed: LEQEMBI, 13%; placebo, 2%. ARIA-H was observed: LEQEMBI, 17%; placebo, 9%. No increase in isolated ARIA-H was observed for LEQEMBI vs placebo.

ApoE ε4 Carrier Status and Risk of ARIA

Of the patients taking LEQEMBI, 16% were ApoE ε4 homozygotes, 53% were heterozygotes, and 31% were noncarriers. With LEQEMBI, ARIA was higher in ApoE ε4 homozygotes (LEQEMBI: 45%; placebo: 22%) than in heterozygotes (LEQEMBI: 19%; placebo: 9%) and noncarriers (LEQEMBI: 13%; placebo: 4%). Symptomatic ARIA-E occurred in 9% of ApoE ε4 homozygotes vs 2% of heterozygotes and 1% of noncarriers. Serious ARIA events occurred in 3% of ApoE ε4 homozygotes and in ~1% of heterozygotes and noncarriers. The recommendations on management of ARIA do not differ between ApoE ε4 carriers and noncarriers.

Radiographic Findings

Most ARIA-E radiographic events occurred within the first 7 doses, although ARIA can occur at any time, and patients can have >1 episode. Maximum radiographic severity of ARIA-E with LEQEMBI was mild in 4%, moderate in 7%, and severe in 1% of patients. Resolution of ARIA-E on MRI occurred in 52% of patients by 12 weeks, 81% by 17 weeks, and 100% overall after detection. Maximum radiographic severity of ARIA-H microhemorrhage with LEQEMBI was mild in 9%, moderate in 2%, and severe in 3% of patients; superficial siderosis was mild in 4%, moderate in 1%, and severe in 0.4% of patients. With LEQEMBI, the rate of severe radiographic ARIA-E was highest in ApoE ε4 homozygotes (5%) vs heterozygotes (0.4%) or noncarriers (0%). With LEQEMBI, the rate of severe radiographic ARIA-H was highest in ApoE ε4 homozygotes (13.5%) vs heterozygotes (2.1%) or noncarriers (1.1%).

Intracerebral Hemorrhage

Intracerebral hemorrhage >1 cm in diameter was reported in 0.7% LEQEMBI vs 0.1% placebo. Fatal events of intracerebral hemorrhage in patients taking LEQEMBI have been reported.

> ***Concomitant Antithrombotic Medication and Other Risk Factors for Intracerebral Hemorrhage:***
> In Clarity AD, baseline use of antithrombotic medication (aspirin, other antiplatelets, or anticoagulants) was allowed if the patient was on a stable dose. Most exposures were to aspirin. Antithrombotic medications did not increase the risk of ARIA with LEQEMBI. The incidence of intracerebral hemorrhage: 0.9% LEQEMBI with a concomitant antithrombotic medication vs 0.6% no antithrombotic; 2.5% LEQEMBI with an anticoagulant alone or with antiplatelet medication/aspirin vs none receiving placebo.
>
> Patients were excluded from Clarity AD if neuroimaging indicated increased risk for intracerebral hemorrhage including cerebral amyloid angiopathy (prior cerebral hemorrhage >1 cm in greatest diameter, >4 microhemorrhages, superficial siderosis, vasogenic edema) or other lesions (aneurysm, vascular malformation). The presence of an ApoE ε4 allele is also associated with cerebral amyloid angiopathy.
>
> Caution should be exercised when considering the administration of anticoagulants or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with LEQEMBI and in patients with factors that indicate an increased risk for intracerebral hemorrhage.

ARIA Monitoring and Dose Management Guidelines

Obtain a recent baseline brain MRI prior to initiating treatment with LEQEMBI and prior to the 5th, 7th, and 14th infusions. Enhanced clinical vigilance for ARIA is recommended during the first 14 weeks of treatment. Depending on ARIA-E and ARIA-H clinical symptoms and radiographic severity, use clinical judgment when considering whether to continue dosing or to temporarily or permanently discontinue LEQEMBI. If a patient experiences ARIA symptoms, clinical evaluation should be performed, including MRI if indicated. If ARIA is observed on MRI, careful clinical evaluation should be performed prior to continuing treatment.

HYPERSENSITIVITY REACTIONS

Hypersensitivity reactions, including angioedema, bronchospasm, and anaphylaxis, have occurred with LEQEMBI. Promptly discontinue the infusion upon the first observation of any signs or symptoms consistent with a hypersensitivity reaction and initiate appropriate therapy.

INFUSION-RELATED REACTIONS (IRRs)

IRRs were observed—LEQEMBI: 26%; placebo: 7% — and most cases with LEQEMBI (75%) occurred with the first infusion. IRRs were mostly mild (69%) or moderate (28%). Symptoms included fever and flu-like symptoms (chills, generalized aches, feeling shaky, and joint pain), nausea, vomiting, hypotension, hypertension, and oxygen desaturation.

In the event of an IRR, the infusion rate may be reduced or discontinued, and appropriate therapy initiated as clinically indicated.

Consider prophylactic treatment prior to future infusions with antihistamines, acetaminophen, nonsteroidal anti-inflammatory drugs, or corticosteroids.

ADVERSE REACTIONS

The most common adverse reactions reported in ≥5% with LEQEMBI and ≥2% higher than placebo were IRRs (LEQEMBI: 26%; placebo: 7%), ARIA-H (LEQEMBI: 14%; placebo: 8%), ARIA-E (LEQEMBI: 13%; placebo: 2%), headache (LEQEMBI: 11%; placebo: 8%), superficial siderosis of central nervous system (LEQEMBI: 6%; placebo: 3%), rash (LEQEMBI: 6%; placebo: 4%), and nausea/vomiting (LEQEMBI: 6%; placebo: 4%).

Please see full Prescribing Information for LEQEMBI, including Boxed WARNING.

Dr. Cooper:

Thank you for watching. I hope you feel more confident that you can take the appropriate steps to identify, treat, support, and counsel appropriate patients, and take them and their families through the patient journey with LEQEMBI.

Narrator:

For more information about LEQEMBI, visit www.LeqembiHCP.com.

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