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BEYOND THE ANTI-VEGFS: AN UPDATE ON CURRENT AND FUTURE AMD TREATMENT STRATEGIES

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CONTENT SOURCE

This continuing medical education (CME) activity captures content from a virtual round table discussion.

ACTIVITY DESCRIPTION

The current state of neovascular age-related macular degeneration (nAMD) treatment in terms of anti-VEGF agents and the treatments expecting FDA approval on the near future are highlighted in this supplement. Faculty members also share their experiences in caring for patients during a pandemic.

TARGET AUDIENCE

This certified CME activity is designed for retina specialists involved in the management of retinal diseases.

LEARNING OBJECTIVES

Upon completion of this activity, the participant should be able to:

- **Discuss** real-world vision outcomes and durability/treatment frequency of anti-VEGF therapy for neovascular AMD
- **Describe** the barriers to achieving the same vision outcomes in the real-world clinical setting as those reported in clinical trials
- **Evaluate** the rates of intraocular inflammation as reported in clinical studies and in clinical practice
- **Describe** therapies in the pipeline that are near FDA approval that would decrease treatment burden and potentially improve treatment adherence in clinical practice

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Please complete prior to accessing the material and submit with Posttest/Activity Evaluation/Satisfaction Measures Instructions for CME Credit.

1. Please rate your confidence in your ability to evaluate intraocular inflammation as reported in clinical studies and in clinical practice (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. An 80-year-old male with new onset neovascular age related macular degeneration (nAMD) presents to your practice. You explain the pathophysiology and treatment of his disease, and discuss the need to initiate anti-VEGF therapy. The patient asks about the necessary duration of his therapy. What is the most appropriate answer:

a. 3 months of treatment followed by observation
b. 1 year of monthly treatment followed by observation
c. 2 years of monthly treatment and as needed treatment thereafter
d. Exact treatment interval will be tailored to his response to treatment, but he should be prepared for a long, frequent dosing schedule

3. What is the risk of endophthalmitis with intravitreal anti-VEGF therapy?

a. 1/100
b. 1/1,000
c. 1/10,000
d. 1/100,000

4. A 78-year-old female with nAMD receiving intravitreal ranibizumab is switched to aflibercept due to poor anatomical response. One week after her injection she calls your practice with the chief complaint of increasing floaters. On examination, you notice 2+ cells in the anterior chamber and 1+ cell in the anterior vitreous. Which of the following is the next appropriate step?

a. Rule out endophthalmitis. If endophthalmitis is ruled out, start anti-inflammatory therapy with aggressive monitoring, starting with topical steroids
b. Inject steroid intravitreally or in the sub-tenons space
c. Start oral steroids
d. Observe

5. The MAPLE study investigated the incidence of inflammation in eyes that received abicipar. What rate of inflammation was noted in this study?

a. 3%
b. 5%
c. 7%
d. 9%

6. Many novel approaches to anti-VEGF therapy are currently being investigated. What is a difference between OPT-302 and conbercept?

a. OPT-302 is a VEGF-A, VEGF-C, and VEGF-D inhibitor while conbercept is a soluble receptor decoy that blocks all isoforms of VEGF-A, VEGF-B, VEGF-C, and PLGF
b. OPT-302 blocks all isoforms of VEGF and conbercept blocks PLGF
c. OPT-302 blocks PLGF and conbercept blocks all isoforms of VEGF
d. Both OPT-302 and conbercept block all VEGF isoforms and PLGF

Beyond the Anti-VEGFs: An Update on Current and Future AMD Treatment Strategies

This roundtable discussion reviews the current state of neovascular age-related macular degeneration (nAMD) treatment in terms of current anti-VEGF agents as well as future treatments. In addition, this group of esteemed retina specialists from across the country will share their experiences in caring for patients during the COVID-19 pandemic, and how longer duration therapies can reduce treatment burden to keep everyone safer while providing efficacious treatment.

—Peter K. Kaiser, MD, Moderator

NOTE: This roundtable discussion occurred before the June 26, 2020, US FDA rejection of the drug candidate abicipar pegol.

INITIATING TREATMENT: PATIENT DISCUSSIONS

Q | PETER K. KAISER, MD: You have a patient who comes in with newly diagnosed nAMD. Can you describe the discussion you have with this patient regarding what their life will be like after initiating treatment?

JEREMY D. WOLFE, MD: With patients like this, I universally explain to them that we have good treatments and the current standard is potentially monthly injections that could continue for their lifetime.[1] Then I explain to them that for many people the treatment is not required forever, but I don't know how they're going to respond, and that we must take it one step at a time. I prepare them for a long, frequent dosing schedule with the hope that they won't need it.

DR. KAISER: In the back of your mind, what is your default treatment strategy? Do you always treat *pro re nata* (PRN), with a fixed schedule, treat and extend, or something different?

DR. WOLFE: I begin with a treat-and-extend approach until the patient extends to a quarter, and then I'll try PRN.

JENNIFER LIM, MD: I tend to use the treat-and-observe approach. Ideally, I give three initial monthly anti-VEGF injections, then use a treat-and-observe PRN regimen.[2] However, if there are issues with the patient coming back for follow-up, I will more than likely use a treat-and-extend regimen to limit the number of times the patient has to come to the office.

In terms of how I discuss treatment with patients, I typically set their expectations from the beginning and tell them it's going to require both a lot of injections, especially up front, and a lot of office visits for monthly monitoring. That being said, with the treat-and-observe approach, I evaluate patients monthly for an extended duration in order to determine their personalized treatment interval. Then, I extend their treatment interval to match their personalized dosing treatment and try to extend from there.

Lastly, I also tell them the drug choice is not only based on published efficacy and safety, but also on selecting a drug that is proven to have the lowest risk of producing an inflammatory reaction during clinical use (after FDA approval).

BARUCH D. KUPPERMANN, MD, PHD: I'm not a straight treat-and-extend provider either; all of us have different variations. I generally use a kind of hybrid between PRN and treat-and-extend regimen. I like to inject just when fluid is developing. I determine the interval of recurrence and then inject at that interval.

I frequently use a treat-and-observe approach, similar to Dr. Lim, and eventually reach treat-and-extend. I like to inject when there is a small amount of fluid and time it around that because even though treat-and-extend is the most popular treatment modality, I'm concerned about over treating.

I like what Dr. Wolfe said about treating out to 12 weeks, then trying PRN to see what's needed, and then determining the interval. It appears that we are all similar; none of us utilize the traditional treat-and-extend approach, which dominates the specialty according to the American Society of Retina Specialists Preferences and Trends survey.[3]

FLUID AND DOSING INTERVALS

Q | DR. KAISER: I think the difference is partly because treat-and-extend really requires the aggressive treatment described by Dr. Lim that involves monthly therapy until the patient is dry.[4,5] Some retina specialists seem to prefer to leave some fluid, and we're learning a lot more about what fluid matters and what fluid may be okay to watch.[6,7,8]

Dr. Wolfe, how much fluid do you tolerate on your treat-and-extend regimen? When you see fluid, do you reduce the interval, or do you maintain the interval?

DR. WOLFE: That really depends on the patient and how frequently I'm treating them. If I'm seeing someone every 5 weeks and their visual acuity (VA) is 20/25 with a small amount of fluid, I'll just keep doing

what I'm doing. However, if the patient starts developing intraretinal edema as opposed to subretinal fluid (SRF), or their vision is not as good and I think there's vision to be gained, then I'll treat that patient more frequently or try a different agent.

DR. KAISER: Dr. Lim, does the type of lesion sway you in any way? In other words, does the baseline type of lesion influence how much fluid you're going to tolerate or not tolerate?

DR. LIM: For eyes that have a pigment epithelial detachment (PED), I'm more aggressive and use frequent anti-VEGF injections because those eyes tend to be polypoidal choroidal eyes, which are at risk of bleeding and are generally more difficult to get under control. So, I don't like to tolerate fluid in those eyes.

I agree completely with Dr. Wolfe in that if there is intraretinal fluid (IRF), I want to resolve that fluid. If it's an eye that doesn't have a PED component and it has responded very nicely to an anti-VEGF, and then you see some SRF that's not immediately threatening the foveal area and the fovea is flat, I can tolerate a little bit of that fluid. However, if that SRF starts increasing, I'll treat. In contrast, if there is subfoveal fluid, I will most likely recommend treatment.

Q | **DR. KAISER:** At Cole Eye, we start our AMD patients on bevacizumab based on the Comparison of AMD Treatment Trials (CATT) study.[9] We keep patients on bevacizumab, when possible. Some patients don't do as well with bevacizumab, so we switch them to treat-and-extend with other medications. How do you manage your patients? What do you start with, and if you start with one, what makes you decide when to switch?

DR. KUPPERMANN: At UC Irvine, we have a good payor mix and I don't have a lot of step therapy required of me. It's case by case, but without step therapy, I tend to predominantly start with aflibercept because perhaps the intervals tend to be slightly longer,[10] though admittedly, there's not a lot of good data. The only data that ever showed anything convincing was the first year of the DRCR.net Protocol T trial,[11] but that was for diabetics. There's this implication that aflibercept may last longer.

When step therapy is required, which is mandated for about 20% of my patients, then we certainly start with bevacizumab and keep them on bevacizumab as long as it makes sense. Many of them actually stay on bevacizumab, because they do well.

I do have other patients who have been on ranibizumab for a very long time and are quite happy with it, so I use that therapy as well. I have all types of patients in whom I use different anti-VEGFs, but I would say my choice is more weighted toward aflibercept than the others.

DR. KAISER: If you look at the clinical studies, CATT, VIEW 1/2, HAWK/HARRIER, that were all head-to-head studies, none actually reported a better VA benefit of any one of these treatments over another. The studies have shown differences in durability between the drugs, but certainly not in efficacy.[6,12,13]

Dr. Wolfe, you're shooting for that 12-week (q12) interval with your patients. Are you able to achieve this with bevacizumab and ranibizumab, or are you doing this in general with aflibercept and brolucizumab?

DR. WOLFE: My approach includes a little of everything. I tend to start my patients on bevacizumab unless they have a strong preference otherwise. I definitely have fewer patients at q12 on bevacizumab than I do on ranibizumab and aflibercept. I agree with Dr. Kuppermann in that I feel like there may be longer duration with aflibercept. Currently, we are not using brolucizumab in our practice.

DR. KAISER: Dr. Lim, what are your top two choices to get patients to q12 intervals, and do you ever push even longer, perhaps to 16-week (q16) or longer intervals?

DR. LIM: I like to use aflibercept predominantly if the patient presents with a PED component. I believe it actually gets the retina flatter in a shorter amount of time. However, because of the rare inflammatory reaction that can occur—I've had two patients have that happen—I prefer not to start with aflibercept every single time. I would start with either ranibizumab or bevacizumab. There are some insurance mandates here that also require us to sometimes start with aflibercept, while others require we start with bevacizumab.

In terms of q12, I can actually get some patients on a q12 interval with ranibizumab or aflibercept more often than with bevacizumab. There are some patients who are able to go longer than 12 weeks on the treat-and-observe regimen and may not need an injection for a while. I have not tried brolucizumab. It was going to be a part of our formulary but then the inflammatory problems arose and we're holding off on using it for now.

DR. WOLFE: For patients who do well at q12, I move to PRN. If they come back with fluid on the next visit, I will treat them and then keep them at the 14- to 16-week range, so I will go longer than q12 in the select patient.

DR. KAISER: And when you switch to PRN at that extended interval, do you keep the q12 PRN, or do you actually switch back to a monthly visit schedule to make sure they are not leaking?

DR. WOLFE: I switch back to monthly. If I've been giving the patient quarterly injections and they appear stable, I offer the patient the option of either an injection today and come back in another quarter, or no injection and come back in a month.

DR. KAISER: Does anyone have experience using brolucizumab?

DR. KUPPERMANN: I don't have any experience with brolucizumab. Similar to the situation described by Dr. Lim, it took us a while to get it to the Pharmacy and Therapeutics committee; we got it fully approved. It then took a while to have it added into the Epic software so we could do that injection. That's when the concerns about

inflammation from brolucizumab began to arise.[14] Based on those reports, we're holding off for now on using brolucizumab until we understand better what's going on there.

DR. KAISER: At Cole Eye, we have been using brolucizumab since around early December. We started using it on patients who needed very frequent treatment with aflibercept, eg, patients who needed injections every 4 weeks (q4) and still had fluid. We just couldn't get them to dry up with our most aggressive treatment. We thought these would be good patients to try brolucizumab and we've now had several patients who have returned for follow-up and been reinjected.

Although we have not conducted an official study, our patients seem to be doing very well from a drying, anatomic standpoint, which is something we saw in the HAWK/HARRIER studies.[13] Those studies showed patients on brolucizumab had better fluid resolution and in some patients, vision improved. For most patients the treatment interval was able to be lengthened which we couldn't do before. That is the positive side, but unfortunately since then we have learned of safety issues with brolucizumab. These inflammatory events certainly give us pause. I think all of us want to figure out what's going on and hopefully solve the issue if possible because from a drying standpoint, the drug was very impressive in the patients in whom we used it.

BARRIERS TO TREATMENT

Q | **DR. KAISER:** There are many barriers to treatments that our patients must overcome. These barriers come to light in the results of real-world studies, which have mostly been conducted with ranibizumab and bevacizumab, although more data is emerging with aflibercept. When we look at these real-world studies,[15] the results are nowhere near as good as what is reported in the clinical trials. Why do you think this disparity exists between real-world outcomes and clinical trial outcomes?

DR. LIM: I believe there are several reasons for this. I think the predominant one is undertreatment, followed by patient selection.

Let me start with undertreatment. In a clinical trial, patients are motivated to come back, and patients are selected because they don't have other comorbidities that would limit their ability to return. In real life, some patients have other illnesses, they can't come back because of scheduling issues, or transportation problems. They also might have financial issues that limit their ability to be treated. Another reason some patients in clinical practice do not achieve the same level of fluid resolution is that in a clinical trial, a specific type of patient with CNV is chosen. For instance, a patient with PED may be excluded or there may be a limited duration of CNV activity or a vision cut-off for inclusion. In contrast, when we use a drug in the clinic, I tend to treat a patient who has CNV and decreased vision and fluid. I don't really consider the VA as long as there's no geographic atrophy that explains severe visual loss or fibrosis that would indicate chronicity and limit visual outcomes. Instead, I'll go ahead and try the drug on that patient. So that patient may have a worse VA than was included in the clinical trial, and may also have other components that make the lesion more severe than was included in the clinical trial.

DR. KAISER: Do your patients ask after an extended period of time if they need to continue treatment? How do you keep patients coming back?

DR. KUPPERMANN: It's an ongoing challenge for all of us. The patients are tolerant of the frequent office visits up to a point. I think that's part of the success of all the attempts to extend the intervals and make the visits as efficient as possible. I believe we always worry that our patients wait too long to return, and we are concerned about the burden on the family. I think that's always in the back of our minds. I believe most patients have accepted their situation because they can see the benefit from the injections and so they're willing to come in. But there's no question that if we could get the same results but extend the intervals to as long as possible, that would be a complete win-win.

DR. KAISER: It always surprises me in the United States that we have so many patients who are undertreated, even in that first year[4] when, as Dr. Lim mentioned, it's so important for patients to receive aggressive treatment. We have excellent health care insurance coverage and no one telling us we can only use a certain number of injections like they have in many other countries. It's surprising how few injections many of the doctors out there are giving. Is this a problem caused by the patients or a problem that results from physicians not understanding the study results?

DR. WOLFE: I think it's some of both.

DR. LIM: I agree. I think patients don't want to come back that frequently and their comorbidities may also impact their ability to follow up, or they may not have the support system for transportation to the office. That's part of the reason patients are undertreated. And then possibly the other part of the equation is that physicians are trying to extend treatment intervals too soon, so the retina is not receiving enough treatment up front. Instead, one starts treat and extend before the retina is dry. So, you're not going to get the best VA results.

DR. KUPPERMANN: I think it also has to do with the heterogeneity of the patients. Not all of them are deriving as much benefit as we had hoped because of the state of the disease, etc. Even with regular injections and doing the best we can, there is progressive vision loss that we encounter in some patients.[16] That's an ongoing concern that we all have. Despite the benefits of the therapies that exist, we're still looking for better options.

HOME MONITORING

Q | **DR. KAISER:** One option undergoing intense research, especially given the COVID-19 pandemic, is this idea of home monitoring of nAMD. There is currently one product on the market for home monitoring of AMD, but in the future we

may have home optical coherence topography (OCT) devices that use artificial intelligence (AI) algorithms to determine when a clinically relevant change has occurred on the OCT, at which point the patient would be called into the office. How would you anticipate this will change our practice?

DR. LIM: If this product was to gain approval, I think it would be really useful. Personally, if my patients can have it, I would be really excited because that would allow these patients to actually have a totally personalized treatment interval. In other words, they could be monitored very frequently; some would want to check their OCT every day. If there were an AI program with the home OCT obviating need for physician interpretation of the OCT image, that would make overall monitoring even easier.

Let's say a patient uses the home monitoring device once a week, or on some schedule mandated at the start of treatment. Then we can actually find out at what point after an injection the IRF or SRF comes back; we can treat just when the retina needs to be treated. As you know, not every patient needs monthly treatment and not every patient can be placed on 6-week, 8-week (q8), or q12 intervals. With home OCT we can really implement an optimized personalized treatment scheme for the patient. So, I'm excited if we ever get there. I think it would be great.

DR. KAISER: I think we're going to get there. From a regulatory standpoint, the issue relates to saying you can use this device and have insurance coverage. The regulatory requirement probably will be to show that a device actually results in an improvement in vision over not using the device. Just getting an OCT device approved by the FDA doesn't require all that much; it's the AI algorithm that's needed to make a medical decision that may take a lot more work to gain FDA approval. There will likely be some very high hurdles. I certainly don't want to be sent all those OCTs and have to analyze them myself. That would be pure torture at the end of a long day. However, once the kinks are worked out, I agree that this will really be a game changer.

DR. KUPPERMANN: As a result of COVID-19, all of us have been pushed more in the direction of telemedicine. There's a mandate from our institution, probably other institutions, too. It's just very difficult for ophthalmology, and especially for retina, to do adequate exams with a smartphone or computer camera. It would be great if we had home imaging that would also allow us to participate more fully because I believe telemedicine will become part of our postpandemic practice strategies. This may allow for patients to come into the office less often for monitoring, possibly coming in only when there's fluid noted or another significant change. In fact, that technology could be used for more than just helping us on some patients or in between visits. Who knows what the future holds? That may become the standard over time, if it's successful.

PATIENT-FOCUSED CARE DURING COVID-19

Q | **DR. KAISER:** Let's talk more about COVID-19. How are you seeing patients, what types of patients do you see, and what changes have you made to your clinics because of the pandemic?

DR. WOLFE: At Beaumont, we've made pretty drastic changes to our practice. Michigan was one of the earlier affected locations, and Detroit was one of the hotspots, so we closed most of our satellite offices and moved to a team-based system. Each retina specialist was paired with a photographer, scribe, and front desk person so as to prevent the spread of the virus throughout the practice should one of the providers or support staff become infected. The ophthalmologist would stick with that team and see about 20 to 25 patients a day. In our practice the doctor reviewed their schedules to determine which patients needed to come into the office. The patients that were offered appointments were typically those with vision-threatening disease requiring intervention. We did that for 3 to 4 weeks and then started opening some of the satellite offices while maintaining the team approach in an attempt to limit the effect of a COVID-19 exposure in the practice. After we were comfortable that our personal protective equipment (PPE) and cleaning protocols were effective (no cases within the practice), we transitioned away from the strict team approach and re-opened the remainder of our satellite offices. In order to maintain distancing in the office, we have removed 75% of the chairs from our waiting room and only allow patients (no guests) into the office, except for established exceptions (pediatrics, dementia, etc.). This has allowed us to gradually increase our volumes to approximately 80% of pre-COVID levels while still maintaining distancing. We have plans to further increase our patient volumes and believe we can do this in a distanced manner using our current protocols.

DR. KAISER: We took a similar approach at Cole Eye Institute. At the start of the pandemic, we dramatically cut the volume of patients in our clinics and only really saw urgent and emergent patients. We considered patients requiring injections as a part of the urgent category as our state had all nonessential visits banned. We normally do a lot of OCTs because we use the treat-and-extend regimen, but we didn't do them early on. Now we are slowly working back to a more regular schedule and have purchased more OCT devices to allow us to separate patients in time and space. We try to minimize movement from exam rooms to waiting rooms and clean after every patient. For now, we also are not allowing visitors to accompany the patients to reduce the number of touch points. What are you guys doing in Chicago?

DR. LIM: We are putting PPE on every patient. Every patient that comes into the office gets a temperature check and receives a mask. Physicians are required to wear goggles, masks, and gloves. We have installed large plastic barriers to protect the reception and front desk staff. We also have installed custom plastic barriers onto the slit lamps. We do still get OCTs on our patients, but we're no longer getting routine OCTAs and we are limiting other imaging tests. We are seeing the same urgent and emergent patients, which of course includes the patients who require intravitreal injections. When I see a patient now with AMD, I'll see them back at the regular interval for that particular patient. However, if I'm seeing a non-AMD patient, for example, a patient with diabetic macular edema (DME), I'll try to stretch that interval because it's not as crucial to see them back in


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a month or 2 because some can go longer and it's not crucial if the fluid returns; you can still get back the vision.

DR. KAISER: Dr. Kuppermann, tell us how your institution returned to seeing patients?

DR. KUPPERMANN: I serve as one of the 10 people at my institution on a committee planning for the post-surge part of the pandemic. We kept an eye on data from the University of Washington epidemiology website, and California didn't really have much of a surge peak in April. California was one of the earliest states to institute social distancing. The early predictions of mortality were more than 6,000 and then changed to less than 1,500.

We reopened clinics, including surgeries, throughout our institution on May 25 based on the data from various resources and agencies.

The retina division has been operating much as the others. I still do regular injections and we do get OCTs, but we made modifications that include requiring both the patients and everyone in the office wear a mask, and wiping down every horizontal surface in the room and every piece of equipment.

We modified the waiting rooms to allow for social distancing space between each chair, and we allowed only the patient to come inside unless they need a caregiver for health care reasons. We're also taking the temperatures of employees but we are not currently taking patients' temperatures; we may do that in the near future. Things like that will be done to make sure it's as safe as possible. Patients would have to fill out a questionnaire about symptoms and have a temperature check before being allowed in the building or in beyond the front desk.

We anticipated that a few weeks after the surge there would be a feeling of calm and after that it would be safe to return to pre-pandemic office practices—with certain precautions in place—and thought we may even need to extend our OR days and open up Saturdays for surgery. The plan was to anticipate when it is safe.

DR. KAISER: Dr. Wolfe, I know that Beaumont was one of the first large health systems to test providers and staff for antibodies to COVID-19. Please share the details with us.

DR. WOLFE: At Beaumont, all 40,000 health care providers and employees were offered the antibody test in April to look for IgG and IgM. The plan was to test everybody twice. I think it's a great public health project for us to understand a bit more about asymptomatic carriers, but I'm not aware that it impacted how facilities reopened.

DR. LIM: Antibody testing was offered at our medical center. I think this was the smart thing to do because we needed to know who is immune, figure out the widespread nature of this disease, and determine the level of asymptomatic carriers. In Chicago, our peak occurred in early to mid-May during the initial surge of the pandemic. We opened our clinics in late May to include nonurgent patients and routine surgery.

DR. KUPPERMANN: California was hit early in the pandemic, but in Orange County, CA, where the population is 3.2 million, we had only 19 COVID-related deaths in mid-April. So, we reopened earlier than most places in the country.

DR. WOLFE: Michigan peaked in early to mid-April, so we began to open satellite offices in early May and increased incrementally the number of days they were open.

DR. KAISER: In Ohio, our lockdown began on March 23. I think because everything closed down, the number of COVID cases in Ohio was far below the original estimate. At Cole Eye, we started discussions with the Clinic leadership in mid-April about slowly increasing the number of patients we would see while maintaining social distancing as we returned to a somewhat normal schedule.

We expect a second wave. We know that if we're not careful, we could be part of the problem for that second wave as opposed to a solution. I think this is all really uncharted waters for everybody, but we're all just trying to do the best we can.

DR. LIM: Is anyone doing telemedicine? I know it's hard for retina patients.

DR. KAISER: We are using telemedicine. We've dramatically increased virtual visits. I think it's interesting how the pandemic has changed our thinking about what's really important about patient exams and how we follow patients and what is obviously less important.

What type of precautions are you taking when you know you have a patient who tested positive for COVID-19?

DR. WOLFE: If we know a patient is positive, we will not see them in the clinic. That said, we are basically treating every person who enters the clinic as if they have COVID-19. Early into the pandemic, all providers and employees wore masks, but we did not require patients to do so, although about 80% were wearing them. Also, caregivers were not allowed in the room. I was actually notified that I saw a COVID-positive patient two days prior to their diagnosis. But with all the precautions we've taken, quarantining our team was not necessary. Beaumont's rule for exposure requires being within 6 feet of a confirmed COVID-19—positive person for more than 10 minutes, without a mask.

TREATMENT SAFETY DISCUSSIONS WITH PATIENTS

Q | **DR. KAISER:** Let's talk about safety. Dr. Lim, when you first talk to a patient about initiating treatment, what does your safety discussion involve?

DR. LIM: My discussion involves the risk of endophthalmitis, which I tell them is about 1/1,000, and also the risk of inflammatory reactions. Lastly, I tell them there are three FDA-approved drugs that come in a hermetically sealed container, as opposed to bevacizumab, which is compounded for each patient. If they ask further about safety issues, I inform them that the bevacizumab used at the University of Illinois is compounded in-house by our pharmacy. It is still a compounded drug, but it's tested to make sure there's no infectious component before we're allowed to use it. The drug must sit for about 2 weeks before we can use it, so if the patient is uncomfortable with any of that, I tell them the best drug would be ranibizumab because it comes in a sealed vial and it doesn't have the inflammatory component as opposed to aflibercept or brolucizumab.

DR. KAISER: I'm going to push back a little bit on that last statement, only because it's interesting. Obviously, ranibizumab is one of our oldest and most commonly used anti-VEGF medications. However, recall that there were several reports of inflammation associated with ranibizumab when it was first approved,[17] but that wasn't so much of a concern because we didn't have alternatives. Over the ensuing years, Genentech has improved their CMC techniques and the inflammation rate now is exceedingly low. If you switch a patient's anti-VEGF agent, do you have an additional discussion about inflammation at that point?

DR. LIM: I don't emphasize inflammation if I switch from ranibizumab to aflibercept because at that point the switch is a result of their vision being affected because the ranibizumab hasn't resolved the fluid. I explain that the best drug for them at that point is one that potentially can better dry the retina, resulting in better vision. I do tell them there's a risk of inflammation, but also that I believe the improved vision outweighs the inflammatory risks.

DR. KUPPERMANN: My conversation is similar to Dr. Lim's. I mention the risk of endophthalmitis and retinal detachment,[18] but I don't really discuss inflammation with patients because historically it's been very rare. I've seen inflammation with bevacizumab, ranibizumab, and aflibercept, but it's rare, as are all the complications, including stroke and endophthalmitis.[19,20] So I don't really focus on the inflammation part in my conversation, but I do mention it during the first visit. I let them know that if there are ever any problems after an injection to please contact us right away. I discuss inflammation but I don't focus on it.

Dr. Lim, I agree with what you do. I have not been spending much time talking about inflammation with my patients. That will change if and when we start using some of the new agents, brolucizumab in particular.

Q | **DR. KAISER:** Dr. Wolfe, how do you monitor for intraocular inflammation (IOI) after injections? Do you simply tell patients to look for these signs and call if they have them? Do you bring patients back at an interval when you start a medication? Or do you bring them back when you expected to treat them next?

DR. WOLFE: I don't specifically monitor for IOI at this point. I have a similar discussion as Dr. Kuppermann and tell every patient that if they're concerned about something to call me. That rarely happens, but I think there's some inflammation that we miss. I get a lot of patients who tell me they had "some floaters for a week or so, and then they went away." Therefore, I think I probably am missing some inflammation, but not a clinically significant amount from what I can tell.

DR. KAISER: From my standpoint, I don't really stare at the anterior chamber given everything that's going on right now. Dr. Lim, how do you feel about the slit lamp exam, and how have things changed in your mind with recent events with brolucizumab?[14]

DR. LIM: That's a good point. I don't necessarily have the patient focus on the possibility of inflammation after an injection. Nor do I bring them back sooner than I otherwise would. That being said, we do know if you were to use brolucizumab that you shouldn't use it in an eye that has some inflammation. The recommendation by the manufacturer is that it shouldn't be used in an eye that has any uveitis present.[21] I'm not actually using brolucizumab, so I'm not looking for inflammation in particular. I generally do a regular anterior chamber and posterior chamber slit-lamp exam on every patient before giving an injection.

DR. KAISER: In our brolucizumab patients, we've been looking very carefully for both anterior chamber and vitreous cell, as well as looking closely at the retinal vasculature, since the ASRS notice sent out in February detailing cases of vasculitis.[14] It's a phase change for me from my previous experiences with other anti-VEGF agents. Previously, unless the patient came in for a specific problem, I would really only look at the posterior segment. Now I'm looking very closely at the anterior segment. This has definitely changed because of the brolucizumab issues. I'm now doing the same thing for patients on other anti-VEGFs because I think it's something that I was remiss about, quite frankly, and should have been doing in the first place. Maybe I missed a bunch of those in the past. The issues with brolucizumab have definitely changed how I monitor these patients.

Dr. Kuppermann, when you see IOI, what's the first way you treat this? What is your management course? How do you handle these patients?

DR. KUPPERMANN: It depends on the degree of inflammation. Most of the IOI that I've seen has been mild. It's a bit like Dr. Wolfe described. I feel like when it happens, I've missed it most of the time. The patients will mention it in passing on the next visit, when in fact, the first concern of course is differentiating it from endophthalmitis. It depends on the timing, severity, symptoms, etc. That's the first step. Again, if it's within the first week after an injection, I'm most concerned about this being infectious rather than inflammatory as its etiology. So that needs to be sorted out first.

Next, depending on the amount and the timing, the easy solution, if I believe it's not infectious, is to administer topical steroids versus just observation and followup, depending on the severity and symptoms. It's not a common finding in my setting, but I agree with all of you in that I think we've been under-examining our patients. I think I've been examining the anterior chamber of each patient before I put the 90.00 D lens in front of the eye, but I'm not sure that I've spent much time focusing on the findings there. That's something on which we've all increased our focus.

For me, and I'm not using brolucizumab, the bulk of them to date have been mild. I also did not have any bad cases of aflibercept-related uveitis. It's really been more of an endophthalmitis versus uveitis decision and then appropriate management based on that.

DR. KAISER: In the CEDAR/SEQUOIA studies, there were episodes of severe inflammation, even episodes of retinal occlusive vasculitis.[22] We've also heard about very similar types of issues sporadically with the use of brolucizumab.[13]

Dr. Wolfe, at what point do you move from topical to oral steroids, assuming you ruled out infectious etiologies? When do you add intravitreal steroids to these patients with more severe inflammation and vasculitis?

DR. WOLFE: Fortunately, we didn't have those issues with abicipar in my clinical trial patients, but I would say that in the cases where there is a significant vision change or evidence of vasculitis, whether on your clinical exam or on an angiogram, I would probably start with oral steroids and then consider either periocular or intraocular steroids depending on the severity.

DR. KAISER: I would echo that because I served on the Novartis Safety Review Committee and we've reviewed as many cases as we could of the inflammation seen post-marketing. One conclusion that we've come to mirrors what Dr. Wolfe said: We need to be really aggressive with the treatment of the inflammation in general. The patients who had a poor outcome were treated with topical steroids and really not as aggressively as they probably should have been.

The takeaway point from this discussion should be that if you see inflammation—and it doesn't matter from what drug—you should be really aggressive with therapy.[23] At a minimum, those patients should be put on oral steroids. If you're really concerned, a local injection of steroids, obviously after ruling out an infection, may be warranted. These patients seem to do better when treated aggressively.

DR. KUPPERMANN: Dr. Kaiser, have you ever treated a patient that aggressively on aflibercept, ranibizumab, or bevacizumab? Or are you referring primarily to the newer therapies that have a potential greater risk of retinal vasculitis, for example?

DR. KAISER: I've never treated a patient that aggressively on ranibizumab. I have had some patients with pretty significant inflammation with aflibercept and bevacizumab and have had to use oral steroids for them. In my brolucizumab patients, I've had no patients with inflammation. But the reports of IOI give you pause as to what the true rate may be. One important point is that the drug that's being used now is different from what was used in HAWK/HARRIER, which appears to have a lower rate.[13] This gives me hope that we can figure out what change may have increased the rate. I mentioned previously, the drug works great. It's an amazing drying agent. It's the inflammation rates that cause concern about using the drug.

DR. KUPPERMANN: It's also worth noting that the manufacturers of both brolucizumab and abicipar are likely working on the possibility of modifying the manufacturing process. I know that the

makers of abicipar intend to be even more aggressive and clean out those few remaining host cell proteins. I'm not sure the makers of brolucizumab have made the same statements. Certainly, within the manufacturing process, they're continuously improving. The likelihood is that these products are likely to become safer over time if they continue to exist.

DR. KAISER: I think that's the important point. All these biologics have to be made in some sort of biologic agent. Many of them are made in either a Chinese hamster ovary cell line or *Escherichia coli.* If you have host cell proteins, in other words little pieces of *E. coli* sticking around, it's going to cause inflammation since our body has mounted an immune reaction to *E. coli* for millennia. I don't think this is an endotoxin because if you look at the timing of some of these severe events, they're not occurring right after the event. There is time in between. This raises the idea of wholesale impurities remaining in the drug. It's hard to purify them, and the higher the dose you use, the purer it has to be.

With a drug like ranibizumab, in which you're giving 0.5 mg, it doesn't have to be as pure as if you're giving, for example, 6.0 mg. A 6.0-mg drug has to be nearly 12 times as pure to have a similar host cell response. I think, as with any drug, ranibizumab and aflibercept have each gone though many process improvements. Abicipar has already had numerous process improvements.[22] Based on this, I believe the manufacturer of brolucizumab will likely go through the same process and improve the drug. I believe the incidence of inflammation is going to dramatically drop as this exercise is successful.

LOOKING AHEAD
Abicipar

Q | **DR. KAISER:** Let's talk about abicipar. The phase 3 CEDAR/SEQUOIA clinical studies showed that from an efficacy standpoint, the drug could be delivered q12 versus the control, which was monthly ranibizumab.[22] That already addresses one of our unmet needs of having extended dosing. Dr. Kuppermann, could you walk us through the inflammation cases seen in the CEDAR/SEQUOIA studies?

DR. KUPPERMANN: What was unique about the CEDAR/SEQUOIA studies was that participants were presorted to q8 versus q12 of abicipar versus q4 of ranibizumab. They had different loading doses, two versus three, depending on whether it was q8 or q12 dosing. They were maintained on those doses, and they tended to see inflammation in about 15% of eyes during the first year of treatment. The inflammation was observed relatively early, within the first four to five injections. Something like 13% of the 15% that were seen by 1 year were actually seen at 6 months. So, it happens early.[22]

At year 2, the rates of inflammation were low in all groups. Those who made it to the second year did not have higher rates than patients in the ranibizumab arm. Therefore, it's an early event, within the first four to five injections. Again, typically seen within the first 6 months, with a distribution between mild, moderate, and severe degrees of inflammation.

There were also some cases of retinal vasculitis that I do not believe was occlusive. Some of those eyes had reversible vision loss, others did not. There was a certain percentage of eyes that had severe vision loss, as designated by 30 letters lost.

I want to mention an important lesson learned from the CEDAR/SEQUOIA studies. Eyes with inflammation were allowed to be reinjected, and the eyes that were reinjected had an increased risk of recurrent severe inflammation and vision loss. The incidence of severe vision loss could have been cut in half if they had avoided reinjecting. The incidence and severity of inflammation was much reduced in the MAPLE study.[22]

DR. KAISER: Let's discuss MAPLE. This open-label bridge study (NCT03539549) was conducted because they made changes to the chemistry, manufacturing, and controls of abicipar to reduce host cell proteins. Dr. Wolfe, can you explain the changes made to abicipar and walk us through the MAPLE study?

DR. WOLFE: The MAPLE study was really a safety study looking to see if the change in the process of making abicipar led to a reduction in inflammation. The investigators were unmasked and were instructed to look for inflammation, and there was still inflammation noted in that trial at about 9% (no cases of retinal occlusive vasculitis). It was a smaller trial, and looking at the patient-level data the inflammation was really quite mild. So, it appears as though there's a big change in the right direction, and I think we probably still need a little more information.

DR. KUPPERMANN: There were 11 eyes out of the 123 study eyes that had inflammation, and none lost any significant vision. Their outcomes were good, and in the two eyes that lost vision, one went from 20/20 to 20/25, and the other went from 20/50 to 20/60. Not only was the inflammation milder, there was no vasculitis, the outcomes were good, and there was no vision loss associated with the inflammation. So that was a very significant finding. Again, with a limited sample size.

DR. KAISER: I think that's a really important point. With what we're seeing with brolucizumab now, hopefully they can use some of the lessons learned in the manufacturing of abicipar to continue to improve the brolucizumab. The improvements in the drug tested in MAPLE dramatically reduced the IOI rate, particularly in terms of the severe cases.

Dr. Lim, what would you personally consider to be an acceptable rate of IOI, and what do you think the FDA will find acceptable?

DR. LIM: I think it depends on not only the rate of IOI but the severity of the IOI. For instance, any severe IOI such as retinal vasculitis and any appreciable rate of say 1/1,000 is unacceptable. If you had a severe occlusive retinal vasculitis occurring 1/1,000 times, that would be a deal-breaker for me. If you had moderate inflammatory reactions that required significant steroids, I would say that rate would still have to be rather low—less than 1% in order for me to

feel comfortable using it because currently all of the anti-VEGF drugs we're using are not causing significant uveitis at that rate. I don't want to add another problem to patients who are already burdened by AMD.

Let's say only mild inflammatory uveitis occurs, and if it was really mild and caused only mild photophobia that doesn't last very long, and if it were 1/500, that would be acceptable if the drug provided something really beneficial. For example, brolucizumab really dries the retina. All these factors have to be weighed out, but I think anything that causes visual loss, requires significant treatment of complications, or causes permanent damage is a deal-breaker no matter what the rate of occurrence.

Biosimilars

Q | DR. KAISER: Let's talk about other products expected in the future: biosimilars. Ranibizumab's patent runs out this summer and I know of several biosimilar drugs for ranibizumab that are in front of the FDA and likely to be approved. Dr. Wolfe, how do you see yourself using a biosimilar in your clinical practice?

DR. WOLFE: I have a hard time right now figuring out how a ranibizumab biosimilar fits into my practice. The reason I use ranibizumab, and I think most people use ranibizumab, is because we are confident in the efficacy and really love the safety profile that comes with it.[24,25,26]

And the discussion we've just been having about how tricky it is to manufacturer and clean a biologic drug gives me some pause on wanting to use a biosimilar because I'm giving up maybe the biggest reason I'm using it: the ranibizumab. For me, right now, I'm not sure how it's going to fit in. And, of course, all of that will also depend on how the payors deal with it.

DR. KAISER: Dr. Lim, do you think that payors are going to make a step through the biosimilars before going to ranibizumab?

DR. LIM: I'm not really sure, but I think it will depend on the price of those biosimilars. I totally agree with Dr. Wolfe in that I wouldn't trade the safety of ranibizumab now for a biosimilar, whose safety profile is yet unproven. I hope payors won't make us do that. In order to compete with ranibizumab, it's possible the biosimilars could be priced at a much lower level than ranibizumab once ranibizumab goes off-patent. I think only time will tell, but I personally would not be too excited about it. Secondly, just the fact that it's a biosimilar means it doesn't have the added durability of these newer agents that are coming out. So, if I was going to switch from ranibizumab, I would switch to a drug that had longer durability or a better drying ability. I wouldn't just switch to something that's similar unless it was a cost-mandated issue by the insurer.

DR. KUPPERMANN: I agree, and it's worth noting that biosimilar biologics are products that are tricky to manufacture. They're not the same as a generic class of drugs that people think about.[27] The safety issues that only come out after tens of thousands or hundreds of thousands of doses are used is concerning because that's really what happened with brolucizumab. So, I agree with all the comments. I think I'm intrigued by biosimilars, but again, I would hate to trade any safety to get a lower price.

DR. KAISER: I agree with Dr. Kuppermann. These drugs are biosimilars, they're biologics, they're made in a different way; it's not a generic version. Generics use a chemical formula with a small molecule that's identical to the reference product. Biosimilars are made differently. They have different host cell impurities. In fact, one of the first ranibizumab biosimilars that was approved in India actually had that issue. It had to be withdrawn for a period of time because there were extensive inflammatory issues with it. It's since been relaunched and it's doing better. But it's something we will all watch for, I'm sure.

Novel Approaches

Q | DR. KAISER: We have many potential treatment options in clinical studies right now that may offer us even longer durability, including KSI-301, faricimab, the port-delivery system with ranibizumab, a higher dose of aflibercept, conbercept, and maybe eventually gene therapy. Dr. Kuppermann, based on your expertise, how would you use these drugs in rank order, say, 5 years from now?

DR. KUPPERMANN: Faricimab looks the furthest along, and that would be at the top of the list. With the blockage of Ang2 and bispecific agent, I think that looks very intriguing. The hope is that it can be used for q12 and q16 intervals between injections.[28]

I think the technology used in KSI-301 looks very compelling.[29,30]

The port-delivery system is certainly intriguing. but there are concerns about the risk of infection and bleeding.[31] So that I think remains to be seen.

As for gene therapy, we've seen exciting newer data from those compounds, and stem cells will also make a significant impact. I think it's a very exciting time with new products coming downstream. It's going to be a very exciting time over the next 5 years. I'm always impressed by the entrepreneurship and the willingness of companies to take significant financial risks to develop new agents.

DR. KAISER: Dr. Lim, the idea of combining some of these pathways is exciting, and there's also a VEGF-C and VEGF-D inhibitor, OPT-302, that being investigated.[32] We know that if you block VEGF-A, then VEGF-C, D, and placental growth factor (PLGF) actually become elevated. This has been shown in cancer patients with bevacizumab as well as in patients with macular degeneration.[33,34] The OPT-302 phase 2 study results, which combined OPT-302 with ranibizumab, were interesting, resulting in almost a pan-VEGF blockade, absent PLGF and VEGF-B. The study reported visual results significantly better than ranibizumab alone.[32,35]

If these results hold through in phase 3 and the drug is approved by the FDA, how do you see the use of a treatment that requires a second injection fitting into your practice?

DR. LIM: OPT-302 blocks VEGF-C and D,[32] and conbercept is a soluble receptor decoy that blocks all isoforms of VEGF-A, VEGF-B, VEGF-C, and PLGF.[36] So, using OPT302 has only added benefit of blocking VEGF-D. I think it would have to have a huge effect in terms of VA. I don't think it's going to make that big of a difference in durability because we already have drugs with increased durability becoming available soon. For example, faricimab may be dosed at q16 weeks.[28] We also have the port-delivery system with ranibizumab that doesn't require a refill in 80% of patients until after 6 months, with the median time to refill being 15 months.[37]

The only reason I would consider a second injection is if it really bumped the efficacy as a combination treatment. And I would be curious to see if you could use OPT-302 with a drug like faricimab; could you get even more efficacy that could result in longer durability? However, if the combination worked, then I would say I would be willing to do two injections in a patient in order to achieve that added durability and that added efficacy.

DR. KAISER: I really appreciate everyone spending the time discussing a wide gamut of the use of anti-VEGFs in AMD. Thank you, everyone, for a great discussion. Stay safe, socially distant, wear your mask, and keep washing your hands. ■

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BEYOND THE ANTI-VEGFS: AN UPDATE ON CURRENT AND FUTURE AMD TREATMENT STRATEGIES

Release Date: September 2020
Expiration Date: September 2021

INSTRUCTIONS FOR CREDIT

To receive credit, you must complete the attached Pretest/Posttest/Activity Evaluation/Satisfaction Measures Form and mail or fax to Evolve Medical Education LLC; 353 West Lancaster Avenue, Second Floor, Wayne, PA 19087; Fax: (215) 933-3950. To answer these questions online and receive real-time results, please visit evolvemeded.com and click http://evolvemeded.com/online-courses/2004-supplement. If you are experiencing problems with the online test, please email us at info@evolvemeded.com. Certificates are issued electronically; please be certain to provide your email address below.

Please type or print clearly, or we will be unable to issue your certificate.

Name _____ ❑ MD/DO participant ❑ OD ❑ non-MD participant

Phone (required) _____ ❑ Email (required) _____

Address _____

City _____ State _____ Zip _____

License Number _____

OE Tracker Number _____

DEMOGRAPHIC INFORMATION

Profession
___ MD/DO
___ OD
___ NP
___ Nurse/APN
___ PA
___ Other

Years in Practice
___ > 20
___ 11-20
___ 6-10
___ 1-5
___ <1

Patients Seen Per Week (with the disease targeted in this educational activity)
___ 0
___ 1-15
___ 16-30
___ 31-50
___ 50+

Region
___ Northeast
___ Northwest
___ Midwest
___ Southeast
___ Southwest

Setting
___ Solo Practice
___ Community Hospital
___ Government or VA
___ Group Practice
___ Other
___ I do not actively practice

Models of Care
___ Fee for Service
___ ACO
___ Patient-Centered Medical Home
___ Capitation
___ Bundled Payments
___ Other

LEARNING OBJECTIVES

DID THE PROGRAM MEET THE FOLLOWING EDUCATIONAL OBJECTIVES?	AGREE	NEUTRAL	DISAGREE
Discuss real-world vision outcomes and durability/treatment frequency of anti-VEGF therapy for neovascular age-related macular degeneration (nAMD)	_____	_____	_____
Describe the barriers to achieving the same vision outcomes in the real-world clinical setting as those reported in clinical trials	_____	_____	_____
Evaluate the rates of intraocular inflammation as reported in clinical studies and in clinical practice	_____	_____	_____
Describe therapies in the pipeline that are near FDA approval that would decrease treatment burden and potentially improve treatment adherence in clinical practice	_____	_____	_____

POSTTEST QUESTIONS

Please complete prior to accessing the material and submit with Posttest/Activity Evaluation

1. Based on this activity, please rate your confidence in your ability to evaluate intraocular inflammation as reported in clinical studies and in clinical practice (based on a scale of 1 to 5, with 1 being not at all confident and 5 being extremely confident).

a. 1
b. 2
c. 3
d. 4
e. 5

2. An 80-year-old male with new onset neovascular age-related macular degeneration presents to your practice. You explain the pathophysiology and treatment of his disease, and discuss the need to initiate anti-VEGF therapy. The patient asks about the necessary duration of his therapy. What is the most appropriate answer:

a. Three months of treatment followed by observation
b. One year of monthly treatment followed by observation
c. Two years of monthly treatment and as needed treatment therafter
d. Exact treatment interval will be tailored to his response to treatment, but he should be prepared for a long, frequent dosing schedule.

3. What is the risk of endophthalmitis with intravitreal anti-VEGF therapy?

a. 1/100
b. 1/1,000
c. 1/10,000
d. 1/100,000

4. A 78-year-old female with neovascular age-related macular degeneration receiving intravitreal ranibizumab is switched to aflibercept due to poor anatomical response. One week after her injection, she calls your practice with the chief complaint of increasing floaters. On examination, you notice 2+ cells in the anterior chamber and 1+ cell in the anterior vitreous. Which of the following is the next appropriate step?

a. Rule out endophthalmitis. If endophthalmitis is ruled out, start anti-inflammatory therapy with aggressive monitoring, starting with topical steroids.
b. Inject steroid intravitreally or in the sub-tenons space
c. Start oral steroids
d. Observe

5. The MAPLE study investigated the incidence of inflammation in eyes that received abicipar. What rate of inflammation was noted in this study?

a. 3%
b. 5%
c. 7%
d. 9%

6. Many novel approaches to anti-VEGF therapy are currently being investigated. What is a difference between OPT-302 and conbercept?

a. OPT-302 is a VEGF-A, VEGF-C, and VEGF-D inhibitor while conbercept is a soluble receptor decoy that blocks all isoforms of VEGF-A, VEGF-B, VEGF-C, and PLGF.
b. OPT-302 blocks all isoforms of VEGF and conbercept blocks PLGF
c. OPT-302 blocks PLGF and conbercept blocks all isoforms of VEGF
d. Both OPT-302 and conbercept block all VEGF isoforms and PLGF

ACTIVITY EVALUATION

Your responses to the questions below will help us evaluate this CME activity. They will provide us with evidence that improvements were made in patient care as a result of this activity.

Rate your knowledge/skill level prior to participating in this course: 5 = High, 1 = Low _____

Rate your knowledge/skill level after participating in this course: 5 = High, 1 = Low _____

This activity improved my competence in managing patients with this disease/condition/symptom. _____ Yes _____ No

Probability of changing practice behavior based on this activity: _____ High _____ Low _____No change needed

If you plan to change your practice behavior, what type of changes do you plan to implement? (check all that apply)

Change in pharmaceutical therapy _____

Change in nonpharmaceutical therapy _____

Change in diagnostic testing _____

Choice of treatment/management approach _____

Change in current practice for referral _____

Change in differential diagnosis _____

My practice has been reinforced _____

I do not plan to implement any new changes in practice ___

Please identify any barriers to change (check all that apply):

_____ Cost

_____ Lack of consensus or professional guidelines

_____ Lack of administrative support

_____ Lack of experience

_____ Lack of time to assess/counsel patients

_____ Lack of opportunity (patients)

_____ Reimbursement/insurance issues

_____ Lack of resources (equipment)

_____ Patient compliance issues

_____ No barriers

Other. Please specify: _____

_____

_____

_____

The design of the program was effective for the content conveyed. ___ Yes ___ No

The content supported the identified learning objectives. ___ Yes ___ No

The content was free of commercial bias. ___ Yes ___ No

The content was relative to your practice. ___ Yes ___ No

The faculty was effective. ___ Yes ___ No

You were satisfied overall with the activity. ___ Yes ___ No

Would you recommend this program to your colleagues? ___ Yes ___ No

Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced through your participation in this activity:

_____ Patient Care

_____ Practice-Based Learning and Improvement

_____ Professionalism

_____ Medical Knowledge

_____ Interpersonal and Communication Skills

_____ System-Based Practice

Additional comments:

_____

_____ I certify that I have participated in this entire activity.

This information will help evaluate this CME activity; may we contact you by email in 3 months to see if you have made this change? If so, please provide your email address below.

_____