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Optimizing Medical Management of Uterine Fibroids: Achieving Patient-Centered Goals and Outcomes

Announcer:
Welcome to CME on ReachMD. This activity entitled "Optimizing Medical Management of Uterine Fibroids: Achieving Patient-Centered Goals and Outcomes" was presented during Omnia Education's Women's Health 2022, Beyond the Annual Visit.

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Dr. Kaunitz:
Hello, I'm Andrew Kaunitz, and today we'll be discussing best practices in the management of uterine fibroids, focusing on medical management and achieving patient-centered goals and outcomes. At the end of this presentation, my goal is that participants will be able to describe the definition, epidemiology, risk factors, natural history, and clinical impact of uterine fibroids, and also review the roles of imaging and laboratory testing in initial evaluation of women with fibroids who go on to view medical options for the treatment of women with symptomatic fibroid tumors, while engaging patients in discussions about their symptoms, and therapy preferences. Finally, it's my hope that participants, by the end of this presentation, will understand the importance of culturally sensitive care and their role in improving outcomes for women with symptomatic fibroids. And finally, we'll review the latest evidence looking at not only the efficacy but also safety of GnRH antagonists in the management of women with symptomatic uterine fibroids.

Leiomyoma or fibroids represent common benign smooth muscle monoclonal tumors. They're the most common solid and symptomatic neoplasm that we encounter in women. All studies that have looked at fibroids have consistently found that these are hormone-sensitive tumors. Their prevalence increases during reproductive years. And between one-quarter and one-half of women with fibroids are symptomatic. We also note very consistently that delays in diagnosis of fibroids are very common.

If we screen populations of reproductive-age women, approximately three-quarters can be identified as having fibroids with ultrasound. But keep in mind, many women who are screened on a population basis as opposed to a clinical setting, many women where we can identify fibroids with ultrasound, may not have symptoms.

Black women bear a disproportionate burden from symptomatic fibroids. When we look at older reproductive-age women, we can detect clinically relevant fibroids and about one-third of white and about one-half of black women. About one-quarter of black women will suffer from fibroids as early as age 25. And by the time black women reach menopause, about 80% will have had symptoms from uterine fibroids. The burden of suffering in black women is two to three times that of white women. And unfortunately, black women experience more severe disease, including larger fibroids, greater duration of bleeding, greater likelihood of needing surgery compared with white women. Some of these differences may reflect the delay in care faced by African American women.

As most of us who have been practicing gynecology for a long time know, we sometimes encounter huge fibroids that can be large enough to fill not only the pelvis, but extend up into the abdominal cavity and even put pressure against the diaphragm. The average growth, however, with uterine fibroids is a little over 1 centimeter every 2 to 3 years, but the rate of growth is extremely variable. Commonly, fibroids will calcify over time. Less commonly, they may outgrow their blood supply and degenerate or necrose.

When women with fibroids reach menopause, their tumors in general will shrink as estradiol levels calm down. However, so-called shrinkage during the menopause is not predictable. In some menopausal patients I have, I would love and they would love it if their fibroids would shrink menopause but doesn't always happen unfortunately.

In this slide, we look in the top component at the FIGO classification of abnormal uterine bleeding, the PALM-COEIN classification. And then in the lower part of this slide, we look at FIGO's leiomyoma anatomic classification of tumors. And notice that the tumors closest to or in fact within the endometrial cavity include category 0, 1, 2, and 3. Without question, the most common key symptom that women with fibroids present with is heavy menstrual bleeding. But we may also see dysmenorrhea or noncyclic pelvic pain, urinary problems including frequency, nocturia, and less commonly, urinary retention. Constipation may occur particularly when fibroids extend posteriorly towards the sigmoid and sacrum. Although it's controversial, some experts believe that fibroids can play a role in fertility, and when the cavity is impacted, recurrent pregnancy loss can occur, and dyspareunia can occur as well. We also know that fibroids can cause problems from an obstetric or pregnancy perspective.

So without question, heavy menstrual bleeding represents the most common, the key symptom of uterine fibroids. And heavy menstrual bleeding can often cause iron deficiency and anemia.

When we look at the symptom anemia, it represents the number one cause of years lived with disability in women, and the anemia can be severe. Dr. Anita Nelson and her colleagues in Southern California, published on women admitted to their center with abnormal bleeding and hemoglobins less than 5. Almost half of these women were found to have uterine fibroids. And highlighting women with profound anemia just underscores how symptomatic fibroids can very tangibly diminish quality of life and productivity.

Some have pointed out that uterine fibroids cause disability similar to that of other chronic diseases. And one group of investigators pointed out that the negative impact on vitality and social function with symptomatic fibroids exceeds that of women with breast cancer which is an eye-opening observation. We know that hysterectomies from fibroids account for almost half of all U.S. hysterectomies. We also know that the lifetime likelihood of hysterectomy in women with fibroids is almost 50%. So these statistics just emphasize the very large economic costs of fibroids.

In addition to clinical and economic costs, fibroids also can have a very negative emotional impact on our patients. Here are results from two surveys pointing out that more than half of women with symptomatic fibroid tumors may feel sad or hopeless. Almost two-thirds worry about bleeding or soiling clothes or bedding. Emphasizes that when you're taking an initial history of women with heavy menstrual bleeding and fibroids, you know, asking have they ever had to leave home or change their clothing at work due to heavy menses? And you'll find that the answer all too often is yes.

Also we need to recognize that many women with fibroids are concerned about cancer. So emphasizing that fibroids are not related to cancer is important. Tthey're also concerned very commonly about a need for hysterectomy or other health complications. When taking the history of a woman with symptomatic fibroids, keep in mind that although women may in fact already be anemic, and may be experiencing progressively heavy and prolonged menses, they may or may not recognize that this is the case because very often in women with fibroids as the tumors slowly grow, menstrual duration and intensity slowly creeps up. And so it may not be clear to all women that what they're experiencing is in fact abnormal.

Also keep in mind that fibroids that are closer to the endometrial cavity, particularly FIGO classification, 0 through 3 tumors, may not present with regular cyclical heavy menstrual bleeding but rather irregular or continuous bleeding. Also keep in mind that iron deficiency with or without anemia can cause fatigue.

And then also in many women with fibroids, non-bleeding symptoms, so-called pressure or bulk symptoms related to uterine anatomy and/or size can be important. So if fibroids are pressing against the bladder as we might see with advanced pregnancy, urinary frequency, including nocturia, may be an important presenting symptom. Less commonly, urinary retention can occur. And then lower back pain and dyspareunia are certainly not unusual in women with symptomatic fibroids.

In terms of physical examination, bimanual exam usually, not always, will suggest an enlarged uterus that may be perceived as having irregular contours from subserosal tumors. Once tumors become large, they may also be palpable abdominally. And then on vaginal speculum exam, the position of the cervix may be distorted in women with enlarged fibroid uteri.

In terms of initial diagnostic imaging, far and away the most appropriate choice would be vaginal ultrasound. It's very sensitive in detecting fibroids. It doesn't require radiation, it's accessible, and cost effective.

You can see in the unenhanced sagittal view of a woman with a posterior uterus and an intramural fibroid in the left-hand image, you can get a sense that that fibroid may be projecting somewhat into the cavity but it's not completely clear how much. However, when you put fluid in as with a saline infusion sonogram, sometimes called a sonohysterogram, you can see that in fact, this is a type 1 tumor, an

intramural tumor with a substantial proportion of the tumor, in this case, the majority of the tumor projecting into the endometrial cavity. And this is important from a therapeutic perspective, as many would consider this particular fibroid to be hysteroscopically resectable.

Here's another unenhanced image of a vaginal ultrasound of a woman with an intramural fibroid to the left of the screen. But switching on the left to the right-hand image, we see a 3D ultrasound of the same patient in uterus. And you can see quite clearly that this is a type 1 or 2 tumor with substantial portion of the tumor projecting into the left-hand cornual component of the endometrial cavity. So both fluid infusion or sonohysterogram, as well as 3D imaging can enhance the value of vaginal ultrasound in women with fibroids.

I only rarely order MRs in women with fibroids. But I do note that my colleagues will often want to image the uterus and fibroids with MR prior to hysteroscopic or abdominal myomectomy. We also know that our colleagues in interventional radiology at the center I work at, I know, universally, will want to look at an MR men assess the fibroids in their position prior to performing uterine artery embolization.

In this particular image, we can see about five dark fibroids, all which are intramural fibroids. And then we can see the long arrow pointing to a less dark fibroid that where a good proportion of this particular fibroid is involving the endometrial cavity, most likely a type 1 or 2 tumor. With the short arrowhead in the lower right-hand portion of this slide, we actually can see an ovarian cyst, and the dark component of the cyst contents is a clot. So this is in fact, a resolving hemorrhagic cyst.

So beyond imaging, we also want to perform laboratory assessment in women with fibroids. And I would recommend that most, if not all, new patients presenting with symptomatic fibroids, it's appropriate to check not only a CBC, but also a ferritin level. When we perform a ferritin level, we don't need to do any other tests for iron such as an iron binding capacity. The ferritin is the only assessment of iron status that we need. It's important to check a ferritin because even in women with heavy bleeding but who have a normal hemoglobin, no anemia, low iron stores, which will be associated with a low ferritin level, can cause symptoms even in women again who are not anemic. Brain fog, shortness of breath, pica, and other symptoms have been well documented in non-anemic iron deficient women.

Let's talk about a few slides in terms of treatment of iron deficiency because there's a lot of newer data, and I think some confusion about best practices here. I , and I imagine many in the audience were trained to prescribe 325 milligram over-the-counter ferrous sulfate tablets which contain 65 milligrams of elemental iron either daily or two or three times a day in women with iron deficiency anemia. But we now understand that lower-dose iron is better absorbed and better tolerated. And the hematologists who focus on iron deficiency in anemia encourage us to recommend slow Fe formulations to our patients. At any chain pharmacy, your patients can find next to the Slow Fe, which is a brand name, they can find house versions of Slow FE, which are just as good and less expensive. So I no longer recommend daily administration of iron tablets or multiple daily tablets. In fact, taking oral iron low dose every other day is not only associated with fewer GI side effects, it's actually better absorbed, and therefore, more effective in addressing iron deficiency.

In recent years, as several newer gender ration formulations of I.V. iron have come on the market, I've noticed that when I first see women with heavy menstrual bleeding and fibroids, in many cases, they've been seeing a hematologist and getting iron infusions for months before I first see them. And certainly I.V. iron is appropriate in women who can't tolerate oral iron, or if oral iron hasn't been effective in resolving iron deficiency in anemia. However, I'd just like to emphasize that if non-GYN bleeding is not present, and therefore, we assume that low iron or anemia is from vaginal bleeding, if the iron deficiency or anemia is severe enough to warrant referral to a hematologist for I.V. infusion, such patients should also be referred to a gynecologist at the same time, and there's no point in waiting until they're well into their I.V. infusion therapy.

Okay, so we've talked about epidemiology, we've talked about history, clinical manifestations, and laboratory and imaging assessment of uterine fibroids. For the rest of this presentation, I'd like to talk about treatment of uterine fibroids, focusing on medical management and focusing on a patient-centered approach to treatment.

So when we're first reviewing treatment options with our patients who have symptomatic fibroids, I think we can start by making it very clear that fibroids are not associated with cancer. Assessing a patient's fertility desires right from the get go, I think is important because this will help point the way to treatments that may be appropriate and allow us to avoid recommending treatments that would not be appropriate.

Patients often want to hear what size their fibroids are, what sites their fibroids occupy, and how many fibroids might be present. In terms of medical management versus surgical management, medical management plays a much more important role when the main symptom of fibroids is heavy menstrual bleeding. We discussed bulk symptoms earlier. And bulk symptoms in general are going to be better addressed by interventions which cause fibroid necrosis or surgical treatment.

Keep in mind that patient preference really is the name of the game here. And there are, as we'll discuss, a lot of different approaches, medically, procedure wise, and surgically in terms of addressing symptomatic fibroids. And so, becoming a partner with your patient in what we often call shared decision-making, I think is really important. And that way the patient will feel you and she are on the same

team.

Also keep in mind that depending on insurance and depending on different formulations, and this is particularly in the case with newer formulations, there may be insurance and access and financial issues that will impact which therapies a given patient may have access to. In terms of procedural and surgical interventions, so three procedures which are intended to destroy fibroids include uterine artery embolization, MRI-guided focused ultrasound, and radiofrequency ablation of fibroids.

In terms of surgical procedures for fibroids, some gynecologists employ endometrial ablation selectively in this setting, but we need to keep in mind that most of the data on endometrial ablation dresses women with anatomically normal appearing uteruses, not women with uterine fibroids. And of course, the mainstay surgical treatment for fibroids include hysteroscopic or abdominal myomectomy as well as hysterectomy.

So how can we make our counseling and treatment selection more patient centered? How can we best employee shared decision-making in helping our women with symptomatic fibroids make good decisions? First of all, we need to recognize that many women with fibroids may have few, if any, symptoms. And in such women, expectant management while monitoring for symptoms and performing periodic vaginal ultrasounds and laboratory assessment might be most appropriate, and then only intervening if symptoms start becoming an issue for a particular patient. Among women with fibroids who do require treatment, keep in mind that if our first recommendation right from the get go in the first visit where the patient has met us if our first recommendation is, you know, ‘Ma'am we're going to need to discuss surgery,’ that can be very off-putting to patients, and it's not unusual in my practice that women will see a gynecologist who immediately recommends surgery and then the patient will essentially fire that gynecologist and they'll end up in my office and we'll discuss different treatment options.

And then keep in mind among women with symptomatic fibroids, where the main symptoms are abnormal uterine bleeding, particularly cyclical heavy menstrual bleeding, those are the patients where initial medical management is most appropriate.

So again, encourage your patient to recognize that you and she are on the same team, but listen to her experiences, asking her about what are the worst experiences she has had from her fibroids? I mean, such as soiling her clothes at work and not having a change of clothes, or having to go home from work because of excessive bleeding. Asking to hear about those kinds of clinical anecdotes from patients with symptomatic fibroids, again that helps your patient understand that you and she are on the same team.

When you're reviewing different treatments, help your patient understand not only the benefits, but also any risks or side effects. Help her recognize that many of the medical managements we'll discuss will not treat the fibroids. Some of the medical management options we'll discuss will, but many will not. And so, for instance, a goal of therapy might be to reduce heavy bleeding without shrinking the fibroids. But with other medical options, it might be both reducing or eliminating bleeding and shrinking the fibroids. So the type of symptoms that are bothering a given patient should play a critical role in terms of which treatment options we're going to be emphasizing for individual patients.

And again, I'd like to emphasize side effects. All of the treatments, all the medical management options we’ll discuss have side effects. It's really important to address the side effects up front rather than waiting until they've occurred. And I'm talking about common side effects, not unusual ones.

All right, we've talked about safety and side effects issues. But keep in mind when you're recommending medical treatment options for patients with symptomatic fibroids, very often patients will be talking with their relatives, their siblings, their sisters, their cousins, their girlfriends about what experience they've had with fibroids and treatment of fibroids. Again, I can't emphasize enough that understanding where the patient is coming from in terms of her short- and long-term fertility goals is paramount in helping women make good decisions about fibroid treatment.

And then ease of administration also is important. Treatments that can only be conducted in a hospital setting, for instance, hysteroscopic myomectomy or uterine artery embolization of fibroids, you know, might be very different and much less desirable for some of our symptomatic patients, compared with treatments that can be given at home or in the office.

I'd like to present two cases briefly starting with 30-year-old G0 woman of African American ethnicity who presents with heavy menstrual bleeding, which she's had for many years. Her mom had a hysterectomy early in life. The patient has required a transfusion in the past. She's tried hormonal contraceptives, but felt that they had little if any impact on reducing her bleeding. She has been told she needed a hysterectomy. But now she's moved to a new gynecologist because she was put off by that recommendation, and she's asking you why should something that is not malignant needs such drastic treatment. So listening to that patient's fears and understanding the frustration she's experienced, not only from her fibroids, but also from her negative experience with the earlier gynecologist, again, this can help her understand that you and she are on the same team. If she's already had bloodwork, imaging, endometrial biopsy, do your best to obtain those records so that you can avoid duplication because patients appreciate that. Understanding her short- and long-term goals.

Again, I'll emphasize fertility goals is critical. And then finding out details, which hormonal contraception did you use? And specifically, what problem did you have?

Also, keep in mind that when patients experience bothersome side effects, sometimes the patient may get so focused on the side effects that they may lose track of important symptom of improvement occurring in the setting of side effects. So for instance, a woman who's using oral contraceptives or high-dose oral norethindrone acetate continuous therapy, initially, those women may experience irregular light bleeding, which may be very annoying. But when you're talking to patients about such annoying, irregular, unpredictable bleeding, also don't allow the patient to lose track of, you know, the big picture. For instance, now that she's on medical management, has she had any more of that flooding, hemorrhagic type menstrual bleeding that caused her to soil her bedlinen or clothes at work? And in fact, sometimes patients will get so focused on more minor but, for them very important side effects, that they may lose track of the fact that actually from the big picture, the hormonal management is really helping and has actually eliminated heavy bleeding.

A second case would be an older reproductive-age woman approaching menopause with heavy menstrual bleeding associated with bulky uterine fibroids, who is not interested in hysterectomy and she wants to know, can she just wait until menopause? And it's certainly true that I don't know any group of patients who look forward to menopause more than women with symptomatic fibroids with heavy menstrual bleeding. Keep in mind though, that in women with symptomatic fibroids, and this is also true by the way with adenomyosis, when such women have heavy menstrual bleeding, the heavy menstrual bleeding, as perimenopausal and ovulation begins, that cyclical predictable bleeding might become heavy, continuous, or unpredictable bleeding and start causing big problems for women with symptomatic fibroids as they become perimenopausal. So helping soon-to-be perimenopausal women with fibroids anticipate the changes that may occur with perimenopause, perhaps seeing them more often as they get into their late 40s, early 50s.

And then also recognizing that women like the one we've described in case two might be ideal candidates for bridge therapy, which we'll talk about in a minute when we discuss the use of GnRH analogs.

Okay, so what are medical management options for women with heavy menstrual bleeding from fibroids? There is the tranexamic acid which is an antifibrinolytic formulation, combination hormonal contraceptives estrogen/progestin 25:58 methods, which include pills, patches, and rings, progestin-only contraceptives, notably progestin or levonorgestrel IUD and depo-medroxyprogesterone acetate, high-dose oral progestational agents, which in particular includes continuous norethindrone 5-milligram tablets. And then finally, GnRH analogs which include agonists, which have been available now for decades, and then antagonists which have only recently become available and are formulated with estrogen/progestin add-back.

So in an observational study looking at women 10 or 20 years ago, commercially insured U.S. women who were treated for fibroids-associated heavy menstrual bleeding, you can see that almost 80% of such women were prescribed combination hormonal contraceptives, almost 9% progestin methods, including IUD, injections, and the implant. Fewer than 9% were prescribed GnRH analogs, and this would have been agonists because this was before the antagonists were available. And less than 3% were prescribed antifibrinolytic therapy with tranexamic acid.

But one group performed a systemic review of oral contraceptives for treating symptomatic fibroids. And although a number of studies were found in the author's literature search, only two met criteria for inclusion in a meta-analysis. And it's important to recognize that combination oral contraceptives, and this would presumably also apply to combination rings and patches, performed less well in reducing heavy menstrual bleeding, than did the progestin-releasing IUD or the levonorgestrel 52-milligram IUD.

What about Depo-Provera for treating heavy menstrual bleeding and uterine fibroids? Not much data is available. But one small study comes to us from South Africa where Depo-Provera is more commonly used in contraception than in the U.S. This study of 20 women in South Africa with symptomatic fibroids actually found that DMPA was relatively effective, almost one-third of women became amenorrheic by 6 months. And then with 6 months of treatment, almost three-quarters noted a reduction in bleeding. And also of note, and this likely reflects the hypoestrogenic impact of Depo-Provera, almost 50% of women at 6 months therapy, in other words two injections, assessment suggested that there is a decrease in mean uterine volume. Of course, there are side effects with Depo-Provera, which is a high-dose injectable progestin, include weight gain, and that was an adverse event reported by these South African authors.

How effective is the progestin-releasing IUD? In fact, it's quite effective. You can see the menstrual blood loss decreased among women who retained their IUD. Hemoglobin and hematocrit and ferritin levels rose. Irregular bleeding was common though. And several studies noted higher expulsion rates when IUDs were used in women with fibroids than when IUDs are used in women with a normal uterus. And for this reason, if you're going to place an IUD to control heavy menstrual bleeding in a woman with fibroids if it's available, you might consider ultrasound-guided IUD placement.

So other medical options include GnRH agonists, which are parenteral agents, which have been available now for decades. And these are most commonly used preoperatively to shrink, to reduce the dimensions of uterine fibroids, to facilitate surgery, and also to improve

hemoglobin prior to surgery.

Concerns with GnRH agonists are the hypoestrogenic side effects, including vasomotor symptoms and fairly substantial loss of bone mineral density.

More recently, GnRH antagonists have become available. The two FDA approved antagonists are formulated with estrogen and progestin add-back. The two available recently FDA approved agents are elagolix and relugolix. These are both oral nonpeptide GnRH antagonists. They're rapidly reversible, and their onset of action is also rapid. They're both FDA approved for the treatment of fibroid-related heavy menstrual bleeding for up to two years. And both elagolix and relugolix are formulated with add-back estradiol 1 milligram with norethindrone acetate 0.5 milligrams. And some of you may recognize this estrogen/progestin add-back as being the doses of an estrogen and progestin used in a popular menopausal combination agent. So add-back should be considered a menopausal dose of estrogen, not a contraceptive dose of estrogen.

So if the first available GnRH antagonist, elagolix with add-back, in this graph aggregating the results of the two pivotal phase 3 studies, you can see that compared with placebo, the upper gray line, even within 1 month of initiation, there is an approximately 50% reduction in menstrual blood loss. And look how high baseline menstrual blood loss was in these study participants. The mean menstrual blood loss and baseline was well over 200 mL's. And keep in mind that of the definition of heavy menstrual bleeding is greater than 80 mL's. So these are women who had profound heavy menstrual bleeding. And then by 3 months of use, there was more than an 85% reduction in menstrual blood loss which was sustained until the end of the trial at month 6. So elagolix with add-back, extremely effective in reducing menstrual blood loss and very rapid in achieving efficacy as well.

We see a similar pattern with the second to be approved GnRH antagonist, relugolix. This second agent with add-back you can see on the left, and the right the two phase 3 pivotal studies, placebo controlled. And again, you can see a profound reduction in menstrual blood loss achieved as early as 1 month after initiation of therapy, and increasingly effective with 2 months and with that high efficacy extended to the end of the trial at 6 months or week 24.

So both of these new GnRH antagonists formulated with estrogen/progestin low-dose, add-back therapy, highly effective and rapidly effective in reducing menstrual blood loss in women with symptomatic fibroids.

What about bone mineral density impact of these GnRH antagonists with add-back? In contrast with GnRH agonists used without add-back, the GnRH antagonists used with add-back seem to have very minimal impact. In phase 3 study published in the *New England Journal*, the phase 3 study of relugolix with add-back, you can see only minimal changes at 6 months therapy compared with placebo. So the conclusion I would reach is that relugolix combination therapy with add-back at 6 months, had a little impact on spine or hip bone mineral density.

So when we're using GnRH analogs, including both agonists and antagonists, we need to recognize that these are highly effective agents that reduce patient's symptoms, and substantially reduce symptoms. It gives patients time to consider other options, and can be used as a bridge to therapy, including giving time to correct anemia or improve comorbidities prior to surgery. Or as we discussed in the second case, serving as a bridge from perimenopause to menopause. And their reassuring BMD data with GnRH antagonist plus add-back therapy raises the possibility that more than 2 years of therapy, which with current labeling would be off label, may be appropriate. So perhaps that's something we add our patients can look forward to with longer-term follow-up of women using these new generation GnRH antagonists with add-back. It would be great if in the future, these agents become approved for more than 2 years of use. But keep in mind, current labeling approved for only up to 2 years.

We also need to keep in mind that GnRH analogs, although very effective, may be associated with barriers our patients face when trying to access them. Because these agents are more expensive, pre-authorization may be required prior to insurance approving use of agonists or antagonists. Some insurance policies may insist that patients fail other therapies, other medical management options prior to authorizing use of GnRH analogs.

We also need to keep in mind that some of our patients with symptomatic fibroids may have contraindications to use of add-back estrogen/progestin therapy. For instance, a premenopausal woman with symptomatic fibroids who's been treated for breast cancer, use of estrogen and progestin therapy would be considered contraindicated in her.

So to conclude this review of clinical issues with fibroids with a focus on patient-centered medical options, where are we today? Well, we recognize that fibroids are common and have tremendous potential to impair patient's health as well as quality of life. We've discussed traditional medical options, recognizing that they offer variable efficacy, and we've discussed antifibrinolytics, combination hormonal contraceptives, progestin contraceptives, high-dose oral progestin therapy, and finally GnRH agonists. Recently, oral GnRH antagonists have become available and these are formulated with estrogen and progestin add-back therapy, and they have the advantage of rapid onset very high efficacy and tolerability as well as patient acceptability.

Thank you for this opportunity to discuss uterine fibroids with you today.

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