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New Horizons in the Medical Management of Endometriosis: The Role of GnRH Antagonists: A “Voice of Patient/Voice of Provider” Curriculum

Announcer:

Welcome to CME on ReachMD. This activity, entitled “New Horizons in the Medical Management of Endometriosis: The Role of GnRH Antagonists: A “Voice of Patient/Voice of Provider” Curriculum” is provided by **Omnia Education**.

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Dr. Al-Hendy:

Despite its profound impact, endometriosis remains critically undermanaged. Diagnostic delay persists despite efforts promoting early intervention. In addition, we’re still determining the short- and long-term impact of the pandemic on patients with endometriosis, including those underserved populations who grapple with health inequities.

I am Dr. Ayman Al-Hendy, and I am in San Diego at the annual meeting for clinicians in the obstetrics and gynecology professions. My colleagues, Dr. Andrea Lukes, and Lee Shulman, presented with me data regarding current and emerging practice patterns in the management of endometriosis, including the evolving role of GnRH antagonists and their potential use as an earlier and/or augmentative treatment option. I am here to provide a recap of the data that we presented, as well as the conclusions that we reached during our dynamic discussion.

This is CME on ReachMD, and I’m Dr. Ayman Al-Hendy.

So, most of the information I’m going to present in the next few minutes is based on a survey that we conducted in preparation for this event. We surveyed 170 patient and 100 healthcare providers. From the patient side, these are endometriosis patients, and the survey is designated to collect patient views on the impact of endometriosis on quality of life, barriers to treatment, and we asked questions such as demographics, experience with endometriosis, how many years it took the patient to confirm and to reach a diagnosis of endometriosis, the treatment provided, and the preferred treatment methods. On the provider side, we distributed the survey to our existing network of ob-gyns, nurse practitioners, and physician assistants via Omnia Education. This was designated to collect providers’ views on the impact of endometriosis on patients, the root causes of the barriers, and clinical inertia. And we asked questions, again, about demographics, patient population, the different treatment lines, and their preferred or offered methods of intervention.

And as you can see on this slide, we had an even geographic diversity. Almost everywhere in the United States, unfortunately, there was a major delay in the diagnosis. We asked the patient to rank their number of years to diagnosis from under 1 year, 1-3 years, 3-7 years, 7-10 years, or even more than 10 years. And as you can see, almost everywhere in the country, unfortunately, there was major delay in the diagnosis, in the 7- to 10-years range or in the more-than-10-years range, which really emphasized the significant issue of delay today in diagnosis of endometriosis.

As you would expect with this major delay in the diagnosis, the cost is also going very high. So, we divided this into 3 groups: short diagnosis – those diagnosed less than a year; and then intermediate; and then long – those who were diagnosed 7-10 years or more

than 10 years.

As you can imagine, with this major delay in diagnosis, the cost of managing endometriosis also goes up. In this study, the researchers looked at the impact of delay in diagnosis on the cost and divided the patients into 3 groups: those who have short diagnosis; intermediate; or long delay in diagnosis. And as you can see, especially with the long and intermediate delay, the cost of managing endometriosis goes significantly higher.

This slide actually talks about the disconnect between patient versus provider perception of the severity of the disease. So, they asked the patient how they rank their symptom severity from severe to moderate to mild, and then they asked their provider also to rank the symptom severity in their patient. And particularly if you pay attention to the severe column – we have the patient column on the left and then the provider on the right – and as you can see, 50% of the patients in this particular survey ranked their symptoms as severe, while their provider ranked it as severe only in about 19% of the patients. This major disconnect really is a major challenge in the management of endometriosis. Now, this difference then is manifested in the moderate and the mild, where you actually see more providers ranking the symptoms as moderate or mild, while the patient is less than that.

The European Society of Human Reproduction, the European equivalent to ACOG, had this statement issued recently in one of their guidelines. Although currently no evidence exists that a symptom diary, questionnaire, or app reduced the time to diagnosis or leads to earlier diagnosis, their guideline development group considers their potential benefit in complementing the traditional history-taking as it empowers women to demonstrate their symptoms. So, all of these attempts using, of course, the traditional history-taking but these newer options such as questionnaires and apps, all aiming to shorten the time to diagnosis of endometriosis. ACOG also has a website and app with endometriosis material for patients.

For those just tuning in, you are listening to CME on ReachMD. I'm Dr. Ayman Al-Hendy, and I'm just about to discuss the importance of patient-centered care and how GnRH antagonists are shifting the endometriosis treatment paradigm.

The key considerations in managing patients with endometriosis are the following: first, managing the acute symptoms and problems the patient is dealing with that directly impact their quality of life and relationships, also addressing possible comorbidities.

Their reproductive life plans are very central to developing an effective and patient-centered treatment plan. For example, the patient who wants to attempt or pursue pregnancy right away probably will have a different management plan than those who want to control the symptoms, such as pain, etc., but will pursue pregnancy later on in their reproductive journey. We also need to pay attention to long-term health consequences, patient preference, and expectation from the patient – treatment versus cure. I think it's probably time to start thinking of endometriosis as a chronic disease and manage patient expectation versus aiming for a cure.

Now we will talk about the results of the phase 3 clinical trials of the 3 members of the oral GnRH antagonist family of compounds. And we'll start from the results of elagolix, which was evaluated through the Elaris EM-I and Elaris EM-II clinical research program. Here we present the data on the low-dose elagolix, 150 mg once a day, and also data on the high-dose elagolix, 200 mg twice a day, for treatment of pelvic pain associated with endometriosis.

And as we can see here, the low dose, the 150 mg once a day, about half of the patients showed significant decrease in their pelvic pain and dysmenorrhea symptoms, which was highly statistically more than the placebo group. But particularly in the high dose, the 200 mg twice a day, we see about three-quarters, about 75% of patients responded favorably and showed significant decrease in dysmenorrhea, which of course, this was highly statistically more than placebo. Also, when we looked at the nonmenstrual pelvic pain, the difference was also statistically significant between both elagolix low dose and high dose compared to placebo.

In this next slide, we will discuss the results of the second member of that family of compounds: relugolix. Relugolix was evaluated into a clinical research program called SPIRIT-1 and 2. And these are the results after 6 months' treatment with relugolix. And these results actually have been presented recently at the ASRM [American Society for Reproductive Medicine] meeting. And as you can see here, this is the total score of the pain scale that we use to evaluate the response of patients treated with relugolix. And this particular questionnaire, the EHP-30, has several factors: total score, pain, emotional well-being, control and powerlessness, self-image, and social support. And you can see here at baseline, both the placebo group and the relugolix combination therapy group had fairly high scores, suggesting severe pain and severe symptoms related to endometriosis. But if you look at the results after 6 months' treatment, the score significantly decreased, on average, about 30 to 35 points in the relugolix combination therapy group while it decreased only, on average, between 14 and 19 points in the placebo group. This difference was highly statistically significant on all the different parameters of this particular questionnaire.

And finally, we'll end up with the results with the phase 3 EDELWEISS program which evaluated the linzagolix treatment of endometriosis-related pelvic pain. Here, linzagolix was evaluated at 2 doses. One is the low dose, which is linzagolix 75 mg once a day, versus the high dose linzagolix 200 mg once a day with the add-back therapy. And the add-back therapy was 1 mg of estradiol and 0.5

mg of norethindrone acetate. And as you see here on the results, the placebo group unfortunately continued to have significant pain through the 6-month study of treatment. However, both the low dose linzagolix, but particularly the high dose, showed significant statistically significant decrease in dysmenorrhea, as well as nonmenstrual pelvic pain very quickly. You can see the results showing as early as 4 weeks and reached a maximum around 8 weeks. And of course, the patient continued to show this significant decrease in symptoms through the 6 months of the study, in both dysmenorrhea and also nonmenstrual pelvic pain.

In the University of Chicago, we are actually undergoing now a clinical trial to evaluate another potential use of these newer options, which is after surgery – post-surgical. So, we know surgery for endometriosis is effective. But then we know also that the recurrence rate is extremely high, about 70% in the next 5 years.

So, to avoid the recurrence, or at least delay it as much as we can, we are evaluating the possible use of relugolix combination therapy in patients right after endometriosis surgery and to see if using these medications can delay or avoid the return of symptoms and provide patients with longer time with higher pain-free and higher quality of life.

The panel concludes endometriosis is a public health problem. It has a major negative impact on quality of life, beside the economic cost on the healthcare system. Diagnosis now is based on structural process of patient interview, clinical examination, and imaging. The traditional reliance on surgical biopsy and pathological evaluation is no longer valid. Need to rethink the old approach with immediate surgery. Consider patient endometriosis life. I think it's time to start thinking of endometriosis as a medical disease and, as any other medical condition, we start with simple, medical, noninvasive approaches and only leave surgery as the last resort for those who have failed or are not eligible for medical treatment. Medical management is first-line therapeutic option for women with pelvic pain with no desire for immediate pregnancy. Modern endometriosis care should be individualized, with a patient-centered, multimodal, and interdisciplinary integrated approach.

I want to thank our audience for listening in and thank my colleagues, Dr. Andrea Lukes, and Dr. Lee Shulman, for their insight, experience, and participation in this symposium.

Announcer:

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