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How Early Initiation of a High Efficacy Therapy May Benefit Your RMS Patients

Announcer:
Welcome to ReachMD.
This medical industry feature, titled, "How Early Initiation of a High Efficacy Therapy May Benefit Your RMS Patients," is sponsored by Novartis Pharmaceuticals Corporation and the presenters have been compensated for their time.

Dr Ryerson:
Hello, and welcome! I'm Dr Lana Zhovtis Ryerson, and I'm very happy to talk with you today about some of the data that show benefits to starting a high efficacy therapy early during the course of a relapsing multiple sclerosis patient's disease.
A little background about me is that I am a board-certified neurologist practicing at the Jersey Shore MS Center and the Director of Research for neuroscience. I'm joined today by my colleague, a nurse practitioner Kathleen Harris. Hi, Ms Harris

Ms Harris:
Thank you for that introduction, Dr Ryerson. For those of you listening, I am a nurse practitioner at the Cleveland Clinic Mellen Center for MS in Ohio, which is one of the leading MS centers in the US. I'm excited to be here today to share my experience and discuss the topic of high efficacy therapies because over the past few years we've seen how they may offer RMS patients several benefits. And before we jump in, I need to mention that Dr Ryerson and I are being compensated for our time today.

In my practice, we generally start patients on a high efficacy therapy rather than starting them on something with lower efficacy and escalating in the event of breakthrough disease. A high efficacy therapy early in disease treatment may offer our patients benefits such as the potential for preventing disability progression over time and potential for side effects comparable to lower efficacy therapies though further studies are needed to answer this question. Let's dive in, Dr Ryerson, what has been your approach for managing your patients with RMS?

Dr Ryerson:
I also use high efficacy therapies early in the course of a patient's disease. I think that is when the benefit-risk ratio is at its best. That is because we know the benefit is typically greatest for patients who begin high efficacy therapy earlier.

Consider my patient, a male in his 30s with RMS. He presented with double vision, two to three periventricular lesions, one cord lesion, and he had positive clonal bands in his cerebral spinal fluid, or CSF. He has a family and is a very fit individual who works as a fireman. Given his young age and active lifestyle, we chose to start him on KESIMPTA (ofatumumab) right at diagnosis to reduce his risk of breakthrough disease activity so he can continue with his current activities.

For a variety of reasons, not every patient is started on a high efficacy therapy at diagnosis. With that in mind, knowing the best time for an appropriate patient to switch to a high efficacy therapy is an important consideration.

What we look for in all my patients is an outcome called no evidence of disease activity, or NEDA-3. That's no relapses, no new or enlarging lesions, and no confirmed disability worsening. This parameter is very important in my clinical practice.

Today we're going to talk about KESIMPTA, so before I go any further, let's quickly review some important information about KESIMPTA. We know that KESIMPTA is indicated for the treatment of relapsing forms of MS and also addresses clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease in adults. KESIMPTA is contraindicated in patients with active hepatitis B virus infection.

To summarize the Important Safety Information, which can be heard in full at the end of this podcast, KESIMPTA can cause infections, injection-related reactions, reduction in immunoglobulins, and fetal risk. Most common adverse reactions with an incidence greater than 10% are upper respiratory tract infection, headache, injection-related reactions, and local injection site reactions. The full Prescribing Information can be accessed on this website.

So, Ms Harris, let's switch over to you. Earlier you said you typically start patients on high efficacy therapy early. Can you explain what factors go into that decision?

Ms Harris:
Sure. I see similarities between the patient you discussed and the patients that I see. Some factors that drive my decision include age, sex, degree of lesion burden, and the need for family planning. However, I typically start my patients on a high efficacy therapy unless there is a patient preference to take a different approach, because there are still some situations where I use other therapies. And for those patients that are on lower efficacy therapies, like oral therapies, I agree that I look for breakthrough disease as a sign to change to a high efficacy therapy.

Now, Dr Ryerson, how did efficacy data support your choice of KESIMPTA for your patient whose priority was early disease control?

Dr Ryerson:
So, in Phase 3 clinical trials, KESIMPTA demonstrated superior annualized relapse rate, or ARR, reductions compared to teriflunomide. In ASCLEPIOS I, we see that the ARRs for KESIMPTA and teriflunomide were 0.11 and 0.22, respectively. In ASCLEPIOS II, the ARRs for KESIMPTA and teriflunomide were 0.10 and 0.25, respectively. KESIMPTA significantly reduced relapses by 51 percent in ASCLEPIOS I and 58 percent in ASCLEPIOS II compared to the active comparator, teriflunomide.

What I personally find to be most notable is the MRI data. In ASCLEPIOS I, the mean number of gadolinium-enhancing lesions for KESIMPTA and teriflunomide were 0.01 and 0.46, respectively. In ASCLEPIOS II, results for KESIMPTA and teriflunomide were 0.03 and 0.52, respectively. That's a relative risk reduction in gadolinium-enhancing lesions of 98 percent in ASCLEPIOS I and 94 percent in ASCLEPIOS II.

And finally, in ASCLEPIOS I, the number of new or enlarging T2 lesions for KESIMPTA and teriflunomide were 0.72 and four, respectively. In ASCLEPIOS II, results for KESIMPTA and teriflunomide were 0.64 and 4.16, respectively. That's a relative risk reduction of 82 percent in ASCLEPIOS I and 85 percent in ASCLEPIOS II.

A 94 to 98 percent reduction in gadolinium-enhancing lesions is not far off from 100 percent resolution of gadolinium-enhancing lesions. This is a pretty solid point to talk about with my patients when we're talking about putting them on, or switching them to, a high efficacy therapy.

Ms Harris:
Certainly impressive. These are the data I look for when choosing a high efficacy therapy for both my treatment-naïve patients and patients changing therapies. And I can count on KESIMPTA knowing more than 80 percent of patients in the Phase 3 studies were either treatment-naïve or previously treated with commonly used first-line therapies like interferon and dimethyl fumarate.

Dr Ryerson:
And what's reassuring to me and my patients are the long-term efficacy data. Up to five years of data in over 1300 patients are available from the ALITHIOS single-arm, open-label, extension study evaluating KESIMPTA in subjects from ASCLEPIOS I and II trials who continued KESIMPTA treatment and those that switched from teriflunomide.

The data shows ARR of 0.06 for patients who continued KESIMPTA and for those who switched to KESIMPTA. That's a 73 percent risk reduction in ARR for patients who switched from teriflunomide to KESIMPTA. The mean number of gadolinium-enhancing lesions is 0.01 and 0.02 for patients who continued and those who switched, respectively. That's a 97 percent risk reduction in gadolinium-enhancing lesions for those patients who switched from teriflunomide to KESIMPTA. As for the number of new or enlarging T2 lesions: 0.07 and 0.44 for patients who continued and those who switched, respectively. That's an 84 percent risk reduction for those patients who switched from teriflunomide to KESIMPTA.

Overall, patients who stayed on or switched to KESMIPTA had favorable results. However, data shows that those who started KESIMPTA treatment earlier in their disease course were better off than those who started later. Now, Ms Harris, what does the availability of long-term efficacy data offer you and your RMS patients?

Ms Harris:
My patients want to see the outcomes of 5 years on KESIMPTA–both my newly diagnosed patients and patients changing therapy. They are very scared, this is a huge decision for them; it's a big part of their life. I think offering the data to the patient is a big part of their

decision-making. This kind of data can support my description of what their disease could look like in 5 years.

Dr Ryerson:
I agree. It's a nice way to demonstrate the potential for consistent results with KESIMPTA over time. And 83 percent of patients who were enrolled in the extension study were still on treatment at the end of the ALITHIOS study. This tells me that patients are comfortable using this therapy and suggests there are tolerable side effects, which has been my clinical experience.

Let's talk about tolerability a bit more. When selecting a high efficacy therapy to use in your patients, how does safety factor into your decision-making?

Ms Harris:
KESIMPTA can cause infections, sometimes severe, so it's important to counsel patients about this potential adverse reaction. If patients are more prone to respiratory infections, pneumonia, urinary tract infections, things like that, we'll talk to them about infection and always check immunoglobulins prior to, during, and after starting anyone on KESIMPTA.

We talked earlier about knowing that time to switch a patient to high-efficacy therapy. I have a patient who has suffered with persistent infections despite her stable disease on teriflunomide, which was her second oral therapy, we actually just recently discussed new options and landed on KESIMPTA for the safety aspect.

The most common adverse reactions with incidence greater than 10% in patients taking KESIMPTA were upper respiratory tract infections, headache, injection-related reactions, and local injection-site reactions.The overall rate of infections and serious infections in KESIMPTA-treated patients was similar to teriflunomide-treated patients: 51.6% vs 52.7%, and 2.5% vs 1.8%, respectively.

As we know, MS is a challenging disease, so if I can provide data that makes my patients feel confident in their treatment selection and gives them the freedom to continue with the current lifestyle, I feel very rewarded as their prescriber.

It's been a pleasure discussing KESIMPTA and the potential benefits of starting a high efficacy therapy early. Any final thoughts you would like to share?

Dr Ryerson:
I feel confident prescribing KESIMPTA given its large body of evidence and clinical data spanning over 5 years.

Ms Harris:
I completely agree. Clinicians and patients should partner to find the treatment that works best for them and their lifestyles.

Dr Ryerson:
Thank you, Kathleen, for joining me today to talk about such an important topic!

Ms Harris:
It was my pleasure, Dr Ryerson. To our listeners, please continue listening for the full Important Safety Information. The Prescribing Information can be accessed on this very website.

Announcer:
INDICATION AND IMPORTANT SAFETY INFORMATION

KESIMPTA (ofatumumab) is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

IMPORTANT SAFETY INFORMATION

Contraindication: KESIMPTA is contraindicated in patients with active hepatitis B virus (HBV) infection.

WARNINGS AND PRECAUTIONS

Infections: Serious, including life-threatening or fatal, bacterial, fungal, and new or reactivated viral infections have been observed during and following completion of treatment with anti-CD20 B-cell depleting therapies. The overall rate of infections and serious infections in KESIMPTA-treated patients was similar to teriflunomide-treated patients (51.6% vs 52.7%, and 2.5% vs 1.8%, respectively). The most common infections reported by KESIMPTA-treated patients in relapsing MS (RMS) trials included upper respiratory tract infection (39%) and urinary tract infection (10%). Delay KESIMPTA administration in patients with an active infection until resolved.

Consider the potential increased immunosuppressive effects when initiating KESIMPTA after an immunosuppressive therapy or initiating an immunosuppressive therapy after KESIMPTA.

Hepatitis B Virus: *Reactivation:* No reports of HBV reactivation in patients with MS treated with KESIMPTA. However, HBV reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, has occurred in patients treated with ofatumumab at higher intravenous doses for chronic lymphocytic leukemia (CLL) than the recommended dose in MS and in patients treated with other anti-CD20 antibodies.

Infection: KESIMPTA is contraindicated in patients with active hepatitis B disease. Fatal infections caused by HBV in patients who have not been previously infected have occurred in patients treated with ofatumumab at higher intravenous doses for CLL than the recommended dose in MS. Perform HBV screening in all patients before initiation of KESIMPTA. Patients who are negative for HBsAg and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], should consult liver disease experts before starting and during KESIMPTA treatment.

Progressive Multifocal Leukoencephalopathy: No cases of progressive multifocal leukoencephalopathy (PML) have been reported for KESIMPTA in RMS clinical studies; however, PML resulting in death has occurred in patients being treated with ofatumumab at higher intravenous doses for CLL than the recommended dose in MS. In addition, JC virus infection resulting in PML has also been observed in patients treated with other anti-CD20 antibodies and other MS therapies. If PML is suspected, withhold KESIMPTA and perform an appropriate diagnostic evaluation. If PML is confirmed, KESIMPTA should be discontinued.

Vaccinations: Administer all immunizations according to immunization guidelines: for live or live-attenuated vaccines at least 4 weeks and, whenever possible at least 2 weeks prior to starting KESIMPTA for inactivated vaccines. The safety of immunization with live or live-attenuated vaccines following KESIMPTA therapy has not been studied. Vaccination with live or live-attenuated vaccines is not recommended during treatment and after discontinuation until B-cell repletion.

Vaccination of Infants Born to Mothers Treated with KESIMPTA. During Pregnancy. For infants whose mother was treated with KESIMPTA during pregnancy, assess B-cell counts prior to administration of live or live-attenuated vaccines. If the B-cell count has not recovered in the infant, do not administer the vaccine as having depleted B-cells may pose an increased risk in these infants.

Injection-Related Reactions: Injection-related reactions with systemic symptoms occurred most commonly within 24 hours of the first injection, but were also observed with later injections. There were no life-threatening injection reactions in RMS clinical studies.

The first injection of KESIMPTA should be performed under the guidance of an appropriately trained health care professional. If injection-related reactions occur, symptomatic treatment is recommended.

Reduction in Immunoglobulins: As expected with any B-cell depleting therapy, decreased immunoglobulin levels were observed. Monitor the levels of quantitative serum immunoglobulins during treatment, especially in patients with opportunistic or recurrent infections and after discontinuation of therapy until B-cell repletion. Consider discontinuing KESIMPTA therapy if a patient with low immunoglobulins develops a serious opportunistic infection or recurrent infections, or if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.

Fetal Risk: Based on animal data, KESIMPTA can cause fetal harm due to B-cell lymphopenia and reduce antibody response in offspring exposed to KESIMPTA in utero. Transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 B-cell depleting antibodies during pregnancy. Advise females of reproductive potential to use effective contraception while receiving KESIMPTA and for at least 6 months after the last dose.

Most common adverse reactions (>10%) are upper respiratory tract infection, headache, injection-related reactions, and local injection-site reactions.

Please see full Prescribing Information, including Medication Guide at the bottom of this presentation.

Announcer:
This program was sponsored by Novartis Pharmaceuticals Corporation. If you missed any part of this discussion, visit reachmd.com/industry-feature. This is ReachMD. Be part of the knowledge.

Important Safety Information for KESIMPTA will be available underneath the player of this audio presentation and a link to the full Prescribing Information, including the Medication Guide, is available at the bottom of this presentation.

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