Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/frontlines-multiple-sclerosis/diving-into-data-relapsing-ms-treatment-option/12204/

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Diving into the Data on a Relapsing MS Treatment Option

Announcer:
This Medical Industry Feature, titled “Diving into the Data on a Relapsing MS Treatment Option” is sponsored by Novartis. This program is intended for US healthcare professionals. The Important Safety Information for KESIMPTA will be available at all times underneath the presentation. A link to the full Prescribing Information is available at the bottom of the presentation.

Dr. Doghramji:
This is ReachMD, and I'm Dr. Paul Doghramji. Joining me to discuss the safety and efficacy of KESIMPTA, is Dr. Gabriel Pardo, Director of the Oklahoma Medical Research Foundation Multiple Sclerosis Center of Excellence, and Associate Member of the OMRF Arthritis and Clinical Immunology Research Program. Dr. Pardo, thanks for being here today.

Dr. Pardo:
Well, thank you very much for having me. I hope this is very instructional for all that look at it.

Dr. Doghramji:
So, to start off, there are currently more than 18 FDA-approved treatments for multiple sclerosis. What are some of the things that you and your patients consider when selecting a treatment for relapsing multiple sclerosis?

Dr. Pardo:
That is a very important question, because certainly there is a lot of thought that goes into making a decision regarding treatment for relapsing multiple sclerosis. First thing that we need to discuss with the patient is that relapsing MS is a chronic, progressive disease with a prolonged and variable clinical course, where disability accumulates over time. The current therapies for relapsing MS may modify the course by reducing disease activity and slowing down the accumulation of disability. In addition to minimizing disease activity, treating relapsing MS should also focus on safety and individual patient factors.

Dr. Doghramji:
Today, we are here to talk about one of those FDA-approved treatments, KESIMPTA. What is KESIMPTA?

Dr. Pardo:
Well, KESIMPTA is indicated for the treatment of relapsing forms of multiple sclerosis to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease in adults. KESIMPTA is contraindicated in patients with active hepatitis B infection, and it is available in single-dose, prefilled Sensoready pens that are intended for once-monthly patient self-administration following an initial dose that is given at weeks 0, 1, and 2.

We also need to quickly review some warnings and precautions. One needs to monitor immunoglobulins at the beginning, during, and after discontinuation of KESIMPTA until B-cell repletion has been achieved. For patients who develop serious or recurrent infections, consider discontinuing KESIMPTA if immunoglobulin levels indicate immune compromise. Finally, females of reproductive potential should be advised that KESIMPTA may cause fetal harm based on animal data. Now, there is full Important Safety Information attached in the panel adjacent to this video.

Announcer:
INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION: 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 infection.

WARNINGS AND PRECAUTIONS

Infections: An increased risk of infections has been observed with other anti-CD20 B-cell depleting therapies. KESIMPTA has the potential for an increased risk of infections including serious bacterial, fungal, and new or reactivated viral infections; some have been fatal in patients treated with other anti-CD20 antibodies. 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 hepatitis B virus (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, on this site or at www.kesimptahcp.com.

Dr. Doghramji:
And, can you tell us how KESIMPTA actually works?

Dr. Pardo:
Yes, so the precise mechanism by which ofatumumab exerts its therapeutic effects in MS is unknown, but is presumed to involve binding to CD20, a cell surface antigen that is present on pre-B and mature B lymphocytes. Now, following that cell surface binding to B lymphocytes, ofatumumab results in lysis of CD20-positive B-cells. KESIMPTA achieved sustained B-cell depletion over the dosing period of this medication.

Dr. Doghramji:
Let's jump right into the Phase 3 clinical program. Which patients were included in the ASCLEPIOS I and II trials for KESIMPTA?

Dr. Pardo:
Great question. We always have to look at that data to apply to our patients, so the demographics and baseline characteristics were well-balanced across treatment arms and the two different trials. The mean age was 38 years, the mean duration of disease was 8.2 years since onset of first symptoms, the mean EDSS score was 2.9, and approximately 5% of the population had secondary progressive MS. About 40% of patients had not been previously treated with a disease-modifying therapy, and approximately 40% had Gd-enhancing T1 lesions on their baseline MRI scan.

Dr. Doghramji:
How do these demographics compare with the patients you might see in your clinic? Can you give us an example of a patient who may be a good candidate for KESIMPTA?

Dr. Pardo:
Sure. So, I think that a good way to go about doing that is to present a hypothetical patient based on real-world clinical data that might show the appropriate characteristics for treatment with KESIMPTA. So, this is Amy, she's 29 years old, she's a small business owner who was diagnosed with relapsing MS two years ago and is currently taking an oral DMT. She presents with signs of active disease to include weakness and lesions on the MRI, and on Amy's own words, she is looking for a powerful treatment that gives her the freedom to do the job she loves without sacrificing time to run her business. This is important, because when we are discussing treatment options with patients, in addition to the characteristics of the disease and the patient's characteristics as it pertains to comorbidities, we also have to incorporate the patient's views, likes, and dislikes into the discussion process, and having this statement from Amy, it is very important for us to take into consideration.

Dr. Doghramji:
Going back to the Phase 3 clinical program, how was KESIMPTA evaluated in relapsing multiple sclerosis patients?

Dr. Pardo:
So, the objective of the ASCLEPIOS trials was to evaluate the efficacy and safety of KESIMPTA compared with teriflunomide. The primary endpoint of both studies was the annualized relapse rate over the treatment period. There were a series of additional outcome measures, and those included things like the time to 3-month confirmed disability progression for the pool populations, the number of Gd-enhancing T1 lesions per scan, and the annualized rate of new or emerging T2 MRI lesions.

Dr. Doghramji:
Well, that's very helpful to know. Can you tell me about the efficacy results for KESIMPTA as demonstrated in Phase 3 clinical trials?

Dr. Pardo:
Certainly. In both Phase 3 studies, ASCLEPIOS I and II, KESIMPTA 20 mg demonstrated significant reductions compared to teriflunomide 14 mg, as seen in a 51% rate of reduction of the annualized relapse rate for ASCLEPIOS I, and 59% for ASCLEPIOS II, and that was the primary end point of the studies. There was also benefit as seen in reduction in the number of Gd-enhancing T1 lesions at 98 and 94% respectively, and reduction of the number of new or enlarging T2 lesions compared to teriflunomide, at a rate of 82 and 85% for ASCLEPIOS I and II. Finally, the prospective pooled analysis showed that KESIMPTA significantly reduced the risk of 3-month confirmed disability progression by 34.4% compared with teriflunomide.

Dr. Doghramji:
For those just joining us, you're listening to ReachMD. I'm Dr. Paul Doghramji and today I'm speaking with Dr. Gabriel Pardo about

KESIMPTA, a treatment option for relapsing multiple sclerosis.

Let's go deeper into the clinical trial. So, we know N-E-D-A 3 or NEDA-3 was a post hoc analysis on the ASCLEPIOS studies. How important is NEDA and how do we use it in clinical practice?

Dr. Pardo:
It is important, and we do use it. So, NEDA-3, or no evidence of disease activity in the analysis was defined as a composite of three elements that is the percentage of patients who were relapse-free, one, were free from both Gd-enhancing and T2 lesions, two, and were free from 6-month confirmed disability progression, three. So, evaluating these different types of parameters will give us a sense for how well-controlled the disease process is in a given patient.

Dr. Doghramji:
What can you tell us about the NEDA-3 data for KESIMPTA?

Dr. Pardo:
Based on the clinical data, we saw that 47% of patients taking KESIMPTA achieved no evidence of disease activity in year 1 versus 25% of the patients that were taking teriflunomide. Now, 88% of patients, or nearly 9 out of 10 taking KESIMPTA, achieved no evidence of disease activity in year 2 compared to 48% of those taking teriflunomide. Now, no conclusions of clinical outcomes can be drawn from this data.

Dr. Doghramji:
Very helpful. Let's move forward. What was the rate of adverse events as demonstrated in clinical trials?

Dr. Pardo:
In the pool analysis, the proportion of patients experiencing adverse events was 83.6 compared to 84.2%, and adverse events leading to drug discontinuation 6% compared to 5%, so they were very similar in the KESIMPTA and the teriflunomide groups. Treatment was discontinued because of decreased immunoglobulins in 3.4% of patients treated with KESIMPTA, and in 0.8% of those taking teriflunomide.

Dr. Doghramji:
So, can you tell us about any systemic and local injection-related adverse events associated with KESIMPTA?

Dr. Pardo:
Injection-related reactions were predominantly mild to moderate in severity for 99.8% of the patients, and local injection reactions were reported in 21% and 11% of patients receiving KESIMPTA, respectively. Injection-related reactions with systemic symptoms of certain clinical studies occurred most commonly within 24 hours of the first injection, but were also observed with later injections. Symptoms observed included fever, headache, myalgia, chills, and fatigue. Now, the most frequently reported symptom of local injection-site reaction at a rate of 2% or greater included erythema, pain, itching, and swelling.

Dr. Doghramji:
Very important to know as physicians. What should patients know before starting treatment with KESIMPTA?

Dr. Pardo:
Prior to initiating KESIMPTA, a physician should perform hepatitis B screening and test for quantitative serum immunoglobulins. In addition, because vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation until B-cell repletion, physicians should also administer all immunizations according to immunization guidelines. And this has to be done at least four weeks prior to initiation of KESIMPTA for live or live-attenuated vaccines, and whenever possible, at least two weeks prior to initiation of KESIMPTA for inactivated vaccines.

Dr. Doghramji:
We've covered a lot of important information. In summary, what would you say KESIMPTA has to offer your patients?

Dr. Pardo:
So, risk of relapse, reduction of lesion burden, probability of disability progression, likelihood of achieving NEDA-3, and risk of adverse events are all important factors to consider when selecting a treatment. And we go back to our patient, Amy, that was concerned about potential worsening of her relapsing MS and was seeking a powerful treatment that allows her to continue working, I think that KESIMPTA certainly is a highly effective therapy that also offers flexibility for a patient like Amy, as she's given the ability to self-administer.

Dr. Doghramji:

That's a great comment for us to think about as we come to the end of today's program. I want to thank my guest, Dr. Gabriel Pardo, for helping us better understand the efficacy and safety of KESIMPTA. Dr. Pardo, it was great speaking with you today.

Dr. Pardo:
Well, it was a great pleasure, thank you very much.

Dr. Doghramji:
I'm Dr. Paul Doghramji and thanks for listening.

Announcer:
This program was sponsored by Novartis. If you missed any part of this discussion, visit ReachMD.com. Please see Prescribing Information, including Medication Guide, which is available at the link below.