Transcript Details
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MSperceptions: Candid HCP/Patient Clinical Conversations About MS

Announcer
Welcome to ReachMD. This Medical Industry Feature titled, MSperceptions: Candid HCP and Patient Clinical Conversations About MS, is sponsored by Biogen. This program is intended for U.S. healthcare professionals. Continue listening for Important Safety Information including **Boxed Warning** and see full Prescribing Information at tysabri.com.

Dr. Barry Singer
Hi, my name is Dr. Barry Singer and I'm the director of the MS Center for Innovations in Care in St. Louis. And today I'll be talking to Rosario, a person living with MS, about the impact MS may have on a patient's quality of life.

Rosario
Hi, Dr. Singer, so nice to meet you. As you mentioned, my name is Rosario and I'm an artist and photographer from this beautiful, yet complicated Caribbean Island of Puerto Rico. I've been living with MS for over 10 years now, and I've been taking TYSABRI since 2013. I look forward to sharing my experience with you.

Dr. Barry Singer
And I as well. So welcome Rosario. Actually, I paint myself, so we have that in common. For healthcare providers who treat MS, we routinely assess a patient's disease activity in response to treatment, by monitoring things like relapses, lesion activity, and disability progression. However, it's harder for us to measure the hidden or invisible symptoms, which are symptoms that a patient's experiencing, but that others may not see. These can include things like fatigue, cognitive problems, anxiety, and depression. It can really have an impact on the quality of life. And because these symptoms may not be as apparent as physical symptoms, it's important for healthcare providers to ask about, and discuss these symptoms during every visit. Rosario, could you please tell us about how you were diagnosed with multiple sclerosis?

Rosario
I first noticed feeling something was different back in 2008. And at that time, I suddenly was exhausted all the time and had difficulty concentrating and focusing on my work. So, I thought I was just working too much, and my job and personal life were taking a toll physically and mentally. And as an artist and photographer, I was feeling burnt out and my creative juices were decreasing. And I felt I was losing my

passion and I didn't know why. A few years after that, I started to experience more physical symptoms like fatigue, cognitive issues, and depression that couldn't be explained by my internal medicine doctor. So, I was eventually sent for an MRI and after seeing many different doctors, I was finally referred to a neurologist. So, when the results of the MRI came back, my neurologist finally had a diagnosis for me, four years after my first symptoms, and it was relapsing multiple sclerosis.

Dr. Barry Singer
Wow. That's really a rough journey to get a diagnosis. And I know some of my patients have gone through similar experiences. So how has MS affected your life after you finally received a diagnosis of multiple sclerosis?

Rosario
In the beginning, I was shocked and scared, but I was also relieved and hopeful because I finally had a diagnosis. And at first, I stopped doing certain activities and jobs, afraid that I would have a relapse. And because of the symptoms I was experiencing, it was a challenge to keep up with work and friends. You know, I was exhausted, couldn't concentrate and physically couldn't keep up. As an artist, it

affected my work and art significantly.

Dr. Barry Singer
Wow, really MS had a significant impact on your quality of life and how you were functioning. And we do see that with our patients living with MS, that it can really disrupt a person's life and cause them to miss out on things that are really important to them. And that's why I think it's important for patients to discuss their treatment goals with their care team so we can develop the right treatment plan. When you were discussing treatment options, what were some of the goals you discussed with your doctor and why did you choose TYSABRI?

Rosario
Because my MS was causing such a disruption in my life, and to the things that are important to me, my main treatment goal was to stop the disease progression. As a photographer and someone who loves outdoor activities, treating my MS was an important goal to discuss with my doctor. There were two major factors that helped me in deciding my treatment. First were the positive study results that showed the efficacy of TYSABRI. Second was the fact that it was once a month, and I wouldn't have to think about my treatment daily. This fit perfectly in with my lifestyle, and psychologically it made a huge difference in my daily life and for maintaining positive thinking. My provider told me about all the potential benefits and possible side effects, including the risk of PML. And after reviewing all the options and analyzing the pros and cons, I personally decided, and you know it's a very personal decision, to choose to start TYSABRI.

Dr. Barry Singer
Yeah, that's really great. And I'm really happy to hear that you discussed your treatment goals with your doctor. And we like to use shared decision making when trying to make these decisions together with our patients. So, when talking to my patients about treatment, every patient is different, so we discuss a number of factors to select the right treatment for an individual patient. I'll assess factors that include risk of disease progression, their other medical problems, medication effectiveness, and even their lifestyle. So, we have to weigh out the benefits of medications with the risk of treatment, including potential serious infections. For many of my MS patients, the goal is to prevent disease progression, reduce relapses, and stop new lesions from forming.

Rosario, when we looked at the data from the 2-year AFFIRM pivotal trial, 83% of patients taking TYSABRI had no sustained disability progression for 12 weeks compared to only 71% with placebo. The same study also showed there was a 67% relative reduction in the annualized relapse rate with TYSABRI versus placebo. And an incredible 97% of TYSABRI-treated patients showed full suppression of contrast gadolinium enhancing MRI activity, versus only 72% with placebo. In addition, there were more recent data were generated after pivotal trial. There's a recent publication from Hersh and colleagues, which describes the effect of TYSABRI on various aspects of a patient's quality of life.

Rosario
Wow. That's interesting. Can you tell me about the study?

Dr. Barry Singer
Sure, happy to. Since this is a podcast and I'm not actually able to display the data, it's important for listeners to know they can see more details about the study methodology and results I'm about to discuss in the Overview section of the podcast description. So, in this study, 164 patients reported their experience after starting TYSABRI using a standard Quality of Life in Neurologic Disorders (Neuro-QoL) Assessment of 12 Domains. Data were collected at routine visits from large real-world cohort of MS patients from 10 healthcare institutions in three countries, including the U.S. And studies like this are important for providing real world evidence that can help support HCP decision making. The study looked at the percentage of TYSABRI patients who experienced clinically meaningful improvement or worsening in two groups. There was the overall population, and within that group, they also looked at patients with baseline impairment.

Rosario
So, what were the results of the study?

Dr. Barry Singer

Before I jump into the results, there was a few limitations to the study we should have the listeners be aware of. Because this is a real-world study that lacks randomization, the results may have been impacted by unconsidered variables or incomplete adjustment. Also, there's no consensus regarding what constitutes a clinically relevant change in patient reported outcomes. The studies showed that in the overall MS patient population, a greater proportion of patients reported clinically meaningful improvement than worsening, for all domains, except for lower extremity function and participation in social roles and activities, for which there was an equal number of patients worsened or improved. Over 75% of patients improved or remained stable across each of the domains. This means that over

75% of patients improved or remained stable in domains that could have a positive impact on an MS patient's life.

Rosario
Yeah. I agree with you that all of those aspects are important aspects of life for patients living with MS. You mentioned that the study also looked at patients with baseline impairment. Can you tell me more about the results for that group?

Dr. Barry Singer
Yeah, happy to. So, in the baseline impairment group, the clinically meaningful improvement was higher than the overall population for most domains. So over 89% of patients improved or remained stable in each of the domains that were measured. This means that almost 90% of patients improved or remained stable in the measured quality of life domains.

Rosario
You know, those results sound great for MS patients. And I'm happy to hear that Biogen continues to sponsor new studies looking at the effects of TYSABRI. My personal experience with TYSABRI, so far, is that it has helped me meet my treatment goals. You know, thankfully I haven't had major side effects, and the ones I have gotten are manageable. In addition to managing my MS through medication, some other things that help me include improving my nutrition and exercise routine and taking time for myself. You know, MS continues to challenge me, but it has not defeated me and has made me a fighter. Overall, I still feel that I have good quality of life. I know I'm blessed, and I feel lucky that I can still pursue my passion for art and photography.

Dr. Barry Singer
Rosario, I'm so happy that you're really in a good place and that you're back to your art and photography. You know, while TYSABRI can slow down disease progression, which can impact different aspects of life, it doesn't address all of the symptoms that a patient develops over the years. And if someone out there living with MS does experience symptoms that affect the quality of life, we need to determine whether these symptoms can be treated without medicine, using approaches like physical therapy, exercise, or lifestyle adjustments, or if the medication is required. So how do you monitor your changes with your provider?

Rosario
Well, my provider always asks if I have new symptoms or if I've had any relapses. My provider is very, very down to earth and I feel so comfortable just telling him everything that has been going on with me since our last checkup. He also monitors my MS by doing MRIs to make sure the lesions are under control. He does labs every six months, as well as checking my physical reflexes and balance at his office.

Dr. Barry Singer
Yeah. I'm really glad that you can have an open discussion with your provider. I think it's really critical about how you mention your provider is down to earth. And I think it's really important that HCPs listen to their patients. You know, as healthcare providers, it's very important that we have these open conversations so patients feel comfortable bringing up and going over symptoms that they're experiencing. When I meet with my patients, I tend to go through a list of symptoms with them. I ask them about specific symptoms, such as fatigue, cognition. And then I follow up with more detailed questions. For example, with fatigue, I'll ask them, are you sleeping well at night? Are you experiencing motor fatigue where your legs get weak? After I get an understanding of how these symptoms are affecting their quality of life, we can decide on the best way to manage these problematic symptoms.

Another thing I routinely do is screen people for cognition, using a digital assessment tool, designed to evaluate cognitive function in patients with MS, in my office. I encourage all our listeners out there to take the time to go through potential symptoms with your patients. I find that by asking about specific symptoms in detail, we can come up with a guided plan for our patients to help improve their quality of life. Thanks so much Rosario for taking time to speak with me and helping us understand the impact that MS may have on someone's quality of life. Any final thoughts you would like to share with us?

Rosario
You're very welcome, Dr. Singer. It was my pleasure. My experience with TYSABRI has been positive so far. You know, I hope the treatment continues in slowing my progression. And even though it's been nine years since my first infusion, changing treatment is not something I want since I feel the benefits in my body. And it's also given me a chance to help and inspire others.

Dr. Barry Singer
Well, thanks so much Rosario for that commitment to the MS community, and for sharing your experience with us. Keep painting and I'd love to see your work.

Announcer
TYSABRI HCP Indication and Important Safety Information

INDICATION:

TYSABRI® (natalizumab) is indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. TYSABRI increases the risk of PML. When initiating and continuing treatment with TYSABRI, physicians should consider whether the expected benefit of TYSABRI is sufficient to offset this risk.

IMPORTANT SAFETY INFORMATION

WARNING: Progressive Multifocal Leukoencephalopathy (PML)

TYSABRI® (natalizumab) increases the risk of PML, an opportunistic viral infection of the brain that usually leads to death or severe disability. Risk factors for the development of PML include the presence of anti-JCV antibodies, duration of therapy, and prior use of immunosuppressants. These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI.

Healthcare professionals should monitor patients on TYSABRI for any new sign or symptom that may be suggestive of PML. TYSABRI dosing should be withheld immediately at the first sign or symptom suggestive of PML. For diagnosis, an evaluation including a gadolinium-enhanced MRI scan of the brain and, when indicated, cerebrospinal fluid analysis for JC viral DNA are recommended.

Because of the risk of PML, TYSABRI is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the TOUCH® Prescribing Program.

- Infection by the JC Virus (JCV) is required for the development of PML
- There are no known interventions that can reliably prevent PML or that can adequately treat PML if it occurs
- Postmarketing data suggest that the risk of developing PML may be associated with relative levels of serum anti-JCV antibody compared to a calibrator as measured by ELISA (often described as an anti-JCV antibody index value)
- MRI findings may be apparent before clinical signs or symptoms suggestive of PML. Monitoring with MRI for signs that may be consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present. Consider monitoring patients at high risk for PML more frequently. Lower PML-related mortality and morbidity have been reported following TYSABRI discontinuation in patients with PML who were initially asymptomatic compared to patients with PML who had characteristic clinical signs and symptoms at diagnosis
- PML has been reported after discontinuation of TYSABRI in patients who did not have findings suggestive of PML at the time of discontinuation. Patients should continue to be monitored for any new signs or symptoms that may be suggestive of PML for at least 6 months after discontinuation of TYSABRI

- Adverse events that may occur during plasma exchange (PLEX) include clearance of other medications and volume shifts, which have the potential to lead to hypotension or pulmonary edema. Although PLEX has not been prospectively studied in TYSABRI-treated patients with PML, it has been used in such patients in the postmarketing setting to remove TYSABRI more quickly from the circulation. There is no evidence that PLEX has any benefit in the treatment of opportunistic infections such as PML. JCV infection of granule cell neurons in the cerebellum, i.e., JCV granule cell neuronopathy (GCN), with symptoms similar to PML, has been reported in patients treated with TYSABRI. JCV GCN can occur with or without concomitant PML and can cause cerebellar dysfunction. Diagnosis and management of JCV GCN should follow guidance provided for PML
- Immune reconstitution inflammatory syndrome (IRIS) has been reported in the majority of TYSABRI-treated patients who developed PML and subsequently discontinued TYSABRI. In almost all cases, IRIS occurred after PLEX was used to eliminate circulating TYSABRI. It presents as a clinical decline in the patient's condition after TYSABRI removal (and, in some cases, after apparent clinical improvement) that may be rapid, can lead to serious neurological complications or death, and is often associated with characteristic changes in the MRI. TYSABRI has not been associated with IRIS in patients discontinuing treatment with TYSABRI for reasons unrelated to PML. In TYSABRI-treated patients with PML, IRIS has been reported within days to several weeks after PLEX. Monitoring for development of IRIS and appropriate treatment of the associated inflammation should be undertaken

Contraindications

- TYSABRI is contraindicated in patients who have or have had PML
- TYSABRI is contraindicated in patients who have had a hypersensitivity reaction to TYSABRI

TYSABRI TOUCH Prescribing Program

- Because of the risk of PML, TYSABRI is available only through a restricted distribution program under a REMS called the TOUCH® Prescribing Program
- Patients must be enrolled in the TOUCH Prescribing Program, read the Medication Guide, understand the risks associated with TYSABRI, and complete and sign the Patient-Prescriber Enrollment Form

Herpes Infections – Encephalitis, Meningitis and Acute Retinal Necrosis

- TYSABRI increases the risk of developing encephalitis and meningitis caused by herpes simplex and varicella zoster viruses
- Serious, life-threatening, and sometimes fatal cases have been reported in the postmarketing setting in multiple sclerosis patients receiving TYSABRI
- The duration of treatment with TYSABRI prior to onset ranged from a few months to several years
- Monitor patients receiving TYSABRI for signs and symptoms of meningitis and encephalitis. If herpes encephalitis or meningitis occurs, TYSABRI should be discontinued, and appropriate treatment for herpes encephalitis/meningitis should be administered
- Patients being administered TYSABRI are at a higher risk of acute retinal necrosis (ARN), a fulminant viral infection of the retina caused by the family of herpes viruses. Patients with eye symptoms such as decreased visual acuity, redness or eye pain should be referred for retinal screening as serious cases of ARN can lead to blindness of one or both eyes
- Following clinical diagnosis of ARN, consider discontinuation of TYSABRI

Hepatotoxicity

- Clinically significant liver injury, including acute liver failure requiring transplant, has been reported in patients treated with TYSABRI in the postmarketing setting
- Signs of liver injury, including markedly elevated serum hepatic enzymes and elevated total bilirubin, occurred as early as six days after the first dose; signs of liver injury have also been reported for the first time after multiple doses
- TYSABRI should be discontinued in patients with jaundice or other evidence of significant liver injury (e.g., laboratory evidence)

Hypersensitivity/Antibody Formation

- Hypersensitivity reactions have occurred in patients receiving TYSABRI, including serious systemic reactions (e.g., anaphylaxis) which occurred at an incidence of <1%
- Reactions usually occur within 2 hours of the start of the infusion. Symptoms associated with these reactions can include urticaria, dizziness, fever, rash, rigors, pruritus, nausea, flushing, hypotension, dyspnea, and chest pain
- If a hypersensitivity reaction occurs, discontinue administration of TYSABRI and initiate appropriate therapy. Patients who experience a hypersensitivity reaction should not be re-treated with TYSABRI
- Hypersensitivity reactions were more frequent in patients with antibodies to TYSABRI compared with patients who did not develop antibodies to TYSABRI in both MS and CD studies
- Patients who receive TYSABRI for a short exposure (1 to 2 infusions) followed by an extended period without treatment are at higher risk of developing anti-natalizumab antibodies and/or hypersensitivity reactions on re-exposure, compared to patients who received regularly scheduled treatment

Immunosuppression/Infections

- The immune system effects of TYSABRI may increase the risk for infections
- In Study MS1, certain types of infections—including pneumonias and urinary tract infections (including serious cases), gastroenteritis, vaginal infections, tooth infections, tonsillitis, and herpes infections—occurred more often in TYSABRI-treated patients than in placebo-treated patients. One opportunistic infection, a cryptosporidial gastroenteritis with a prolonged course, was observed in a patient who received TYSABRI in Study MS1
- In Studies MS1 and MS2, an increase in infections was seen in patients concurrently receiving short courses of corticosteroids. However, the increase in infections in TYSABRI-treated patients who received steroids was similar to the increase in placebo-treated patients who received steroids
- In a long-term safety study of patients, opportunistic infections (pulmonary mycobacterium avium intracellulare, aspergilloma, cryptococcal fungemia and meningitis, and Candida pneumonia) have been observed in <1% of TYSABRI-treated patients
- Concurrent use of antineoplastic, immunosuppressant, or immunomodulating agents may further increase the risk of infections over

the risk observed with use of TYSABRI alone
- In Studies MS1 and MS2, the rate of any type of infection was approximately 1.5 per patient-year in both TYSABRI-treated patients and placebo-treated patients
- In Study MS1, the incidence of serious infections was approximately 3% in TYSABRI-treated patients and in placebo-treated patients. Most patients did not interrupt treatment with TYSABRI during infections

Laboratory Test Abnormalities

- In clinical trials, TYSABRI was observed to induce increases in circulating lymphocytes, monocytes, eosinophils, basophils, and nucleated red blood cells. Observed changes persisted during TYSABRI exposure, but were reversible, returning to baseline levels usually within 16 weeks after the last dose. Elevations of neutrophils were not observed. TYSABRI induces mild decreases in hemoglobin levels (mean decrease of 0.6 g/dL) that are frequently transient

Thrombocytopenia

- Cases of thrombocytopenia, including immune thrombocytopenic purpura (ITP), have been reported with the use of TYSABRI in the postmarketing setting. Symptoms of thrombocytopenia may include easy bruising, abnormal bleeding, and petechiae. Delay in the diagnosis and treatment of thrombocytopenia may lead to serious and life-threatening sequelae. If thrombocytopenia is suspected, TYSABRI should be discontinued
- Cases of neonatal thrombocytopenia, at times associated with anemia, have been reported in newborns with *in utero* exposure to TYSABRI. A CBC should be obtained in neonates with *in utero* exposure to TYSABRI

Adverse Reactions

- The most common adverse reactions reported at an incidence of ≥10% with TYSABRI and ≥2% difference with placebo were headache (38% vs 33%), fatigue (27% vs 21%), infusion reactions (24% vs 18%), urinary tract infections (21% vs 17%), arthralgia (19% vs 14%), depression (19% vs 16%), pain in extremity (16% vs 14%), rash (12% vs 9%), gastroenteritis (11% vs 9%), and vaginitis (10% vs 6%)
- The most frequently reported serious adverse reactions in Study MS1 were infections (3.2% vs 2.6% placebo), including urinary tract infection (0.8% vs 0.3%) and pneumonia (0.6% vs 0%), acute hypersensitivity reactions (1.1% vs 0.3%, including anaphylaxis/anaphylactoid reaction [0.8% vs 0%]), depression (1.0% vs 1.0%, including suicidal ideation or attempt [0.6% vs 0.3%]), and cholelithiasis (1.0% vs 0.3%)
- Based on animal data, TYSABRI may cause fetal harm. TYSABRI should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

Please see full Prescribing Information, including **Boxed Warning**.

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