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MSperceptions: Candid HCP/Patient Clinical Conversations about MS

Announcer:
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Dr. Barry Singer:
Hi everyone. I'm Dr. Barry Singer. I'm the director of the MS Center for Innovations and Care at Missouri Baptist Medical Center in St. Louis. Today I'll be talking with Dr. Jacqueline Nicholas, and Kim, a patient living with multiple sclerosis, about the mechanism of action of different treatment options for MS and their immunological impact. And then, we'll discuss mechanism of action, safety profile of TYSABRI. So, Dr. Nicholas, can you introduce yourself?

Dr. Jacqueline Nicholas:
Hi Dr. Singer. Thanks, I'd be happy to. So, I'm Dr. Jackie Nicholas, and I serve as the System Chief of Neuroimmunology and MS at the Ohio Health Multiple Sclerosis Center in Columbus, Ohio. I also direct the Research and Fellowship Programs in MS at Ohio Health. So, Kim, could you tell us a little bit about yourself?

Kim:
Hi Dr. Nicholas, it's nice to speak with you again. And Dr. Singer, it's so nice to meet you. My name is Kim, and I was diagnosed with MS seven years ago, and I'm happy to share my experience with you today.

Dr. Jacqueline Nicholas:
Thanks, Kim. We're glad to have you here and excited to hear what you have to share from a patient perspective. So, Dr. Singer, let's start off by talking about how we discuss mechanism of action and safety considerations of our MS disease-modifying therapies when talking to our patients in clinic.

Dr. Barry Singer:
Yeah, I think that's really great. One of the things that we have to do, first of all, is kind of explain what MS is, so that it is an autoimmune disease. And I like to talk about autoimmune diseases as immune system turning against the body. And we know in the case of multiple sclerosis, the immune system attacks the myelin, which is the coating that protects nerves in the central nervous system. So, I like to start off talking about the disease itself.

Dr. Jacqueline Nicholas:
Yeah, that's a great explanation and very similar to what I do. I oftentimes find it helpful when I'm explaining that to my patients to actually use a marker board and draw some pictures about how the immune system in people with MS attacks the central nervous system or the neurons within the brain and spinal cord, just like you described. And then I oftentimes will also draw how some of our disease-modifying therapies may work to treat MS by altering different aspects of the immune system. So, I'm curious to hear from you, Kim. When your physician or provider described how treatments for MS might work, how did they do that?

Kim:
Actually, when I was formally diagnosed with MS, my provider talked to me about how the immune system is altered in someone with MS, and how different classes of treatment for MS are thought to work through either modulating or depleting immune cells.

Dr. Barry Singer:

Yeah, that's really a great way of your provider, Kim, kind of explaining classes of medications. And typically, I talk about the disease-modifying therapies affecting MS through various ways. Some affect or modulate immune-cell trafficking. So, this is how cells move through the body. Some affect the functioning of immune cells in terms of how inflammatory they're going to be. Some prevent cells from replicating rapidly. And some actually destroy specific immune cells.

So, these interesting different mechanism of actions are important, and may not only just affect the efficacy of the medications, but also the risk of certain immune-related adverse events. And treatments may weaken immune response to infection or impact future considerations. An important aspect of DMTs is the long-term consequences for patients. And so, we have to kind of think about how that medication may affect you long-term, you know particularly with aging and family planning.

Dr. Jacqueline Nicholas:
Those are all certainly incredibly important points to discuss and consider when we're selecting DMTs for our patients. I also talk about mechanism of action in how it may relate to side effects and risks based on each individual disease-modifying therapy. And we talk about these benefits and risks together and find the choice that fits best for that individual patient. Now, this decision is really based on their disease course and also the individual's risk tolerance. And that certainly varies from individual to individual. For example, some of our treatments are associated with an increased risk of infection, and some with potential risk of malignancy. And so, for patients who are already at a higher risk for these issues, we might tend to discuss other options as being more favorable for them.

Dr. Barry Singer:
Yeah, I think it's really important to kind of personalize or tailor that treatment. And when we do that, we really have to think about what those risks are for that individual patient, and really kind of explain it to them so they have a good understanding, especially if a medication has an increased risk of serious infection or malignancy. So, Kim, if you don't mind sharing, you know, what concerns did your healthcare provider bring up with you when you were making a treatment decision?

Kim:
Sure. Infection was a big concern of mine since I frequently travel, so I spoke to my neurologist about the effects that different treatments have on my immune system. My neurologist explained that TYSABRI worked by blocking immune cells from entering the brain. Because of my background as a nurse, it was critical that I chose a treatment with strong efficacy data. So, my provider and I spoke about the benefits and the risks of treatment options available. I felt we made the right choice for me based on the information. And we decided on TYSABRI, and I've been on TYSABRI now for seven years.

Dr. Jacqueline Nicholas:
That's great. I'm so glad to hear your decision worked out so well for your MS. Let's talk a little bit more specifically about the mechanism of action and the safety profile of TYSABRI. When I talk to healthcare professionals about the mechanism of action of TYSABRI, I like to explain how it's believed to work. And we believe that TYSABRI binds to a receptor on the surface of lymphocytes, certain types of white blood cells, and that receptor is called the alpha 4 beta 1 integrin. And once TYSABRI binds that receptor, it blocks their migration across the blood–brain barrier. TYSABRI may also further inhibit recruitment and inflammatory activity of activated immune cells, which are believed to cause lesions associated with MS.

And when I talk to patients about the mechanism of TYSABRI, it's really not much different. I go back to that drawing board, and I explain how the binding of TYSABRI to the white blood cells themselves, the lymphocytes, takes away these lymphocytes' or white blood cells' key to be able to cross that blood–brain barrier. And so, they're not entering into the central nervous system. But a really important point that I share with my patients is that TYSABRI does not actually destroy or deplete white blood cells. It just takes away that key from allowing them to cross the blood–brain barrier. And that's why we think it has such an impact in MS.

Dr. Barry Singer:
Yeah, that's really a great explanation, Dr. Nicholas. And I also talk to my patients about trying to prevent these white blood cells from crossing the blood vessel wall and getting into the brain and spinal cord. And specifically, I talk about how TYSABRI binds onto these immune cells, which are a type of white blood cell called lymphocytes, and really prevents them from docking against the blood vessel wall. So really keeping them, locking them out, as you mentioned, outside of the brain and spinal cord.

Dr. Jacqueline Nicholas:
Yeah, absolutely. And you know in addition to mechanism of action, I think it's really important to discuss the effectiveness of this therapy with my patients. So certainly, I discuss this with many patients with MS, definitely with those who have active disease or those who are specifically interested in taking a high-efficacy therapy. We know that TYSABRI is a high-efficacy treatment. And when we look at data from the two-year AFFIRM pivotal trial, 83% of patients taking TYSABRI had no sustained disability progression for 12 weeks. And that was compared to 71% for those on placebo. In the same study, it was shown that there was a 67% relative reduction in annualized relapse rate with TYSABRI as compared to placebo. So, if we look at the annualized relapse rate for those on TYSABRI, it

was 0.22 versus 0.67 for those on placebo. And 97% of TYSABRI-treated patients did not have gadolinium-enhancing lesions on MRI in this study, as compared to 72% with placebo.

Dr. Barry Singer:
Yeah, Dr. Nicholas. Actually, I think that's a really important point that I bring up frequently in the clinic, is that 97% of the patients on TYSABRI did not show the active lesions on their MRI scan. And I think that's a strong consideration. So, let's turn this around, look at safety. So, what do you discuss with your patients about the safety when you prescribe TYSABRI?

Dr. Jacqueline Nicholas:
Yeah, so that's incredibly important. So, before I prescribe TYSABRI, we talk a lot about the safety profile. It's really important to talk about potential adverse events, including infections and potential hypersensitivity reaction, which were all reported in the AFFIRM trial. I also review that with TYSABRI, there is a boxed warning for PML, which we well are aware of in the neurology community that this is an opportunistic viral infection of the brain that can lead to death or severe disability. It's important though to understand as providers that there are risk factors on TYSABRI that can increase the risk of developing PML. And these are, if a patient has a positive anti-JC virus serum antibody test result, we look at the duration on therapy. So how long they've been on therapy can increase that risk. And also, we want to really understand if they've ever been on any prior medications that suppress the immune system, because prior immunosuppression in the patient can increase that risk of PML in TYSABRI-treated patients.

Now, if we break it down and we look at folks on TYSABRI who are JC virus antibody negative, the risk of developing PML is rare. So, it's actually one in 10,000, or 0.01%. And if we look at JC virus-positive patients, the risk does not exceed 0.7%, looking all the way out to eight years. Regardless of the JC virus status, the risk of developing PML is less than 1%. So, Dr. Singer, how do you talk to your patients about safety on TYSABRI?

Dr. Barry Singer:
Yeah, I think it's very important, as you mentioned, what the risk is of PML. So, patients definitely want to know about that. But they also want to know about my own personal experience in treating people with TYSABRI. And you know some of my patients have done exceptionally well for 15 years on the treatment. And so, I think I tend to highlight that we have a well understanding of the safety profile of this agent. And I think some of the real-world experience, in addition to the clinical trial experience, is important. One of the real-world studies, an observational study, is called TYGRIS. And it was a five-year observational study collected from 2207 real-world TYSABRI-treated MS patients in the US on long-term safety and clinical practice.

Dr. Jacqueline Nicholas:
Yeah, that's really interesting. Now, can you share with us a little more about the results of the TYGRIS study?

Dr. Barry Singer:
Yeah. Before I jump into that though, I should probably talk about some limitations of the study. As I mentioned, it was an observational study, so there was not randomization or placebo control group in the study. So, it may not be totally representative of the global MS population. And 24.1% of patients did withdraw from the study, so that may have led to some selection bias or underestimating the number of adverse events. In addition, a fixed dosing regimen was not required. Comorbidities were not assessed. In addition, the anti-JC virus antibody test was not available at the time TYGRIS was initiated.

But you know turning to the results from the US patients only, we found that 82.5% of patients had no serious adverse events. And there were low rates of opportunistic infection and malignancy over five years. And you know if you look at the rate of non-PML serious opportunistic infections, it was less than 0.1%, occurring in only two out of 2207 patients. And even the rate of PML was 0.1%, occurring in only three out of 2207 patients. In terms of malignancies, the rates were similar in the general US population and no relationship between treatment duration, malignancy incidence was observed in the TYSABRI cohort.

Dr. Jacqueline Nicholas:
That's really useful information, and definitely helps to put some of that risk into perspective. As an MS specialist, you know I think you'd agree it's incredibly important to educate our patients so they're aware of why we're doing the monitoring, and how it can help to maintain their safety.

Dr. Barry Singer:
Totally agree. And depending on the practice setting, monitoring protocols may vary. So how do you monitor your patients in your practice, Dr. Nicholas?

Dr. Jacqueline Nicholas:
Yeah. So, at our MS center, we have guidelines for lab work monitoring and MRI scan monitoring for patients with MS. And this is really based on each individual and their disease-modifying therapy that they're taking. But when we talk specifically about TYSABRI, the

recommendation is to do the JC virus antibody testing prior to initiation, and then every six months while patients are on treatment.

As a group at our center, we actually check the JC virus antibody every three months. That's been relatively easy, because that test is able to be drawn when patients come in for their infusion, that IV is being placed. And our infusion nurses actually just pull that blood sample off at the time of the IV placement, and we send that over to the lab. The nice thing is, that it comes back within our electronic medical record system so our patients can see it, and we also keep them up to date by letting them know when that returns, if that result alters their risk in any way of PML. And if it does, then we have a conversation about whether we recommend continuation, or if we need to talk about doing something different.

Now, I would also like to mention that I do have JC virus-positive patients with MS that I am comfortable treating with TYSABRI, and that's something that, you know, we regularly have a discussion about their risk. And many of these patients will continue on TYSABRI with continued close monitoring.

Now, I will mention that my center has a system of 12 infusion centers located throughout the state of Ohio. So, most patients can actually just visit a center to get their infusion close to home, and we receive those results directly in our office. And so, Dr. Singer, I'm curious what the monitoring process has been like for you at your center with TYSABRI.

Dr. Barry Singer:
Yeah. So similar to what you're doing, Dr. Nicholas. I think we have our own infusion center that's part of the hospital infusion center. And so, we have six chairs and two nurses that really help make sure that everything's moving smoothly. And you know really having great relationships with our patients is important, because they're coming in every month. So, they've developed great relationships with our nurses.

One of the things that we can do through the TOUCH program is use infusion centers that are not our own infusion center. And so, you do not need to be on staff at an infusion center. As long as they're in the TOUCH program, they can receive TYSABRI. This is a huge benefit for many of our rural patients. Some of them live three, four hours away. I saw patients from different states today. And so, they can go ahead and get their infusions locally, and I do not need to be on staff. So same thing for all of you out there. You can definitely get TYSABRI. And these rural patients should not be limited in terms of their access to very effective monoclonal antibody therapy.

Dr. Jacqueline Nicholas:
That's such a great point. And certainly, every practice is different, but I think you've made it really clear, Dr. Singer, that no matter your practice size or location, TYSABRI is very easily accessible to all patients through TOUCH infusion centers. And for us as providers, not having to be on staff is certainly a big advantage. So, I'm also glad you mentioned TOUCH Online. Just if you're not aware, it's a great resource to help assist with TOUCH prescribing program participants, and it helps to support safe administration of TYSABRI. So, through this program, it gives you real-time access to patient data for those on TYSABRI, including their JC virus status, and when they've received their infusions, and when they're due. But it also helps to reduce the administrative burden for healthcare professionals as well as infusion sites and helps to enhance that communication between the two. So, Kim, I'm curious. Since you've been on TYSABRI for seven years, what has that communication looked like between you and your provider regarding safety over time?

Kim:
Throughout my seven years on TYSABRI, I've kept communication very open with my provider on whether TYSABRI is still the right treatment choice for me, especially with all the new treatment options that are available now. I've questioned if TYSABRI was safe to use for more than two years, similar to what you both have just discussed. My provider reassured me that TYSABRI has real-world data with ongoing studies to support its long-term safety far beyond two years. And we talked about the number of people taking TYSABRI, including the number of side effects reported.

Because TYSABRI has continued to control my MS for over seven years and I have not experienced any noticeable side effects, I've not considered switching therapies. In addition to safety, my one-hour infusion means I can have it done over a lunch break. I don't have to take any pre-medications that would affect my ability to return to work on infusion days. So, when I'm done, I can go back to work and continue on with my day.

Dr. Barry Singer:
So, Kim, I'm really glad to hear that you've had a positive experience on TYSABRI. And I get similar comments from my patients about the one-hour infusion. In fact, there's been an update to the TYSABRI administration instructions, and it made it a lot easier. So, once you've received that 12th infusion, if you've not experienced any reactions, your provider may decide to shorten or even skip the observation period altogether. So as a long-time TYSABRI-treated patient, Kim, do you have any advice for providers on how to discuss things like the safety of TYSABRI with their patients?

Kim:

Based on my personal experience, I would recommend that providers who are discussing safety of DMTs with their patients consider the benefits relative to the potential risks. All treatments for MS have safety risks. In fact, everything in life has an inherent risk. But ask your patients to balance safety considerations with the importance of maintaining their health and preventing disease progression.

Dr. Jacqueline Nicholas:
That's very well said, Kim, and excellent advice. Thank you, Kim, and Dr. Singer, for this wonderful discussion today.

Dr. Barry Singer:
Yeah, it was really great talking to both of you. And hopefully all the healthcare providers out there listening to us learned a little bit more about TYSABRI, will consider it for the appropriate patients in their practice.

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**.

Announcer:
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