

INDICATION

TYSABRI® (natalizumab) is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. 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. See important information regarding the risk of PML with TYSABRI.

IMPORTANT SAFETY INFORMATION

WARNING

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 duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. 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.

Progressive Multifocal Leukoencephalopathy (PML)

- Infection by the JC Virus (JCV) is required for the development of PML.
- Anti-JCV antibody testing should not be used to diagnose PML.
- There are no known interventions that can reliably prevent PML or that can adequately treat PML if it occurs. It is not known whether early detection of PML and discontinuation of TYSABRI will mitigate the disease.

CANCEL AND QUIT

CONTINUE »

Adverse Reactions

- The most common adverse reactions reported at an incidence of $\geq 10\%$ with TYSABRI and $\geq 2\%$ 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%).
*Percentage based on female patients only.
- 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. If a woman becomes pregnant while taking TYSABRI, consider enrolling her in the TYSABRI Pregnancy Exposure Registry, by calling 1-800-456-2255.



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CANCEL AND QUIT

CONTINUE



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*Percentage based on female patients only.
- The most common serious adverse reactions reported with TYSABRI were infection (10%), infusion reaction (8%), anaphylaxis (4%), and cholestatic hepatitis (3%).
- Based on the potential for TYSABRI to cause serious adverse events, the manufacturer has recommended that TYSABRI be used only by healthcare professionals who have received special training in the safe use of TYSABRI.

CLOSE

You must read the **TYSABRI® (natalizumab) Important Safety Information** to continue.

CANCEL AND QUIT

READ TYSABRI ISI

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By clicking continue, I acknowledge that I have read and understand the **TYSABRI Important Safety Information**.

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- 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 approximately 6 months after discontinuation of TYSABRI.

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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 that are frequently transient.

Adverse Reactions

- The most common adverse reactions reported at an incidence of $\geq 10\%$ with TYSABRI and $\geq 2\%$ 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%).

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TYSABRI safely and effectively. See full prescribing information for TYSABRI.

TYSABRI (natalizumab) injection, for intravenous use

Initial U.S. Approval: 2004

WARNING: PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

See full prescribing information for complete boxed warning

- TYSABRI increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability (5.1)
- Risk factors for the development of PML include duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI (5.1)]
- Monitor patients, and withhold TYSABRI immediately at the first sign or symptom suggestive of PML (4, 5.1)
- TYSABRI is available only through a restricted distribution program called the TOUCH® Prescribing Program (5.1, 5.2)

RECENT MAJOR CHANGES

Warnings and Precautions

Boxed Warning	11/2013
Indications and Usage, Multiple Sclerosis (MS) (1.1)	11/2013
Progressive Multifocal Leukoencephalopathy (5.1)	11/2013
Herpes Encephalitis and Meningitis (5.3)	11/2013
Hepatotoxicity (5.4)	11/2013

INDICATIONS AND USAGE

TYSABRI is an integrin receptor antagonist indicated for treatment of:

Multiple Sclerosis (MS) (1.1)

- TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. 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 the risk of PML. See important information regarding the risk of PML with TYSABRI. [see Boxed Warning, Warnings and Precautions (5.1)].

Crohn's Disease (CD) (1.2)

- Inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate conventional CD

DOSAGE AND ADMINISTRATION

- 300 mg infused intravenously over approximately one hour, every four weeks. Do not give as an intravenous push or bolus (2.1, 2.2).
- TYSABRI solution must be administered within 8 hours of preparation (2.3).
- Observe patients during the infusion and for one hour after the infusion is complete (2.4).
- In CD, discontinue in patients that have not experienced therapeutic benefit by 12 weeks of induction therapy, and in patients that cannot discontinue chronic concomitant steroids within six months of starting therapy (2.2).

DOSAGE FORMS AND STRENGTH

- Solution [300 mg per 15 mL vial] for dilution prior to infusion (3).

CONTRAINDICATIONS

- Patients who have or have had PML (4).
- Patients who have had a hypersensitivity reaction to TYSABRI (4, 5.3).

WARNINGS AND PRECAUTIONS

- Herpes encephalitis and meningitis: Life-threatening and fatal cases have occurred. Discontinue TYSABRI if this occurs and treat appropriately (5.3).
- Hepatotoxicity: Significant liver injury, including liver failure requiring transplant, has occurred. Discontinue TYSABRI in patients with evidence of liver injury (5.4).
- Hypersensitivity reactions: Serious hypersensitivity reactions (e.g., anaphylaxis) have occurred. Permanently discontinue TYSABRI if such a reaction occurs (5.5).
- Immunosuppression/Infections: TYSABRI may increase the risk for certain infections. Monitor patients for development of infections due to increased risk with use of TYSABRI (5.6).

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥ 10%) in MS were headache, fatigue, arthralgia, urinary tract infection, lower respiratory tract infection, gastroenteritis, vaginitis, depression, pain in extremity, abdominal discomfort, diarrhea NOS, and rash; and in CD were headache, upper respiratory tract infections, nausea, and fatigue (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Biogen Idec at 1-800-456-2255 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 11/2013

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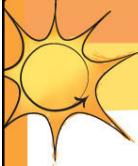
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Tap to collapse

▼ Indication

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Healthcare professionals should monitor patients on TYSABRI for any new sign or symptom that may be

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Tap to collapse

► Indication

▼ Important Safety Information (ISI)

TOUCH Prescribing Program.

Progressive Multifocal
Leukoencephalopathy (PML)

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- Anti-JCV antibody testing should not be used to diagnose PML.
- There are no known interventions that can reliably prevent PML or that can adequately treat PML if it occurs. It is not known whether early detection of PML and discontinuation of TYSABRI will mitigate the disease.
- 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 approximately 6 months after discontinuation of TYSABRI.
- In MS patients, an MRI scan should be obtained before initiating therapy with TYSABRI. This MRI may be helpful in differentiating subsequent multiple sclerosis symptoms from PML.

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- In MS patients, an MRI scan should be obtained before initiating therapy with TYSABRI. This MRI may be helpful in differentiating subsequent multiple sclerosis symptoms from PML.
- Three sessions of plasma exchange over the course of 5 to 8 days were shown to accelerate TYSABRI clearance in a study of 12 patients with MS who did not have PML, although in the majority of patients, alpha-4 integrin receptor binding remained high. Adverse events that may occur during plasma exchange include clearance of other medications and volume shifts, which have the potential to lead to hypotension or pulmonary edema. Although plasma exchange has not been 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.
- Anti-JCV antibody testing should not be performed during, or for at least 2 weeks after, plasma exchange because of the removal of antibodies from the serum.
- 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 plasma exchange 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 plasma exchange. 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 should not be administered to a patient who has had a hypersensitivity reaction to TYSABRI.

Prescribing Program.

- For prescribers and patients, the TOUCH Prescribing Program has two components: MS TOUCH® (for patients with multiple sclerosis) and CD TOUCH® (for patients with Crohn's disease).
- Prescribers must be certified and must comply with the following:
 - Review the TOUCH Prescribing Program prescriber educational materials, including the Full Prescribing Information.
 - Educate patients on the benefits and risks of treatment with TYSABRI, ensure that patients receive the Medication Guide, and encourage them to ask questions.
 - Review, complete, and sign the Patient-Prescriber Enrollment Form.
 - Evaluate patients 3 months after the first infusion, 6 months after the first infusion, every 6 months thereafter, and for at least 6 months after discontinuing TYSABRI.
 - Determine every 6 months whether patients should continue on treatment, and if so, authorize treatment for another 6 months.
 - Submit to Biogen Idec the "TYSABRI Patient Status Report and Reauthorization Questionnaire" 6 months after initiating treatment and every 6 months thereafter.
 - Complete an "Initial Discontinuation Questionnaire" when TYSABRI is discontinued, and complete a "6-Month Discontinuation Questionnaire" after discontinuation of TYSABRI.
 - Report cases of PML, hospitalizations due to opportunistic infections, or deaths to Biogen Idec at 1-800-456-2255 and to the Food and Drug Administration's MedWatch Program at 1-800-FDA-1088 as soon as possible.
- 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.
- To dispense or infuse TYSABRI, pharmacies and infusion centers must be specially certified.

Herpes Encephalitis and Meningitis

- 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.
- 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.

Hepatotoxicity

- Clinically significant liver injury, including acute liver failure requiring transplant, has been reported in patients treated with TYSABRI in the postmarketing setting. In some patients, liver injury recurred upon rechallenge, providing evidence that TYSABRI caused the injury.
- The combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that may lead to death or the need for a liver transplant in some patients.
- 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. Generally, these reactions are associated with antibodies to TYSABRI.
- 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 after an extended period without treatment may be at higher risk of hypersensitivity reactions.

Immunosuppression/Infections

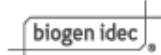
- The immune system effects of TYSABRI may increase the risk for infections.
- In Study MS1, certain types of infections—including pneumonias and urinary tract infections (including serious cases), gastroenteritis, vaginal infections, tooth infections, tonsillitis, and herpes infections—occurred more 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.
- Concurrent use of antineoplastic, immunosuppressant, or immunomodulating agents may further increase the risk of infections over the risk observed with use of TYSABRI alone. The safety and efficacy of TYSABRI in combination with antineoplastic, immunosuppressant, or immunomodulating agents have not been established.
- 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.
- In postmarketing experience, serious herpes infections have occurred.

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 that are frequently transient.

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%).
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Progressive Multifocal Leukoencephalopathy (5.1)	11/2013
Herpes Encephalitis and Meningitis (5.3)	11/2013
Hepatotoxicity (5.4)	11/2013

INDICATIONS AND USAGE

TYSABRI is an integrin receptor antagonist indicated for treatment of:

Multiple Sclerosis (MS) (1.1)

- TYSABRI is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. 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 the risk of PML. See important information regarding the risk of PML with TYSABRI [see Boxed Warning, Warnings and Precautions (5.1)].

Crohn's Disease (CD) (1.2)

- Inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate conventional CD therapies and inhibitors of TNF-α.

Important Limitations:

- In CD, TYSABRI should not be used in combination with immunosuppressants or inhibitors of TNF-α.

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

1 INDICATIONS AND USAGE

- 1.1 Multiple Sclerosis (MS)
- 1.2 Crohn's Disease (CD)

2 DOSAGE AND ADMINISTRATION

- 2.1 Multiple Sclerosis
- 2.2 Crohn's Disease
- 2.3 Preparation Instructions
- 2.4 Administration Instructions

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Progressive Multifocal Leukoencephalopathy (PML)
- 5.2 Distribution Program for TYSABRI
- 5.3 Herpes Encephalitis/Meningitis
- 5.4 Hepatotoxicity
- 5.5 Hypersensitivity/Antibody Formation
- 5.6 Immunosuppression/Infections
- 5.7 Laboratory Test Abnormalities
- 5.8 Immunizations

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Immunogenicity
- 6.3 Postmarketing Experience

7 DRUG INTERACTIONS

DOSAGE AND ADMINISTRATION

- 300 mg infused intravenously over approximately one hour, every four weeks. Do not give as an intravenous push or bolus (2.1, 2.2).
- TYSABRI solution must be administered within 8 hours of preparation (2.3).
- Observe patients during the infusion and for one hour after the infusion is complete (2.4).
- In CD, discontinue in patients that have not experienced therapeutic benefit by 12 weeks of induction therapy, and in patients that cannot discontinue chronic concomitant steroids within six months of starting therapy (2.2).

DOSAGE FORMS AND STRENGTH

- Solution [300 mg per 15 mL vial] for dilution prior to infusion (3).

CONTRAINDICATIONS

- Patients who have or have had PML (4).
- Patients who have had a hypersensitivity reaction to TYSABRI (4, 5.3).

WARNINGS AND PRECAUTIONS

- Herpes encephalitis and meningitis: Life-threatening and fatal cases have occurred. Discontinue TYSABRI if this occurs and treat appropriately (5.3).
- Hepatotoxicity: Significant liver injury, including liver failure requiring transplant, has occurred. Discontinue TYSABRI in patients with evidence of liver injury (5.4).
- Hypersensitivity reactions: Serious hypersensitivity reactions (e.g., anaphylaxis) have occurred. Permanently discontinue TYSABRI if such a reaction occurs (5.5).
- Immunosuppression/Infections: TYSABRI may increase the risk for certain infections. Monitor patients for development of infections due to increased risk with use of TYSABRI (5.6).

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥ 10%) in MS were headache, fatigue, arthralgia, urinary tract infection, lower respiratory tract infection, gastroenteritis, vaginitis, depression, pain in extremity, abdominal discomfort, diarrhea NOS, and rash; and in CD were headache, upper respiratory tract infections, nausea, and fatigue (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Biogen Idec at 1-800-456-2255 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm. (8.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 11/2013

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility
- 13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

- 14.1 Multiple Sclerosis
- 14.2 Crohn's Disease

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the Full Prescribing Information are not listed.

MS ISN'T WAITING...

...and NEITHER AM I

NOW IS THE TIME

EVERY 4 WEEKS 300mg IV

TYSABRI®
(natalizumab)

Realize the potential

Jun 25, 2013 4:41 PM

Ver. 0.10

page

2

▼ Indication

TYSABRI® (natalizumab) is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. 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. See important information regarding the risk of PML with TYSABRI.

▼ Important Safety Information (ISI)

WARNING

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 duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. 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

ISI

PI

REF

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Important Safety Information (ISI)

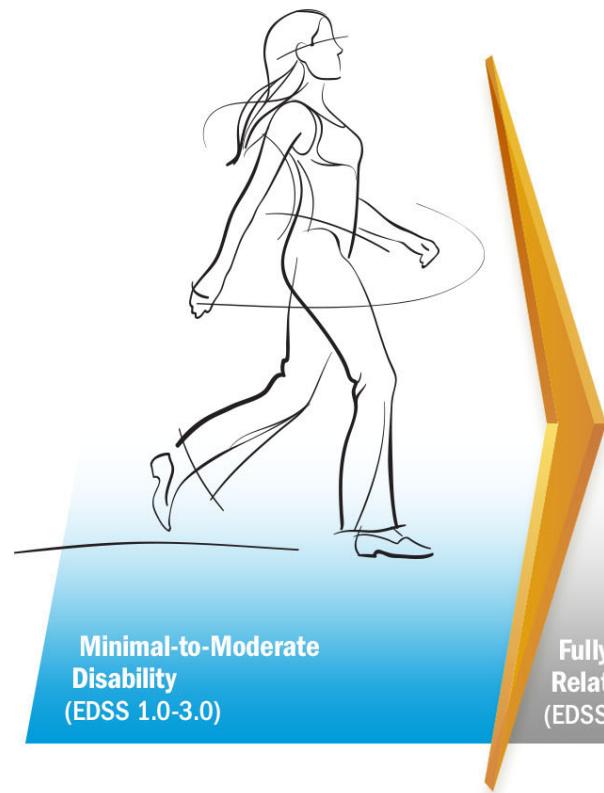
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ISI PI REF



SHE MAY SEEM ACTIVE NOW, BUT: HER RISK OF PROGRESSING MAY BE HIGHER THAN EXPECTED



Even 1 additional relapse in the first **2** years may **accelerate** disability progression¹

- Almost **1/2** of relapses result in an increase in **residual disability**²

EDSS scale³



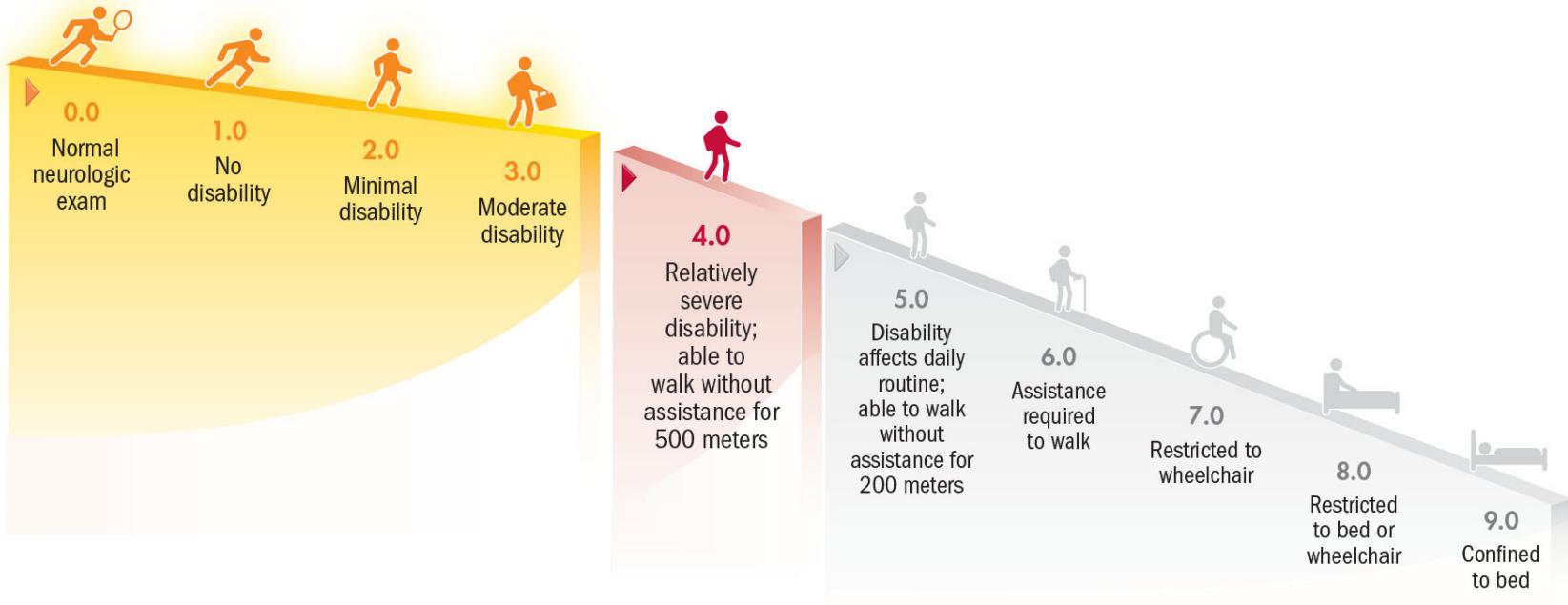
ISI

PI

REF

EXPANDED DISABILITY STATUS SCALE (EDSS)³

CLOSE 



EDSS scale³



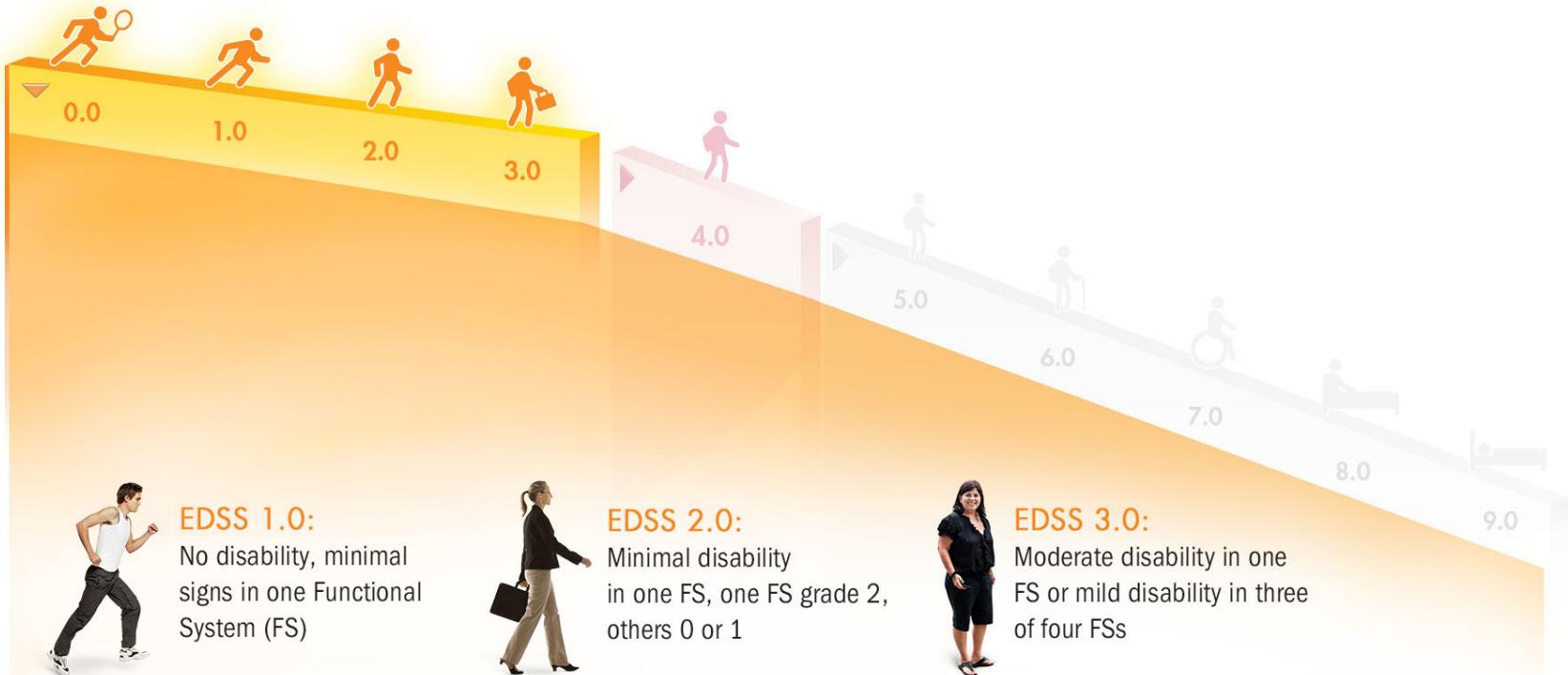
ISI

PI

REF

EXPANDED DISABILITY STATUS SCALE (EDSS)³

CLOSE 



Minimal-to-Moderate Disability (EDSS 1.0-3.0)³

EDSS scale³



ISI

PI

REF

EXPANDED DISABILITY STATUS SCALE (EDSS)³

CLOSE 



Fully Ambulatory Despite Severe Disability (EDSS 4.0)³

EDSS scale³



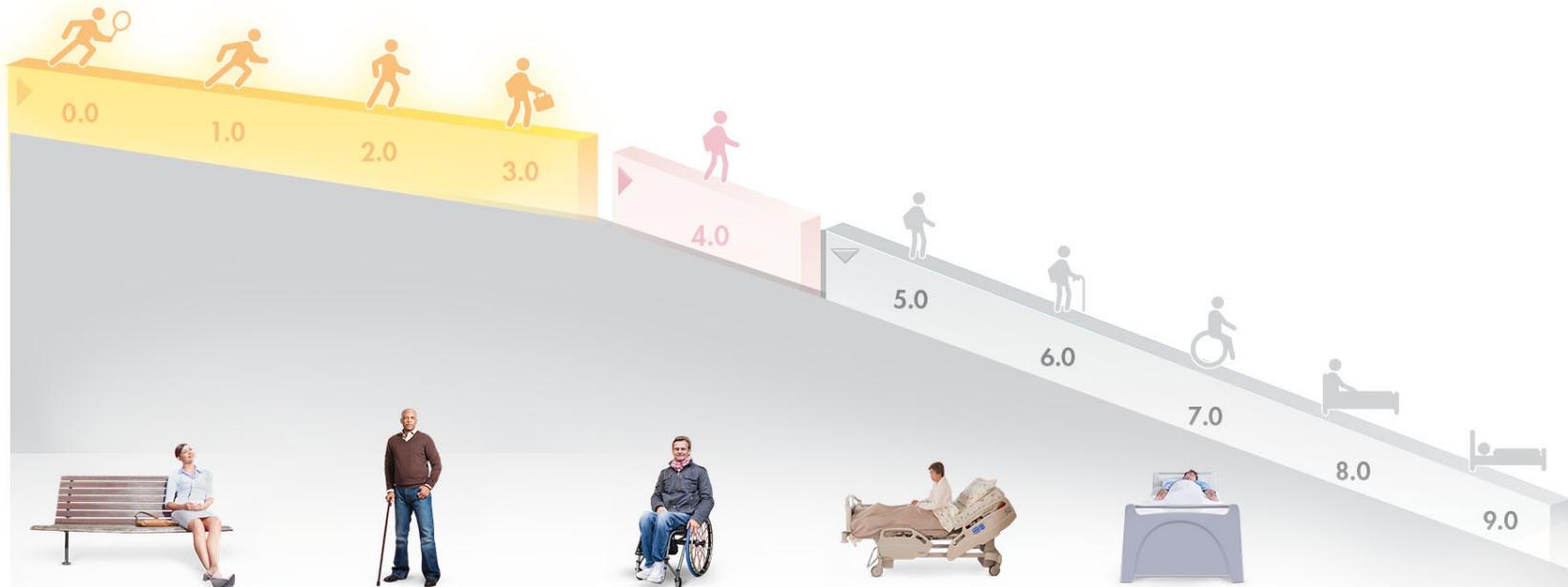
ISI

PI

REF

EXPANDED DISABILITY STATUS SCALE (EDSS)³

CLOSE 



EDSS 5.0:
Disability affects daily
routine; able to walk
without assistance
for 200 meters

EDSS 6.0:
Assistance required
to walk

EDSS 7.0:
Restricted to
wheelchair

EDSS 8.0:
Restricted to
bed or chair

EDSS 9.0:
Confined to bed

Loss of Ambulation, Full Daily Activities Impaired (EDSS 5.0-9.0)³

EDSS scale³



ISI

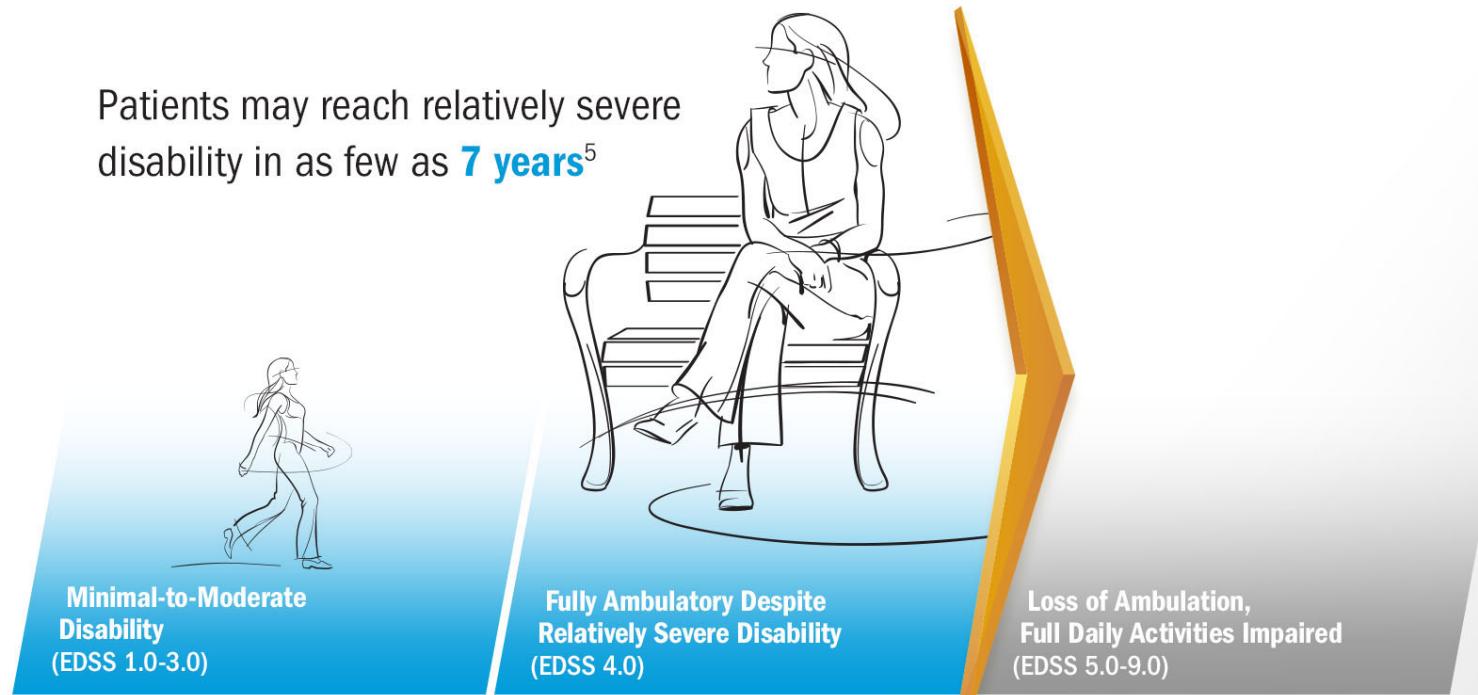
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HER RISK OF PROGRESSING: MS IS THE LEADING CAUSE OF NONTRAUMATIC, YOUNG-ADULT DISABILITY⁴

Patients may reach relatively severe disability in as few as **7 years**⁵



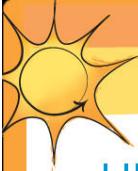
EDSS scale³



ISI

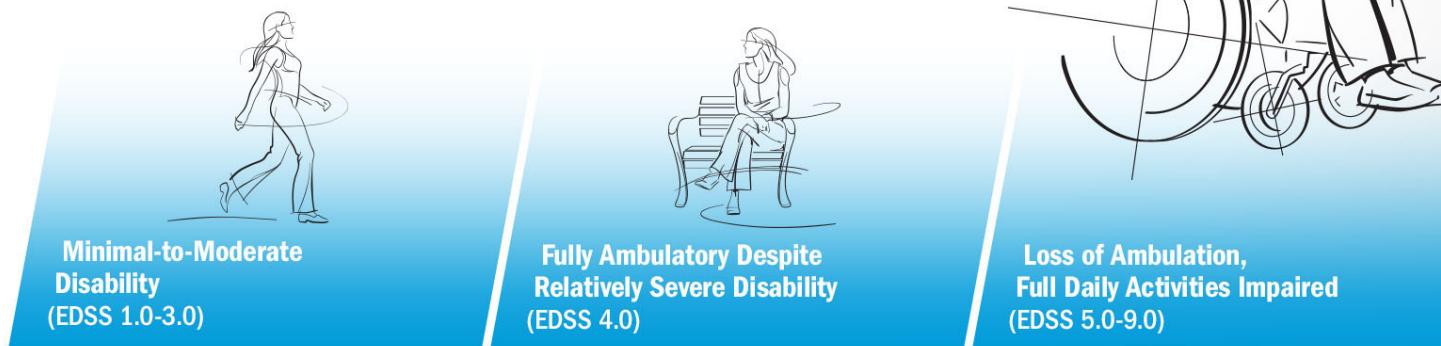
PI

REF



HER RISK OF PROGRESSING: A RAPID INCREASE IS SEEN ONCE MODERATE DISABILITY IS REACHED

Once an **EDSS** of **4.0** is reached,
more rapid-loss of ambulation and
impairment of daily activity are likely²



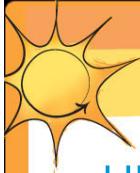
EDSS scale³



ISI

PI

REF



HER RISK OF PROGRESSING: A RAPID INCREASE IS SEEN ONCE MODERATE DISABILITY IS REACHED



Minimal-to-Moderate
Disability
(EDSS 1.0-3.0)



Fully Ambulatory Despite
Relatively Severe Disability
(EDSS 4.0)



Loss of Ambulation,
Full Daily Activities Impaired
(EDSS 5.0-9.0)



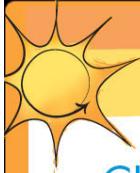
EDSS scale³



ISI

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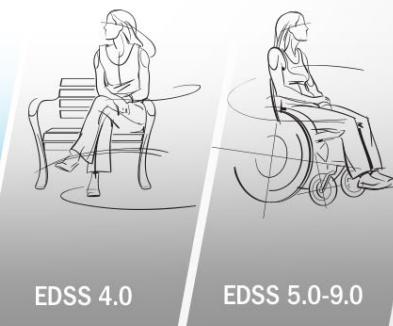
CLOSELY MONITOR THE SMALLER CHANGES SHE'S MAKING NOW: DELAY FUTURE DISABILITY PROGRESSION



Minimal-to-Moderate
Disability
(EDSS 1.0-3.0)

EDSS scale³

The Leray article suggests:
There may be a **therapeutic
window of opportunity**
in **optimizing** treatment⁶



ISI

PI

REF



RELAPSING MS PATIENTS CAN
**BENEFIT FROM THE POWERFUL EFFICACY
OF TYSABRI FROM THE START**



In the AFFIRM study

42%

relative reduction
in the risk of
increased
physical disability
sustained for
12 weeks
vs placebo
(0.17 vs 0.29)^{7,8}

In the AFFIRM study

67%

relative reduction
in annualized
relapse rate
at 2 years
vs placebo
(0.22 vs 0.67)⁷

In the AFFIRM study

92%

relative reduction
in the mean
number of
Gd+ lesions
at 2 years
vs placebo
(0.1 vs 1.2)⁸

83% OF PATIENTS HAD NO SUSTAINED PHYSICAL DISABILITY PROGRESSION AT 2 YEARS VS **71%** OF PLACEBO PATIENTS
($P<0.001$)⁷

Proven experience with >7 years of clinical use⁹

>1.5 million infusions have been administered in the US alone,
representing more than 115,000 patient-years of experience⁹

- You know your patients are **seen by an HCP each month** at their infusions

Risk of TYSABRI and PML

- TYSABRI® (natalizumab) increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability

Expand ISI for additional risk information.

Tap to expand

- Indication
- Important Safety Information (ISI)

ISI

PI

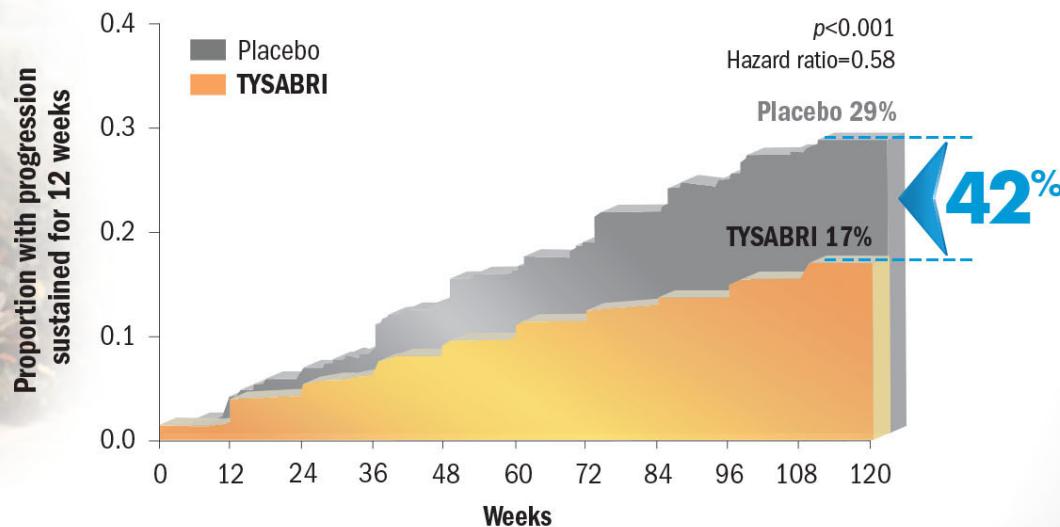
REF



NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI



Significant relative reduction in sustained physical disability in the AFFIRM Study^{7,8}



Risk of TYSABRI and PML (cont'd)

- Risk factors for the development of PML include duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI

Expand ISI for additional risk information.

Patient Characteristics ^{7,9}	In the AFFIRM trial...	Tap to expand
The AFFIRM Study ^{7,8}	AFFIRM (Natalizumab Safety and Efficacy in Relapsing-Remitting MS)...	Tap to expand
2-year Endpoint ^{7,9}	The primary endpoint at 2 years was time to onset of sustained increase in...	Tap to expand

Tap to expand

► Indication

► Important Safety Information (ISI)

ISI

PI

REF



NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI



Significant relative reduction in sustained physical disability in the AFFIRM Study^{7,8}



Patient Characteristics⁷⁻⁹

In the AFFIRM trial, baseline patient characteristics included:

- ~94% of overall patients who entered the study were treatment-naïve to the disease-modifying therapies interferon-beta and glatiramer acetate
 - Patients enrolled did not receive any interferon-beta or glatiramer acetate for at least the previous 6 months prior to study entry
- Median disease duration of 5 years
- Median age of 37
- Mean EDSS score of 2.3
- ~70% of patients had ≤ 1 Gd+ lesion at baseline

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and Efficacy in Relapsing-Remitting MS)...

Tap to expand

2-year Endpoint^{7,9}

The primary endpoint at 2 years was time to onset of sustained increase in...

Tap to expand

Tap to expand

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ISI

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NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI



Significant relative reduction in sustained physical disability in the AFFIRM Study^{7,8}



Patient Characteristics^{7,9}

In the AFFIRM trial...

[Tap to expand](#)

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFicacy in Relapsing-Remitting MS)

- Pivotal 2-year, double-blind, randomized controlled trial
- 942 RRMS patients randomized to receive either:
 - TYSABRI monotherapy (300 mg by intravenous infusion [n=627]) or placebo (n=315)
- Infusions administered every 4 weeks for up to 28 months (30 infusions)

2-year Endpoint^{7,9}

The primary endpoint at 2 years was time to onset of sustained increase in...

[Tap to expand](#)

[Tap to expand](#)

► Indication

► Important Safety Information (ISI)

ISI

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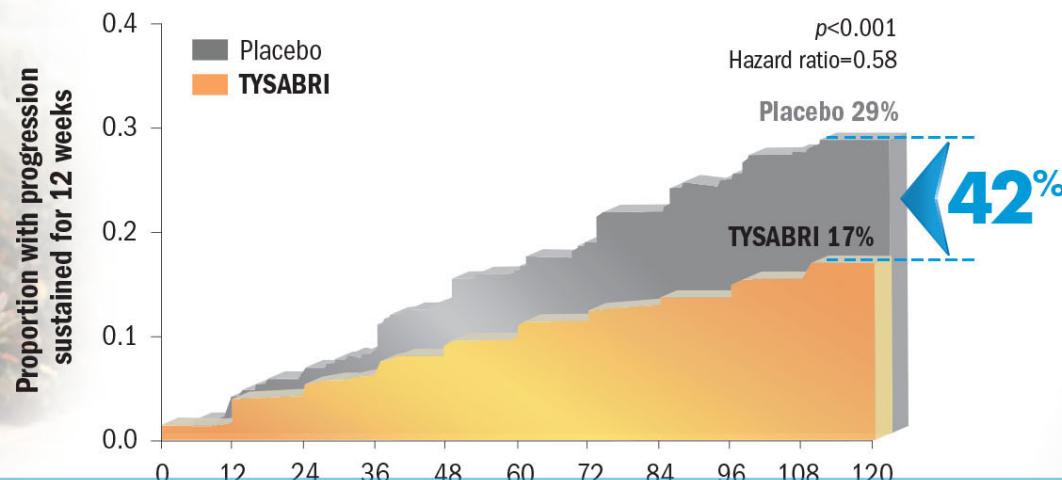
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Significant relative reduction in sustained physical disability in the AFFIRM Study^{7,8}



Patient Characteristics^{7,9}

In the AFFIRM trial, baseline patient characteristics included:

[Tap to expand](#)

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFicacy in Relapsing-Remitting MS)...

[Tap to expand](#)

2-year Endpoint^{7,9}

The primary endpoint at 2 years was time to onset of sustained increase in disability, defined as:

- An increase of ≥ 1.0 point on the EDSS from baseline EDSS ≥ 1.0 that was sustained for 12 weeks
- An increase of ≥ 1.5 points on the EDSS from baseline EDSS=0 that was sustained for 12 weeks

Increase excluded disability confirmation within 30 days of relapse.

[Tap to expand](#)

► Indication

► Important Safety Information (ISI)



ISI

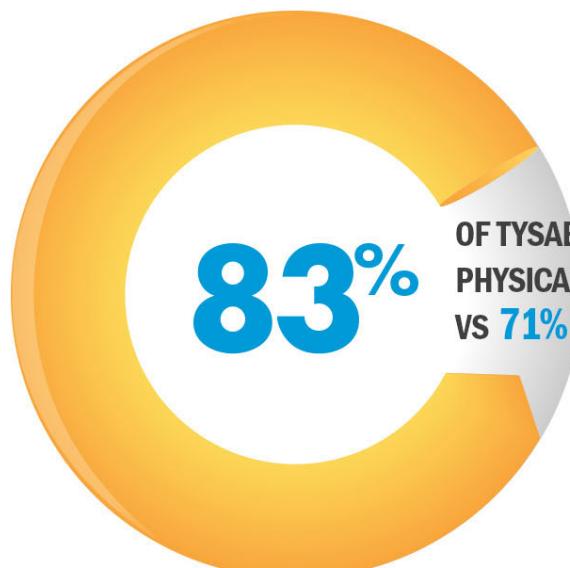
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REF



NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI

The majority of patients demonstrated no sustained disability progression⁷



OF TYSABRI PATIENTS HAD NO SUSTAINED
PHYSICAL DISABILITY PROGRESSION AT 2 YEARS
VS 71% OF PLACEBO PATIENTS ($P<0.001$)⁷



Patient Characteristics⁷⁻⁹

In the AFFIRM trial, baseline patient characteristics included:

[Tap to expand](#)

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFicacy in Relapsing-Remitting MS)...

[Tap to expand](#)

2-year Endpoint^{7,9}

The primary endpoint at 2 years was time to onset of sustained increase in

[Tap to expand](#)



Risk of TYSABRI and PML (cont'd)

- Risk factors for the development of PML include duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI

Expand ISI for additional risk information.

[Tap to expand](#)

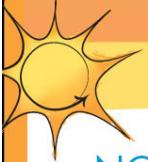
► **Indication**

► **Important Safety Information (ISI)**

ISI

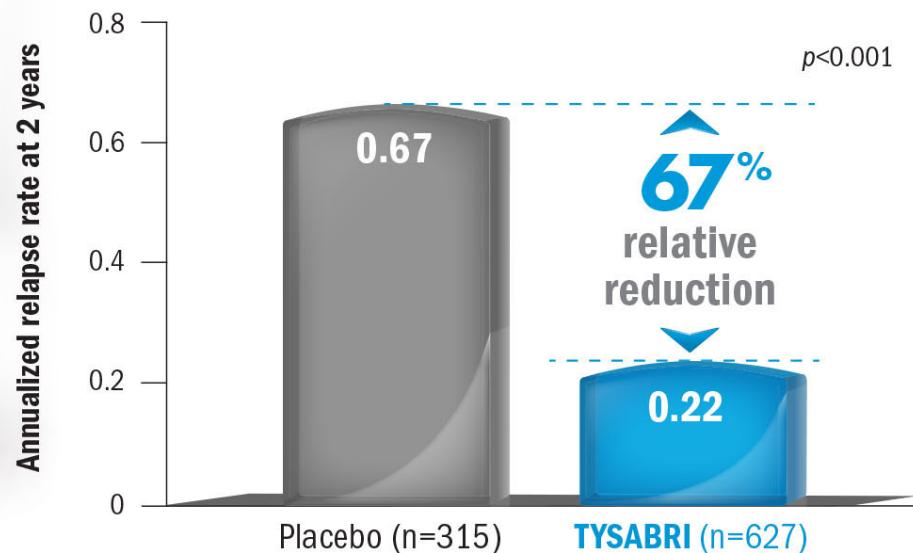
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NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI®

Significant relative reduction in annualized relapse rate in the AFFIRM Study⁷



Patient Characteristics^{7,9}

In the AFFIRM trial...

[Tap to expand](#)

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFIcacy in Relapsing-Remitting MS)...

[Tap to expand](#)



Tap to expand

► Indication

► Important Safety Information (ISI)

ISI

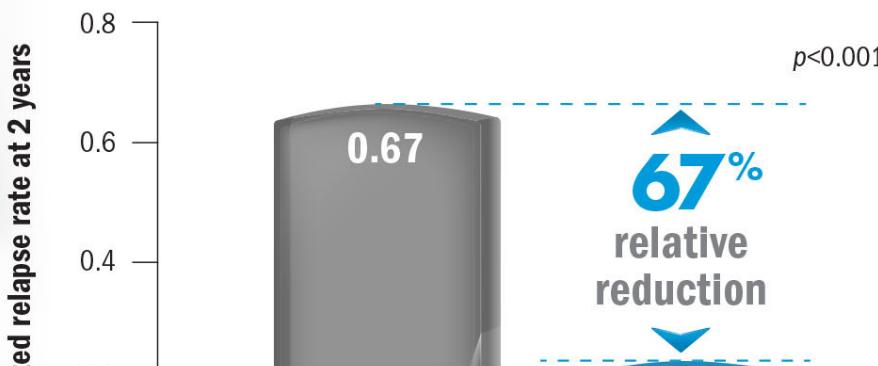
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Patient Characteristics^{7,9}

In the AFFIRM trial, baseline patient characteristics included:

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- Median age of 37
- Mean EDSS score of 2.3
- ~70% of patients had ≤1 Gd+ lesion at baseline

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and Efficacy in Relapsing-Remitting MS)...

[Tap to expand](#)



Tap to expand

► Indication

► Important Safety Information (ISI)

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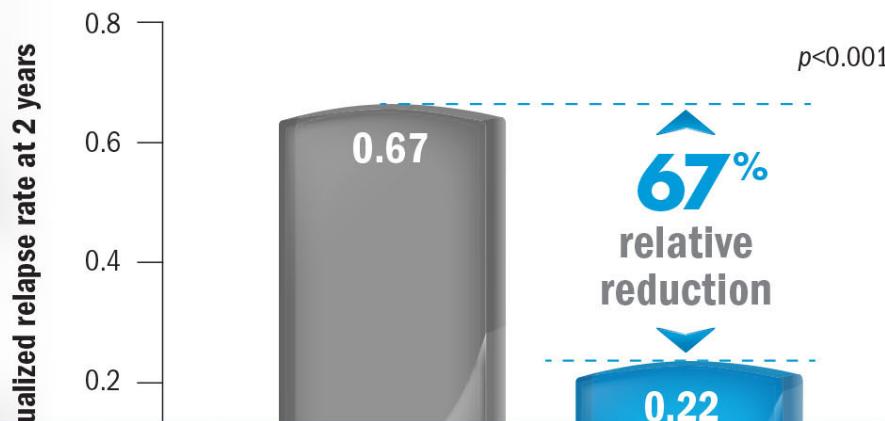
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NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI®

Significant relative reduction in annualized relapse rate in the AFFIRM Study⁷



Risk of TYSABRI and PML (cont'd)

- 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

Patient Characteristics⁷⁻⁹

In the AFFIRM trial...

Tap to expand

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFicacy in Relapsing-Remitting MS)

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- Infusions administered every 4 weeks for up to 28 months (30 infusions)

Tap to expand

► Indication

► Important Safety Information (ISI)

ISI

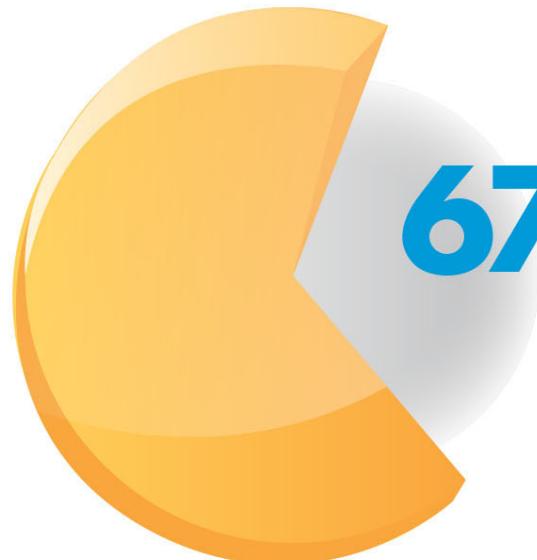
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NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI

The majority of patients demonstrated no relapse activity⁷



67% OF TYSABRI PATIENTS WERE FREE
OF RELAPSE AT 2 YEARS VS
41% OF PLACEBO PATIENTS (P<0.001)⁷



Risk of TYSABRI and PML (cont'd)

- 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

Expand ISI for additional risk information.

Tap to expand

- Indication
- Important Safety Information (ISI)

ISI

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Patient Characteristics^{7,9}

In the AFFIRM trial...

[Tap to expand](#)

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFIcacy in Relapsing-Remitting MS)...

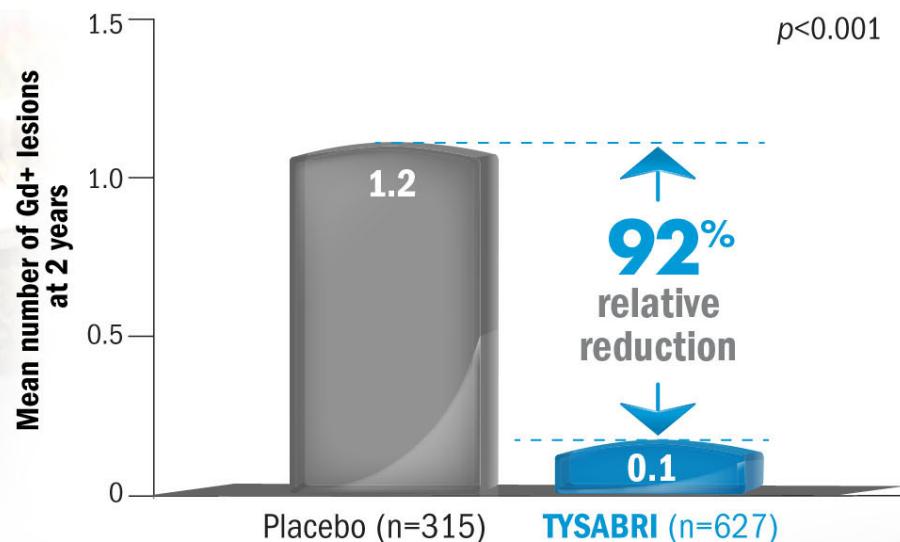
[Tap to expand](#)





NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI

Significant relative reduction in Gd+ lesions at 2 years in the AFFIRM Study⁸



Patient Characteristics^{7,9}

In the AFFIRM trial...

[Tap to expand](#)

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFIcacy in Relapsing-Remitting MS...)

[Tap to expand](#)



Changes in MRI findings often do not correlate with changes in the clinical status of patients (e.g., disability progression). The prognostic significance of these MRI findings has not been evaluated.⁷

Risk of TYSABRI and PML (cont'd)

- 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

Expand ISI for additional risk information.

Tap to expand

► **Indication**

► **Important Safety Information (ISI)**

ISI

PI

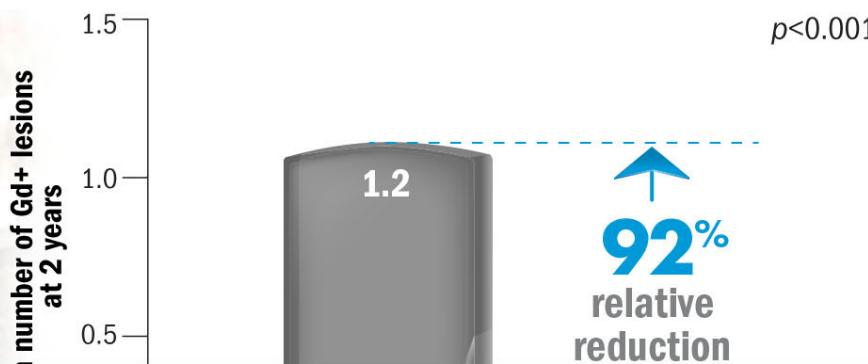
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NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI



Significant relative reduction in Gd+ lesions at 2 years in the AFFIRM Study⁸



Patient Characteristics^{7,9}

In the AFFIRM trial, baseline patient characteristics included:

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- Mean EDSS score of 2.3
- ~70% of patients had ≤1 Gd+ lesion at baseline

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and Efficacy in Relapsing-Remitting MS...)

Tap to expand



Risk of TYSABRI and PML (cont'd)

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

Tap to expand

► Indication

► Important Safety Information (ISI)

ISI

PI

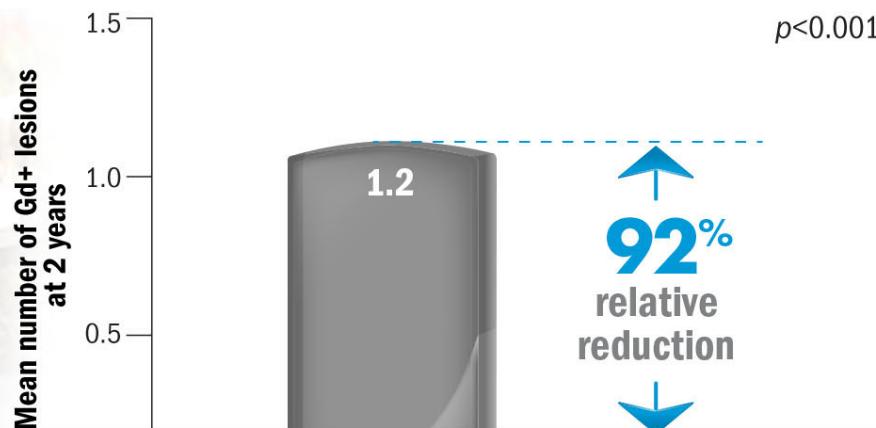
REF



NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI



Significant relative reduction in Gd+ lesions at 2 years in the AFFIRM Study⁸



Patient Characteristics^{7,9}

In the AFFIRM trial...

Tap to expand

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and Efficacy in Relapsing-Remitting MS)

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Tap to expand

► Indication

► Important Safety Information (ISI)

ISI

PI

REF



NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI

The majority of patients demonstrated no Gd+ MRI activity⁷



OF TYSABRI PATIENTS WERE
FREE OF GD+ LESIONS AT 2 YEARS
VS 72% OF PLACEBO
PATIENTS ($P<0.001$)⁷

Patient Characteristics^{7,9}

In the AFFIRM trial...

[Tap to expand](#)

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFIcacy in Relapsing-Remitting MS...)

[Tap to expand](#)



Risk of TYSABRI and PML (cont'd)

- 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

Expand ISI for additional risk information.

Tap to expand

► [Indication](#)

► [Important Safety Information \(ISI\)](#)

ISI

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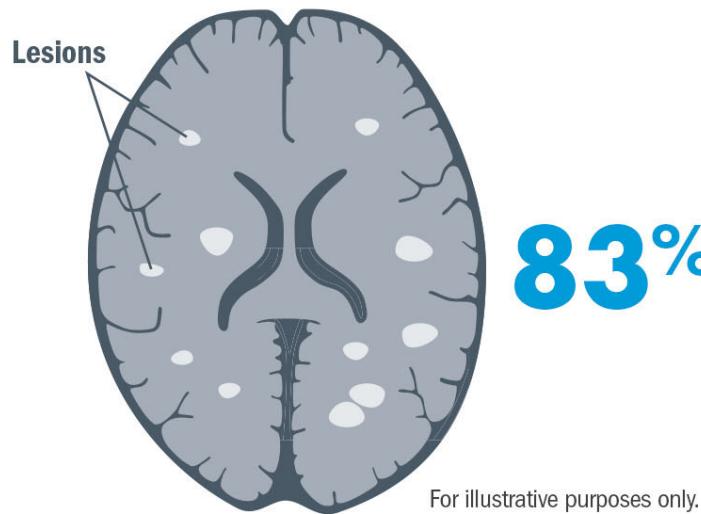
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NOW IS THE TIME TO CONSIDER THE POWERFUL EFFICACY OF TYSABRI



Significant relative reduction in T2 lesions at 2 years in the AFFIRM study^{8,9}



83% RELATIVE REDUCTION IN THE MEAN
NUMBER OF NEW OR ENLARGING
T2-HYPERINTENSE LESIONS AT 2 YEARS
($P<0.001$)^{8,9}

Placebo

TYSABRI

Patient Characteristics^{7,9}

In the AFFIRM trial...

[Tap to expand](#)

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFIcacy in Relapsing-Remitting MS)...

[Tap to expand](#)



Tap to expand

► Indication

► Important Safety Information (ISI)

ISI

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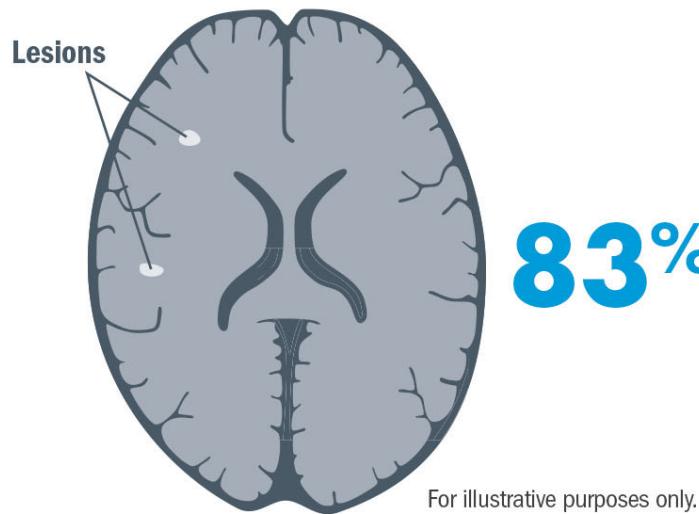
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Patient Characteristics^{7,9}

In the AFFIRM trial...

[Tap to expand](#)

The AFFIRM Study^{7,8}

AFFIRM (Natalizumab Safety and EFFicacy in Relapsing-Remitting MS...)

[Tap to expand](#)



Tap to expand

► Indication

► Important Safety Information (ISI)

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REF



REALIZE THE IMPACT ON TRADITIONAL SIGNS OF DISEASE ACTIVITY

Significant efficacy: impact of TYSABRI at 2 years

NO SUSTAINED PHYSICAL DISABILITY PROGRESSION

in **83%** of TYSABRI patients vs **71%** of placebo patients ($p<0.001$)⁷

NO RELAPSES

in **67%** of TYSABRI patients vs **41%** of placebo patients ($p<0.001$)⁷

MRI activity: impact at 2 years

NO NEW OR ENLARGING GD+ LESIONS

in **97%** of TYSABRI patients vs **72%** of placebo patients ($p<0.001$)⁷

NO NEW OR ENLARGING T2-HYPERINTENSE LESIONS

in **57%** of TYSABRI patients vs **15%** of placebo patients ($p<0.001$)⁷

Changes in MRI findings often do not correlate with changes in the clinical status of patients (e.g., disability progression). The prognostic significance of these MRI findings has not been evaluated.



TYSABRI is contraindicated in

- Patients who have or have had PML
- Patients who have had a hypersensitivity reaction to TYSABRI

Expand ISI for additional risk information.

The AFFIRM Study^{7,8}

AFFIRM (NAtalizumab Safety and EFFIcacy in Relapsing-Remitting MS)...

[Tap to expand](#)

Tap to expand

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► Important Safety Information

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- Patients who have or have had PML
- Patients who have had a hypersensitivity reaction to TYSABRI

Expand ISI for additional risk information.

The AFFIRM Study^{7,8}

AFFIRM (NAtalizumab Safety and EFFIcacy in Relapsing-Remitting MS)

- Pivotal 2-year, double-blind, randomized controlled trial
- 942 RRMS patients randomized to receive either:
 - TYSABRI monotherapy (300 mg by intravenous infusion [$n=627$]) or placebo ($n=315$)
- Infusions administered every 4 weeks for up to 28 months (30 infusions)

Tap to expand

- Indication
► Important Safety Information

ISI

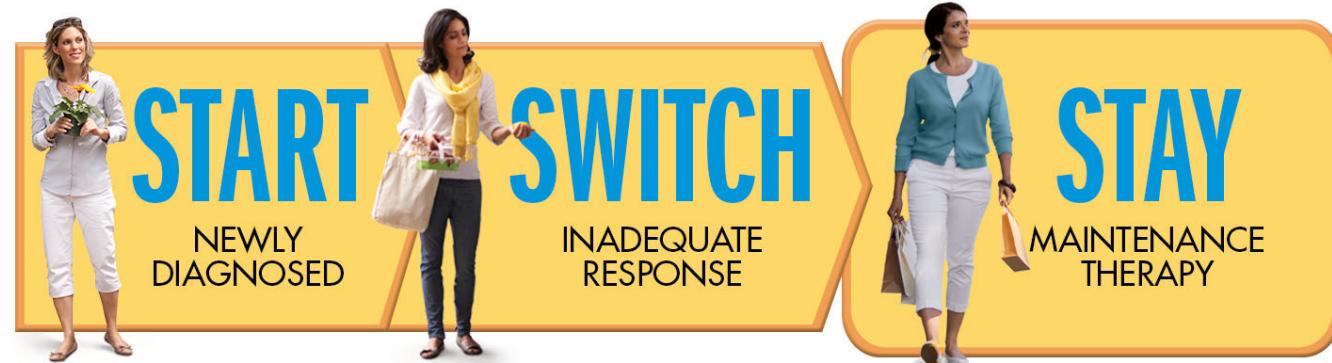
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CONSIDER THE PROVEN EFFICACY OF TYSABRI AT EVERY STAGE

Assess the benefits and risks of TYSABRI alongside her risk of disease progression



Indication

TYSABRI® (natalizumab) is indicated as monotherapy for the treatment of patients with relapsing forms of multiple sclerosis. 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. See important information regarding the risk of PML with TYSABRI.

► The decision to start or continue TYSABRI requires an individualized assessment



Risk of TYSABRI (cont'd)

- 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 MS patients receiving TYSABRI

Expand ISI for additional risk information.

Tap to expand

- Indication
- Important Safety Information (ISI)

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REF



CONSIDER THE PROVEN EFFICACY OF TYSABRI® AT EVERY STAGE



Assess the benefits and risks of TYSABRI alongside her risk of disease progression

▼ The decision to start or continue TYSABRI requires an individualized assessment

TYSABRI label includes estimated PML risk out to 6 years⁷

TYSABRI Exposure ^a	Anti-JCV Antibody Negative ^b	Anti-JCV Antibody Positive ^c	
		No Prior Immunosuppressant	Prior Immunosuppressant
1-24 months		<1/1000	1/1000
25-48 months	<1/1000	3/1000	13/1000
49-72 months		7/1000	9/1000

^aData beyond 6 years of treatment are limited.

^bCalculation based on 2 cases of anti-JCV antibody negative PML in patients exposed for at least 1 month of therapy as of September 3, 2013.

Data for anti-JCV antibody negative patients reflects worldwide exposure.

^cBased on US postmarketing PML data as of September 3, 2013, and TYSABRI use data as of August 31, 2013.

- There are 3 known risk factors for PML⁷
 - Anti-JCV antibody positive status
 - Prior treatment with an immunosuppressant
 - Longer duration of TYSABRI treatment (especially beyond 2 years)
- These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI



Risk of TYSABRI (cont'd)

- 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 MS patients receiving TYSABRI

Expand ISI for additional risk information.

Tap to expand

- ▶ Indication
- ▶ Important Safety Information (ISI)

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PROACTIVELY IDENTIFY PATIENTS WHO MAY BENEFIT FROM THE PROVEN EFFICACY OF TYSABRI

Assess the benefits and risks of TYSABRI alongside her risk of disease progression



START with the efficacy of TYSABRI

Newly diagnosed patients with disease activity are potential candidates for TYSABRI

- Disease activity as indicated by EDSS progression, relapse rate, and/or MRI activity
- The AFFIRM study included patients with the following characteristics⁷:
 - Approximately 94% were treatment-naïve
 - Median disease duration of 5 years
 - Mean EDSS score of 2.3

► The decision to start or continue TYSABRI requires an individualized assessment



Risk of TYSABRI (cont'd)

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Expand ISI for additional risk information.

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PROACTIVELY IDENTIFY PATIENTS WHO MAY BENEFIT FROM THE PROVEN EFFICACY OF TYSABRI

Assess the benefits and risks of TYSABRI alongside her risk of disease progression



SWITCH to the efficacy of TYSABRI

Patients with inadequate response to their current therapy may benefit from TYSABRI

- Various definitions for inadequate responses to therapy have been defined in the literature and based on:

► **Physical Disability^{10,11}** ► **Relapse^{10,12}** ► **MRI^{11,12}**

► The decision to start or continue TYSABRI requires an individualized assessment



Risk of TYSABRI (cont'd)

- 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 MS patients receiving TYSABRI

Expand ISI for additional risk information.

Tap to expand

- **Indication**
► **Important Safety Information (ISI)**

ISI

PI

REF



PROACTIVELY IDENTIFY PATIENTS WHO MAY BENEFIT FROM THE PROVEN EFFICACY OF TYSABRI

Assess the benefits and risks of TYSABRI alongside her risk of disease progression



SWITCH to the efficacy of TYSABRI

Patients with inadequate response to their current therapy may benefit from TYSABRI

- Various definitions for inadequate responses to therapy have been defined in the literature and based on:

▼ **Physical Disability^{10,11}**

Increase in EDSS score in first month on new therapy
Rio et al, 2012.

► **Relapse^{10,12}**

► **MRI^{11,12}**

≥1 point increase
Prosperini et al, 2009.

EDSS INCREASE

► The decision to start or continue TYSABRI requires an individualized assessment



Risk of TYSABRI (cont'd)

- 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 MS patients receiving TYSABRI

Expand ISI for additional risk information.

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PROACTIVELY IDENTIFY PATIENTS WHO MAY BENEFIT FROM THE PROVEN EFFICACY OF TYSABRI

Assess the benefits and risks of TYSABRI alongside her risk of disease progression



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- Various definitions for inadequate responses to therapy have been defined in the literature and based on:

► Physical Disability^{10,11} ▽ Relapse^{10,12} ▶ MRI^{11,12}

1.2
Rio et al, 2012.

≥2
Coyle et al, 2009.

MEAN ANNUALIZED RELAPSE RATE INCREASE

-
- The decision to start or continue TYSABRI requires an individualized assessment



Risk of TYSABRI (cont'd)

- 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 MS patients receiving TYSABRI

Expand ISI for additional risk information.

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PROACTIVELY IDENTIFY PATIENTS WHO MAY BENEFIT FROM THE PROVEN EFFICACY OF TYSABRI

Assess the benefits and risks of TYSABRI alongside her risk of disease progression



SWITCH to the efficacy of TYSABRI

Patients with inadequate response to their current therapy may benefit from TYSABRI

- Various definitions for inadequate responses to therapy have been defined in the literature and based on:

► Physical Disability^{10,11} ► Relapse^{10,12} ▽ MRI^{11,12}

≥1 Gd+ lesion
Prosperini et al, 2009.

≥1 Gd+ or T2 lesion within 1 year
Coyle et al, 2009.

LESION LOAD INCREASE

- The decision to start or continue TYSABRI requires an individualized assessment



Risk of TYSABRI (cont'd)

- 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 MS patients receiving TYSABRI

Expand ISI for additional risk information.

Tap to expand

- Indication
► Important Safety Information (ISI)

ISI

PI

REF



MAINTAIN PATIENTS WHO MAY BENEFIT FROM THE PROVEN EFFICACY OF TYSABRI

Assess the benefits and risks of TYSABRI alongside her risk of disease progression



STAY with the efficacy of TYSABRI

The TYSABRI label clarifies estimated PML risk up to 6 years

- Anti-JCV antibody negative patients have <1/1000 risk⁷
 - Negative status indicates that exposure to JCV has not been detected
- Anti-JCV antibody negative patients have a lower risk of PML than those who are positive⁷
 - There is still a risk for the development of PML due to the potential for a new JCV infection or a false negative test result. Therefore, these patients should be retested periodically
- Continually evaluate treatment response and disease activity to support success

-
- The decision to start or continue TYSABRI requires an individualized assessment



Risk of TYSABRI (cont'd)

- 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 MS patients receiving TYSABRI

Expand ISI for additional risk information.

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- Indication
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SUPPORT AND EXPERIENCE YOU AND YOUR RELAPSING MS PATIENTS NEED



“My monthly infusions allow me to prioritize my health and focus on my fight.”

-Real TYSABRI Patient

24/7 Assistance

Monthly Check-ins

Connection to others

Clinical Experience



Hepatotoxicity

- Clinically significant liver injury, including acute liver failure requiring transplant, has been reported in patients treated with TYSABRI in the postmarketing setting. TYSABRI should be discontinued in patients with jaundice or other evidence of significant liver injury (e.g., laboratory evidence)

Expand ISI for additional risk information.

Tap to expand

- ▶ Indication
- ▶ Important Safety Information (ISI)

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SUPPORT AND EXPERIENCE YOU AND YOUR RELAPSING MS PATIENTS NEED



ActiveNurses™ are available to answer patients' questions with 24/7 phone coaching

ActiveSupport™ coaching by highly trained MS Support Specialists

ActiveVoices™ provides an opportunity for patients to attend live events to learn about TYSABRI

24/7
Assistance with
MS Active Source

Monthly
Check-ins

Connection
to others

Clinical
Experience

EVERY
4 WEEKS
300mg IV
TYSABRI
(natalizumab)
Realize the potential

Hepatotoxicity

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Expand ISI for additional risk information.

Tap to expand

- **Indication**
► **Important Safety Information (ISI)**

ISI

PI

REF



SUPPORT AND EXPERIENCE YOU AND YOUR RELAPSING MS PATIENTS NEED



- Dosing confirmed by the HCP administering the infusion, so you can easily monitor your patients
- Routine access to knowledgeable nurses to answer questions and provide regular support



EVERY
4 WEEKS
300mg IV

TYSABRI®
(natalizumab)

Realize the potential

Hepatotoxicity

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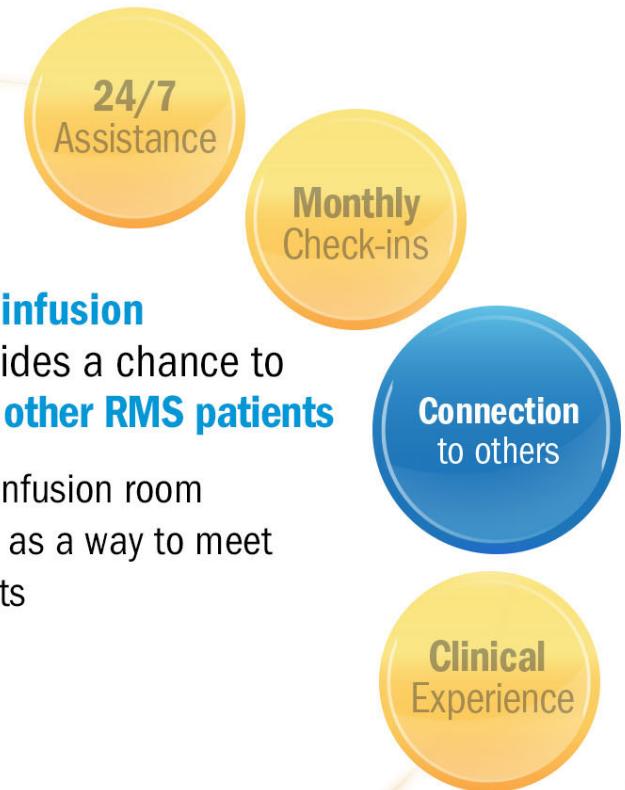


SUPPORT AND EXPERIENCE YOU AND YOUR RELAPSING MS PATIENTS NEED



The **monthly infusion process** provides a chance to **connect with other RMS patients**

- Time in the infusion room often serves as a way to meet other patients



EVERY
4 WEEKS
300mg IV

TYSABRI®
(natalizumab)

Realize the potential

Hepatotoxicity

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REF



SUPPORT AND EXPERIENCE YOU AND YOUR RELAPSING MS PATIENTS NEED



- TYSABRI: **Proven with >7 years** of clinical use⁹
- **>1.5 million infusions** administered in the US alone, representing **>115,000 patient-years** of experience⁹



Hepatotoxicity

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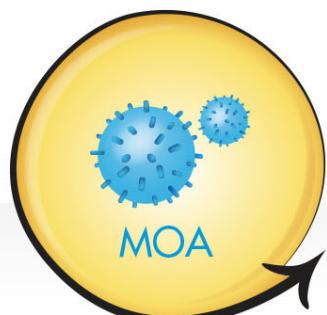
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ADDITIONAL INFORMATION



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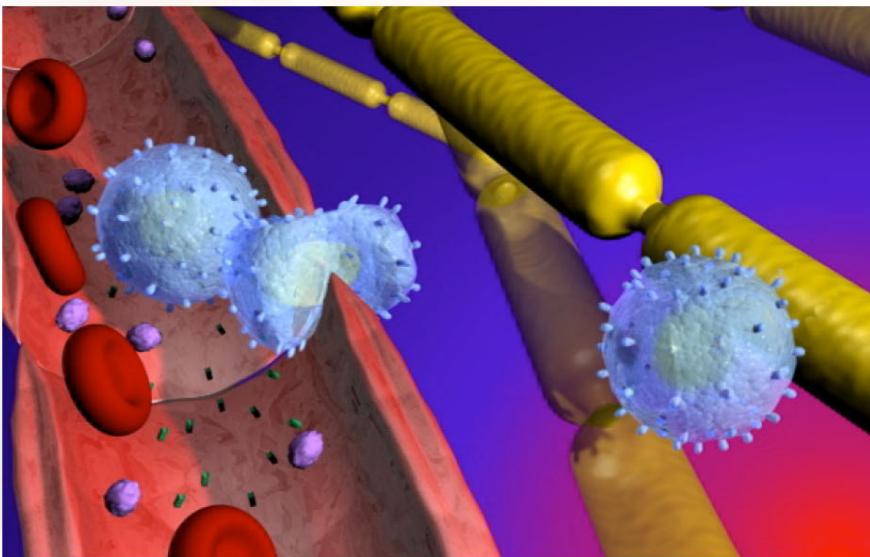


PROPOSED MECHANISM OF ACTION (MOA)



Immunopathology of MS

Proposed TYSABRI MOA



- The blood-brain barrier restricts access to the central nervous system (CNS)
- At the beginning of an MS relapse, activated white blood cells cross the blood-brain barrier and enter the CNS^{7,13}
- Then white blood cells attack the myelin sheath and recruit other immune cells to help attack the myelin sheath¹³

SLIDESHOW

VIDEO



Tap to collapse

► Indication

▼ Important Safety Information (ISI)

WARNING

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 duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI.

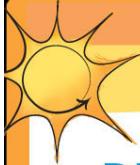
Healthcare professionals should monitor patients on TYSABRI for any new sign or symptom that may be suggestive of PML. TYSABRI dosing should be withheld immediately at the first sign or symptom suggestive of PML. For diagnosis, an evaluation including a gadolinium-enhanced MRI scan of the brain and,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

ISI

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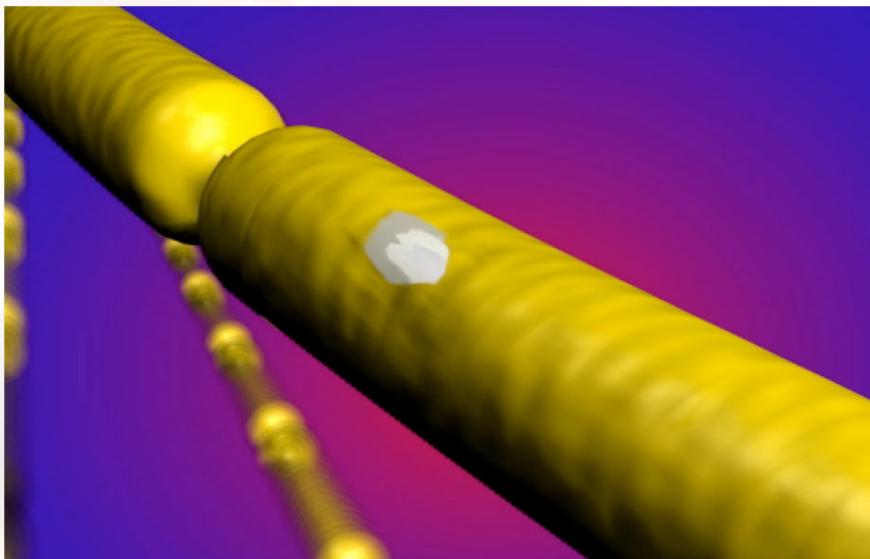
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PROPOSED MECHANISM OF ACTION (MOA)

Immunopathology of MS

Proposed TYSABRI MOA



- When the myelin sheath is first damaged, nerve impulses can still be transmitted
- At this point, the myelin can repair itself and the symptoms disappear, resulting in a remission of the disease

SLIDESHOW

VIDEO



Tap to collapse

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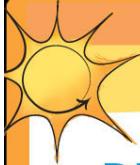
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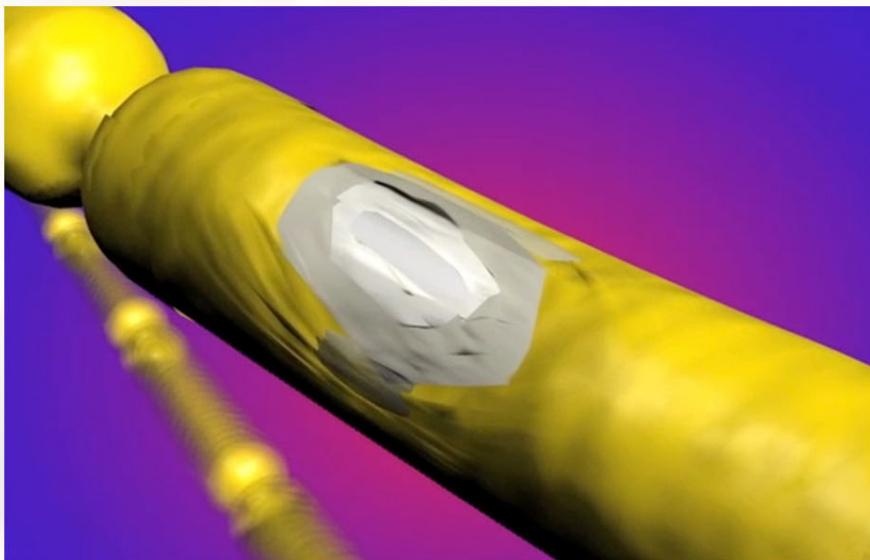
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PROPOSED MECHANISM OF ACTION (MOA)

Immunopathology of MS

Proposed TYSABRI MOA



- As the myelin becomes more damaged, it is replaced by scar tissue and nerve impulses are slowed down
- When the myelin is completely destroyed, the nerve impulses are blocked, which causes a permanent loss of function

SLIDESHOW

VIDEO



Tap to collapse

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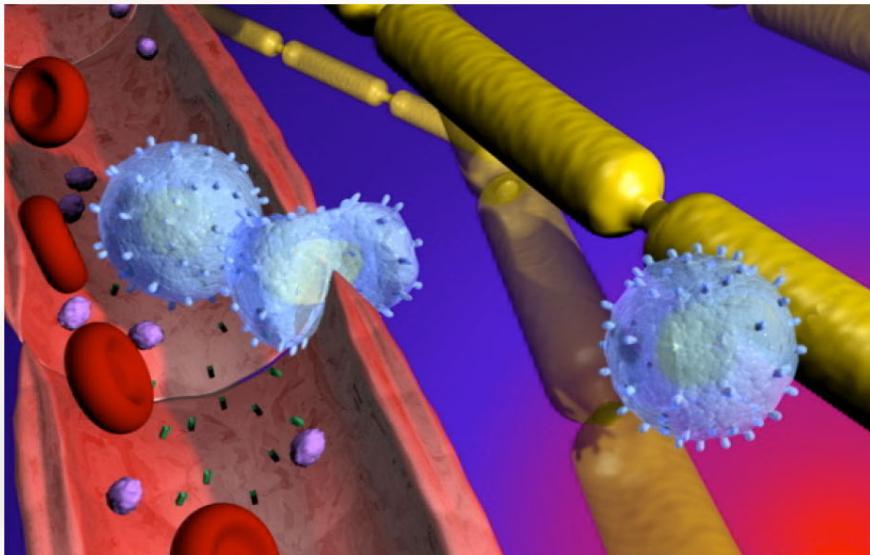


PROPOSED MECHANISM OF ACTION (MOA)



Immunopathology of MS

Proposed TYSABRI MOA



The specific mechanism(s) by which TYSABRI exerts its effects in MS have not been fully defined.

- TYSABRI binds to 2 adhesion molecules expressed on the surface of all white blood cells (except neutrophils)⁷
- TYSABRI prevents white blood cells from crossing the blood-brain barrier and attacking the CNS^{7,13}

SLIDESHOW

VIDEO



Tap to collapse

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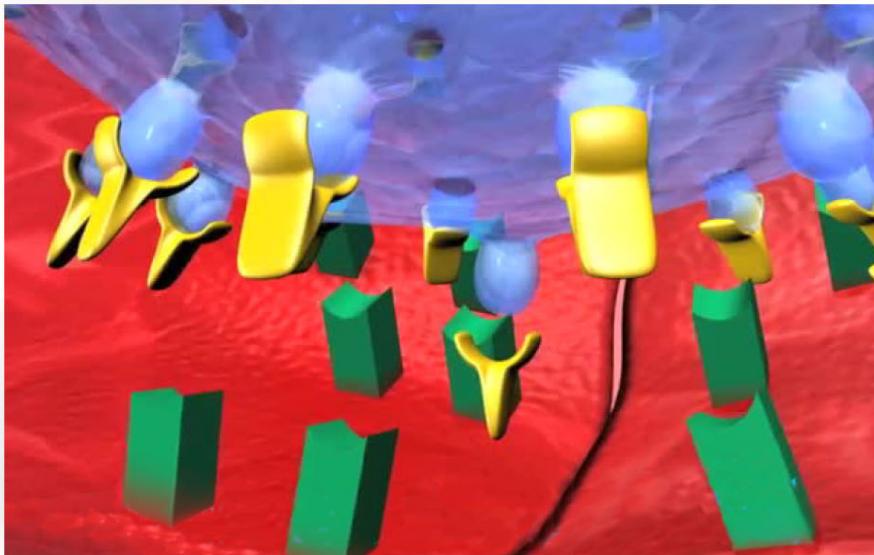


PROPOSED MECHANISM OF ACTION (MOA)



Immunopathology of MS

Proposed TYSABRI MOA



The specific mechanism(s) by which TYSABRI exerts its effects in MS have not been fully defined.

- TYSABRI is a monoclonal antibody that targets alpha4-integrin
- TYSABRI may work by interrupting the activity of inflammatory cells through inhibition of alpha4-integrin-mediated adhesion⁷

SLIDESHOW

VIDEO



Tap to collapse

► Indication

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WARNING

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 duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. These factors should be considered in the context of expected benefit when initiating and continuing treatment with TYSABRI.

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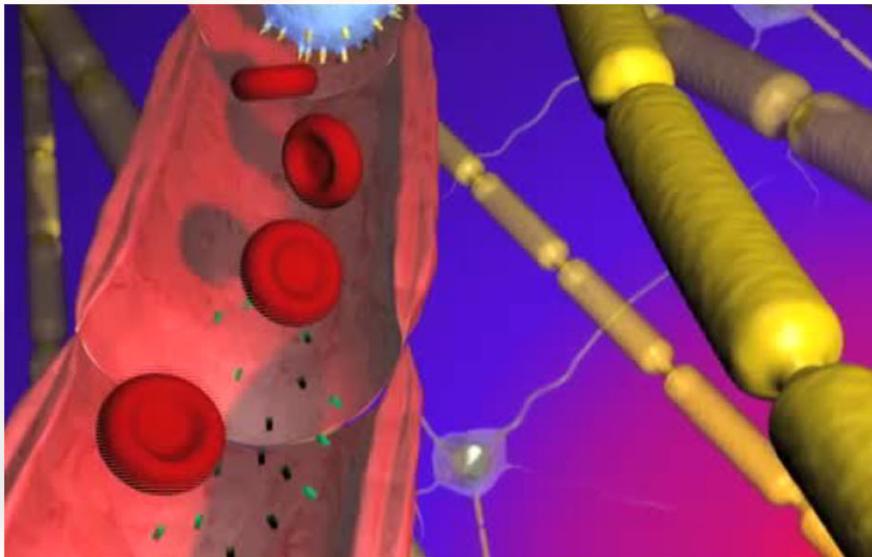


PROPOSED MECHANISM OF ACTION (MOA)



Immunopathology of MS

Proposed TYSABRI MOA



The specific mechanism(s) by which TYSABRI exerts its effects in MS have not been fully defined.

- Disruption of these molecular interactions prevents transmigration of leukocytes across the endothelium into inflamed parenchymal tissue⁷
- TYSABRI may also have effects within the CNS

SLIDESHOW

VIDEO



Tap to collapse

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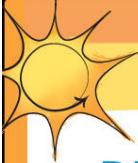
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ISI

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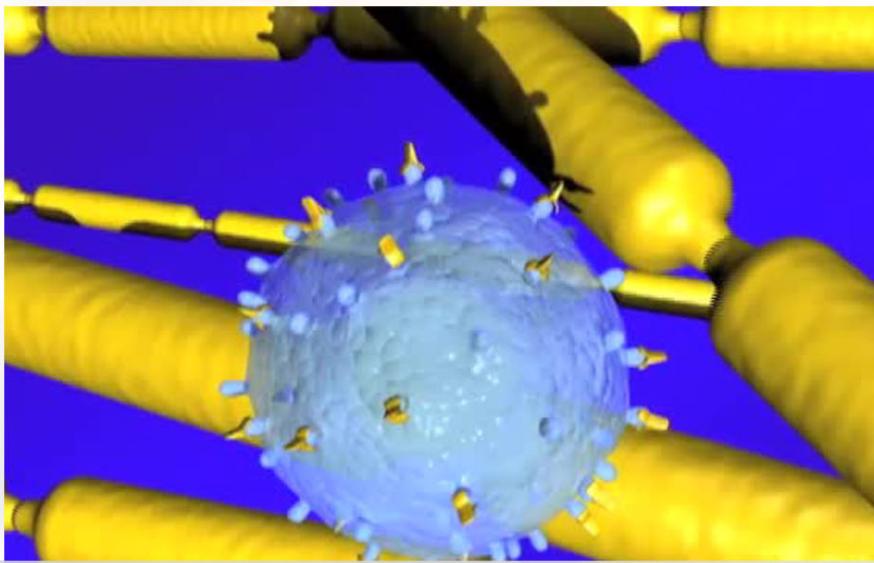


PROPOSED MECHANISM OF ACTION (MOA)



Immunopathology of MS

Proposed TYSABRI MOA



The specific mechanism(s) by which TYSABRI exerts its effects in MS have not been fully defined.

- TYSABRI may further act to inhibit the interaction of alpha4-suppressing leukocytes with their ligand or ligands in extracellular matrix and on parenchymal cells⁷
 - Thereby inhibiting further recruitment and inflammatory activity of activated immune cells

SLIDESHOW

VIDEO



Tap to collapse

► Indication

▼ Important Safety Information (ISI)

WARNING

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 duration of therapy, prior use of immunosuppressants, and presence of anti-JCV antibodies. 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

ISI

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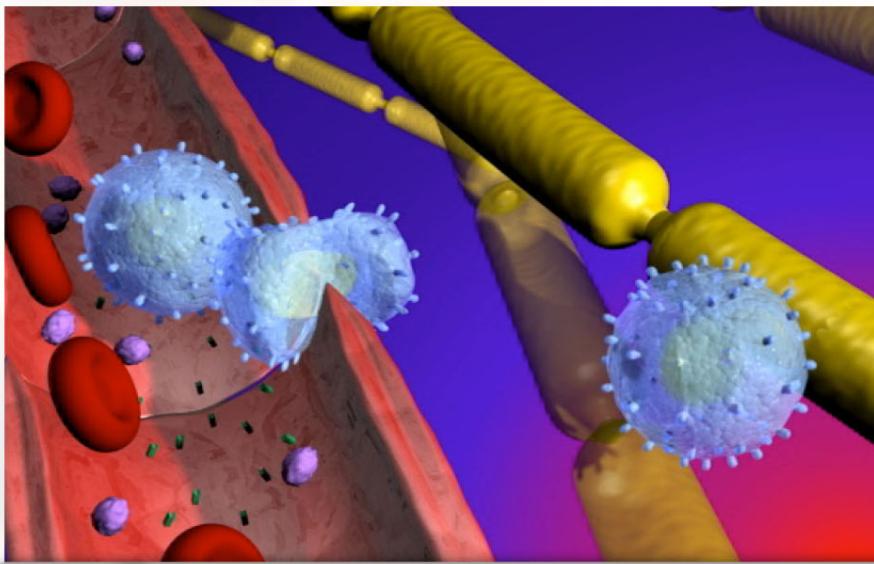


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Immunopathology of MS

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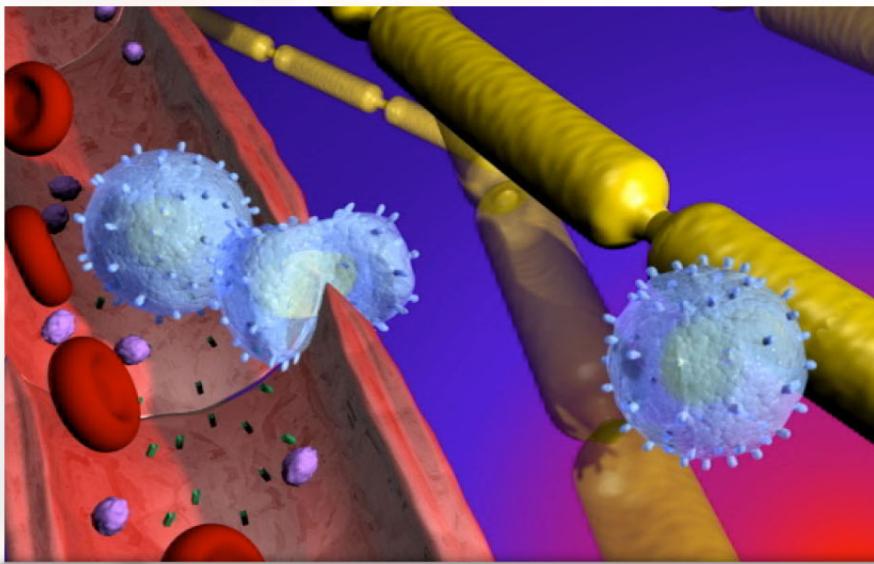


PROPOSED MECHANISM OF ACTION (MOA)



Immunopathology of MS

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ENCOURAGE TREATMENT ADHERENCE



Manage treatment expectations to help your RMS patients stay on therapy

BEFORE initiating TYSABRI

Establish realistic treatment goals for your patient^{14,15}

AFTER initiating TYSABRI

Revisit goals with your patient to determine whether they still match current treatment objectives^{16,17}

ALWAYS

Encourage your patients to **monitor** their disease progression and routinely check in with you^{16,18}

ADDITIONAL INFORMATION



Tap to expand

- ▶ Indication
- ▶ Important Safety Information (ISI)

ISI

PI

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HELPING PATIENTS WITH RELAPSING MS WITH THEIR PRESCRIBED THERAPY



1-800-456-2255
MSACTIVESOURCE.COM



- Active Nurses are available to answer patients' questions about RMS and TYSABRI
- Phone coaching is provided 24/7



- Patients have access to MS Support Specialists who are highly trained in both RMS and TYSABRI
- These specialists offer coaching sessions online or by phone



- ActiveVoices provides an opportunity for patients to attend live events to learn about TYSABRI
- Mentors are available online and by phone



- Offers patients a comprehensive set of financial and insurance support services
- Helps ensure that patients are focused on treatment, not cost

ADDITIONAL INFORMATION

Tap to expand

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