OCREVUS®
ocrelizumab 300MG/10ML INJECTION FOR IV

Delivering a high standard for impacting disability progression in PPMS patients[1,2]

The **FIRST and ONLY** DMT with 2 positive Phase III clinical trials for PPMS—ORATORIO and ORATORIO–HAND (OHAND)[1-3]

IZZY
Taking OCREVUS for PPMS

Indications

OCREVUS is indicated for the treatment of:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Primary progressive MS, in adults.

Contraindications

OCREVUS is contraindicated in patients with active hepatitis B virus infection and in patients with a history of life-threatening infusion reaction to OCREVUS.

Select Important Safety Information

The warnings and precautions for OCREVUS are infusion reactions and infections, which include respiratory tract infections, herpes, hepatitis B virus (HBV) reactivation, and a warning for progressive multifocal leukoencephalopathy (PML). Additional warnings are possible increased risk of immunosuppressant effects with other immunosuppressants, reduction in immunoglobulins, malignancies, immune-mediated colitis, and liver injury.

DMT=disease-modifying treatment; PPMS=primary progressive multiple sclerosis.

Please see additional safety information on pages 9-11 and click here for full OCREVUS Prescribing Information and Medication Guide.

Preserving function longer in patients at risk of disability progression[2]

Function matters at every stage of MS. Therefore, OHAND evaluated preservation of function in a broader set of patients—those who were older and more disabled—compared to those studied in ORATORIO.

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OHAND examined the impact of OCREVUS on PPMS patients with greater levels of disability[2]

OCREVUS is approved in patients with PPMS based on the Phase III ORATORIO pivotal trial[1,3]

ORATORIO STUDY DESIGN[1,3]

N=732

Key Inclusion Criteria

- Diagnosis of PPMS*
- 18-55 years old
- EDSS: 3.0-6.5
- ≥2 on pyramidal FSS due to lower extremity findings
- No history of RMS, SPMS, or PRMS

2:1 RANDOMIZATION

OCREVUS | **Placebo**

Time- or event-driven trial of at least 120 weeks

OCREVUS: n=488[3]
PLACEBO: n=244[3]
*2005 revised McDonald criteria.

OHAND STUDY DESIGN[2]

N=1013

Key Inclusion Criteria

- Diagnosis of PPMS†
- 18-65 years old
- EDSS: 3.0-8.0

1:1 RANDOMIZATION

OCREVUS | **Placebo**

Lasted until the last patient completed 144 weeks or until ≥340 confirmed progression events (9HPT or EDSS) were observed, whichever occurred earlier

OCREVUS: n=505[2]
PLACEBO: n=508[2]
†2007 revised McDonald criteria.

9HPT=9-hole peg test; EDSS=Expanded Disability Status Scale; FSS=functional systems score; MS=multiple sclerosis; PPMS=primary progressive multiple sclerosis; PRMS=progressive-relapsing multiple sclerosis; RMS=relapsing multiple sclerosis; SPMS=secondary progressive multiple sclerosis.

Select Important Safety Information

Infusion Reactions

OCREVUS can cause infusion reactions, which can include pruritus, rash, urticaria, erythema, bronchospasm, throat irritation, oropharyngeal pain, dyspnea, pharyngeal or laryngeal edema, flushing, hypotension, pyrexia, fatigue, headache, dizziness, nausea, tachycardia, and anaphylaxis.

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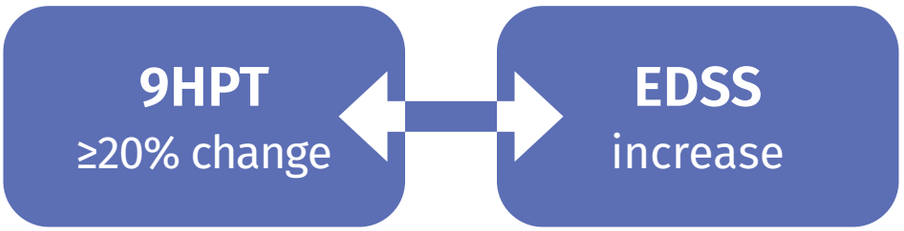
OHAND measured the impact of OCREVUS on cCDP, a novel, more comprehensive composite disability measure[2,4]

To overcome the limitations of using EDSS alone, cCDP also includes 9HPT, which specifically measures upper extremity function and has been shown to be predictive of increases in disability progression[4-6]

OHAND cCDP*=

First occurrence of either event†



A disability event was defined as the first occurrence of either[4]:

- **9HPT:** ≥20% change in 9HPT time from baseline that was sustained on subsequent visits for at least 12 weeks

OR

- **EDSS:** ≥1.0-point increase from a baseline EDSS score of ≤5.5 that was sustained on subsequent visits for at least 12 weeks **or** ≥0.5-point increase from a baseline EDSS score of >5.5 that was sustained on subsequent visits for at least 12 weeks

OHAND primary endpoint: time to onset of 12-week composite CDP

*The components of cCDP may vary from study to study.
†Confirmed at 12 weeks after the event.[2]

9HPT=9-hole peg test; CDP=confirmed disability progression; cCDP=composite confirmed disability progression; EDSS=Expanded Disability Status Scale.

Select Important Safety Information

Infections

Serious, including life-threatening or fatal, bacterial, viral, parasitic and fungal infections have been reported in patients receiving OCREVUS. An increased risk of infections (including serious and fatal bacterial, fungal, and new or reactivated viral infections) has been observed in patients during and following completion of treatment with anti-CD20 B-cell depleting therapies.

A higher proportion of OCREVUS-treated patients experienced infections compared to patients taking REBIF or placebo. In RMS trials, 58% of OCREVUS-treated patients experienced one or more infections compared to 52% of REBIF-treated patients. OCREVUS was not associated with an increased risk of serious infections in MS patients in controlled trials.

Please see additional safety information on pages 9-11 and click here for full OCREVUS Prescribing Information and Medication Guide.

OHAND evaluated PPMS patients with more advanced disease than those in ORATORIO, with a focus on upper extremity (UE) function[1,2]

OHAND: PPMS patients up to age 65 and with an EDSS up to 8.0 were included[2]

	ORATORIO[1,2]		OHAND[1,2]	
	ALL PATIENTS (n=732)		OCREVUS (n=505)	Placebo (n=508)
Age, years, median (range)	**46** (18-56)	**Broader age range** ➡ ≤55 years, n (%) >55 years, n (%)	**48** (18-66) **366** (72.5) **139** (27.5)	**47** (22-66) **371** (73.0) **137** (27.0)
Female, %	**49.3%**	**Higher proportion of female patients** ➡	**57.4%**	**54.7%**
Time since symptom onset, years, median (range)	**5.9** (0.9-32.9)		**9.4** (0.7-27.6)	**9.0** (0.7-37.4)
Prior DMT,* %	**11.6%**		**8.3%**	**6.1%**
EDSS, median (range)	**4.5** (2.5-7.0)	**Higher EDSS scores** ➡ >6.5, n(%)	**6.0** (3.0-8.0) **77** (15.2)	**6.0** (2.5-8.0) **84** (16.5)
9HPT, average both hands, median (SD)	**26.9** (11.1-300.0)	**Lower baseline UE function** ➡	**34.2** (25.1-216.9)	**33.8** (24.5-221.8)
Presence of T1 Gd+ lesions, %	**26.4%**		**24.0%**	**22.3%**

*In ORATORIO, defined as treatment-naive for B-cell therapies and no other immunosuppressive medications in the prior two years. In OHAND, defined as treatment-naive for B-cell therapies; immunosuppressive medications were allowed but required appropriate washout.

9HPT=9-hole peg test; CDP=confirmed disability progression; DMT=disease-modifying treatment; EDSS=Expanded Disability Status Scale; PPMS=primary progressive multiple sclerosis; T1 Gd+=T1 gadolinium-enhancing.

Select Important Safety Information

Progressive Multifocal Leukoencephalopathy (PML)

Cases of progressive multifocal leukoencephalopathy (PML) have been reported in patients with MS treated with OCREVUS in the postmarketing setting. At the first sign or symptom suggestive of PML, withhold OCREVUS and perform an appropriate diagnostic evaluation. Magnetic resonance imaging (MRI) findings may be apparent before clinical signs or symptoms. Monitoring with MRI for signs 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. If PML is confirmed, treatment with OCREVUS should be discontinued.

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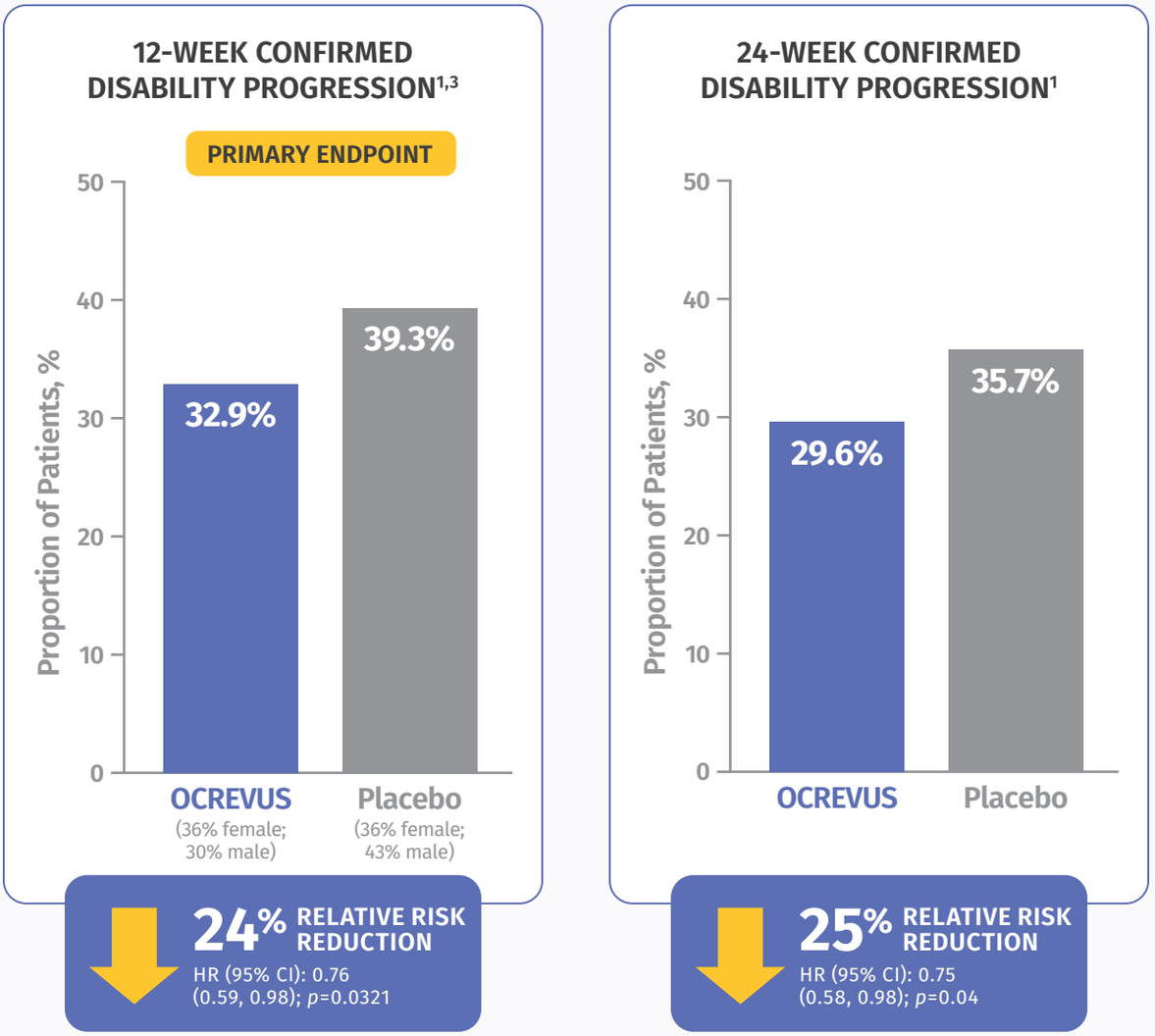
ORATORIO established OCREVUS as the first and only DMT proven to significantly slow disability progression in PPMS[3]

Significant reduction in the risk of confirmed disability progression vs placebo on 2 endpoints (12- and 24-week CDP)[1]



In exploratory subgroup analyses of ORATORIO, the proportion of female patients with disability progression confirmed at 12 weeks after onset was similar in OCREVUS (ocrelizumab)-treated patients and placebo-treated patients (approximately 36% in each group). In male patients, the proportion of patients with disability progression confirmed at 12 weeks after onset was approximately 30% in OCREVUS-treated patients and 43% in placebo-treated patients. Clinical and MRI endpoints that generally favored OCREVUS numerically in the overall population, and that showed similar trends in both male and female patients, included annualized relapse rate, change in T2 lesion volume, and number of new or enlarging T2 lesions. ORATORIO was not powered to detect differences among these subgroups.[1,3]

CDP=confirmed disability progression; DMT=disease-modifying treatment; HR = hazard ratio; MRI=magnetic resonance imaging; PPMS=primary progressive multiple sclerosis; T2=transverse relaxation time.

Select Important Safety Information

Reduction in Immunoglobulins

As expected with any B-cell depleting therapy, decreased immunoglobulin levels are observed with OCREVUS treatment. The pooled data of OCREVUS clinical studies (RMS and PPMS) and their open-label extensions (up to approximately 7 years of exposure) have shown an association between decreased levels of immunoglobulin G (IgG<LLN) and increased rates of serious infections.

Please see additional safety information on pages 9-11 and click here for full OCREVUS Prescribing Information and Medication Guide.

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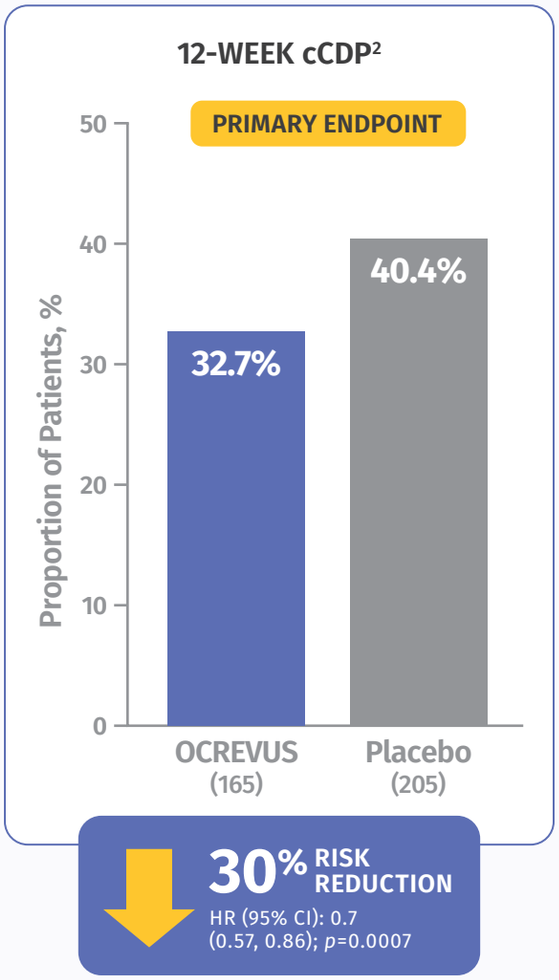
OCREVUS significantly reduced the risk of disability progression as measured by cCDP in the OHAND study[1,2]

OHAND studied a population that had more advanced disease (higher median EDSS) and higher median age than those in ORATORIO



Proportion of patients with 12-week cCDP defined as the first occurrence of either[4]:

- **9HPT:** ≥20% change in 9HPT time from baseline that was sustained on subsequent visits for at least 12 weeks

OR

- **EDSS:** ≥1.0-point increase from a baseline EDSS score of ≤5.5 that was sustained on subsequent visits for at least 12 weeks **or** ≥0.5-point increase from a baseline EDSS score of >5.5 that was sustained on subsequent visits for at least 12 weeks

Choose OCREVUS: Demonstrated reduction in the risk of disability progression as measured by a comprehensive assessment inclusive of upper extremity function.[2]

9HPT=9-hole peg test; cCDP=composite confirmed disability progression; EDSS=Expanded Disability Status Scale; HR=hazard ratio.

Select Important Safety Information

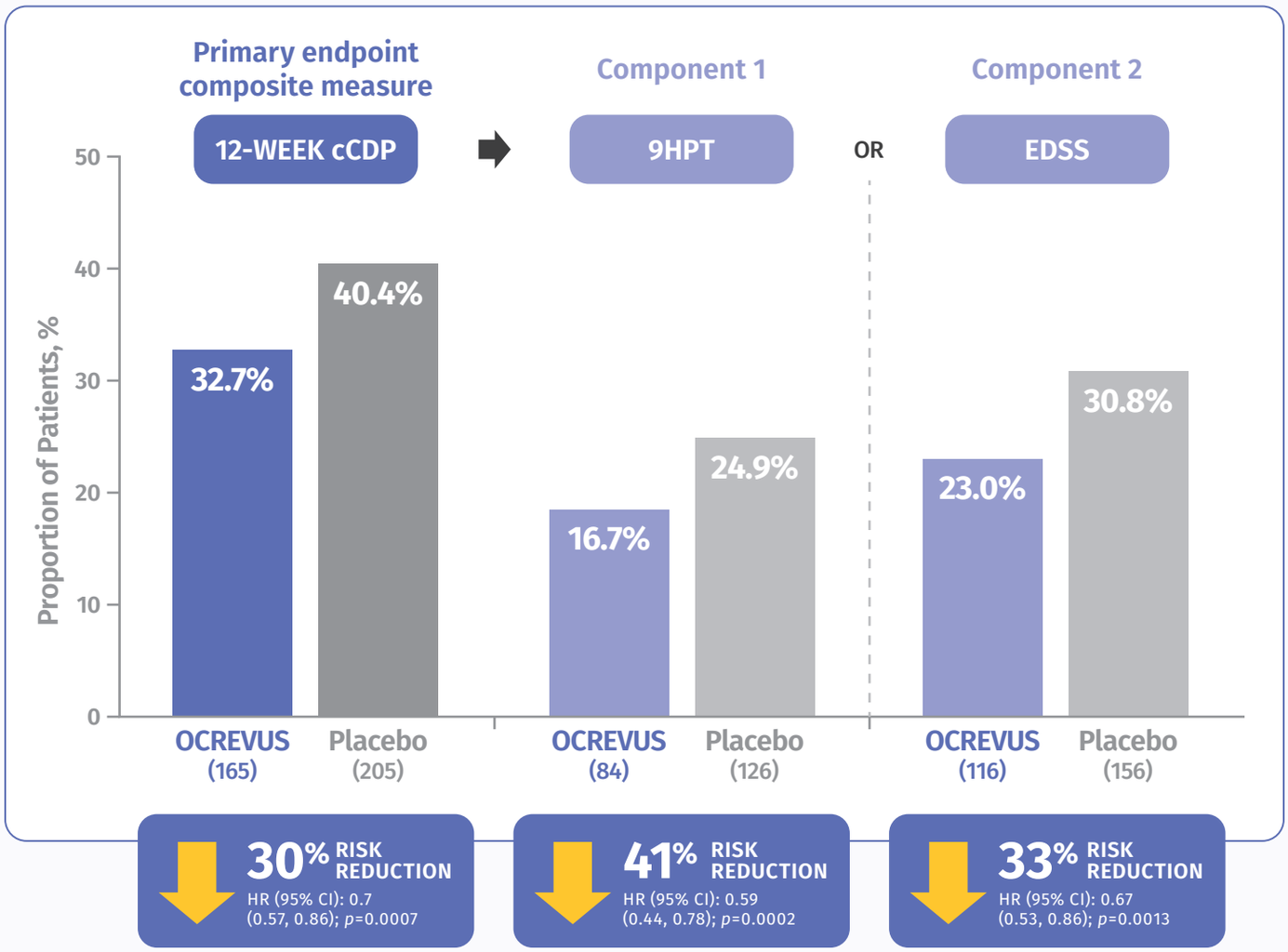
Malignancies

An increased risk of malignancy, including breast cancer, may exist with OCREVUS.

Please see additional safety information on pages 9-11 and click here for full OCREVUS Prescribing Information and Medication Guide.

OHAND demonstrated a significant effect on disability progression, including upper extremity function (9HPT) and EDSS[2]

Both components reinforce the significance of the overall 12-week cCDP result*



*The data presented are not inclusive of all endpoints in the OHAND study.

9HPT=9-hole peg test; cCDP=composite confirmed disability progression; EDSS=Expanded Disability Status Scale; HR=hazard ratio.

Select Important Safety Information

Immune-Mediated Colitis

Immune-mediated colitis, which can present as a severe and acute-onset form of colitis, has been reported in patients receiving OCREVUS in the postmarketing setting. Some cases of colitis were serious, requiring hospitalization, with a few patients requiring surgical intervention. Systemic corticosteroids were required in many of these patients. Monitor patients for immune-mediated colitis during OCREVUS treatment and evaluate promptly if signs and symptoms such as new or persistent diarrhea or other gastrointestinal signs and symptoms occur.

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OHAND provided additional safety data consistent with the known profile for OCREVUS[1,2]

The safety data in OHAND were comparable to ORATORIO

	ORATORIO		OHAND	
	OCREVUS (n=486)	Placebo (n=239)	OCREVUS (n=506)	Placebo (n=506)
AEs, %	95.1%	90.0%	74.9%	71.1%
Serious AEs, %	20.4%	22.2%	12.8%	13.2%
Deaths, % (n)	0.8% (4)	0.4% (1)	2.2% (11)	2.0% (10)
IRRs, %	39.9%	25.5%	20.8%	4.3%
Infections, % Excluding COVID-19	71.4% n/a	69.9% n/a	48.4% 37.5%	44.7% 37.0%
Serious infections, % Excluding COVID-19	6.2% n/a	5.9% n/a	6.3% 2.4%	5.3% 3.8%
Malignancies, % (n)	2.3% (11)	0.8% (2)	1.0% (5)	0.6% (3)

OHAND was conducted during the COVID-19 pandemic, which may have influenced the incidence of AEs, serious AEs, and infections. The OHAND study enrolled older patients with higher levels of disability compared to those studied in ORATORIO. To contextualize these findings for OHAND, rates are presented both including and excluding COVID-19–related events.[2]

OCREVUS has a well-established safety profile with 10+ years of clinical trial data.[7]

Explore OLE safety data

AE=adverse event; IRR=infusion-related reaction; OLE=open-label extension.

Select Important Safety Information

Liver Injury

Clinically significant liver injury, without findings of viral hepatitis, has been reported in the postmarketing setting in patients treated with anti-CD20 B-cell depleting therapies approved for the treatment of MS, including OCREVUS. Signs of liver injury, including markedly elevated serum hepatic enzymes with elevated total bilirubin, have occurred from weeks to months after administration.

Obtain liver function tests prior to initiating treatment with OCREVUS, and monitor for signs and symptoms of any hepatic injury during treatment. Measure serum aminotransferases, alkaline phosphatase, and bilirubin levels promptly in patients who report symptoms that may indicate liver injury, including new or worsening fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice. If liver injury is present and an alternative etiology is not identified, discontinue OCREVUS.

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Important Safety Information

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Indications

OCREVUS is indicated for the treatment of:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Primary progressive MS, in adults.

Contraindications

OCREVUS is contraindicated in patients with active hepatitis B virus infection and in patients with a history of life-threatening infusion reaction to OCREVUS.

Warnings and Precautions

Infusion Reactions

OCREVUS can cause infusion reactions, which can include pruritus, rash, urticaria, erythema, bronchospasm, throat irritation, oropharyngeal pain, dyspnea, pharyngeal or laryngeal edema, flushing, hypotension, pyrexia, fatigue, headache, dizziness, nausea, tachycardia, and anaphylaxis. In multiple sclerosis (MS) clinical trials, the incidence of infusion reactions in OCREVUS-treated patients [who received methylprednisolone (or an equivalent steroid) and possibly other pre-medication to reduce the risk of infusion reactions prior to each infusion] was 34-40%, with the highest incidence with the first infusion. There were no fatal infusion reactions, but 0.3% of OCREVUS-treated MS patients experienced infusion reactions that were serious, some requiring hospitalization.

Observe patients treated with OCREVUS for infusion reactions during the infusion and for at least one hour after completion of the infusion. Inform patients that infusion reactions can occur up to 24 hours after the infusion. Administer pre-medication (e.g., methylprednisolone or an equivalent corticosteroid, and an antihistamine) to reduce the frequency and severity of infusion reactions. The addition of an antipyretic (e.g., acetaminophen) may also be considered. For life-threatening infusion reactions, immediately and permanently stop OCREVUS and administer appropriate supportive treatment. For less severe infusion reactions, management may involve temporarily stopping the infusion, reducing the infusion rate, and/or administering symptomatic treatment.

Infections

Serious, including life-threatening or fatal, bacterial, viral, parasitic and fungal infections have been reported in patients receiving OCREVUS. An increased risk of infections (including serious and fatal bacterial, fungal, and new or reactivated viral infections) has been observed in patients during and following completion of treatment with anti-CD20 B-cell depleting therapies.

A higher proportion of OCREVUS-treated patients experienced infections compared to patients taking REBIF or placebo. In RMS trials, 58% of OCREVUS-treated patients experienced one or more infections compared to 52% of REBIF-treated patients. In the PPMS trial, 70% of OCREVUS-treated patients experienced one or more infections compared to 68% of patients on placebo. OCREVUS increased the risk for upper respiratory tract infections, lower respiratory tract infections, skin infections, and herpes-related infections. OCREVUS was not associated with an increased risk of serious infections in MS patients in controlled trials. Delay OCREVUS administration in patients with an active infection until the infection is resolved.

Respiratory Tract Infections

A higher proportion of OCREVUS-treated patients experienced respiratory tract infections compared to patients taking REBIF or placebo. In RMS trials, 40% of OCREVUS-treated patients experienced upper respiratory tract infections compared to 33% of REBIF-treated patients, and 8% of OCREVUS-treated patients experienced lower respiratory tract infections compared to 5% of REBIF-treated patients. In the PPMS trial, 49% of OCREVUS-treated patients experienced upper respiratory tract infections compared to 43% of patients on placebo, and 10% of OCREVUS-treated patients experienced lower respiratory tract infections compared to 9% of patients on placebo. The infections were predominantly mild to moderate and consisted mostly of upper respiratory tract infections and bronchitis.

Herpes

In active-controlled (RMS) clinical trials, herpes infections were reported more frequently in OCREVUS-treated patients than in REBIF-treated patients, including herpes zoster (2.1% vs. 1.0%), herpes simplex (0.7% vs. 0.1%), oral herpes (3.0% vs. 2.2%), genital herpes (0.1% vs. 0%), and herpes virus infection (0.1% vs. 0%). Infections were predominantly mild to moderate in severity. In the placebo-controlled (PPMS) clinical trial, oral herpes was reported more frequently in the OCREVUS-treated patients than in the patients on placebo (2.7% vs. 0.8%).

Serious cases of infections caused by herpes simplex virus and varicella zoster virus, including central nervous system infections (encephalitis and meningitis), intraocular infections, and disseminated skin and soft tissue infections, have been reported in the postmarketing setting in multiple sclerosis patients receiving OCREVUS. Serious herpes virus infections may occur at any time during treatment with OCREVUS. Some cases were life-threatening.

If serious herpes infections occur, OCREVUS should be discontinued or withheld until the infection has resolved, and appropriate treatment should be administered.

Please see additional safety information on pages 10-11 and click here for full OCREVUS Prescribing Information and Medication Guide.

Important Safety Information (cont'd)

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Hepatitis B Virus (HBV) Reactivation

Hepatitis B reactivation has been reported in MS patients treated with OCREVUS in the postmarketing setting. Fulminant hepatitis, hepatic failure, and death caused by HBV reactivation have occurred in patients treated with anti-CD20 antibodies. Perform HBV screening in all patients before initiation of treatment with OCREVUS. Do not administer OCREVUS to patients with active HBV confirmed by positive results for HBsAg and anti-HB tests. For patients who are negative for surface antigen [HBsAg] and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], consult liver disease experts before starting and during treatment.

Possible Increased Risk of Immunosuppressant Effects With Other Immunosuppressants

When initiating OCREVUS after an immunosuppressive therapy or initiating an immunosuppressive therapy after OCREVUS, consider the potential for increased immunosuppressive effect. OCREVUS has not been studied in combination with other MS therapies.

Vaccinations

Administer all immunizations according to immunization guidelines at least 4 weeks prior to initiation of OCREVUS for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of OCREVUS for non-live vaccines. OCREVUS may interfere with the effectiveness of non-live vaccines. The safety of immunization with live or live-attenuated vaccines following OCREVUS therapy has not been studied, and vaccination with live-attenuated or live vaccines is not recommended during treatment and until B-cell repletion.

Vaccination of Infants Born to Mothers Treated With OCREVUS During Pregnancy

In infants of mothers exposed to OCREVUS during pregnancy, do not administer live or live-attenuated vaccines before confirming the recovery of B-cell counts as measured by CD19+ B-cells. Depletion of B-cells in these infants may increase the risks from live or live-attenuated vaccines.

You may administer non-live vaccines, as indicated, prior to recovery from B-cell depletion, but you should consider assessing vaccine immune responses, including consultation with a qualified specialist, to assess whether a protective immune response was mounted.

Progressive Multifocal Leukoencephalopathy (PML)

Cases of progressive multifocal leukoencephalopathy (PML) have been reported in patients with MS treated with OCREVUS in the postmarketing setting. PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. PML has occurred in OCREVUS-treated patients who had not been treated previously with natalizumab, (which has a known association with PML), were not taking any immunosuppressive or immunomodulatory medications associated with risk of PML prior to or concomitantly with OCREVUS, and did not have any known ongoing systemic medical conditions resulting in compromised immune system function.

JCV infection resulting in PML has also been observed in patients treated with other anti-CD20 antibodies and other MS therapies.

At the first sign or symptom suggestive of PML, withhold OCREVUS and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

Magnetic resonance imaging (MRI) findings may be apparent before clinical signs or symptoms of PML. Monitoring with MRI for signs 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. If PML is confirmed, treatment with OCREVUS should be discontinued.

Reduction in Immunoglobulins

As expected with any B-cell depleting therapy, decreased immunoglobulin levels are observed with OCREVUS treatment. The pooled data of OCREVUS clinical studies (RMS and PPMS) and their open-label extensions (up to approximately 7 years of exposure) have shown an association between decreased levels of immunoglobulin G (IgG<LLN) and increased rates of serious infections. Monitor the levels of quantitative serum immunoglobulins during OCREVUS treatment and after discontinuation of treatment, until B-cell repletion, and especially in the setting of recurrent serious infections. Consider discontinuing OCREVUS therapy in patients with serious opportunistic or recurrent serious infections, and if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.

Malignancies

An increased risk of malignancy with OCREVUS may exist. In controlled trials, malignancies, including breast cancer, occurred more frequently in OCREVUS-treated patients. Breast cancer occurred in 6 of 781 females treated with OCREVUS and none of 668 females treated with REBIF or placebo. Patients should follow standard breast cancer screening guidelines.

Immune-Mediated Colitis

Immune-mediated colitis, which can present as a severe and acute-onset form of colitis, has been reported in patients receiving OCREVUS in the postmarketing setting. Some cases of colitis were serious, requiring hospitalization, with a few patients requiring surgical intervention. Systemic corticosteroids were required in many of these patients. The time from treatment initiation to onset of symptoms in these cases ranged from a few weeks to years. Monitor patients for immune-mediated colitis during OCREVUS treatment and evaluate promptly if signs and symptoms that may indicate immune-mediated colitis, such as new or persistent diarrhea or other gastrointestinal signs and symptoms, occur.

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Important Safety Information (cont'd)

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Liver Injury

Clinically significant liver injury, without findings of viral hepatitis, has been reported in the postmarketing setting in patients treated with anti-CD20 B-cell depleting therapies approved for the treatment of MS, including OCREVUS. Signs of liver injury, including markedly elevated serum hepatic enzymes with elevated total bilirubin, have occurred from weeks to months after administration.

Patients treated with OCREVUS found to have an alanine aminotransferase (ALT) or aspartate aminotransferase (AST) greater than 3x the upper limit of normal (ULN) with serum total bilirubin greater than 2x ULN are potentially at risk for severe drug-induced liver injury.

Obtain liver function tests prior to initiating treatment with OCREVUS, and monitor for signs and symptoms of any hepatic injury during treatment. Measure serum aminotransferases, alkaline phosphatase, and bilirubin levels promptly in patients who report symptoms that may indicate liver injury, including new or worsening fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice. If liver injury is present and an alternative etiology is not identified, discontinue OCREVUS.

Use in Specific Populations

Pregnancy

There are no adequate data on the developmental risk associated with use of OCREVUS in pregnant women. There are no data on B-cell levels in human neonates following maternal exposure to OCREVUS. However, transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 antibodies during pregnancy. OCREVUS is a humanized monoclonal antibody of an immunoglobulin G1 subtype and immunoglobulins are known to cross the placental barrier.

Lactation

There are no data on the presence of ocrelizumab in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. Ocrelizumab was excreted in the milk of ocrelizumab-treated monkeys. Human IgG is excreted in human milk, and the potential for absorption of ocrelizumab to lead to B-cell depletion in the infant is unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for OCREVUS and any potential adverse effects on the breastfed infant from OCREVUS or from the underlying maternal condition.

Females and Males of Reproductive Potential

Women of childbearing potential should use effective contraception while receiving OCREVUS and for 6 months after the last infusion of OCREVUS. Instruct patients that if they are pregnant or plan to become pregnant while taking OCREVUS, they should inform their healthcare provider.

Most Common Adverse Reactions

RMS: The most common adverse reactions in RMS trials (incidence ≥10% and >REBIF) were upper respiratory tract infections (40%) and infusion reactions (34%).

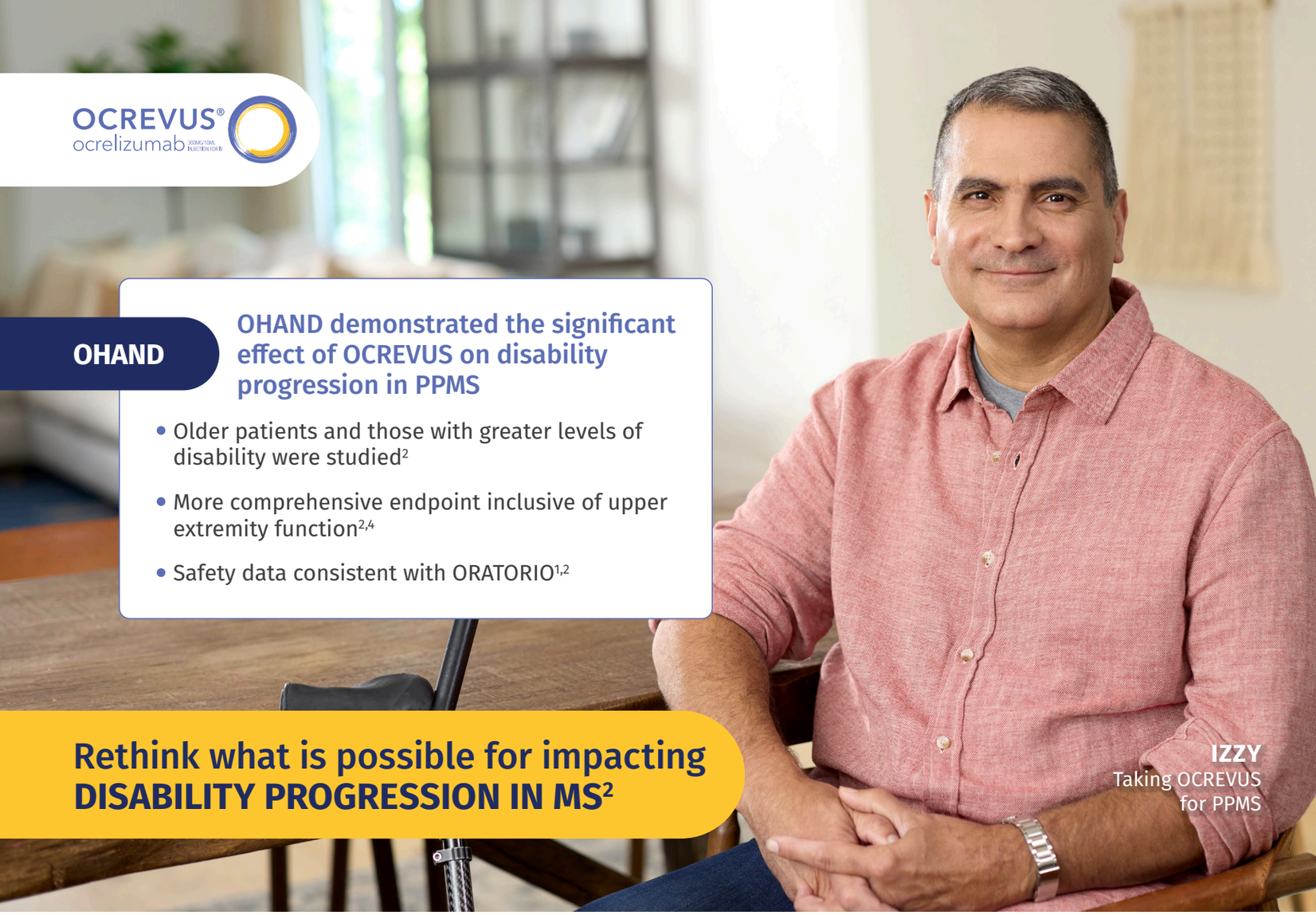
PPMS: The most common adverse reactions in PPMS trials (incidence ≥10% and >placebo) were upper respiratory tract infections (49%), infusion reactions (40%), skin infections (14%), and lower respiratory tract infections (10%).

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

References: 1. Montalban X, Hauser SL, Kappos L, et al; ORATORIO Clinical Investigators. Ocrelizumab versus placebo in primary progressive multiple sclerosis. *N Engl J Med*. 2017;376(3):209-220. doi:10.1056/NEJMoa1606468 **2.** Giovannoni G, Airas L, Bove R, et al. Efficacy and safety of ocrelizumab vs placebo in primary progressive MS: results of the phase IIIb ORATORIO-HAND study. Poster presented at: 41st Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); September 24-26, 2025; Barcelona, Spain. **3.** OCREVUS [prescribing information]. South San Francisco, CA: Genentech, Inc. 2025. **4.** Kappos L, Yiu S, Coetzee T, et al. Composite confirmed disability worsening/progression is a useful clinical endpoint for multiple sclerosis clinical trials. *Neurology*. 2025;104(10):e213558. doi:10.1212/WNL.0000000000213558 **5.** Feys P, Lamers I, Francis G, et al. The Nine-Hole Peg Test as a manual dexterity performance measure for multiple sclerosis. *Mult Scler*. 2017;23(5):711-720. doi:10.1177/1352458517690824 **6.** Fox EJ, Markowitz C, Applebee A, et al. Ocrelizumab reduces progression of upper extremity impairment in patients with primary progressive multiple sclerosis: Findings from the phase III randomized ORATORIO trial. *Mult Scler*. 2018;24(14):1862-1870. doi:10.1177/1352458518808189 **7.** Hauser SL, Kappos L, Montalban X, et al. Safety of ocrelizumab in multiple sclerosis: up to 11 years of updated analysis in patients with relapsing and progressive multiple sclerosis. Poster presented at: 40th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); September 18-20, 2024. Poster P300.

 Please see additional safety information on pages 9-10 and click here for full OCREVUS Prescribing Information and Medication Guide.

OCREVUS®
ocrelizumab



OHAND

OHAND demonstrated the significant effect of OCREVUS on disability progression in PPMS

- Older patients and those with greater levels of disability were studied[2]
- More comprehensive endpoint inclusive of upper extremity function[2,4]
- Safety data consistent with ORATORIO[1,2]

IZZY
Taking OCREVUS
for PPMS

Rethink what is possible for impacting DISABILITY PROGRESSION IN MS[2]

Genentech is committed to helping patients get started on OCREVUS after it has been prescribed.

Indications

OCREVUS is indicated for the treatment of:

- Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults
- Primary progressive MS, in adults.

Contraindications

OCREVUS is contraindicated in patients with active hepatitis B virus infection and in patients with a history of life-threatening infusion reaction to OCREVUS.

Select Important Safety Information

The warnings and precautions for OCREVUS are infusion reactions and infections, which include respiratory tract infections, herpes, hepatitis B virus (HBV) reactivation, and a warning for progressive multifocal leukoencephalopathy (PML). Additional warnings are possible increased risk of immunosuppressant effects with other immunosuppressants, reduction in immunoglobulins, malignancies, immune-mediated colitis, and liver injury.

MS=multiple sclerosis; PPMS=primary progressive multiple sclerosis.

Please see additional safety information on pages 9-11 and click here for full OCREVUS Prescribing Information and Medication Guide.

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