A **decade of data** and 300,000+ patients treated globally[2,3]

[b]From December 2020 to September 2023; IQVIA Claims & IQVIA NSP, rolling 3-month prescriber-based data; includes all patients with an OCREVUS prescription. Includes all patients with an ICD-10-CM of G35 (multiple sclerosis).

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, and immune-mediated colitis.

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

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PROGRESSION BEGINS EARLY IN MS[4-10]

MS is characterized by acute and diffuse inflammation and chronic neurodegeneration[5,7,11]

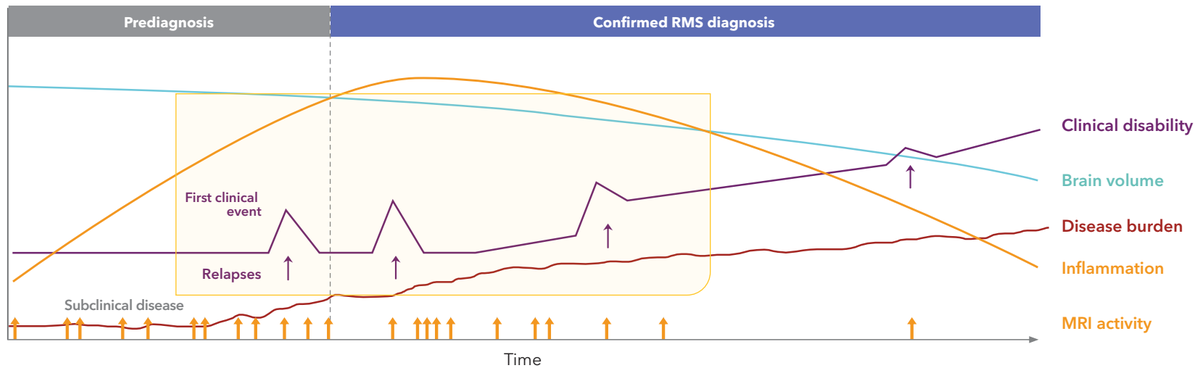
- INFLAMMATORY ACTIVITY IS THOUGHT TO BE **HIGHEST EARLY IN MS** AND IS ASSOCIATED WITH[5]:

Younger age
The average age at diagnosis of MS is 32[12-14]

Lesions
Lesions can contribute to axonal loss/degeneration, which is associated with progression[8]

Relapses
Relapses are the acute clinical manifestation of neurologic damage early in MS[15,16]

INFLAMMATION IS AN IMPORTANT DRIVER OF PROGRESSION EARLY IN MS[5,9-11,17-20]

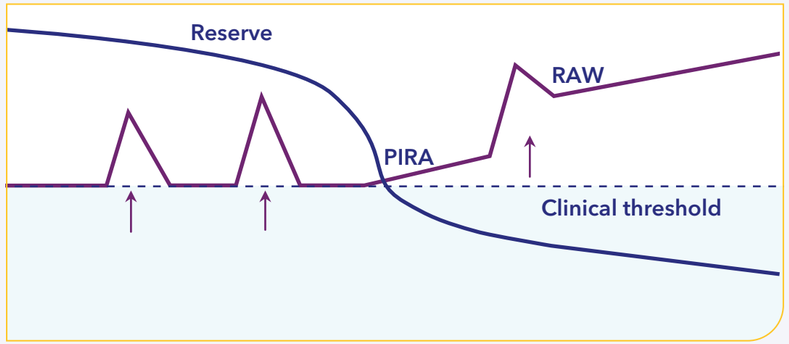


- PROGRESSION REFERS TO BOTH[15,18]:
  - Pathological processes (brain volume loss)
  - Clinical manifestation (disability)

Adapted from Gavin Giovannoni based on Fox RJ, Cohen JA. *Cleve Clin J Med.* 2001;68(2):157-171.

- THE BRAIN **MAY COMPENSATE FOR DAMAGE** EARLY IN MS VIA FUNCTIONAL RESERVE[8,11,17,21-25]

- As functional reserve is lost, the ability to compensate for damage decreases and disability emerges
- Disability may accumulate in 2 ways: relapse-associated worsening (RAW) or progression independent of relapse activity (PIRA)
- In 2 recent studies of CIS and RMS patients, PIRA accounted for a substantial portion of the confirmed disability accumulation observed[24,25]



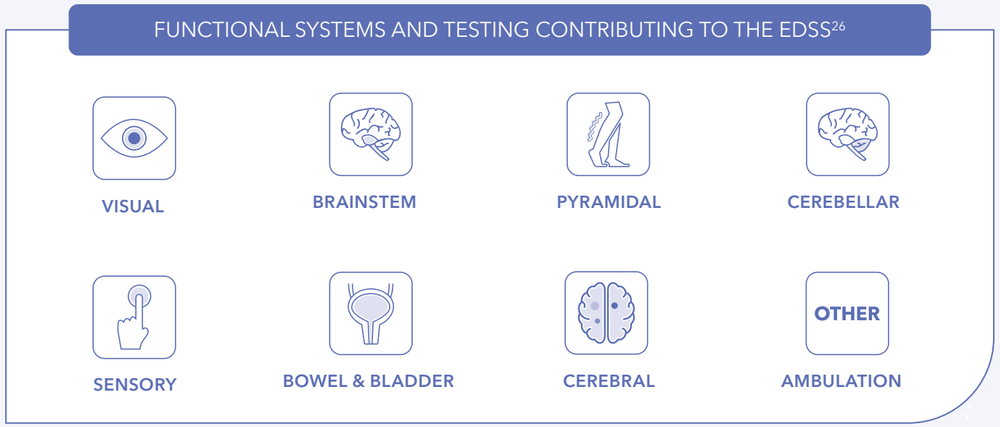
Emerging research suggests that disability progression can manifest in the absence of relapse, as early as CIS.[24,25]

RECOGNIZING PROGRESSION EARLY CAN BE CHALLENGING[26-28]

Disability progression in MS patients goes beyond ambulation[26]

DISABILITY PROGRESSION CAN OCCUR ACROSS **MANY FUNCTIONAL DOMAINS**[11,17,26]

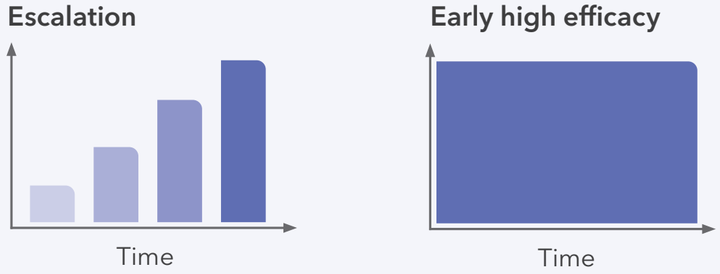
Early deficits assessed during the neurological exam can affect various functional systems, even in patients who are fully ambulatory.



Some signs and symptoms may be difficult to detect on exam, such as changes in mood and cognition, fatigue, and sexual dysfunction.[29-31]

CONTEMPORARY **TREATMENT PARADIGMS** IN MS[32]

When selecting a strategy to manage MS, the early impact of progression should be considered along with factors such as treatment goals, patient preferences, age, and comorbidities.



Reducing the risk of disability progression is a key goal of MS management. What approach do you take with your patients?

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

GENERATION O IN OPERA I AND II

Select baseline characteristics of patients in OCREVUS trials for RMS

60%
of patients studied were **younger than 40 years of age**[33]

3/4
of all patients had no disease-modifying therapy (DMT) **within the previous 2 years**[1]

45%
of all patients were diagnosed within 2 years of screening and **treatment naive**[2,34]

37 years
mean age with approximately **4 years** from MS diagnosis to trial participation[1]

40%
of patients had an EDSS score of **<2.5**[1,33]
Patients in the controlled period had to have an EDSS score between 0 and 5.5.

40%
had ≥1 T1 Gd+ lesions, thought to represent **acute inflammation**[1]

AVERAGE PATIENT IN THE CONTROLLED PERIOD[1,35,36]

Age: **37**
Mean EDSS score: **2.8**

Mean number of T1 Gd+ lesions: **1.8**
Mean number of T2 lesions: **51.0**

Untreated within 2 years: **74%**
Mean time since diagnosis: **4 years**

Gd+=gadolinium-enhancing.

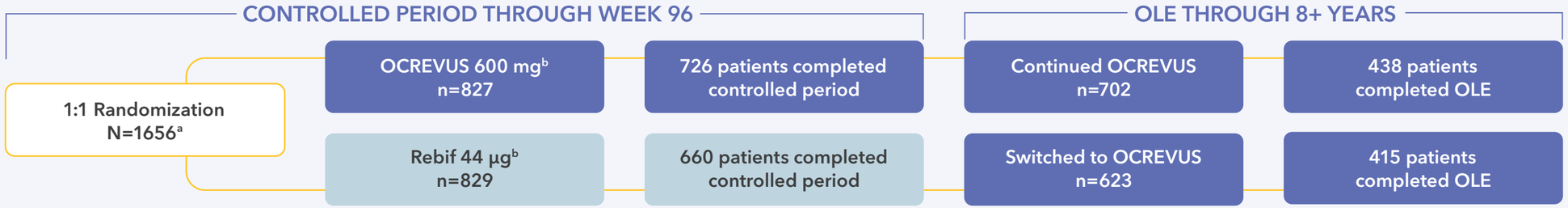
Select Important Safety Information

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.

ONLY aCD20 FOR MS WITH 10+ YEARS OF CLINICAL TRIAL EXPERIENCE[1,3]

OPERA I and OPERA II were identical head-to-head clinical trials of OCREVUS vs Rebif® (interferon β-1a) in RMS[36]

OPERA I AND OPERA II POOLED ANALYSIS[2,3]



- Patients who received Rebif during the controlled period continued to receive Rebif during the open-label extension (OLE) screening period until their first infusion of OCREVUS
- In the OLE phase, the first 600-mg dose of OCREVUS was administered as two 300-mg infusions given 2 weeks apart

KEY INCLUSION CRITERIA[36]

- ≥2 relapses within last 2 years
- ≥1 relapse in last year
- EDSS score from 0.0 to 5.5

CONTROLLED AND OLE **STUDY ENDPOINTS**[3,36,37]

- Annualized relapse rate (primary endpoint)
- 12-week and 24-week confirmed disability progression (CDP) in the controlled period and 24-week and 48-week CDP in the OLE period
- Confirmed disability improvement (CDI) at 12 weeks through 96 weeks
- Mean number of T1 Gd+ lesions and new or enlarging T2 hyperintense lesions per MRI at Week 96
- Exploratory composite endpoint: proportion of patients with No Evidence of Disease Activity (NEDA) in the controlled period
- Safety

Limitations of the open-label, uncontrolled study period

Patients in the OLE period successfully completed the controlled period and are subject to continued dropout; they may represent an enriched population. The endpoints measured were not prespecified or powered to conclude statistical significance; they only convey numerical trends. Conclusions regarding the treatment effect of OCREVUS cannot be drawn on the basis of OLE data.

aCD20=anti-CD20 B-cell depleting antibody.

[a] OCREVUS: OPERA I, n=410; OPERA II, n=417. Rebif: OPERA I, n=411; OPERA II, n=418.[34]

[b] OCREVUS arm: 600-mg intravenous (IV) dose every 24 weeks (first dose: two 300-mg IV infusions 2 weeks apart) or placebo as subcutaneous (SC) injections 3 times/week; Rebif arm: 44-µg SC 3 times/week or placebo IV infusions every 24 weeks.[34]

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, and immune-mediated colitis.

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

SUPERIOR RELAPSE REDUCTIONS VS REBIF AT YEAR 2

OCREVUS reduced relapse rates by nearly half[1]

SUPERIOR RELAPSE REDUCTIONS vs REBIF AT YEAR 2 (CONTROLLED PERIOD)[1]

46% OPERA I | **47%** OPERA II

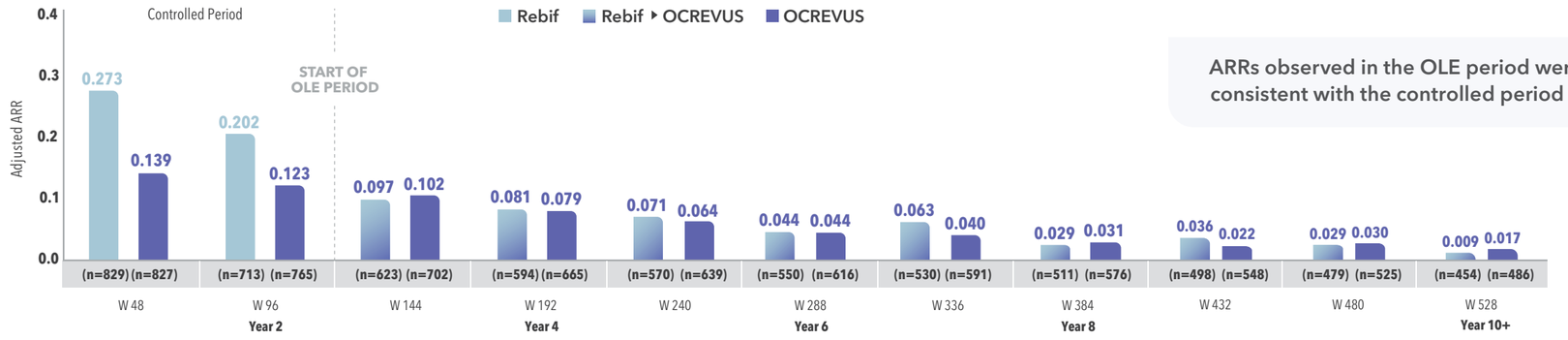
RELATIVE REDUCTIONS
p<0.0001

ARR with OCREVUS vs Rebif:
OPERA I: 0.156 vs 0.292
OPERA II: 0.155 vs 0.290

- **83%/82%** of patients treated with OCREVUS were relapse free at the end of the 2-year controlled period vs **71%/72%** with Rebif (OPERA I/OPERA II)

ANNUALIZED RELAPSE RATE (ARR) DATA THROUGH **10+ YEARS**[3]

CONTROLLED AND OLE PERIODS



ARRs observed in the OLE period were consistent with the controlled period

All patients in the OLE period were treated with OCREVUS.[3]

- Conclusions regarding the treatment effect of OCREVUS cannot be drawn on the basis of OLE data

Relapses were defined as new or worsening neurologic symptoms that were attributable to MS, persisted for more than 24 hours, were immediately preceded by a stable or improving neurologic state for at least 30 days, and were accompanied by objective neurologic worsening as defined in the study protocols.[36]

Measurements performed at intermediate timepoints were not prespecified in the statistical testing hierarchy and reflect numerical trends only.[36]

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.

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

IMPACT ON DISABILITY ACROSS 3 ENDPOINTS AT YEAR 2

The only aCD20 to significantly impact disability in 3 endpoints across 2 identical RMS trials[1,36]

>9 OUT OF 10 PATIENTS TAKING OCREVUS REMAINED FREE FROM DISABILITY PROGRESSION (12- AND 24-WEEK CDP)[1,36]

PRESPECIFIED POOLED ANALYSIS

12-week CDP (proportion of patients)	24-week CDP (proportion of patients)
90.2% OCREVUS vs **84.8%** Rebif	**92.4%** OCREVUS vs **88.0%** Rebif
NO DISABILITY PROGRESSION	NO DISABILITY PROGRESSION
In the individual OPERA studies	**In the individual OPERA studies**
OPERA I: 92.4% OCREVUS vs 87.8% Rebif	**OPERA I: 94.1% OCREVUS vs 90.5% Rebif**
OPERA II: 89.4% OCREVUS vs 84.9% Rebif	**OPERA II: 92.1% OCREVUS vs 88.5% Rebif**
↓ **40%** RISK REDUCTION vs REBIF HR (95% CI): 0.60 (0.45, 0.81) *p*=0.0006	↓ **40%** RISK REDUCTION vs REBIF HR (95% CI): 0.60 (0.43, 0.84) *p*=0.003

>20% OF OCREVUS-TREATED PATIENTS SHOWED CONFIRMED DISABILITY IMPROVEMENT (CDI)[36]

PRESPECIFIED POOLED ANALYSIS

12-week CDI (proportion of patients)

↑ **33%**
DIFFERENCE
p=0.02

Pooled analysis:
20.7% OCREVUS vs 15.6% Rebif

Confirmed disability progression (CDP) was defined as patients with EDSS score ≤5.5 who experienced an EDSS score increase of ≥1.0. For patients with EDSS score >5.5, progression was an EDSS score increase of ≥0.5. Disability progression was categorized as confirmed if it was present at 12 or 24 weeks over the treatment period.[34]

Confirmed disability improvement (CDI) was defined as a reduction from the baseline EDSS score of at least 1.0 point (or 0.5 points if the baseline EDSS score was >5.5) that was sustained for at least 12 weeks in patients with a baseline EDSS score of at least 2.0.[34]

48-WEEK CDP vs REBIF (CONTROLLED PERIOD, POST HOC ANALYSIS)[2,38]

- 57% risk reduction (proportion of patients: 3.2% OCREVUS vs 7.2% Rebif)
- Not prespecified to conclude statistical significance; these data only convey numerical trends

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.

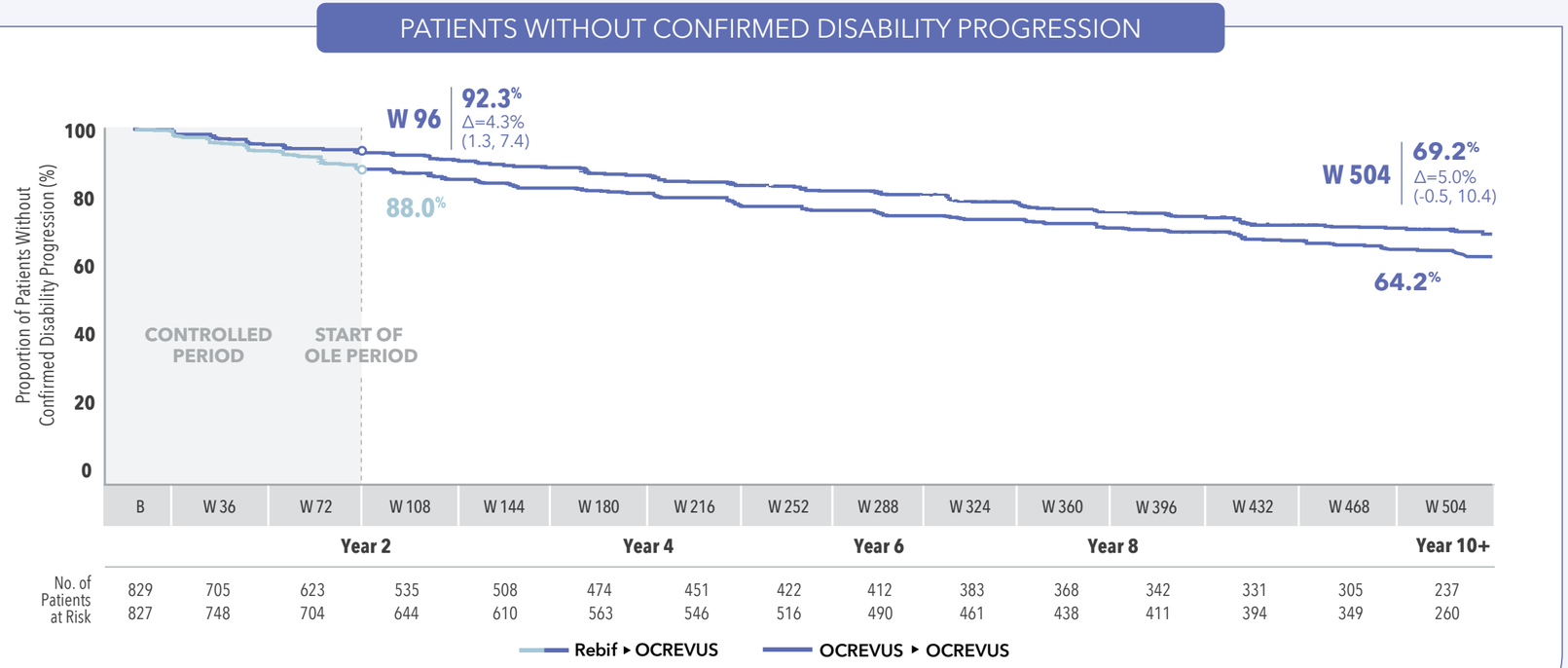
A higher proportion of OCREVUS-treated patients experienced infections compared to patients taking REBIF or placebo. In RMS trials, 58% of OCREVUS-treated patients experienced one or more infections compared to 52% of REBIF-treated patients. OCREVUS was not associated with an increased risk of serious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

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

DISABILITY DATA THROUGH 10+ YEARS

In the controlled period, >90% of patients treated with OCREVUS experienced no disability progression (12- and 24-week CDP)[1,36]

TIME TO ONSET OF **24-WEEK CDP**[2,3]



All patients in the OLE period were treated with OCREVUS.[3]

- Conclusions regarding the treatment effect of OCREVUS cannot be drawn on the basis of OLE data

> It was numbing to know that I had been diagnosed with MS. But I had a little person depending on me. **I had to find a way to keep going**.
>
> —**PASTELL**
> RMS diagnosis 2016, started OCREVUS 2018 at age 34

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.

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

SUPERIOR REDUCTIONS IN MRI LESIONS vs REBIF

OCREVUS demonstrated superior reductions in mean number of T1 Gd+ lesions and T2 lesions over 2 years[1]

NEAR-COMPLETE SUPPRESSION OF T1 Gd+ LESIONS[1,a]

94% OPERA I | **95%** OPERA II

RELATIVE REDUCTIONS
p<0.0001

OCREVUS vs Rebif:

OPERA I: 0.016 vs 0.286
OPERA II: 0.021 vs 0.416

[a]The precise mechanism by which OCREVUS exerts its therapeutic effects in MS is unknown.

SUPERIOR REDUCTIONS IN MEAN NUMBER OF NEW OR ENLARGING T2 LESIONS[1]

77% OPERA I | **83%** OPERA II

RELATIVE REDUCTIONS
p<0.0001

OCREVUS vs Rebif:

OPERA I: 0.323 vs 1.413
OPERA II: 0.325 vs 1.904

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.

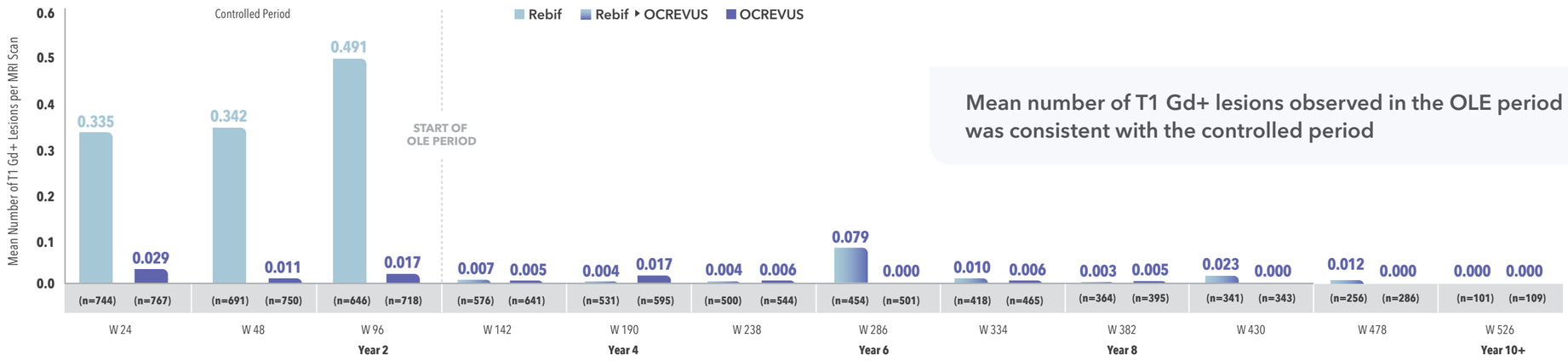
For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

MRI DATA THROUGH 10+ YEARS

T1 Gd+ lesions in the controlled and OLE periods[3]

T1 Gd+ LESIONS[3]

CONTROLLED AND OLE PERIODS



Mean number of T1 Gd+ lesions observed in the OLE period was consistent with the controlled period

All patients in the OLE period were treated with OCREVUS.[3]

- Conclusions regarding the treatment effect of OCREVUS cannot be drawn on the basis of OLE data

Relative reductions vs Rebif in T1 Gd+ lesions were observed in the controlled period at each of the intermediate timepoints–Weeks 24, 48, and 96. The measurements performed at these intermediate timepoints were not prespecified in the statistical testing hierarchy and reflect numerical trends only.[36]

Unadjusted controlled and OLE data include the ITT population; clinical cutoff date: November 2022. Number of T1 Gd+ lesions at each timepoint for all patients in the treatment group divided by the total number of brain MRI scans at that timepoint.[3]

ITT=intent-to-treat.

Select Important Safety Information

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

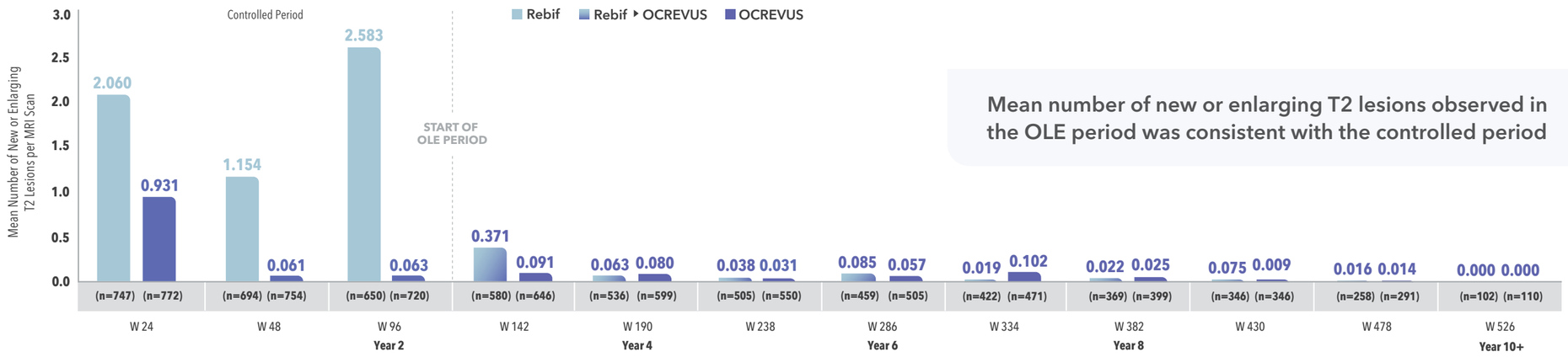
Immune-Mediated Colitis
Immune-mediated colitis, which can present as a severe and acute-onset form of colitis, has been reported in patients receiving OCREVUS in the postmarketing setting. Some cases of colitis were serious, requiring hospitalization, with a few patients requiring surgical intervention. 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.

MRI DATA THROUGH 10+ YEARS

New or enlarging T2 lesions in the controlled and OLE periods[3]

NEW OR ENLARGING T2 LESIONS[3]

CONTROLLED AND OLE PERIODS



Mean number of new or enlarging T2 lesions observed in the OLE period was consistent with the controlled period

All patients in the OLE period were treated with OCREVUS.[3]

- Conclusions regarding the treatment effect of OCREVUS cannot be drawn on the basis of OLE data

Relative reductions vs Rebif in T2 lesions were observed in the controlled period at each of the intermediate timepoints—Weeks 24, 48, and 96. The measurements performed at these intermediate timepoints were not prespecified in the statistical testing hierarchy and reflect numerical trends only.[36]

Unadjusted controlled and OLE data include the ITT population; clinical cutoff date: November 2022. Number of new or enlarging T2 lesions at each timepoint for all patients in the treatment group divided by the total number of brain MRI scans at that timepoint.[3]

ITT=intent-to-treat.

Select Important Safety Information

Contraindications

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NEDA BY WEEK 96 (POST HOC ANALYSIS)

No evidence of disease activity (NEDA) in the controlled period including re-baselined analysis

NEDA IS THE PROPORTION OF RMS PATIENTS WITH[36]:

- NO PROTOCOL-DEFINED RELAPSES
- NO 3-MONTH CDP
- NO T1 Gd+ MRI ACTIVITY
- NO NEW OR ENLARGING T2 LESIONS

Controlled Period NEDA[36]
Pooled Analysis

48% OCREVUS **vs** **27%** Rebif

Weeks 0-96

ASSESSMENT AND LIMITATIONS

- The predefined secondary endpoint of NEDA in the OPERA studies was considered nonconfirmatory because it fell below the break in the statistical hierarchy at change in Multiple Sclerosis Functional Composite Scale score from baseline to Week 96
- Exploratory result based on modified ITT population

Re-baselined NEDA[39]
Pooled Analysis

72% OCREVUS **vs** **42%** Rebif

Weeks 24-96
(re-baselined to 24 weeks)

82% OCREVUS **vs** **57%** Rebif

Weeks 48-96
(re-baselined to 48 weeks)

ASSESSMENT AND LIMITATIONS

- During Weeks 48 to 96, the lower frequency of MRI scans compared with other time periods may have influenced the proportions of patients maintaining NEDA
- Moving into the clinical practice setting, the optimal timing of re-baselining should reflect the anticipated timing for reaching complete DMT efficacy, to give a more reliable indication of subsequent drug failure
- Conclusions from cross-trial comparisons are limited because of differences including comparators, patient populations, MRI techniques, frequency of assessments, analysis methods, and definitions of NEDA

Why re-baseline NEDA data?

NEDA analyses are often re-baselined, or calculated at a later timepoint, in order to minimize any confounding impact of pretreatment disease activity and to better reflect the steady state of DMT impact on disability worsening and disease activity.[39]

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, and immune-mediated colitis.

WELL-ESTABLISHED SAFETY PROFILE WITH 10+ YEARS OF CLINICAL TRIAL DATA

As of November 2022, 6155 patients have received OCREVUS in the all-exposure trial population, resulting in 28,269 PY of exposure[37]

- **In Phase III trials, the most common adverse events (AEs) were infusion reactions and infections (mainly mild to moderate)**[1]
- Other common AE rates were similar with Rebif and placebo[1]
- In the OCREVUS all-exposure population, reported rates of AEs continue to be consistent with those seen during the controlled RMS and primary-progressive multiple sclerosis (PPMS) trials[37]

AEs PER 100 PATIENT-YEARS (PY) IN OCREVUS TRIAL POPULATION[37]

	OPERA (pooled) treatment period[a]			ORATORIO treatment period[a]			OCREVUS all-exposure population[d]
	OCREVUS n=825	Rebif n=826	All RMS[b] n=4558	OCREVUS n=486	Placebo n=239	All PPMS[c] n=1597	Mean number of doses: 9.6 N=6155
	PY=1448	PY=1399	PY=21,080	PY=1606	PY=729	PY=7190	PY=28,269
Any AE	290	296	227	252	259	215	224
AEs leading to discontinuation	2.4	3.9	1.0	1.2	1.1	1.0	1.0
Serious AEs	5.4	6.3	5.7	10.2	12.1	10.9	7.0
Infections	84.5	67.8	66.2	70.8	72.5	61.6	65.1
Serious infections[e]	0.8	1.8	1.5	2.7	3.0	3.7	2.1
Infusion reactions	34.9	7.9	23.2	31.0	20.3	16.8	21.6
Malignancies[f,g]	0.3	0.1	0.4	0.9	0.3	0.9	0.5
Deaths	0.1	0.1	0.1	0.3	0.4	0.4	0.2

COVID-19–related AEs were excluded from this analysis, but patients continued to contribute to the incidence of all other AEs. AEs were classified according to Medical Dictionary for Regulatory Activities (MedDRA) versions 18.0, 18.1, 22.1, and 24.1. Multiple occurrences of the same AE in one patient are counted multiple times, except for malignancies.

[a]Data as of April-July 2015.

[b]Includes patients with RMS who received any dose of OCREVUS during the controlled period and associated OLE periods of the Phase II and Phase III studies plus VELOCE, CHORDS, CASTING, OBOE, ENSEMBLE, LIBERTO, and CHIMES (data as of November 2022).

[c]Includes patients with PPMS who received any dose of OCREVUS during the controlled period and associated OLE periods of OBOE and CONSONANCE (data as of November 2022).

[d]Includes patients who received any dose of OCREVUS during the controlled period and associated OLE periods of the Phase II and Phase III studies plus VELOCE, CHORDS, CASTING, OBOE, ENSEMBLE, LIBERTO, CONSONANCE, and CHIMES, including patients originally randomized to comparator (IFN β-1a or placebo) who switched to open-label OCREVUS treatment (data as of November 2022).

[e]Serious infections are defined using AEs falling into the MedDRA system organ class "Infections and infestations," and using "Is the event nonserious or serious?" from the AE case report form.

[f]Malignancies are identified using AEs falling into the standard MedDRA query "Malignant tumours (narrow)."

[g]For malignancies, incidence rates are reported and exposure in PY was calculated from first treatment to onset of first malignancy.

ORATORIO (PPMS): A randomized, double blind, placebo-controlled clinical trial in 732 patients (OCREVUS, n=488; placebo, n=244 with PPMS treated for at least 120 weeks. Selection criteria included patients aged 18 to 55 and required a baseline EDSS score of 3.0 to 6.5 and a score of 2.0 or greater for the EDSS pyramidal functional systems score due to lower extremity findings. Patients also had no history of RMS, SPMS (secondary progressive multiple sclerosis), or PRMS (progressive relapsing multiple sclerosis).[1,40]

- **Potential serious opportunistic infections in the OCREVUS all-exposure population:** 0.03 per 100 PY (95% CI: 0.01, 0.06) as of November 2022[37]

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

OBSERVED RATES OF INFECTION

Patients who experienced ≥1 infections in the controlled period[1]

INFECTIONS IN THE CONTROLLED PERIOD[1]

OPERA I AND II

58% OCREVUS vs 52% Rebif

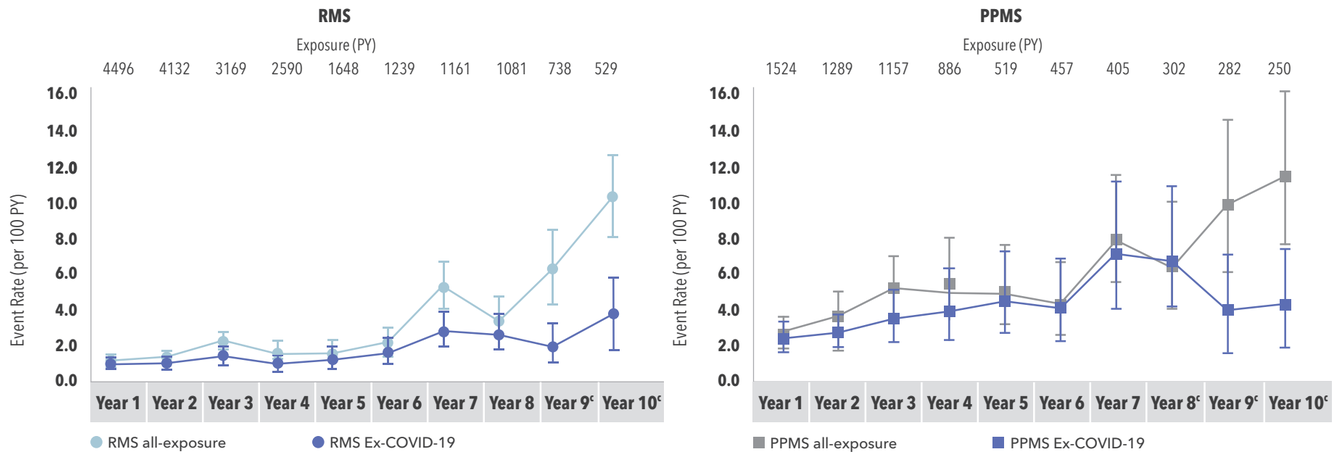
ORATORIO

70% OCREVUS vs 68% Placebo

- In the controlled period, infections were mainly mild to moderate
- In the controlled period, OCREVUS did not increase the risk of serious infections vs Rebif or placebo, though serious infections have occurred
- In the post-marketing period, serious, including life-threatening or fatal, bacterial, viral, parasitic, and fungal infections have been reported in patients receiving OCREVUS. An increased risk of infections has been observed in patients during and following completion of treatment with anti-CD20 B-cell depleting therapies

RATE OF SERIOUS INFECTIONS OBSERVED OVER 10+ YEARS[37,a]

ALL-EXPOSURE POPULATION[b]



Serious infections with OCREVUS (Ex-COVID-19 population as of November 2022)[37]

- All-RMS population: 1.5 per 100 PY (95% CI: 1.3, 1.7)
- All-PPMS population: 3.7 per 100 PY (95% CI: 3.3, 4.2)
- All-exposure population: 2.1 per 100 PY (95% CI: 1.9, 2.2)

The most common serious infections were urinary tract infections, pneumonia, and cellulitis.[41]

Patients with IgG below LLN were not excluded.

[a] For both RMS and PPMS, serious infections data are presented for the full OCREVUS all-exposure population and a subset of this population without COVID-19 infections (Ex-COVID-19). In the Ex-COVID-19 analysis, patients continued to contribute to the incidence of all other AEs.

[b] Includes patients who received any dose of OCREVUS during the controlled period and associated OLE periods of the Phase II and Phase III studies plus VELOCE, CHORDS, CASTING, OBOE, ENSEMBLE, CONSONANCE, and CHIMES, including patients originally randomized to comparator (IFN ß-1a or placebo) who switched to open-label OCREVUS treatment (data as of November 2022).

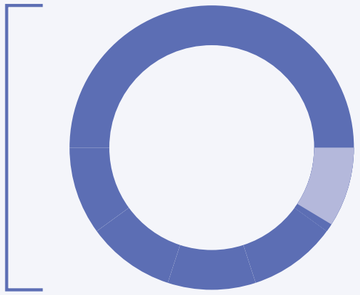
[c] The exposure in PY during Years 8 through 10 is limited for meaningful interpretation.

SERIOUS INFECTIONS AND IgG LEVELS

10+ years of data on serious infections and IgG (as of November 2022)[37]

- MOST PATIENTS TAKING OCREVUS REMAINED **AT OR ABOVE THE LOWER LIMIT OF NORMAL FOR IgG** (LLN; 5.65 g/L)[2]

TOTAL PATIENTS TREATED WITH OCREVUS IN OPERA, ORATORIO, AND OLE
N=2092



84.3%
n=1763
Patients with IgG≥LLN

15.7%
n=329
Patients with IgG<LLN

Out of 2092 patients treated with OCREVUS, 62 serious infections were observed in 46 patients during episodes of IgG<LLN

From the OCREVUS Prescribing Information[1]

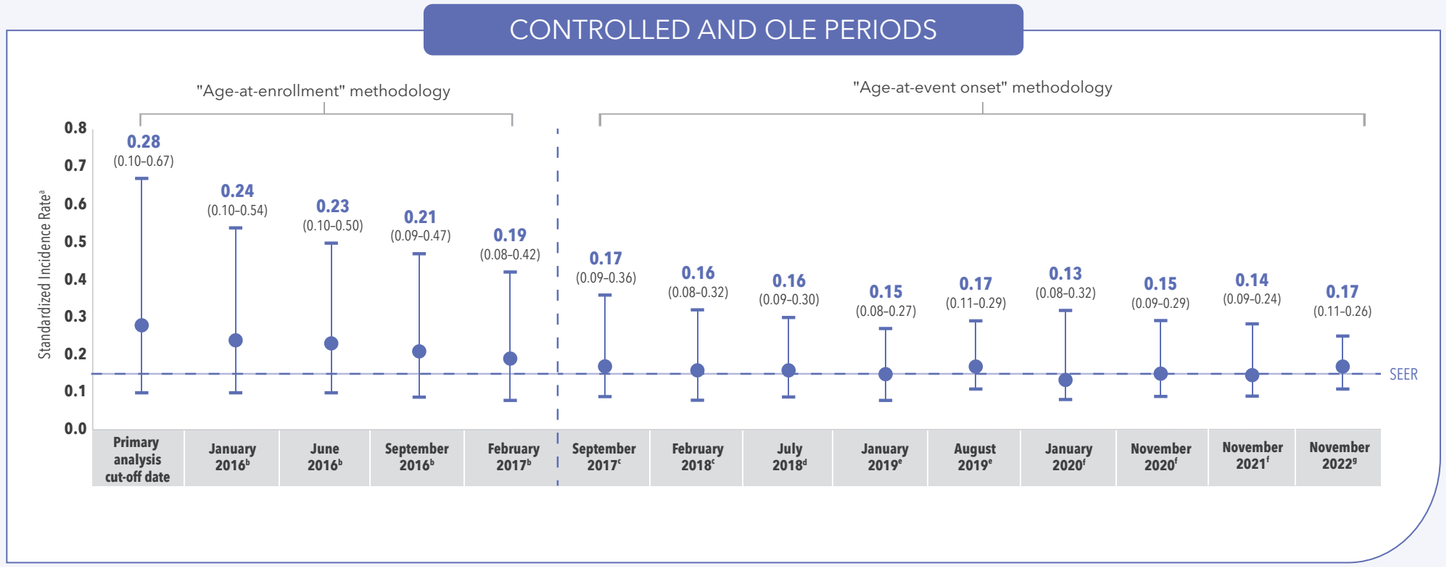
As expected with any B-cell depleting therapy, decreased immunoglobulin levels are observed with OCREVUS treatment. The pooled data of OCREVUS clinical studies (RMS and PPMS) and their open-label extensions (up to approximately 7 years of exposure) have shown an association between decreased levels of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

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

ADDITIONAL IMPORTANT SAFETY INFORMATION

An increased risk of malignancy, including breast cancer, may exist in OCREVUS-treated patients[1]

AGE-STANDARDIZED INCIDENCE RATE OF FEMALE BREAST CANCER OVER OCREVUS-STUDIED POPULATIONS AND SEER POPULATION (PER 100 PY)[2,37,42]



"Age-at-enrollment" methodology only captures how old a patient was at the trial baseline, and not when the event occurred. However, as study follow-up continues and patients become older, the "age-at-event onset" methodology, based on the age of the patient at the onset of malignancy, is a more precise method of calculating the standardized incidence rate.

[a] Nonmelanoma Skin Cancer (NMSC) is not reported in the Surveillance, Epidemiology, and End Results (SEER) program.

[b] Includes patients who received any dose of OCREVUS during the controlled period, extended-controlled period, and associated OLE periods of the Phase II and Phase III studies, including patients originally randomized to comparator (Rebif or placebo) who switched to open-label OCREVUS treatment.

[c] Includes patients described in footnote b plus VELOCE, CHORDS, CASTING, and OBOE.

[d] Includes patients described in footnote c plus ENSEMBLE.

[e] Includes patients described in footnote d plus LIBERTO.

[f] Includes patients described in footnote d plus CONSONANCE.

[g] Includes patients who received any dose of OCREVUS during the controlled period, and associated OLE periods of the Phase II and Phase III studies, plus VELOCE, CHORDS, CASTING, OBOE, ENSEMBLE, LIBERTO, and CONSONANCE, including patients originally randomized to comparator (Rebif or placebo) who switched to open-label OCREVUS treatment.

The SEER Program of the National Cancer Institute (NCI) is an authoritative source of information reporting data on cancer incidence in nearly 50% of the general US (non-MS specific) population. No comparisons should be made due to limitations that have not been fully accounted for, such as variations in patient populations, as well as differences in sample size, temporal changes, and other potential confounding factors.[44]

Breast cancer was found in:

- 6/781 females treated with OCREVUS and 0/668 females treated with Rebif or placebo in the controlled period[1]
- 33/3857 females on OCREVUS (16,864 PY) in the all-exposure population as of November 2022[37]

The FDA recommends that OCREVUS patients follow standard breast cancer screening guidelines

The American Cancer Society recommends that patients age <40 with risk factors for breast cancer should ask their HCP whether mammograms are advisable and how often to have them. Patients age 45 to 54 should get mammograms every year.[1,43]

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

2x-YEARLY OCREVUS DOSING[a]

Shorter 2-hour infusion option after first dose[1,b]

TREATMENT **INITIATION**

INITIAL DOSE

DAY 1: 300 MG — Infusion 1

DAY 15: 300 MG — Infusion 2

≥2.5-HOUR DURATION

2-hour infusion is available for patients who have not experienced serious infusion reactions (IRs) with any previous OCREVUS infusion

2 HOURS if no serious IRs[c] have occurred

3.5 TO 4 HOURS

[a] Three treatments in the first year: first 600-mg dose administered as two 300-mg IV infusions over approximately 2.5 hours, separated by 2 weeks; subsequent doses administered as a single 600-mg IV infusion every 6 months.

[b] Infusion time may take longer if the infusion is interrupted or slowed. No change in premedication, dose, formulation, or posttreatment monitoring between infusion timing options.

[c] Per the study protocol, serious IRs included those that were fatal or life threatening, required or prolonged hospitalization, resulted in persistent or significant disability, or were deemed to be medically significant by the trial investigator.[2]

ONE 600-MG INFUSION EVERY 6 MONTHS BEYOND INITIAL TREATMENT[1]

Delayed or missed doses[1]:

If a planned infusion of OCREVUS is missed, administer it as soon as possible; do not wait until the next scheduled dose. Reset the dose schedule to administer the next sequential dose 6 months after the missed dose is administered. Doses of OCREVUS must be separated by at least 5 months.

PREMEDICATION AND OBSERVATION[1]

Premedication	Infusion	Observation
30 to 60 minutes	2 hours or 3.5 to 4 hours	60 minutes

With the OCREVUS dosing schedule, patients only need 2 infusions every 12 months[1]

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.

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

SHORTER 2-HOUR INFUSION

2-hour infusion is available for patients who have not experienced serious IRs with any previous OCREVUS infusion[1]

Per the ENSEMBLE protocol, serious IRs included those that were fatal or life threatening, required or prolonged hospitalization, resulted in persistent or significant disability, or were deemed to be medically significant by the trial investigator.[2]

NO LIFE-THREATENING, FATAL, OR SERIOUS IRs OCCURRED WITH OCREVUS IN THE ENSEMBLE PLUS STUDY[1,45]

The proportions of patients with IRs were similar between the 2 infusion protocols[1,45]

24.4%
2-HOUR INFUSION

23.3%
3.5- TO 4-HOUR INFUSION

- Overall, in all randomized doses, 27.1% of the patients in the 2-hour infusion group and 25.0% of the patients in the 3.5-hour infusion group reported mild or moderate infusion reactions; two infusion reactions were severe in intensity, with 1 severe infusion reaction (0.3%) reported in 1 patient in each group in this substudy

ENSEMBLE PLUS evaluated the safety of OCREVUS 2-hour infusion[1]

A prospective, multicenter, randomized, double-blind, controlled, parallel-arm substudy of 580 patients with early RRMS. 81% (469/579) of treated patients received a single randomized infusion of OCREVUS for the primary analysis.

3.5- to 4-hour infusion of OCREVUS: 99.7% of infusions did not result in serious IRs in the OPERA and ORATORIO studies (controlled period)[1,46]

- IRs were highest with the first infusion. Of the IRs that occurred, most were mild to moderate in severity
- 0.3% of OCREVUS-treated MS patients experienced IRs that were serious, some requiring hospitalization

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.

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

PERSISTENCE AND ADHERENCE

Clinical trial completion rates and real-world persistence and adherence data

OCREVUS CLINICAL **TRIAL COMPLETION**[1]

Percentage of patients who completed the OCREVUS RMS clinical trials at Year 2:

OPERA I

89% OCREVUS vs **83%** Rebif

OPERA II

86% OCREVUS vs **77%** Rebif

OCREVUS REAL-WORLD **PERSISTENCE AND ADHERENCE**[2,47]

Study design for OCREVUS real-world analysis among patients with 2 years of follow-up[2,47]

OCREVUS was studied with other DMTs using real-world US commercial and Medicare claims data from IBM MarketScan®.

- Persistence and adherence over a 2-year period were evaluated in the IBM MarketScan® Commercial Claims and Medicare Supplemental Databases
- Inclusion criteria included: patients ≥18 years of age with a diagnosis of MS who initiated an FDA-approved DMT between April 2017 and December 2017 and with 2 years of follow-up data (n=1710)
- Exclusion criteria included: patients on alemtuzumab, mitoxantrone, and any off-label therapies; patients initiating multiple DMTs on index; and patients with any claims of index DMT in the prior 12 months

Persistence was defined as no evidence of switching to another DMT or no gap in index DMT coverage of ≥60 days at any time during the evaluation period.[a]

Adherence was calculated based on proportion of days covered (PDC), with ≥80% considered adherent to the DMT initiated.[a]

– PDC = number of days of supply or administration divided by 730 days

[a]For orals and self-injectables, if a patient received their prescription early, the patient was assumed to be persistent/adherent for the total number of days for which they possessed medication. For IV infusions, including OCREVUS, these overlapping days were not considered.

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.

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

OCREVUS REAL-WORLD ANALYSIS

Among patients with 2 years of follow-up concluding December 31, 2019[47]

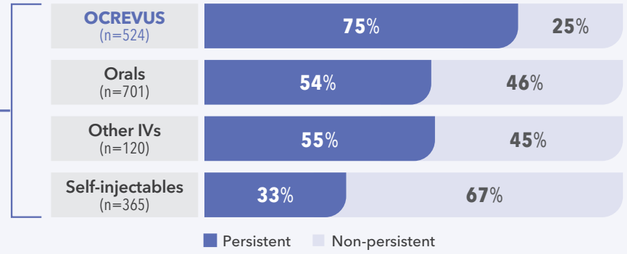
LIMITATIONS FOR OCREVUS REAL-WORLD ANALYSIS AMONG PATIENTS WITH 2 YEARS OF FOLLOW-UP[2,47]

- Potential for selection bias based on requirement that patients have continuous enrollment for 3 years, which may limit generalizability of the results
- Deviations from FDA-approved dosing schedule may cause persistence and adherence to be misclassified
- Caution should be exercised in making any direct comparisons due to differences in DMT dosing schedules and pharmacodynamics
- Claims data have inherent limitations:
  - –Unable to ascertain if patients on injectable and oral medications took DMT as prescribed
  - –ICD-10 codes do not identify patients by MS subtypes
  - –Limited clinical information available may impact interpretation of results (eg, MS disease duration, line of therapy)
  - –Lack of data on reason for discontinuation
  - –Possible coding errors and missing data

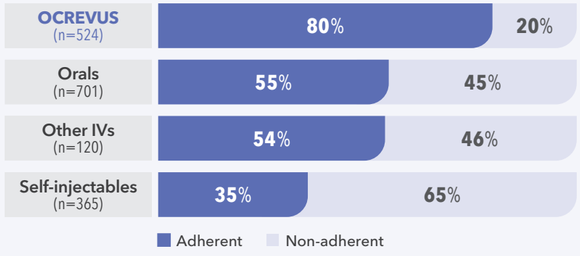
RESULTS FOR OCREVUS REAL-WORLD ANALYSIS INCLUDE ONLY DMTs THAT WERE FDA APPROVED AS OF 2017 AND EXCLUDE ALEMTUZUMAB AND MITOXANTRONE[2,47]

Real-world persistence and adherence rates should not be considered as a comparison of safety and efficacy[47]

PERSISTENCE AMONG PATIENTS WITH 2 YEARS OF FOLLOW-UP



ADHERENCE AMONG PATIENTS WITH 2 YEARS OF FOLLOW-UP



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.

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

ACCESS AND SUPPORT

The majority of patients with MS have unrestricted first-line access to OCREVUS[a]

DEDICATED TO ENSURING A **SMOOTH EXPERIENCE** FOR EVERY PATIENT PRESCRIBED OCREVUS

OCREVUS ACCESS SOLUTIONS

Call 1 (844) OCREVUS (1-844-627-3887)
Monday through Friday 9 AM–8 PM ET

Visit OCREVUS.COM for more information

- **Live Support** from dedicated OCREVUS Patient Navigators
- **Help getting insurance approval**, including benefits investigations and prior authorization resources
- The ability to enroll in **My Patient Solutions**, an online tool for practices and infusion sites to manage OCREVUS patients
- Help with **coordinating infusions and locating infusion sites**, including infusion centers and hospitals, HCP offices, and home infusion providers
- Connections to **patient financial assistance**, including the OCREVUS Co-pay Program[b], the Genentech Patient Foundation[c], or referrals to independent co-pay assistance foundations[d]

With the OCREVUS Co-pay Program, eligible patients with commercial insurance could pay as little as $0 per treatment for OCREVUS. Co-pay assistance of up to $20,000 is provided per calendar year.[b]

[a]As of November 2023, OCREVUS is available for first-line access in 65% of insured patients with published coverage for RMS.

[b]The Co-pay Program ("Program") is valid ONLY for patients with commercial (private or non-governmental) insurance who have a valid prescription for a Food and Drug Administration (FDA)-approved indication of a Genentech medicine. Patients using Medicare, Medicaid or any other federal or state government program (collectively, "Government Programs") to pay for their Genentech medicine are not eligible.

Under the Program, the patient may be required to pay a co-pay. The final amount owed by a patient may be as little as $0 for the Genentech medicine (see Program specific details available at the Program website). The total patient out-of-pocket cost is dependent on the patient's health insurance plan. The Program assists with the cost of the Genentech medicine only. It does not assist with the cost of other medicines, procedures or office visit fees. After reaching the maximum annual Program benefit amount, the patient will be responsible for all remaining out-of-pocket expenses. The Program benefit amount cannot exceed the patient's out-of-pocket expenses for the Genentech medicine.

All participants are responsible for reporting the receipt of all Program benefits as required by any insurer or by law. The Program is only valid in the United States and U.S. Territories, is void where prohibited by law and shall follow state restrictions in relation to AB-rated generic equivalents (e.g., MA, CA) where applicable. No party may seek reimbursement for all or any part of the benefit received through the Program. The value of the Program is intended exclusively for the benefit of the patient. The funds made available through the Program may only be used to reduce the out-of-pocket costs for the patient enrolled in the Program. The Program is not intended for the benefit of third parties, including without limitation third party payers, pharmacy benefit managers, or their agents. If Genentech determines that a third party has implemented a program that adjusts patient cost-sharing obligations based on the availability of support under the Program and/or excludes the assistance provided under the Program from counting towards the patient's deductible or out-of-pocket cost limitations, Genentech may impose a per fill cap on the costsharing assistance available under the Program. Submission of true and accurate information is a requirement for eligibility and Genentech reserves the right to disqualify patients who do not comply from Genentech programs. Genentech reserves the right to rescind, revoke or amend the Program without notice at any time.

Additional terms and conditions apply. Please visit OCREVUS.com/Copay for the full list of Terms and Conditions.

[c]To be eligible for free Genentech medicine from the Genentech Patient Foundation, insured patients who have coverage for their medicine should try to pursue other forms of financial assistance, if available, and meet certain income requirements. Uninsured patients and insured patients without coverage for their medicine must meet a different set of income requirements.

[d]Independent co-pay assistance foundations have their own rules for eligibility. Genentech has no involvement or influence in independent foundation decision-making or eligibility criteria and does not know if a foundation will be able to help your patient. We can only refer your patient to a foundation that supports their disease state. Genentech does not endorse or show preference for any particular foundation. The foundations to which we refer your patient may not be the only ones that might be able to help.

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

STARTING 2x-YEARLY OCREVUS[a]

How to start and manage patients on OCREVUS[1]

PRIOR TO FIRST DOSE

- Perform hepatitis B virus screening
- Test for quantitative serum immunoglobulins
- Complete necessary vaccinations (4 weeks prior for live or live-attenuated vaccines and, when possible, 2 weeks prior for non-live vaccines)

BEFORE EACH INFUSION

- Assess for active infection and administer premedications

AFTER EACH INFUSION

- Monitor patients for 1 hour for possible infusion reactions

Verifiable IV administration can facilitate monitoring of patient adherence[48,49]

[a]The first dose of OCREVUS is split between 2 treatments, for a total of 3 infusions in the first year.

Select Important Safety Information

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

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.

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

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.

Important Safety Information

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.

Click here for full Prescribing Information and Medication Guide.

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 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.

Click here for full Prescribing Information and Medication Guide.

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.

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.

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**.

Click here for full Prescribing Information and Medication Guide.

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For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

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Where they go depends on where you start

#1 most prescribed MS DMT in the US[2,a]

10+ years of data—2 years controlled period, 8+ years of OLE[3]

2x a year. 2-hour infusion option. Verifiable IV administration.[1,48,49,b,c]

[b]The first dose of OCREVUS is split between 2 treatments, for a total of 3 treatments in the first year.

Give your patients the confidence of a decade of OCREVUS experience[3]

[a]From December 2020 to September 2023; IQVIA Claims & IQVIA NSP, rolling 3-month prescriber-based data; includes all patients with an OCREVUS prescription. Includes all patients with an ICD-10-CM of G35 (multiple sclerosis).

[c]2-hour infusion can be administered after the initial dose for patients who do not experience serious IRs with any previous OCREVUS infusion.

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, and immune-mediated colitis.

For additional safety information, please see pages 25, 26, and 27 and **click here** for full Prescribing Information and Medication Guide.

OCREVUS®
ocrelizumab 300MG/10ML INJECTION FOR IV

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