OCREVUS REAL-WORLD ANALYSIS

Initial (1L) vs later-line (2L+) use of OCREVUS in patients with multiple sclerosis (MS)

An assessment of events often associated with a relapse, healthcare resource use, and costs

These HCEI materials were prepared pursuant to FD&C Act Sec. 502(a) standards. They are intended solely for use by payers, formulary committees, or other similar entities with knowledge and expertise in the area of healthcare economic analysis to facilitate drug selection decisions for coverage or reimbursement. These materials are not intended to be used by healthcare practitioners for the purpose of making individual patient prescribing decisions.

START

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Important Safety Information

Prescribing Information

Genentech
A Member of the Roche Group

OCREVUS®
ocrelizumab 300MG/10ML INJECTION FOR IV

Indications and Important Safety Information

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.

Indications and Important Safety Information (cont'd)

Infections (cont'd)

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.

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.

Indications and Important Safety Information (cont'd)

Infections (cont'd)

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.

Indications and Important Safety Information (cont'd)

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.

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.

Indications and Important Safety Information (cont'd)

Use in Specific Populations (cont'd)

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.

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

Overview

INTENDED FOR DISTRIBUTION ONLY TO PAYERS, FORMULARY COMMITTEES, OR SIMILAR ENTITIES FOR HEALTHCARE ECONOMIC ANALYSIS TO FACILITATE DRUG SELECTION, ON A POPULATION BASIS, FOR COVERAGE OR REIMBURSEMENT.

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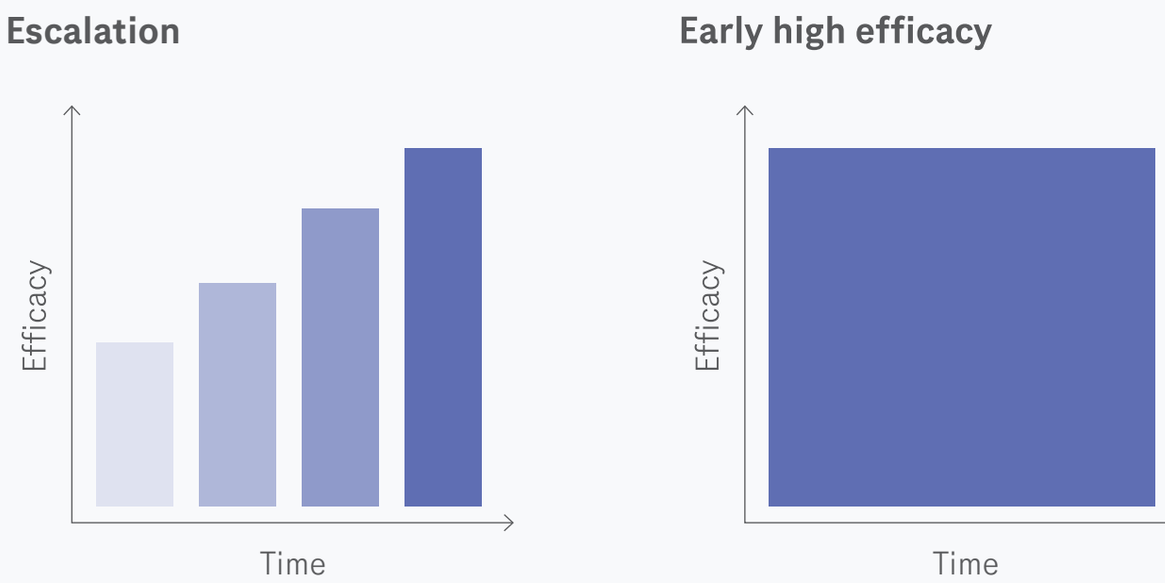
Contemporary treatment paradigms in MS: escalation versus early high-efficacy treatment[1]



- Treatment considerations in MS are evolving and evaluation of clinical outcomes of these approaches is a robust area of research[2,3]
- Worse clinical outcomes are associated with increased healthcare costs[4-7]

References: 1. Ontaneda D, Tallantyre E, Kalincik T, Planchon SM, Evangelou N. Early highly effective versus escalation treatment approaches in relapsing multiple sclerosis. *Lancet Neurol*. 2019;18(10):973-980. doi:10.1016/S1474-4422(19)30151-6 **2.** Simpson A, Mowry EM, Newsome SD. Early aggressive treatment approaches for multiple sclerosis. *Curr Treat Options Neurol*. 2021;23(7):19. doi:10.1007/s11940-021-00677-1 **3.** Spelman T, Magyari M, Piehl F, et al. Treatment escalation vs immediate initiation of highly effective treatment for patients with relapsing-remitting multiple sclerosis: data from 2 different national strategies. *JAMA Neurol*. 2021;78(10):1197-1204. doi:10.1001/jamaneurol.2021.2738 **4.** Jones E, Pike J, Marshall T, Ye X. Quantifying the relationship between increased disability and health care resource utilization, quality of life, work productivity, health care costs in patients with multiple sclerosis in the US. *BMC Health Serv Res*. 2016;16:294. doi:10.1186/s12913-016-1532-1 **5.** Nicholas J, Zhou H, Deshpande C. Annual cost burden by level of relapse severity in patients with multiple sclerosis. *Adv Ther*. 2021;38(1):758-771. doi:10.1007/s12325-020-01570-0 **6.** Patwardhan MB, Matchar DB, Samsa GP, McCrory DC, Williams RG, Li TT. Cost of multiple sclerosis by level of disability: a review of literature. *Mult Scler*. 2005;11(2):232-239. doi:10.1191/1352458505ms1137oa **7.** O'Brien JA, Ward AJ, Patrick AR, Caro J. Cost of managing an episode of relapse in multiple sclerosis in the United States. *BMC Health Serv Res*. 2003;3(1):17. doi:10.1186/1472-6963-3-17

OCREVUS is the #1 prescribed DMT in the United States[1,*]

10 years of clinical data, efficacy and safety[2,3]

2 years controlled and 8 years of open-label extension[2,3]

2 infusions per year[4]

Dose 1 administered as two 300-mg intravenous (IV) infusions 2 weeks apart. OCREVUS is subsequently dosed every 24 weeks.[4]

Identical, robust, head-to-head clinical trials vs Rebif for patients with RMS[4]

- **OPERA I and OPERA II:** 2 double-blind, double-dummy trials evaluating efficacy and safety in more than 1600 patients with RMS in 2 years[4]

Primary endpoint: Annualized relapse rate (ARR)[4]

Superior relapse reductions vs Rebif at year 2 (controlled period)[4]

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

- 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[5]

DMT=disease-modifying therapy.

Rebif® (interferon beta-1a) is a registered trademark of EMD Serono.

*From April 2019 to April 2021; IQVIA Claims & IQVIA NSP, rolling 3-month prescriber-based data; includes all patients with an OCREVUS prescription.

References: 1. Data on file. Genentech, Inc; September 2023. **2.** Weber MS et al. Presented at ECTRIMS; October 11-13, 2023. **3.** Hauser SL et al. Presented at ECTRIMS; October 11-13, 2023. **4.** OCREVUS [prescribing information]. South San Francisco, CA: Genentech, Inc. 2024. **5.** Hauser SL, Bar-Or A, Comi G, et al. Ocrelizumab versus interferon beta-1a in relapsing multiple sclerosis. *N Engl J Med*. 2017;376:221-34. doi:10.1056/NEJMoa1601277

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

REAL-WORLD ANALYSIS

Initial (1L) vs later-line use (2L+) of OCREVUS in patients with multiple sclerosis (MS)

An assessment of events often associated with a relapse, healthcare resource use, and costs

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.

This is a Genentech-sponsored study.

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Analysis overview[1]

Objective

Compare clinical and economic outcomes among patients with MS treated with OCREVUS as initial use (1L) vs later-line (2L+) use.

Outcomes

The following outcomes were assessed during the follow-up period using the Optum® Market Clarity US Commercial, Medicaid, and Medicare claims database:

Events often associated with a relapse (EOAR)

- Time to first EOAR
- Annualized EOAR†

- EOAR was defined as any inpatient stay with primary diagnosis of MS; or an outpatient visit with an MS diagnosis with evidence of high-dose steroids, IV corticosteroids, adrenocorticotropic hormone, or plasma exchange within 30 days of the outpatient visit. All patient characteristics, use of DMTs, and outcomes were identified using claims data

All-cause and MS-related, non-DMT healthcare resource use (HCRU) and costs

- Inpatient hospitalizations
- Emergency room visits
- Outpatient visits
- Prescription fills (all-cause, non-DMT only)
- Total costs (overall and by place of services)

†Annualized EOAR was calculated for each patient based on the total number of events during the follow-up periods.[2]

References: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands. **2.** Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Supplement to poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.

Analysis overview[1]

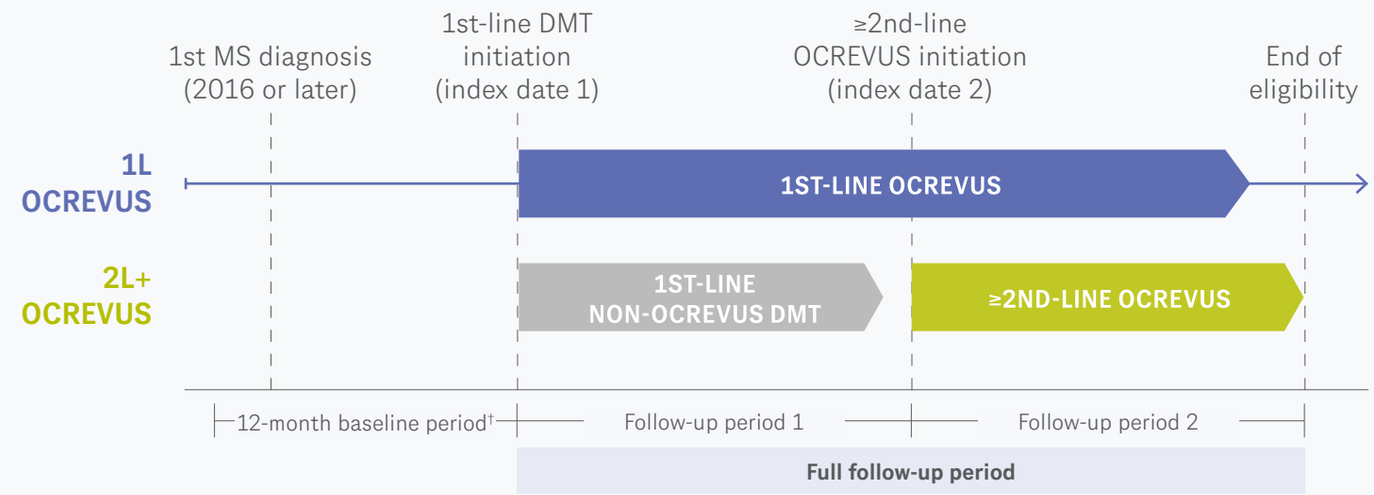
Methods

Retrospective cohort study of 694 patients from the Optum Market Clarity US Commercial, Medicaid, and Medicare claims database for the study period between January 2015 and June 2021.

- Newly diagnosed patients with MS who initiated OCREVUS were divided into 2 cohorts based on when they initiated OCREVUS: 1L cohort if they initiated OCREVUS as the 1st-line treatment after diagnosis or 2L+ cohort if they initiated OCREVUS as a ≥2nd-line treatment after diagnosis
- 1L and 2L+ OCREVUS patients were matched 1:1 on duration of follow-up time
- Patients were weighted based on a propensity score model to ensure the 1L and 2L+ cohorts had similar baseline demographic and clinical characteristics*
- All patient characteristics, use of DMTs, and outcomes were identified using claims data

+ ADDITIONAL FOLLOW-UP PERIOD INFORMATION

Included patients were divided into 2 cohorts based on when OCREVUS was initiated: 1L or 2L+



Index date 1 is the date of initiation of the 1st-line DMT after MS diagnosis. Index date 2 was assigned to 1L patients based on when 1:1 matched 2L+ patients initiated OCREVUS. In both cohorts, the average follow-up period was 25 months for the full follow-up period (follow-up period 1: 17 months; follow-up period 2: 8 months).

*Propensity score model variables included: age, sex, race/ethnicity, payer type, region, baseline annualized EOAR, baseline Charlson comorbidity index score, baseline comorbidities (cerebrovascular disease, hypertension, obesity), any inpatient hospitalization during baseline period, emergency department visits during baseline period, total costs during baseline period.
†Baseline characteristics were evaluated in the 12 months prior to the date of initiation of the 1st-line DMT (index date 1).

Reference: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.

Population[1,2]

Patients were included if they:

- Had first MS diagnosis in 2016 or later
- Initiated OCREVUS at any time following initial MS diagnosis
- Were continuously enrolled for 12 months prior to first MS diagnosis through OCREVUS initiation
- Were aged 18-64 years at initiation of first DMT

Patients were excluded if they:

- Initiated any DMTs prior to first MS diagnosis
- Initiated multiple concurrent DMTs
- Were pregnant during 12-month baseline period or anytime during follow-up

Pre-index

Study sample: newly diagnosed OCREVUS patients

1101

	Study sample (n=1101)	Matched sample* (n=694)
1L OCREVUS	354 (32%)	347 (50%)
2L+ OCREVUS	747 (68%)	347 (50%)

*For each 2L+ OCREVUS patient, a 1L OCREVUS patient "match" was randomly selected from all 1L OCREVUS patients who had a total duration of continuous eligibility after the date of initiation of 1st-line OCREVUS that was at least as long as the time for the 2L+ OCREVUS patient from the initiation of the 1st-line non-OCREVUS DMT until the initiation of ≥2nd-line OCREVUS.

References: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.
2. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Supplement to poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.

Population[1,2]

SELECT BASELINE CHARACTERISTICS AFTER WEIGHTING*		1L OCREVUS (ESS=260)	2L+ OCREVUS (ESS=253)	SMD (weighted)
Age, mean†		41.7	41.4	0.027
Female sex, %†		64.3%	65.2%	0.019
Race/ethnicity, %†				0.040
Caucasian		73.9%	74.4%	
African American		12.0%	11.0%	
Hispanic		5.1%	5.3%	
Asian		0.9%	0.7%	
Other/unknown		8.2%	8.6%	
Payer type, %†				0.040
Commercial		77.9%	77.1%	
Medicaid		18.4%	18.7%	
Medicare		2.9%	3.5%	
Unknown		0.8%	0.7%	
Months from diagnosis to index date 1, mean		7.1	4.8	0.285
Months of follow-up after index date 1, mean		25.0	24.7	0.021
Baseline clinical characteristics	EOAR, mean†	1.95	1.94	0.005
	CCI score, mean†	0.64	0.61	0.032
Baseline healthcare resource use	Any hospitalization, %†	9.0%	10.6%	-0.052
	Any ED visits, %†	52.3%	52.8%	-0.011
12-month baseline costs	Total costs, mean†	$19,933	$19,739	0.010
	Total OP costs, mean	$14,268	$13,097	0.079
	Total IP costs, mean	$1,967	$2,051	-0.010
	Total ED costs, mean	$1,126	$851	0.145

Patients were weighted based on a propensity score model to ensure the 1L and 2L+ cohorts had similar baseline demographic and clinical characteristics.

+ 1ST-LINE NON-OCREVUS DMTs

+ FULL BASELINE CHARACTERISTICS

CCI=Charlson comorbidity score; ED=emergency department; EOAR=events often associated with a relapse; ESS=effective sample size; IP=inpatient; OP=outpatient; SMD=standardized mean difference.

*12-month baseline period before initiation of 1st-line DMT (index date 1). Total costs were calculated based on the standard cost variable from Optum, which represents the amount paid to the provider.

Region and comorbidities (hypertension, obesity, and cerebrovascular disease) are not shown in the table but they were included in the propensity score model. The SMD for those variables was <0.1 both before and after weighting.

†Included in propensity score model.

References: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands. **2.** Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Supplement to poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.

Limitations of real-world data analyses[1,2]

- The treatment choices inherent in real-world data and the design of this study may introduce selection bias
  - 2L+ OCREVUS patients were required to discontinue their 1st-line DMT; therefore, some 2L+ OCREVUS patients may have had breakthrough disease on their first treatment, which may be suggestive of more severe disease
  - 1L OCREVUS patients may have been selected for 1st-line OCREVUS treatment because they were perceived to have more severe disease
  - Since OCREVUS is the only DMT approved for the treatment of PPMS, the 1L OCREVUS cohort is expected to include a greater proportion of patients with PPMS, which may increase costs and HCRU but decrease EOAR in the 1L cohort
- Since the aim of this study was to evaluate 1L vs 2L+ use of OCREVUS in MS patients, comparing the effectiveness of OCREVUS to other DMTs was outside the scope of this study
- The design of the study did not consider the differential time to onset of efficacy of therapy and did not require a washout period to help affirm effects are not attributable to a previous medication prior to the initiation of OCREVUS 2L+
- Patients may not have been on treatment during the entire length of each follow-up period if they discontinued treatment

Claims data have inherent limitations:

- Possible coding errors and missing data
- Inability to ascertain if patients on injectable and oral medications took DMT as prescribed
- Limited clinical information (eg, MS disease duration, MS severity) availability may impact interpretation of results
- Lack of data on reason for discontinuation or switch (eg, lack of efficacy or safety)
- Limited clinical data on MS subtype
- Patients were enrolled for an average of 25 months during the full follow-up period and the majority were enrolled with a single payer. Results may not be generalizable to all patients with MS

References: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.
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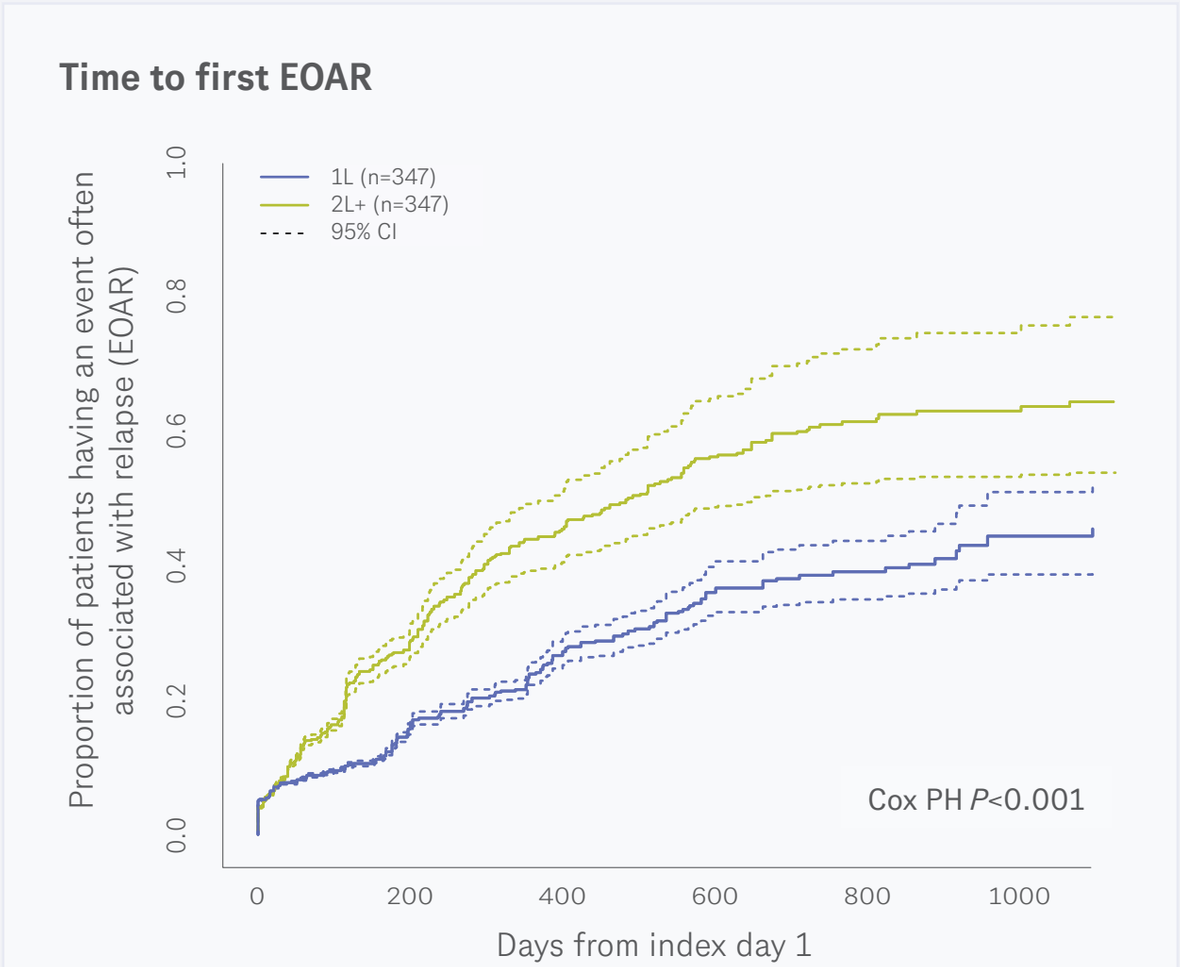
Patients treated with OCREVUS 1L had a **longer time to first EOAR** compared with patients treated with OCREVUS 2L+[1]



Time to first EOAR methods[1,2]

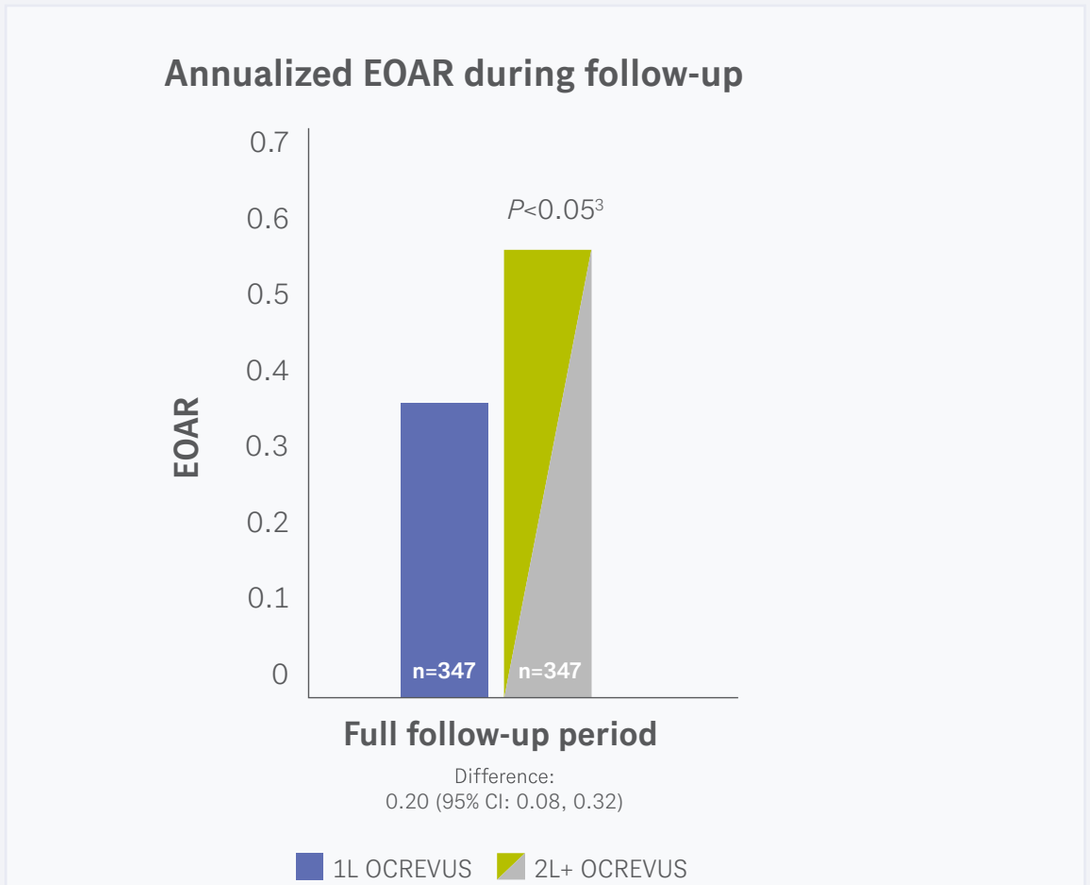
- EOAR was defined as any inpatient stay with primary diagnosis of MS; or an outpatient visit with an MS diagnosis with evidence of high-dose steroids, IV corticosteroids, adrenocorticotropic hormone, or plasma exchange within 30 days of the outpatient visit
  - All qualifying inpatient stays and outpatient visits within 30 days were grouped into single event
- Weighted Kaplan-Meier curves were estimated for the time to first EOAR
  - Weighted Cox proportional hazards (PH) model was fit to test for difference in time between 2 cohorts

Select limitations for EOAR[1,2]:

- There are no diagnosis codes to identify MS relapses in claims data; therefore, MS relapses could not be identified using the exact definition of relapses from the OPERA I and OPERA II clinical trials
- EOAR were identified using an unvalidated claims-based algorithm. The definition of EOAR differs from the definition of adjudicated relapses in the OPERA clinical trials

References: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands. **2.** Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Supplement to poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.

1L OCREVUS patients had a significantly **lower annualized EOAR** when compared with 2L+ OCREVUS patients[1]



EOAR methods[1,2]:

- EOAR was defined as any inpatient stay with primary diagnosis of MS; or an outpatient visit with an MS diagnosis with evidence of high-dose steroids, IV corticosteroids, adrenocorticotropic hormone, or plasma exchange within 30 days of the outpatient visit
  - All qualifying inpatient stays and outpatient visits within 30 days were grouped into single event
- Annualized EOAR was calculated for each patient based on the total number of these events during the follow-up periods
- Annualized EOAR was estimated using inverse probability of treatment (IPT)-weighted zero-inflated negative binomial models with the follow-up time included as an offset variable and bootstrapping was used to generate 95% confidence intervals

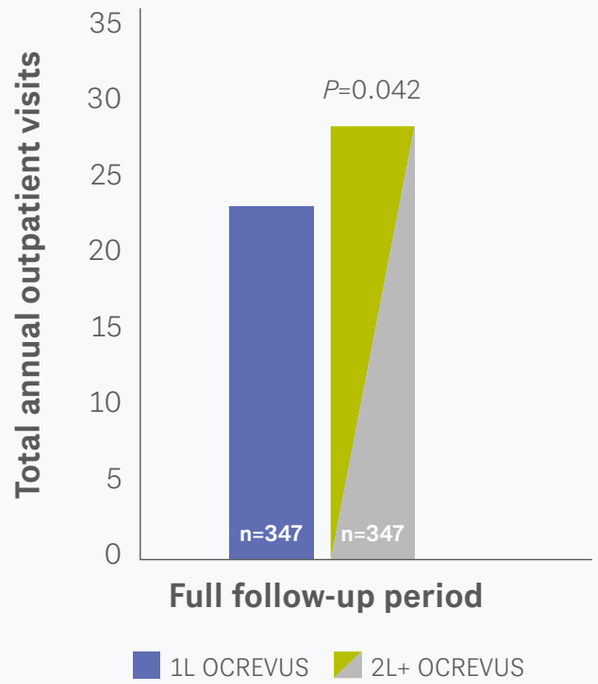
+ FOLLOW-UP PERIOD 1 AND FOLLOW-UP PERIOD 2 DATA

+ FULL LIMITATIONS

Annualized EOAR was evaluated in the sample of 347 1L and 347 2L+ OCREVUS patients during the full follow-up period after the initiation of the 1st-line DMT until the end of continuous eligibility. While the length of the follow-up period varied across individual patients, follow-up time was the same on average in the two cohorts due to the 1:1 matching of 1L and 2L+ OCREVUS patients on follow-up time. The average length of the full follow-up period in both cohorts was 25 months (standard deviation 11) and the median was 24 months (interquartile range 16-33).

References: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.
2. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Supplement to poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.
3. Data on file. Genentech, Inc; 2022.

Patients treated with OCREVUS 1L had **significantly fewer all-cause, non-DMT outpatient visits** compared with patients treated with OCREVUS 2L+[1]



Annualized MS-related, non-DMT outpatient visits

- Similarly, 1L OCREVUS patients had significantly fewer annual MS-related, non-DMT outpatient visits during the full follow-up period (9.1 vs 14.1, *P*<0.001)[2]

Outpatient visit methods:

- All-cause, non-DMT outpatient visits included all outpatient visits that occurred for any reason except for the administration of DMTs
- Summarized using stabilized IPT weights generated from the propensity scores

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+ FOLLOW-UP PERIOD 1 AND FOLLOW-UP PERIOD 2 DATA

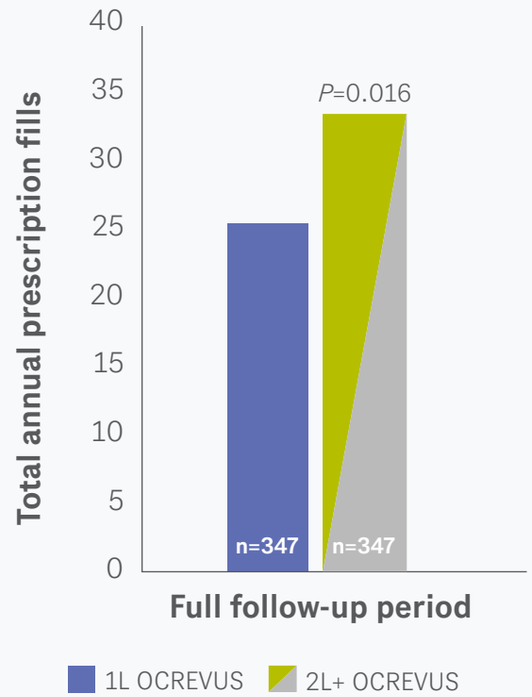
+ FULL LIMITATIONS

IPT=inverse probability of treatment.

References: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands. **2.** Data on file. Genentech, Inc; 2022.

Patients treated with OCREVUS 1L had **significantly fewer non-DMT prescription fills** compared with patients treated with OCREVUS 2L+[1]

Annualized all-cause, non-DMT prescription fills



Non-DMT prescription fill methods:

- Non-DMT prescription fills included all-cause prescription drug claims for all drugs except MS DMTs and may include prescriptions for the treatment of conditions other than MS
- Summarized using stabilized IPT weights generated from the propensity scores

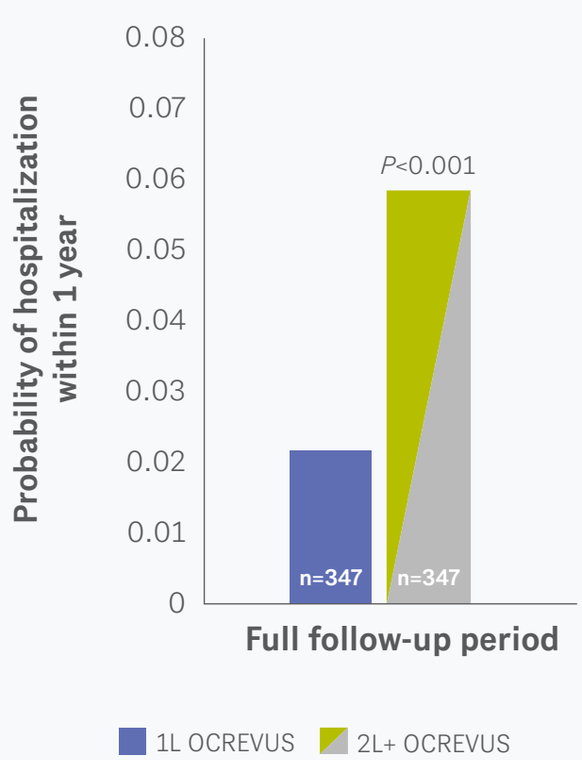
+ FOLLOW-UP PERIOD 1 AND FOLLOW-UP PERIOD 2 DATA

+ FULL LIMITATIONS

IPT=inverse probability of treatment.

Reference: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.

Patients treated with OCREVUS 1L had **significantly lower probability of all-cause hospitalization** compared with patients treated with OCREVUS 2L+[1]



Probability of MS-related, non-DMT hospitalization[1-3]

- Similarly, 1L OCREVUS patients had significantly lower probability of MS-related hospitalizations during the full follow-up period (0.02 vs 0.06, *P*=0.001)

Probability of hospitalization methods[1,2]:

- Probability of hospitalization within 1 year was estimated using IPT-weighted logistic regression with follow-up time included as an offset variable
- Summarized using stabilized IPT weights generated from the propensity scores

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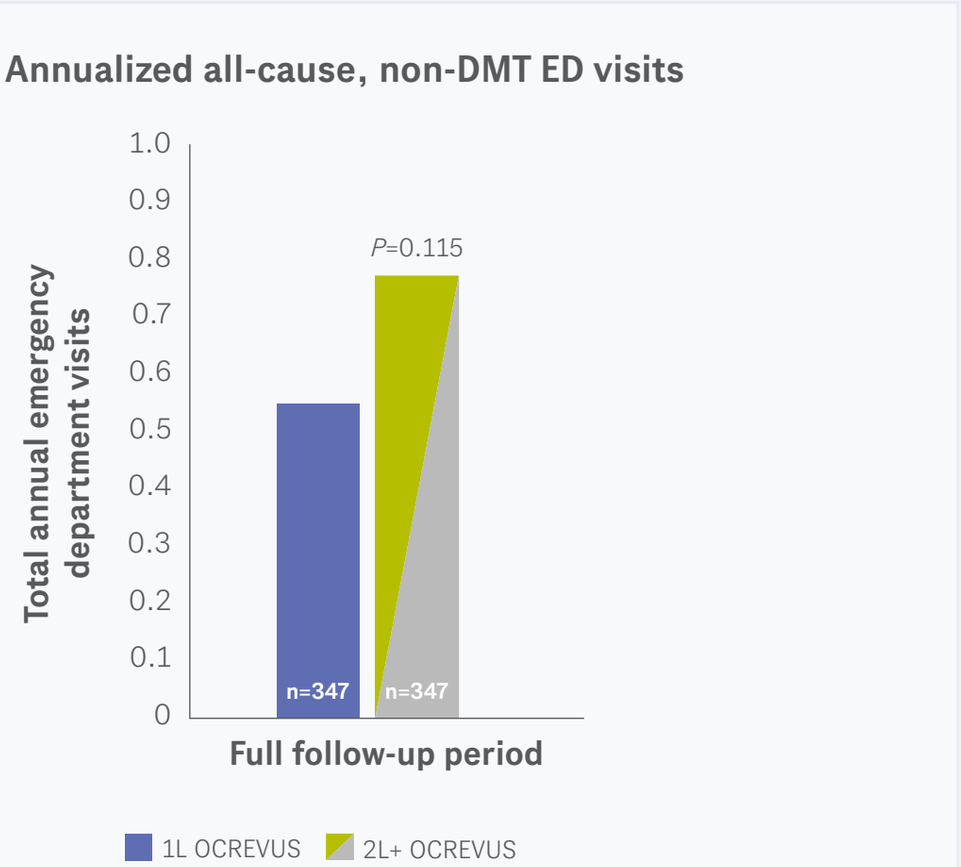
+ FOLLOW-UP PERIOD 1 AND FOLLOW-UP PERIOD 2 DATA

+ FULL LIMITATIONS

IPT=inverse probability of treatment.

References: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands. **2.** Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Supplement to poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands. **3.** Data on file. Genentech, Inc; 2022.

Patients treated with OCREVUS 1L had **similar all-cause ED visits** compared with patients treated with OCREVUS 2L+[1]



Annualized MS-related, non-DMT ED visits[1,2]

- Similarly, 1L OCREVUS patients had a similar number of annual MS-related, non-DMT ED visits during the full follow-up period (0.27 vs 0.46, *P*=0.069)

ED visit methods:

- All-cause, non-DMT emergency department (ED) visits included all visits to the emergency department for any reason except for the administration of DMTs[3]
- Summarized using stabilized IPT weights generated from the propensity scores

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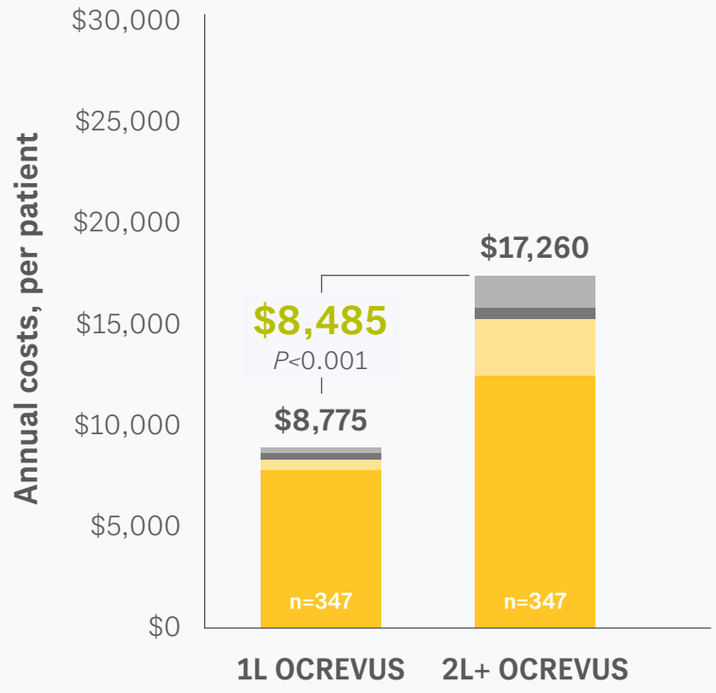
+ FOLLOW-UP PERIOD 1 AND FOLLOW-UP PERIOD 2 DATA

+ FULL LIMITATIONS

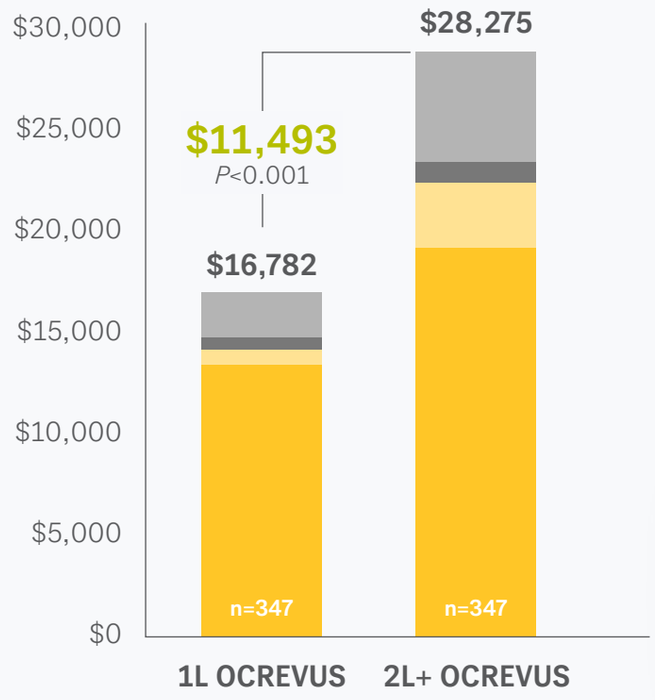
References: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands. **2.** Data on file. Genentech, Inc; 2022. **3.** Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Supplement to poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.

Patients treated with OCREVUS 1L had **lower annualized non-DMT costs during the entire follow-up period and across all places of service** compared with patients treated with OCREVUS 2L+[1]

Annualized MS-related, non-DMT costs: full follow-up period



Annualized All-cause, non-DMT costs: full follow-up period



Outpatient costs | Inpatient costs | Emergency department costs | Prescription costs

Outpatient costs included costs for all outpatient visits and services (e.g., neurologist visits, MRIs, laboratory work, and physical therapy).

Cost methods:

- All cost outcomes were summarized using stabilized IPT weights generated from the propensity scores
- Total costs were calculated based on the standard cost variable from Optum, which represents the amount paid to the provider

+ FOLLOW-UP PERIOD 1 AND FOLLOW-UP PERIOD 2 DATA

+ FULL LIMITATIONS

Reference: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.

Summary

The initiation of OCREVUS as 1st-line treatment following MS diagnosis was associated with lower costs over the full follow-up period[1]

Patients treated with OCREVUS 1L had an annualized all-cause, non-DMT cost savings of $11,493 during the entire follow-up period and lower costs across all places of service compared with patients treated with OCREVUS 2L+[1]

Reference: 1. Geiger C, Sheinson D, To TM, Jones D, Bonine N. Real-world clinical and economic outcomes among persons with multiple sclerosis initiating first versus second-line treatment with ocrelizumab. Poster EP1127 presented at: 38th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS); October 26-28, 2022; Amsterdam, the Netherlands.