OCREVUS REAL-WORLD ANALYSIS AMONG PATIENTS WITH 2 YEARS OF FOLLOW-UP

Adherence and persistence in patients with multiple sclerosis (MS) who were treated with OCREVUS or other disease-modifying therapies (DMTs)

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

Please see Important Safety Information and Full Prescribing Information by tapping the appropriate button below.

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

OCREVUS: for adults with relapsing multiple sclerosis (RMS) and primary progressive multiple sclerosis (PPMS)

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.

Please see additional Important Safety Information and Full Prescribing Information by tapping the appropriate button below.

Important Safety Information | Prescribing Information

OCREVUS is the **first and only** FDA-approved treatment for both RMS and PPMS[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[1]*

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

Identical, robust, head-to-head clinical trials vs Rebif for patients with RMS[1]

2 double-blind, double-dummy trials evaluating efficacy and safety in over 1600 patients with RMS in 2 years[1]

Robust clinical trial vs placebo for patients with PPMS[1]

A double-blind, double-dummy trial evaluating efficacy and safety in 732 patients with PPMS for >2 years (120 weeks)[1]

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

References: 1. OCREVUS [package insert]. South San Francisco, CA: Genentech, Inc; 2024. **2.** Weber MS et al. Presented at ECTRIMS; October 11-13, 2023. **3.** Hauser SL et al. Presented at ECTRIMS; October 11-13, 2023.

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Important Safety Information | Prescribing Information

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

A 2-YEAR REAL-WORLD ADHERENCE AND PERSISTENCE ANALYSIS

Adherence and persistence to OCREVUS compared with other DMTs for MS in US commercial and Medicare claims databases

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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Important Safety Information | Prescribing Information

Analysis overview[1,2]

Objective

Evaluate adherence and persistence of OCREVUS compared with other DMTs for the treatment of MS in the IBM MarketScan US Commercial and Medicare claims database in a 2-year retrospective analysis.

Primary outcomes

The primary outcomes were assessed using data from the IBM MarketScan US Commercial and Medicare claims database.*

Adherence

- In this study, adherence was calculated based on proportion of days covered (PDC), with ≥80% considered adherent to the DMT initiated

Persistence

- In this study, persistence was measured based on switch to another DMT or gap in index DMT coverage of ≥60 days at any time during the evaluation period

$$PDC = \left(\frac{\text{Number of days in period covered}}{\text{Number of days in a specified time period}} \right) \times 100\%$$

Denominator based on follow-up time: 730 days

+ WHY PDC?

*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.

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

WHY PDC?

2 types of calculations are commonly used for adherence data[1,2]

For this particular analysis, PDC was used instead of MPR as it is a more conservative approach to adherence measurement. This outcome measure follows the RWD Good Practices from ISPOR-ISPE and is the metric of choice for real-world analyses for the Pharmacy Quality Alliance (PQA).

MPR

MPR takes the total number of days of supply for a given medication for a set fill period and divides it by the number of days in a specified time period.

$$\text{MPR} = \left(\frac{\text{Sum of days' supply for all fills in period}}{\text{Number of days in a specified time period}} \right) \times 100\%$$

The MPR calculation may lead to a value of **greater than 100% adherence** if a patient gets an early refill or if they have filled their medication only once.

PDC

PDC takes the number of days the patient is covered to receive the medication and divides it by the number of days in a specified time period.

$$\text{PDC} = \left(\frac{\text{Number of days in period covered}}{\text{Number of days in a specified time period}} \right) \times 100\%$$

The PDC calculation considers **any value of 80% or higher adherent**. In this calculation, it is unlikely that a patient will receive a value greater than 100%.

SPOR-ISPE=International Society for Pharmacoeconomics and Outcomes Research-International Society for Pharmacoepidemiology; RWD=real-world data.

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Patel N. The difference between primary measures of medication adherence: PDC and MPR. USciences website. Published November 15, 2018. Accessed May 3, 2021. https://www.usciences.edu/blog/noteworthy/posts/the-difference-between-primary-measures-of-medication-adherence-pdc-and-mpr.html

Analysis overview[1,2]

Methods

Retrospective cohort study of 1710 patients from the IBM MarketScan US Commercial and Medicare claims database for period between April 1, 2016, and December 31, 2019.

The proportion persistent and proportion adherent at 2 years were reported by treatment group.

Poisson regression models, which included several covariates, were used to model the risk of discontinuation and risk of nonadherence (PDC <80%) at 2 years. The relative risk for OCREVUS compared with each of self-injectable, oral, and other IV DMTs was estimated via the model contrast between the effect of OCREVUS and the average effect among the individual drugs within each treatment group.

All models were adjusted for the following covariates:

- Age group
- Gender
- Payer type
- Insurance plan type
- Region
- Relapse in the pre-index period (yes/no)
- Pre-index use of DMTs
- Charlson comorbidity index
- Presence of MS symptoms

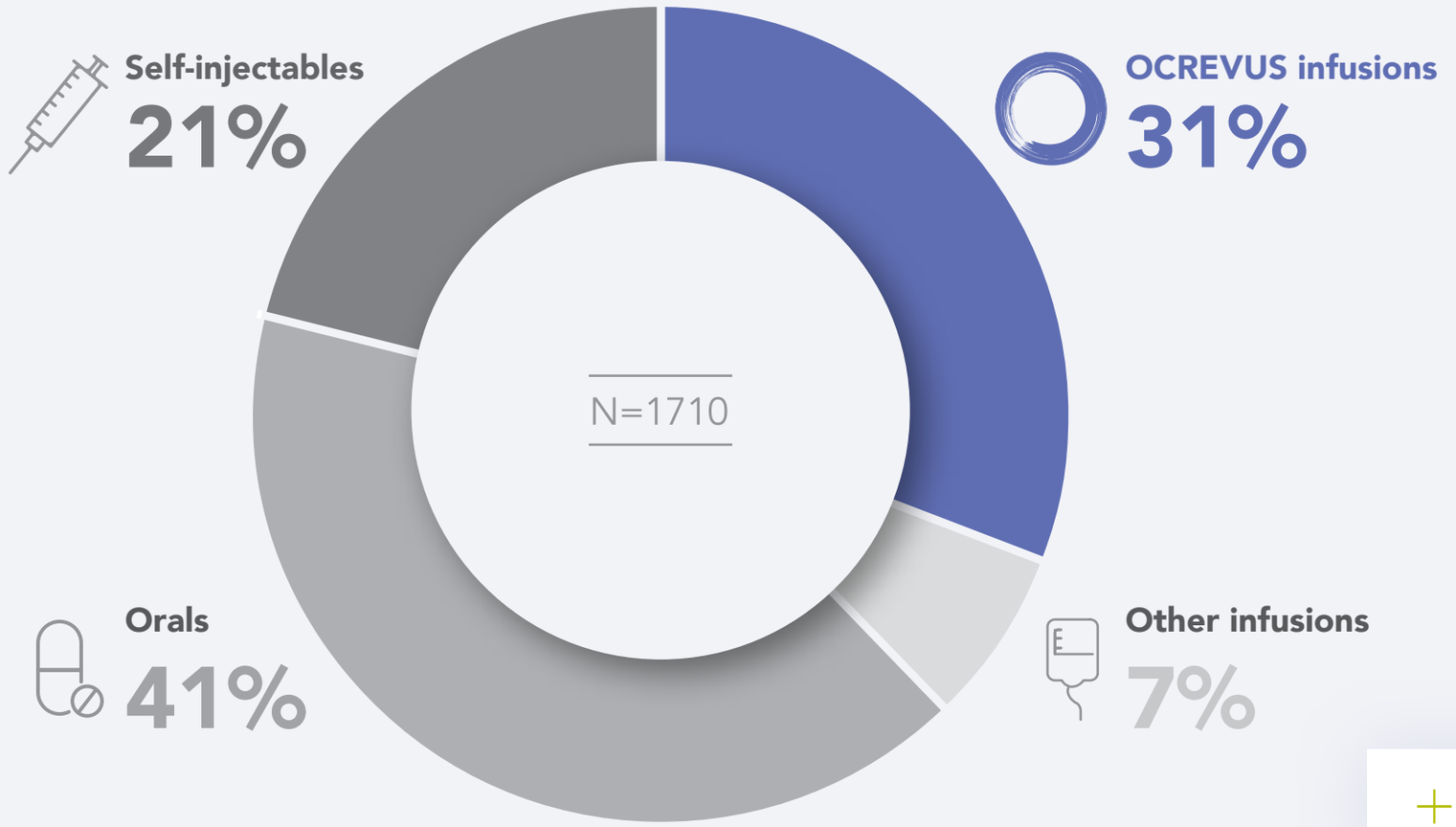
Sensitivity analyses were conducted to assess robustness of data and were consistent with the results from the analysis

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

Analysis overview[1,2]

Routes of administration (ROA) analyzed[1]*

Dosing frequency is highly variable across DMTs, ranging from daily to twice-yearly administration. OCREVUS is dosed twice yearly.†



+ ROA BY DMT

Percentages reflect the proportion of total sample size represented by each DMT.
Analysis included all approved DMTs for MS at time of OCREVUS approval (March 2017) and excluded mitoxantrone and alemtuzumab.

*The following DMTs were part of the analysis: oral DMTs included dimethyl fumarate, fingolimod, teriflunomide; self-injectable DMTs included glatiramer acetate, interferon beta-1a, interferon beta-1b; IV DMTs included natalizumab and OCREVUS.[1]

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

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** OCREVUS [package insert]. South San Francisco, CA: Genentech, Inc; 2024.

ROA BY DMT

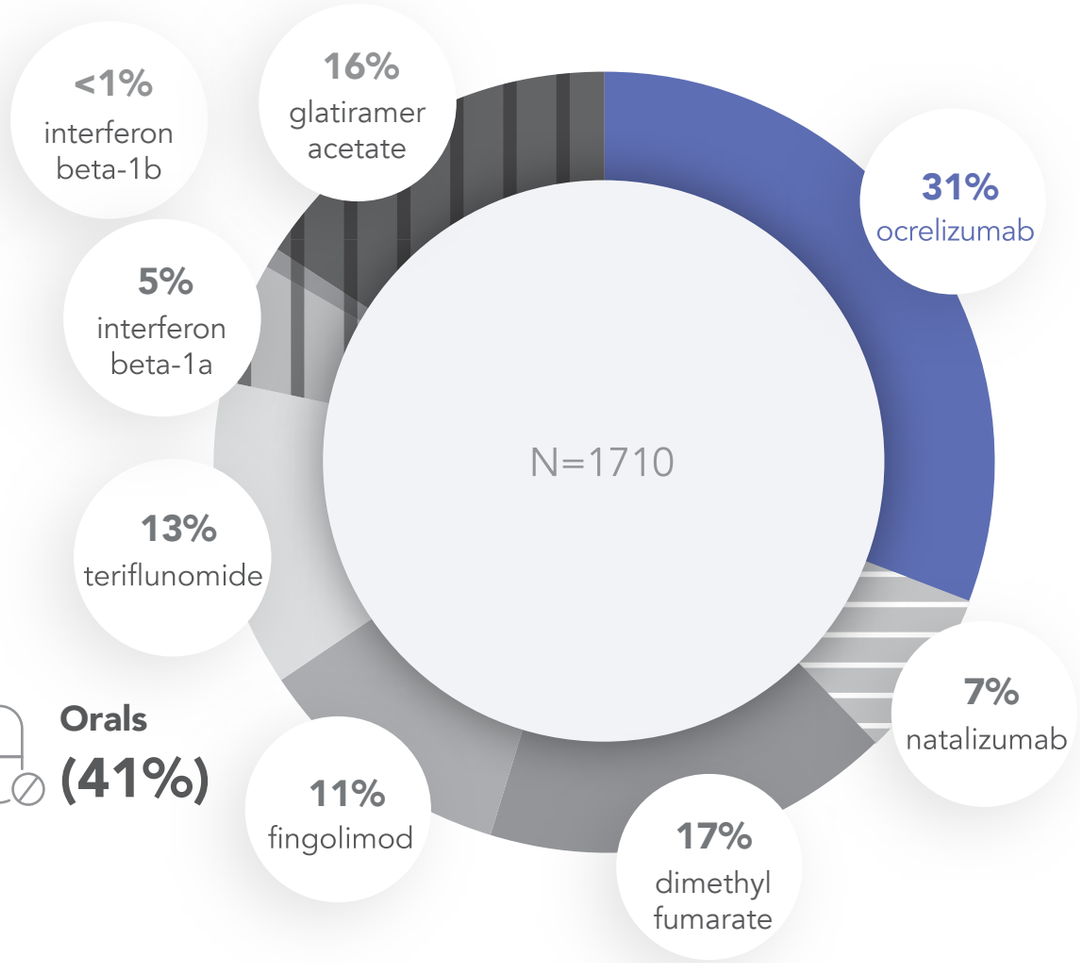
DMTs by ROA[1-10*]

Self-injectables (21%)

Orals (41%)

OCREVUS infusions (31%)

Other infusions (7%)



Glatiramer acetate: dosed 20 mg QD or 40 mg TIW.[2,3]
Interferon beta-1b: dosed QOD.[4]
Interferon beta-1a: dosed TIW.[5]
Teriflunomide: dosed QD.[6]
Fingolimod: dosed QD.[7]
Dimethyl fumarate: dosed BID.[8]
Natalizumab is dosed once every 4 weeks.[9]
OCREVUS is dosed twice yearly. Dose 1 administered as two 300-mg intravenous (IV) infusions 2 weeks apart. OCREVUS is subsequently dosed every 24 weeks.[10]

*Percentages reflect the proportion of total sample size represented by each DMT.
Analysis included all approved DMTs for MS at time of OCREVUS approval (March 2017) and excluded mitoxantrone and alemtuzumab.

References: 1. Data on file. Genentech, Inc. **2.** Copaxone [package insert]. Parsippany, NJ: Teva Pharmaceuticals USA, Inc; 2022. **3.** Glatopa [package insert]. Princeton, NJ: Sandoz, Inc; 2022. **4.** Betaseron [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; 2021. **5.** Avonex [package insert]. Cambridge, MA; Biogen Inc; 2021. **6.** Aubagio [package insert]. Cambridge, MA: Genzyme Corporation; 2021. **7.** Gilenya [package insert]. East Hanover, NJ: Novartis, AG; 2019. **8.** Tecfidera [package insert]. Cambridge, MA: Biogen Inc; 2022. **9.** Tysabri [package insert]. Cambridge, MA: Biogen Inc; 2021. **10.** OCREVUS [package insert]. South 2020 Francisco, CA: Genentech, Inc; 2024.

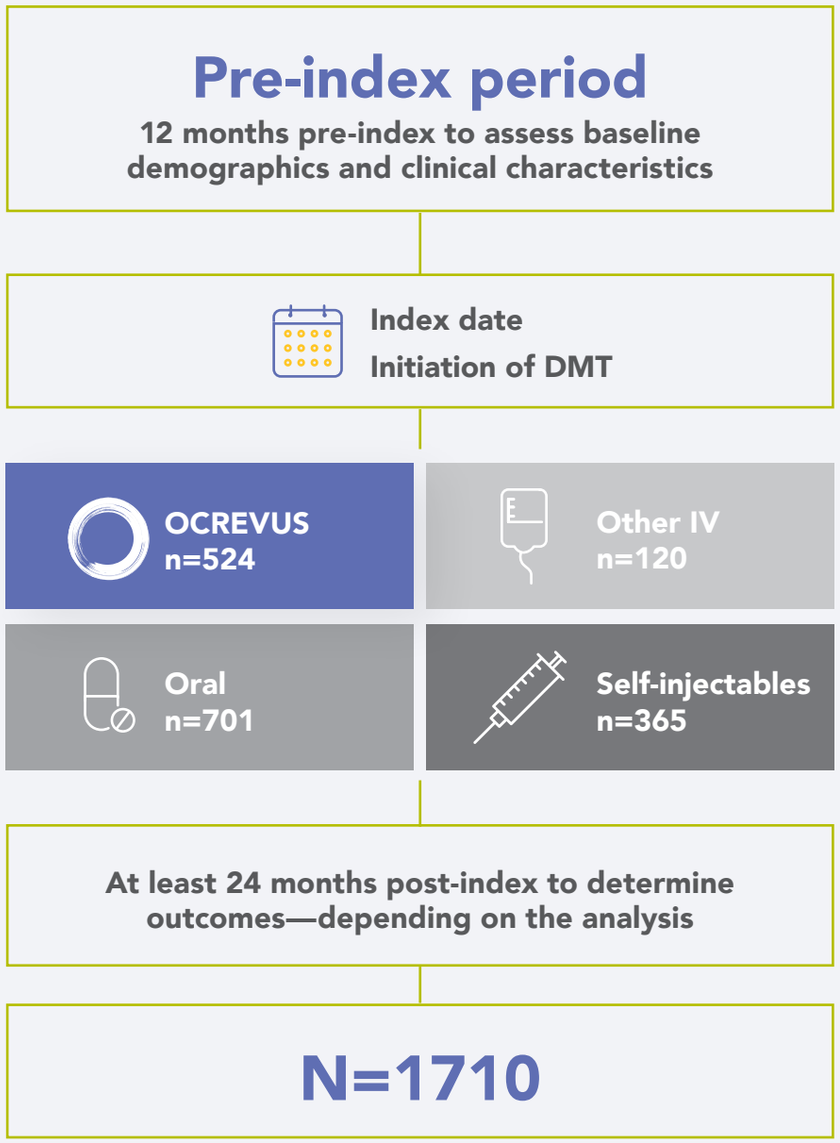
Population[1,2]

Patients were included if they:

- Were ≥18 years with a diagnosis of MS at any time and initiated OCREVUS, fingolimod, dimethyl fumarate, glatiramer acetate, interferon beta-1a/b, natalizumab, or teriflunomide
- Have continuous enrollment ≥12 months pre-index and ≥24 months post-index of DMT initiation

Patients were excluded if they:

- Were treated with alemtuzumab, mitoxantrone, or any off-label therapies
- Were initiated multiple DMTs on index
- Had any claims of index DMT in the prior 12 months



References: 1. Data on file. Genentech, Inc. **2.** Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021.

Population[1]

SELECT BASELINE CHARACTERISTICS	OCREVUS* (n=524)	OTHER IVs (n=120)	ORAL (n=701)	SELF-INJECTABLES (n=365)
AGE AT INDEX, MEAN (SD), YEARS	49 (10)	43 (11)	46 (11)	45 (12)
AGE CATEGORY AT INDEX, n (%)				
<35 y	41 (8)	23 (19)	106 (15)	72 (20)
35-44 y	115 (22)	44 (37)	195 (28)	98 (27)
45-54 y	193 (37)	35 (29)	236 (34)	109 (30)
≥55 y	175 (33)	18 (15)	164 (23)	86 (24)
SEX AT INDEX, n (%)				
FEMALE	353 (67)	95 (79)	541 (77)	289 (79)
PAYER TYPE AT INDEX, n (%)				
COMMERCIAL	501 (96)	117 (98)	676 (96)	356 (98)
MEDICARE	23 (4)	3 (3)	25 (4)	9 (3)
≥1 PRE-INDEX RELAPSE, n (%)†	201 (38)	53 (44)	200 (29)	115 (32)
PRE-INDEX DMT USE, n (%)†	386 (74)	56 (47)	359 (51)	84 (23)
CCI CATEGORY, n (%)†				
0	393 (75)	96 (80)	538 (77)	269 (74)
1	44 (8)	8 (7)	85 (12)	54 (15)
2+	87 (17)	16 (13)	78 (11)	42 (12)

2 / 2

CCI=Charlson comorbidity index; DMT=disease-modifying therapy; SD=standard deviation.
*Patients initiating OCREVUS were older, had a higher CCI score, were more likely to be male, and were more likely to have received a previous DMT compared with other index DMT groups.
†1 year prior to index date.

Reference: 1. Data on file. Genentech, Inc.

Analysis limitations[1,2]

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:

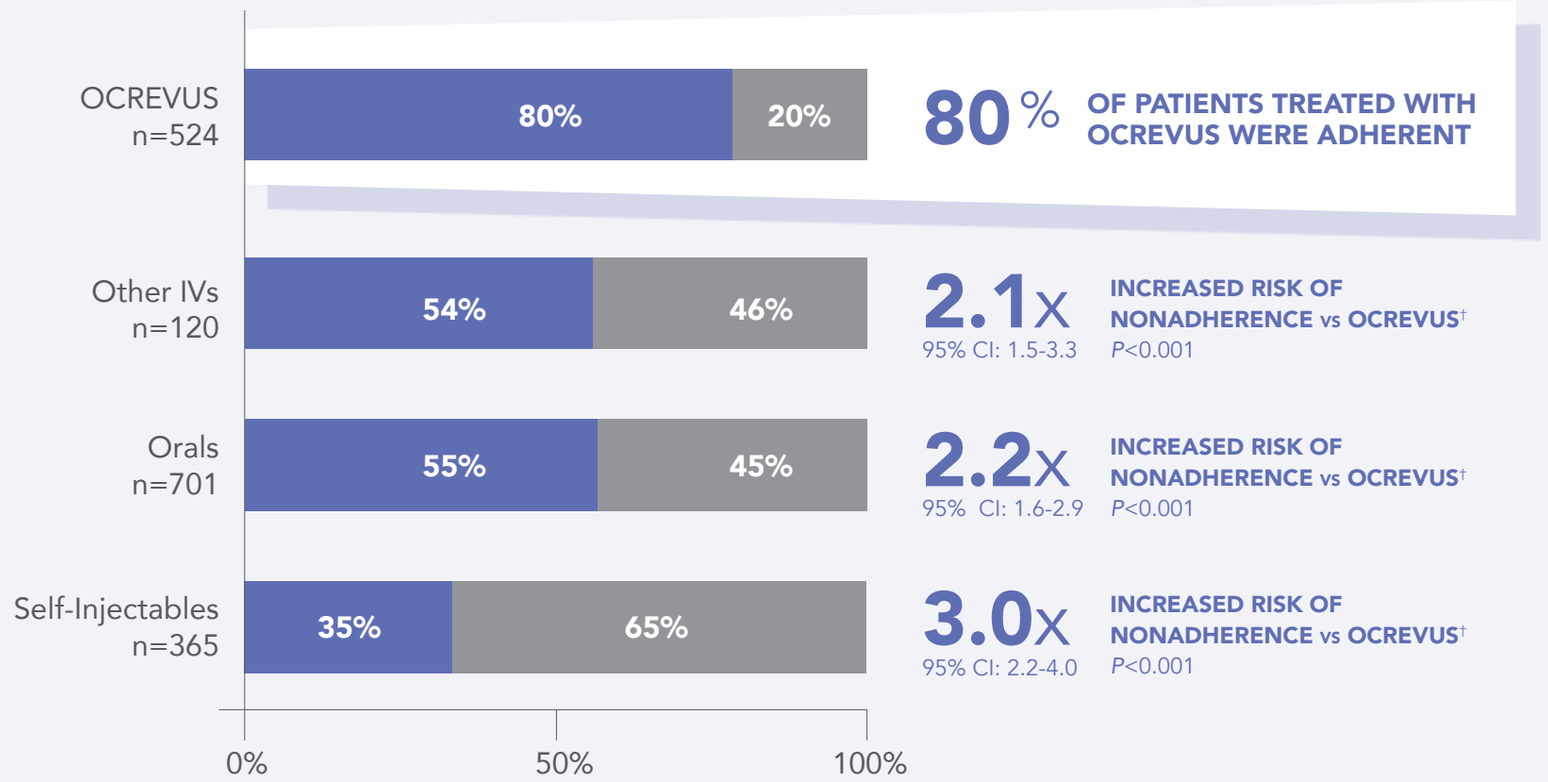
- Unable to ascertain if patients on injectable and oral medications took DMT as prescribed
- ICD-10 codes do not identify patients by MS subtypes
- Limited clinical information available may impact interpretation of results (eg, MS disease duration, line of therapy)
- Lack of data on reason for discontinuation
- Possible coding errors and missing data

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

In a retrospective analysis of 1710 patients with MS,

Among patients with a 2-year follow-up, the proportion of **adherent patients** was higher in the OCREVUS group compared with patients treated with other IVs, orals and self-injectables for MS[1,2]*

Results for OCREVUS real-world analysis among patients with 2 years of follow-up concluding December 31, 2019



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

These data are not intended to show clinical comparisons.

*Monitoring occurred over a 24-month period.

†Multivariable adjusted relative risks.

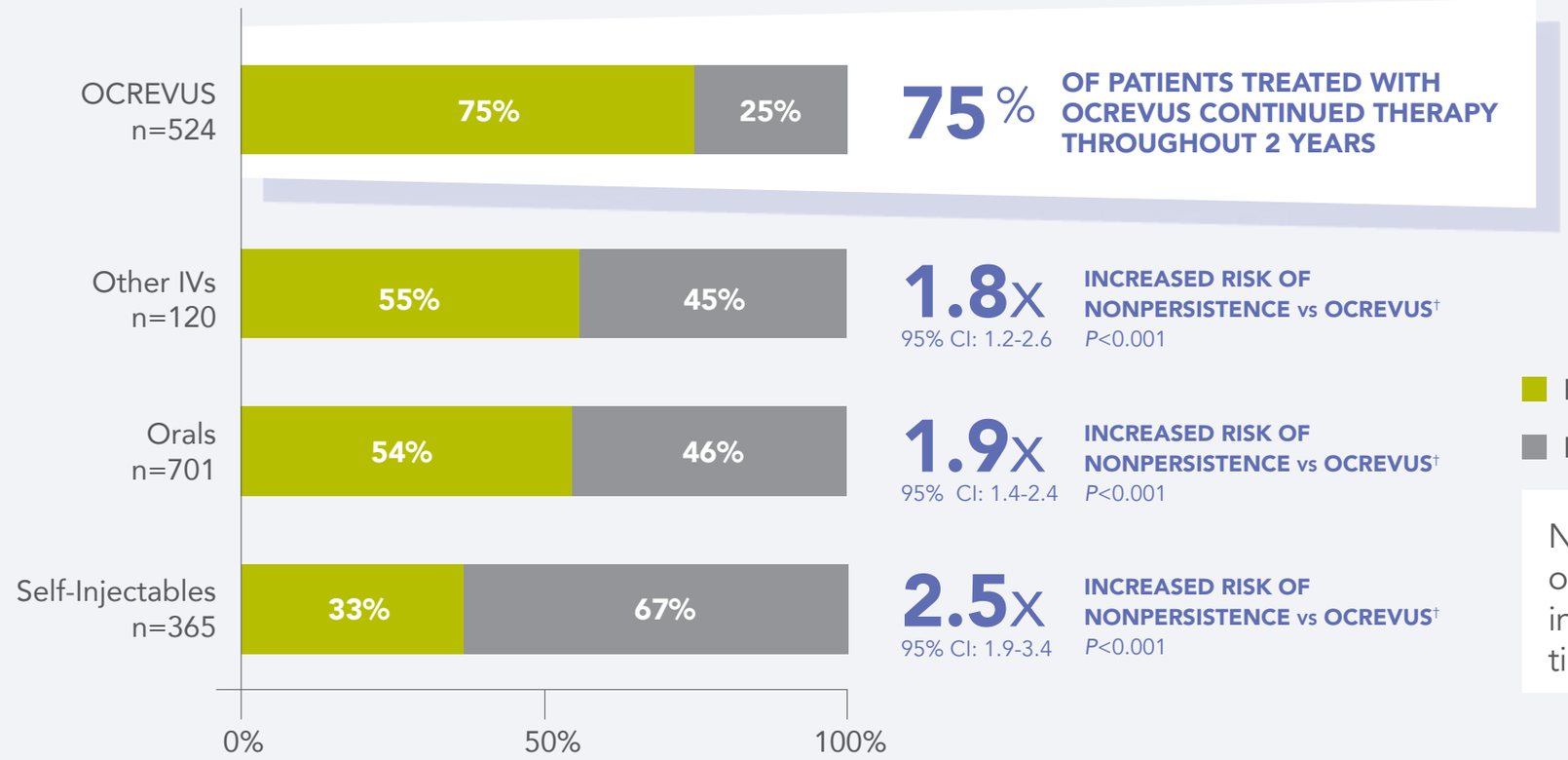
‡For orals and self-injectables, if a patient received their prescription early, the patient was assumed to be persistent/adherent for the total number of days for which they possessed medication. For IV infusions, including OCREVUS, these overlapping days were not considered.

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

In a retrospective analysis of 1710 patients with MS,

Among patients with a 2-year follow-up, those treated with OCREVUS were **more likely to continue treatment** compared with patients treated with other IVs, orals and self-injectables for MS[1,2]*

Results for OCREVUS real-world analysis among patients with 2 years of follow-up concluding December 31, 2019



Nonpersistence is defined as evidence of switch to another DMT or gap in index DMT coverage of ≥60 days at any time during the evaluation period.‡

These data are not intended to show clinical comparisons.

*Monitoring occurred over a 24-month period.

†Multivariable adjusted relative risks.

‡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.

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

REAL-WORLD ANALYSIS

The association between adherence/persistence to DMTs for MS and healthcare resource utilization and costs

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.

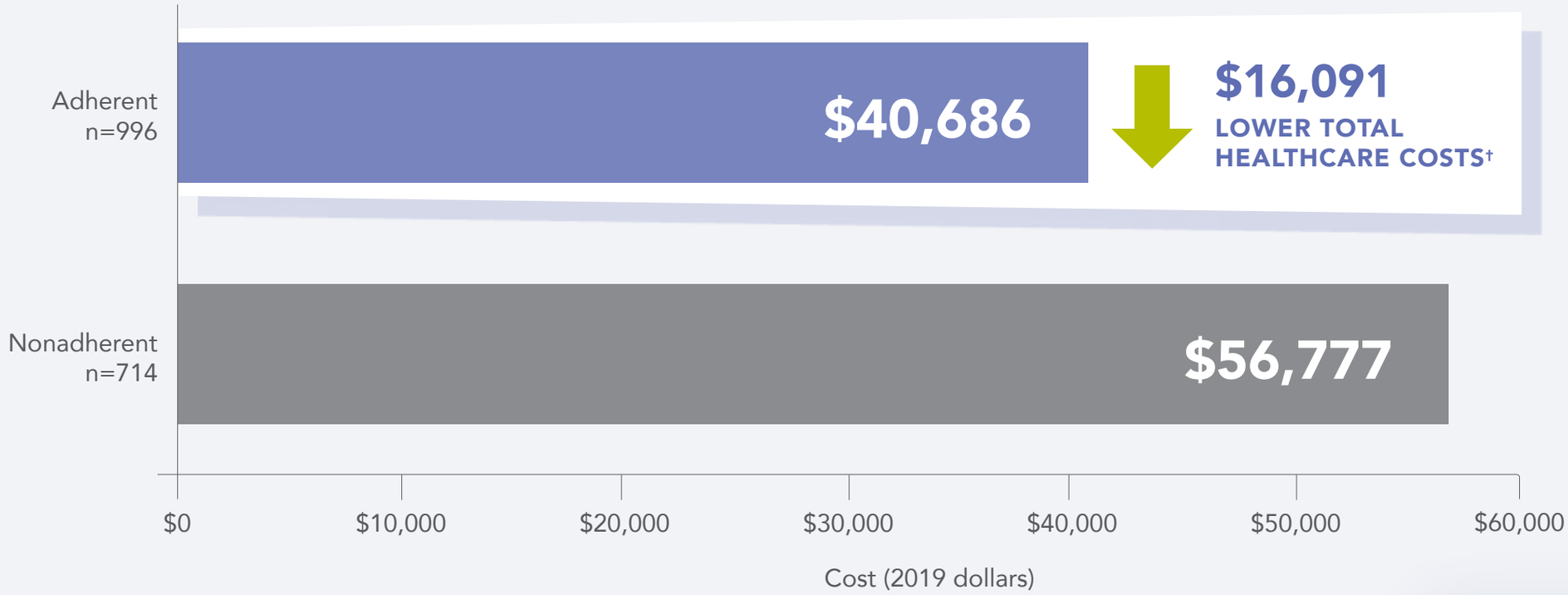
Please see additional Important Safety Information and Full Prescribing Information by tapping the appropriate button below.

Important Safety Information | Prescribing Information

In a 2-year retrospective analysis of 1710 patients with MS,

Adherence to DMTs for MS was associated with lower total healthcare costs vs nonadherence[1,2]*

Total mean-adjusted non-DMT healthcare costs per patient at 2 years†



2 / 3

+ ANALYSIS OVERVIEW

*Adjusted means were estimated using a multivariable general linear model adjusted for age, sex, payer type (commercial vs Medicare), insurance plan type, region, relapse in the prior year (yes/no), CCI, DMT use in the pre-index year (yes/no), pre-index cost, and presence of MS symptoms (yes/no).

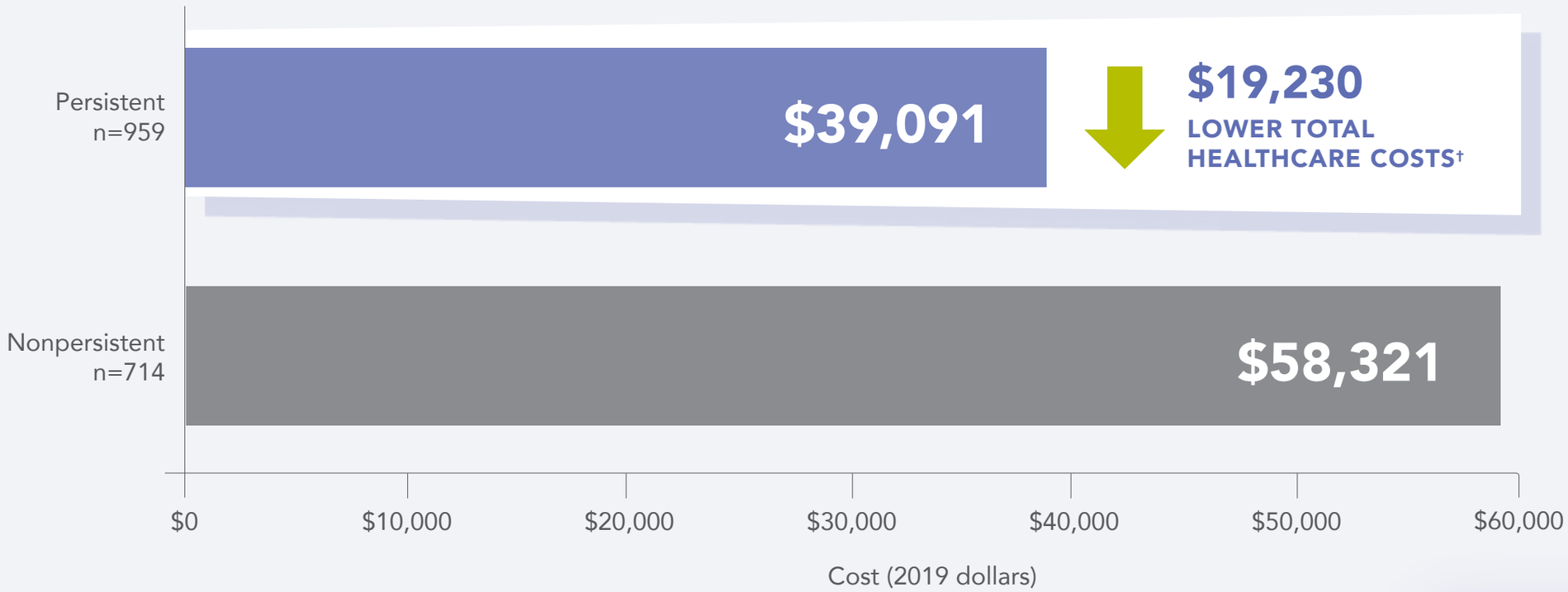
†**Non-DMT healthcare costs include outpatient services, hospitalizations, and emergency department visits.**

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

In a 2-year retrospective analysis of 1710 patients with MS,

Persistence with DMTs for MS was associated with lower total healthcare costs vs nonpersistence[1,2]*

Total mean-adjusted non-DMT healthcare costs per patient at 2 years†



+ ANALYSIS OVERVIEW

*Adjusted means were estimated using a multivariable log link gamma regression model fit adjusted for age, sex, payer type (commercial vs Medicare), insurance plan type, region, relapse in the prior year (yes/no), CCI, DMT use in the pre-index year (yes/no), pre-index cost, and presence of MS symptoms (yes/no).

†Non-DMT healthcare costs include outpatient services, hospitalizations, and emergency department visits.

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

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Please see additional Important Safety Information and Full Prescribing Information by tapping the appropriate button on the right.

Important Safety Information | Prescribing Information

OCREVUS® ocrelizumab 300MG/10ML INJECTION FOR IV

Analysis overview[1,2]

Objective

Estimate healthcare resource utilization and non-DMT costs of patients who are adherent/persistent on DMTs versus patients who are not.

Primary outcomes

The primary outcomes were assessed using data from the IBM MarketScan US Commercial and Medicare claims database during the 2-year post-index period.*

Adherence

- In this study, adherence was calculated based on PDC, with ≥80% considered adherent to the DMT initiated

$$\text{PDC} = \left(\frac{\text{Number of days in period covered}}{\text{Number of days in a specified time period}} \right) \times 100\%$$

Fixed denominator: 730 days

Persistence

- In this study, persistence was measured based on switch to another DMT or gap in index DMT coverage of ≥60 days at any time during the evaluation period

Healthcare resource utilization included hospitalizations, ED visits, and outpatient visits

*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.

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

Analysis overview[1,2]

Methods

Retrospective database analysis of 1710 patients from the IBM MarketScan US Commercial and Medicare claims database for the period between April 1, 2016 and December 31, 2019.

Generalized linear models were used to examine the association of patient factors such as baseline patient demographic and clinical characteristics with total all-cause costs (dependent variables) within 2 years of follow-up.

Explanatory variables (covariates) were selected based on clinical relevance, and depending on the analysis, including:

- Age
- Sex
- Payer type (commercial vs Medicare)
- Insurance plan type
- Pre-index relapse (yes/no)
- Pre-index DMT use (yes/no)
- Charlson comorbidity index (CCI)
- Presence of MS symptoms (yes/no)
- Region
- Pre-index costs

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

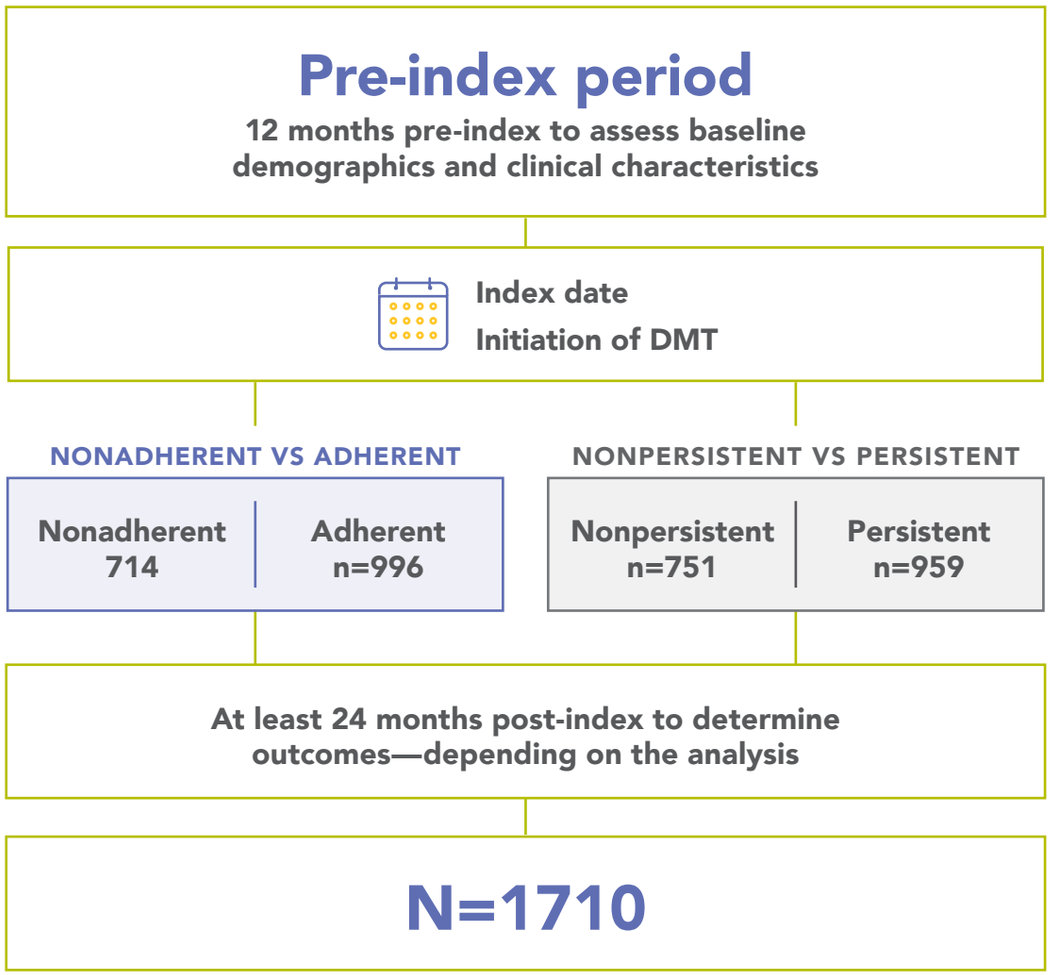
Population[1,2]

Patients were included if they:

- Were ≥18 years and diagnosed with MS at any time and initiated OCREVUS, fingolimod, dimethyl fumarate, glatiramer acetate, interferon beta-1a/b, natalizumab, or teriflunomide
- Were continuously enrolled ≥12 months pre-index and ≥24 months post-index of DMT initiation

Patients were excluded if they:

- Were on alemtuzumab, mitoxantrone, or any off-label therapies
- Were initiated multiple DMTs on index
- Had any claims of index DMT in the prior 12 months



References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

Population[1]

SELECT BASELINE CHARACTERISTICS	NONADHERENT VS ADHERENCE (N=1710)		NONPERSISTENT VS PERSISTENT (N=1710)	
	NONADHERENT (n=714)	ADHERENT (n=996)	NONPERSISTENT (n=751)	PERSISTENT (n=959)
AGE AT INDEX, MEAN (SD), YEARS	46 (12)	47 (10)	46 (12)	47 (10)
AGE CATEGORY AT INDEX, n (%)				
<35 y	126 (18)	116 (12)	133 (18)	109 (11)
35-44 y	197 (28)	255 (26)	249 (26)	203 (27)
45-54 y	208 (29)	365 (37)	351 (37)	222 (30)
≥55 y	183 (26)	260 (26)	250 (26)	193 (26)
SEX AT INDEX, n (%)				
FEMALE	560 (78.4)	718 (72)	580 (77)	698 (73)
PAYER TYPE AT INDEX, n (%)				
COMMERCIAL	683 (96)	967 (97)	718 (96)	932 (97)
MEDICARE	31 (4)	29 (3)	33 (4)	27 (3)
≥1 PRE-INDEX RELAPSE, n (%)*	239 (34)	330 (33)	259 (35)	310 (32)
PRE-INDEX DMT USE, n (%)*	296 (41.5)	589 (59)	312 (42)	573 (60)
CCI CATEGORY, n (%)*				
0	535 (75)	761 (76)	566 (75)	730 (76)
1	82 (12)	109 (11)	87 (12)	104 (11)
2+	97 (14)	126 (13)	98 (13)	125 (13)

CCI=Charlson comorbidity index; DMT=disease-modifying therapy; SD=standard deviation.
*1 year prior to index date.

Reference: 1. Data on file. Genentech, Inc.

Study considerations and limitations[1,2]

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

References: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021. **2.** Data on file. Genentech, Inc.

Summary

In a 2-year retrospective analysis of 1710 patients with MS, patients treated with OCREVUS were[1]:

80% adherent at 2 years

75% persistent in continuing therapy at 2 years

In a 2-year retrospective analysis of 1710 patients with MS[1]:

Adherence to and persistence with DMTs for MS was associated with a reduction of healthcare utilization costs[1]

Reference: 1. Pineda E, Sheinson D, Ng C, Bonine N, Pardo G. Adherence and persistence to disease-modifying therapies for multiple sclerosis and their impact on clinical and economic outcomes in a US claims database. Presented at AAN 2021 Virtual Annual Meeting; April 17-22, 2021.