Indications and Usage

OCREVUS ZUNOVO is a CD20-directed cytolytic antibody 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

Please see Important Safety Information throughout and full Prescribing Information provided with this presentation

Please Note: For FDA approved products please consult the product's full prescribing information for a complete discussion of risks and benefits of the product(s) for its approved indication(s).

The information we provide may additionally include relevant references to non-Genentech product information derived from publicly available sources.

OCREVUS ZUNOVO [prescribing information]. South San Francisco, CA.

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OCREVUS ZUNOVO™ (ocrelizumab and hyaluronidase-ocsq) OVERVIEW

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OCREVUS ZUNOVO

INDICATIONS AND USAGE[1]

Ocrevus Zunovo 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

RECOMMENDED DOSAGE

- The recommended dosage of OCREVUS ZUNOVO is 920 mg/23,000 units (920 mg ocrelizumab and 23,000 units of hyaluronidase) administered by a healthcare professional as a single 23 mL subcutaneous injection in the abdomen over approximately 10 minutes every 6 months.

Ocrevus Zunovo (ocrelizumab SC; OCR SC) contains the same monoclonal antibody as the IV formulation, Ocrevus (ocrelizumab IV; OCR IV), and is combined with recombinant human hyaluronidase PH20, rHuPH20, which facilitates subcutaneous dosing of larger volumes.[1,2]

IV, intravenous; OCR, ocrelizumab; SC, subcutaneous

1. Ocrevus Zunovo [package insert]. Genentech USA, Inc.; South San Francisco, CA. 2. Locke K, et al. *Drug Deliv* 2019;26:98-106.

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RECOMBINANT HUMAN HYALURONIDASE (rHuPH20)

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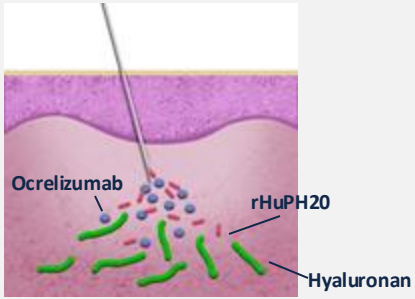
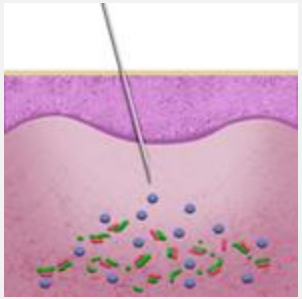
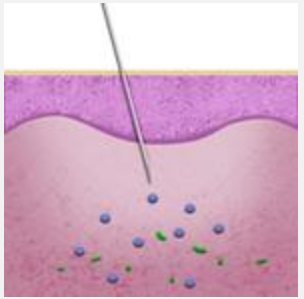
IMPACT OF rHuPH20 ON THE SC INJECTION OF LARGER FLUID VOLUMES



- Hyaluronan (hyaluronic acid) is a key component of SC connective tissue, and plays a role in preventing spread of injected fluids.[1]



- The addition of rHuPH20 temporarily degrades hyaluronan locally at the injection site, with no changes in collagen and elastin.[2]
  - Subcutaneous tissue permeability is restored within 24 to 48 hours.[3]



- The degradation of hyaluronan results in a temporary increase in the local SC dispersion area, facilitating larger volumes of fluids to be administered.[2]

Co-formulation with rHuPH20 facilitates SC administration of larger volumes

rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous.

1. Bittner B, et al. *BioDrugs*. 2018;32(5):425-440. 2. Jackisch C, et al. *Geburtshilfe Frauenheilkd*. 2014;74(4):343-349. 3. Knowles SP, et al. *Expert Opin Drug Deliv*. 2021;18(11):1673-1685.

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PHARMACOKINETIC BRIDGING STUDY

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WHEN CAN A PHARMACOKINETIC (PK) BRIDGING STUDY BE USED?

PK Bridging* Approach

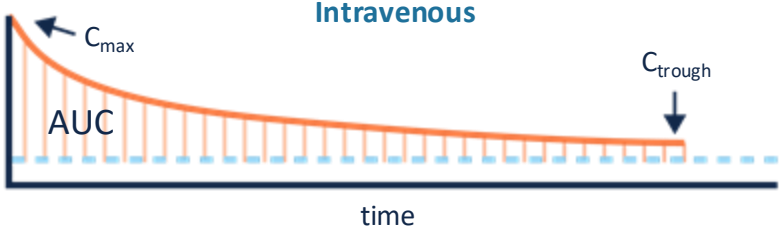
Drug product with same active ingredient

Clinical profile† already established with one administration route

New administration route

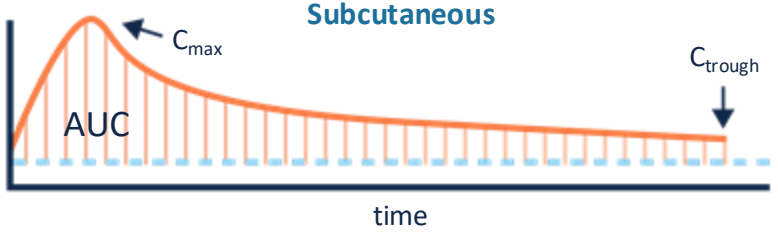
Illustrative only, no actual data

Intravenous



- Fastest way to deliver drug to the bloodstream; no absorption required
- All drug is expected to reach the bloodstream instantaneously

Subcutaneous



- Absorption occurs; concentration* at site of absorption drives movement into the systemic vasculature
- Not all drug is expected to reach the bloodstream

A PK bridging*[1] approach can be considered when the **same active ingredient of a drug product is used across two different routes of administration (SC/IV)** and the clinical profile is already established with one of these routes of administration.[2]

*Bridging study FDA definition: A study performed to provide nonclinical or clinical data that allows extrapolation of the existing data from the drug product produced by the current process to the drug product from the changed process.[2]

IV, intravenous; PK, pharmacokinetics; SC, subcutaneous.

1. FDA. Q5E Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q5e-comparability-biotechnologicalbiological-products-subject-changes-their-manufacturing-process. Accessed May 14, 2024. 2. Xu Z, et al. *Clin Pharmacol Ther.* 2023;113(5):1011-1029.

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THE OCARINA II STUDY

A Phase III, Non-Inferiority, Randomized, Open-Label, Parallel Group, Multicenter Study to Investigate the Pharmacokinetics, Pharmacodynamics, Safety and Radiological and Clinical Effects of Subcutaneous Ocrelizumab versus Intravenous Ocrelizumab in Patients with Multiple Sclerosis

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OCARINA II METHODS: PATIENT POPULATION AND STUDY OBJECTIVES

PATIENT POPULATION

- RMS or PPMS (McDonald 2017)[1]
- Age 18–65 years, inclusive
- EDSS 0.0–6.5 inclusive
- OCR/anti-CD20 naïve patients
- Any disease duration from onset of MS symptoms except <15 years for patients with EDSS score <2.0 at screening

STUDY OBJECTIVES

Primary Objective	**PK**	PK non-inferiority of the SC formulation of OCR in patients with MS on the basis of serum OCR AUC$_{W1–12}$ after SC administration compared with IV infusion up to Week 12
Secondary Objectives	**C$_{max}$**	Maximum serum concentration of OCR SC
	MRI[a]	Total number of T1 Gd+ lesions at Weeks 8 and 24, and total number of N/E T2 lesions at Weeks 12 and 24 by MRI
	Safety	Incidence and severity of AEs following OCR administration
	Immunogenicity	Incidence of ADAs to OCR SC and OCR IV, and antibodies to rHuPH20
Exploratory Objectives	**Relapse**[b]	Annualized PDR rate by Weeks 24 and 48
	PD[c]	Proportion of patients achieving CD19+ B-cell level ≤5 cells/µL at Weeks 12, 24 and 48
	MRI	Total number of T1 Gd+ lesions at Week 48 by MRI
	PRO[d]	Patient satisfaction and experience in patients receiving OCR SC versus IV

[a]Exploratory radiologic objectives included total T1 Gd+ lesions at Weeks 48 and 96, and N/E T2 lesions at Weeks 8, 48 and 96; [b]Exploratory clinical objectives included annualized PDR rate by Weeks 24, 48 and 96 in patients with RMS, and change in EDSS from baseline at Weeks 48, 72 and 96; [c]Exploratory PD objectives included the proportion of patients achieving CD19+ B-cell level ≤5 cells/µL at Weeks 48 and/or 96; [d] Assessed via the Treatment Administration Satisfaction Questionnaires (TASQ) which is a self-reported patient instrument, designed to assess satisfaction with and impact of 2 different routes of treatment administration (IV and SC)[2]

ADA, antidrug antibody; AE, adverse event; AUC, area under the serum concentration–time curve; Cmax, maximum serum concentration; EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; IV, intravenous; MS, multiple sclerosis; N/E, new/enlarging; OCR, ocrelizumab; PD, pharmacodynamic; PDR, protocol-defined relapse; PK, pharmacokinetic; PPMS, primary progressive multiple sclerosis; PRO, patient-reported outcome; rHuPH20, recombinant human hyaluronidase PH20; RMS, relapsing multiple sclerosis; SC, subcutaneous.

1. Thompson AJ, et al. *Lancet Neurol* 2018;17:162–173.

2. Doll H, et al. J Patient Rep Outcomes. 2021;5(1):45.

Newsome SD et al. CMSC 2024; Nashville, TN; May 30, 2024; Presentation DMT06.

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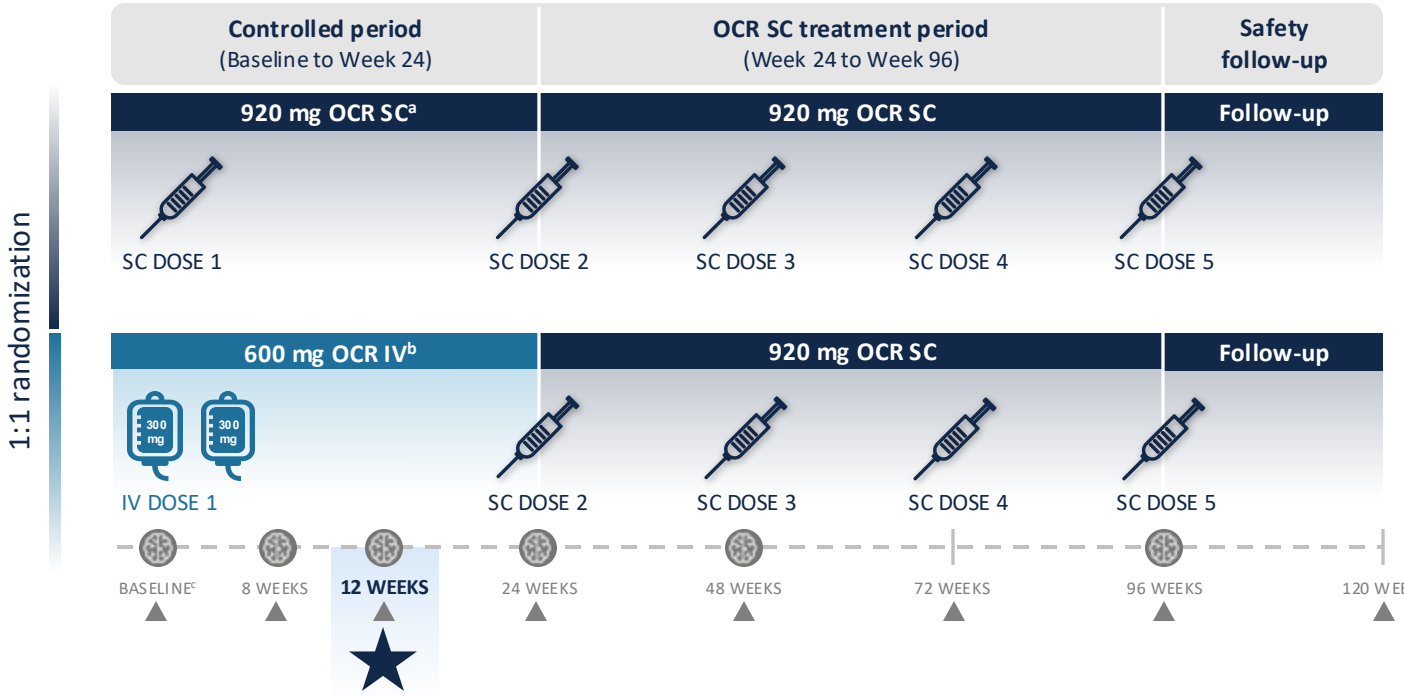
OCARINA II: STUDY DESIGN



[a]The 920 mg OCR SC dose was established as the recommended dose in the OCARINA I study (NCT03972306); [b]The first dose of OCR IV was administered as two 300 mg IV infusions given 2 weeks apart; [c]The screening phase in patients with RMS and PPMS took place before baseline MRI readings and patients were randomized 1:1 between the two arms. [d]Cut-off date is when the last patient completes 12 weeks.

ADA, antidrug antibody; AUC, area under the serum concentration–time curve; EDSS, Expanded Disability Status Scale; IV, intravenous; MRI, magnetic resonance imaging; OCR, ocrelizumab; PD, pharmacodynamic;PK, pharmacokinetic; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis; SC, subcutaneous; W, week.

Newsome SD, et al. CMSC 2024; Nashville, TN; May 30, 2024; Presentation DMT06. Newsome SD et al. ECTRIMS-ACTRIMS 2023; Milan, Italy; October 11-13, 2023. P370

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OCARINA II: WEEK 12 PHARMACOKINETIC ANALYSIS

OCR PK SC vs IV[a]			
	SC 920 mg[b] (n=116)	IV 600 mg[b] (n=116)	GMR[d] SC vs IV[c] (90% CI)
AUC over the first 12 weeks ($AUC_{W1–12}$)	3,500 µg/mL*day	2,750 µg/mL*day	**1.29 (1.23–1.35)**
Max concentration (C_{max})	132 µg/mL	137 µg/mL	0.96 (0.92–1.01)
T_{max}, median (min–max)	3.75 (1.75–13.2) days	–	–

PRIMARY ENDPOINT

The differences in pharmacokinetic exposures following administration of OCR SC 920 mg or OCR IV 600 mg were not clinically significant during the first 12 weeks.[1]

CCOD: March 10, 2023.

[a]Two patients from the OCR SC/SC arm were excluded from the PK-evaluable analysis set due to an incomplete SC dose and an impossible concentration-time profile. Two patients from the OCR IV/SC arm were excluded from the PK-evaluable analysis set due to a delay in the second IV infusion and a missing second IV infusion; [b]Estimated mean exposure for AUC or Cmax; Ocrevus IV 600 mg was administered as two 300 mg IV infusions given 14 days apart. [c]GMR and two-sided 90% CI of SC vs IV between baseline and Week 12. Non-inferiority would be established if the lower end of the two-sided 90% CI is >0.8; the non-inferiority limit of 0.8 corresponds to a maximal 20% loss in AUC for the SC administration compared with IV, as recommended in the regulatory guidance documents for demonstration of bioequivalence for PK bridging.[2,3]

[d] The geometric mean ratio (GMR) is calculated from the geometric mean values for each treatment arm. The geometric mean is used because PK parameters have a log-normal distribution rather than a normal distribution.

AUC, area under the serum concentration–time curve, CCOD, clinical cut-off date; CI, confidence interval; Cmax, maximum serum concentration; GMR, geometric mean ratio; IV, intravenous; OCR, ocrelizumab; PK, pharmacokinetic; SC, subcutaneous; Tmax, time to maximum concentration

1. Ocrevus Zunovo™ [package insert]. Genentech; South San Francisco, CA. 2. European Medicines Agency. Guideline on the investigation of bioequivalence. January 2010. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-investigation-bioequivalence-rev1_en.pdf. Accessed April 12, 2024.
2. Food and Drug Administration. Bioavailability studies submitted in NDAs or INDs – General considerations. April 2022. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/bioavailability-studies-submitted-ndas-or-inds-general-considerations. Accessed April 12, 2024.

Newsome SD et al. AAN 2024; Denver, CO; April 13 -18, 2024; Poster S31.001

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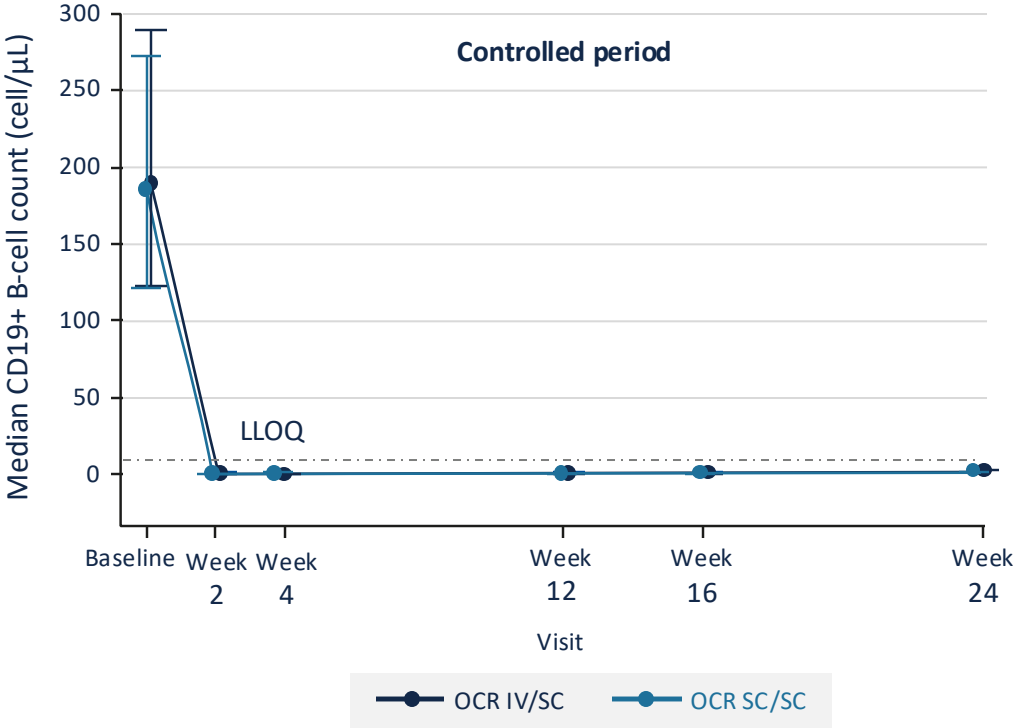
OCARINA II: B-CELL DEPLETION



Treatment led to **CD19+ B-cell depletion** in peripheral blood, which was similar in both treatment arms (OCR SC/SC and OCR IV/SC) up to Week 24

CCOD: December 4, 2023. Error bars represent interquartile range. LLOQ = ≤5 cells/µL.
CCOD, clinical cut-off date; IV, intravenous; LLOQ, lower limit of quantification; OCR, ocrelizumab; SC, subcutaneous.
Newsome SD et al. ECTRIMS 2024; Copenhagen, Denmark; September 18-20, 2024; Poster P797

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EXCERPTS FROM OCREVUS ZUNOVO USPI

The Results of the PK Bridging Study, OCARINA II, was the Basis of the FDA Approval of Ocrevus Zunovo

In Study 4[c], ***the differences in pharmacokinetic exposures*** following the administration of OCREVUS ZUNOVO subcutaneously at 920 mg/23,000 units and ocrelizumab intravenously at 600 mg in MS patients ***were not clinically significant.*** *(from Section 12.3 Pharmacokinetics).*

Studies 1-3[a-c], which established the effectiveness of ocrelizumab for the treatment of RMS and PPMS in adults, were conducted with intravenously-administered ocrelizumab. Study 4 demonstrated ***comparable exposure of OCREVUS ZUNOVO relative to the ocrelizumab intravenous formulation, which established the efficacy of OCREVUS ZUNOVO.***

(from Section 14 CLINICAL STUDIES)

MS, multiple sclerosis; OCR=ocrelizumab; PPMS, primary progressive multiple sclerosis; RMS, relapsing multiple sclerosis; USPI, United States Prescribing Information.

a ***Study 1 and 2*** refer to the (OCR IV) OPERA I and II Phase 3 clinical trials in patients with RMS; b ***Study 3*** refers to the (OCR IV) ORATORIO Phase 3 clinical trial in patients with PPMS; *c* ***Study 4*** refers to the OCARINA II Phase 3, PK noninferiority study comparing OCR SC 920 mg vs OCR IV 600 mg

1. Ocrevus Zunovo [package insert]. Genentech USA, Inc.; South San Francisco, CA.

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OCRELIZUMAB SC EFFICACY DATA: OCARINA II

SC, subcutaneous

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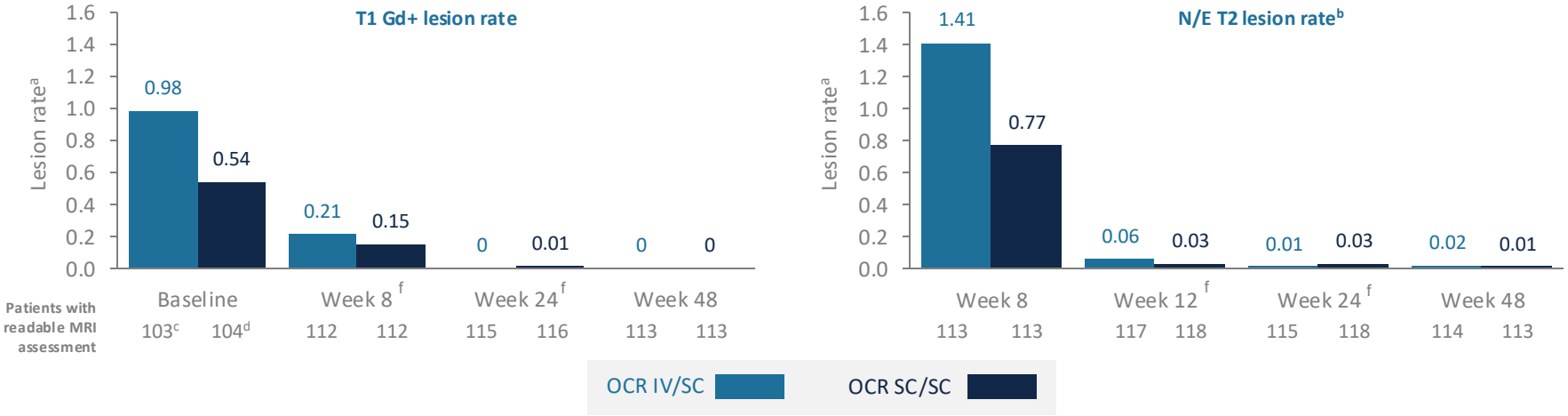
EXPLORATORY ENDPOINTS AT WEEK 48

Radiologic Measures



Clinical Measure at Week 48[e]

- **97.2%** of patients **were free of relapses** following **OCR SC** administration during the treatment phase or safety follow-up

OCR SC/SC
97.2% (n=104/107)

OCR IV/SC
98.1% (n=104/106)

CCOD: December 4, 2023.

[a]The lesion rate is the total number of lesions divided by the number of patients with a readable MRI assessment at the visit; [b]New or enlarging T2 lesion count measurement is performed with respect to the previous scheduled available visit; [c]At baseline for T1 Gd+ lesions, 78/103 (75.7%) patients had no lesions and 11/103 (10.7%) had ≥4 lesions; [d]At baseline for T1 Gd+ lesions, 82/104 (78.8%) patients had no lesions and 5/104 (4.8%) had ≥4 lesions; [e]At Week 48, two patients (1.9%) in each arm had one protocol-defined relapse, and one patient (0.9%) in the OCR SC/SC arm had two protocol-defined relapses; unadjusted relapse rate per year was 0.04 and 0.02 in the SC/SC and IV/SC arms, respectively. The unadjusted annualized relapse rate is the total number of relapses for all patients in the considered group divided by the total follow-up time. [f]Prespecified Secondary Endpoints: T1-Gd+ lesions at Weeks 8 and 24, N/E T2 lesions at Weeks 12 and 24.

CCOD, clinical cut-off date; Gd+, gadolinium-enhancing; IV, intravenous; MRI, magnetic resonance imaging; N/E, new/enlarging; OCR, ocrelizumab; SC, subcutaneous.

Newsome SD et al. CMSC 2024; Nashville, TN; May 30, 2024; Presentation DMT06.

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OCRELIZUMAB SC SAFETY DATA

SC, subcutaneous

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OCARINA II: SAFETY DATA

Patients with ≥1 event, n (%)	OCARINA II[a] OCR SC 920 mg (n=233)
Adverse Events[b]	175 (75.1)
Serious Adverse Events	6 (2.6)
Infections	89 (38.2)
Injection Reactions[c]	120 (51.5)
Local Injection Reactions	117 (50.2)
Systemic Injection Reactions	27 (11.6)

- No patients in OCARINA II that experienced AEs withdrew or had dose modification
- Most patients had AEs of Grade 1 or Grade 2 (96.6%); no Grade 4 or 5 AEs were reported

Over a period of 48 weeks, no new safety concerns were identified beyond the known risks associated with OCR or the new route of administration

[a]Patients who received their first dose of OCR SC were included regardless of which arm they were randomized to;[b]Patients with ≥1 AE, reported terms of AEs are encoded using MedDRA version 26.0; [c]IRs comprise AEs with the MedDRA Preferred Terms injection-related reaction and injection site reaction, which occurred during or within 24 hours after OCR SC administration and which were judged by the investigator to be related to the OCR SC injection.
AE, adverse event; IR, injection reaction; MedDRA, Medical Dictionary for Regulatory Activities; OCR, ocrelizumab; rHuPH20, recombinant human hyaluronidase PH20; RoA, route of administration; SC, subcutaneous.
1. Newsome SD, et al. AAN 2024; Denver, CO; April 13 -18, 2024; Poster P10.003 and S31.001 2. Newsome SD et al. CMSC 2024; Nashville, TN; May 30, 2024. Presentation DMT06.

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OCRELIZUMAB SC
INJECTION REACTION SAFETY DATA

SC, subcutaneous

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USPI: EXCERPTS FROM SECTION 5.1 INJECTION REACTIONS

OCREVUS ZUNOVO can cause injection reactions, which can be local or systemic. Common symptoms of local injection reactions reported by patients treated with OCREVUS ZUNOVO in multiple sclerosis (MS) clinical trials included erythema, pain, swelling, and pruritus. Common symptoms of systemic injection reactions reported by patients included headache and nausea. In an open-label, active-controlled trial, injection reactions were more frequently reported with the first injection; 49% of patients experienced an injection reaction with the first injection.

Monitor patients during and after injections [see Dosage and Administration (2.4)]. Inform patients that injection reactions can occur during or within 24 hours of the injection.

Reducing the Risk of Injection Reactions and Managing Injection Reactions

Administer oral premedication (e.g., dexamethasone or an equivalent corticosteroid, and an antihistamine) at least 30 minutes prior to each OCREVUS ZUNOVO injection to reduce the risk of injection reactions. The addition of an antipyretic (e.g., acetaminophen) may also be considered.

Management recommendations for injection reactions depend on the type and severity of the reaction. For life-threatening injection reactions, immediately and permanently stop OCREVUS ZUNOVO and administer appropriate supportive treatment. For less severe injection reactions, the injection should be interrupted immediately, and the patient should receive symptomatic treatment. The injection should be completed at the healthcare provider's discretion and only after all symptoms have resolved.

1. Ocrevus Zunovo [package insert]. Genentech USA, Inc.; South San Francisco, CA.

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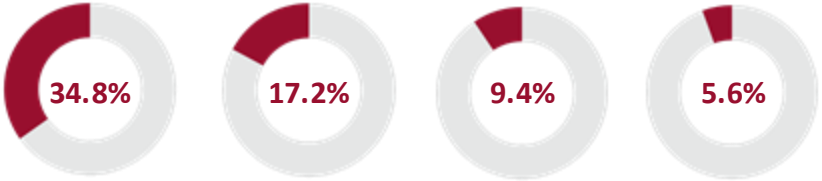
OCARINA II: INJECTION REACTIONS OVER 48 WEEKS[a,b,c]

Most Common Symptoms

Local



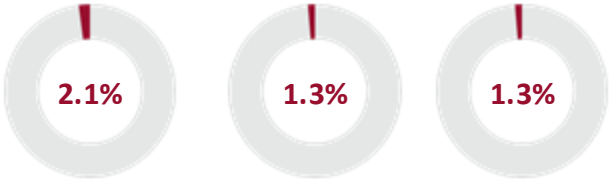
Erythema (81/233)

Pain (40/233)

Swelling (22/233)

Pruritus (13/233)

Systemic



Headache (5/233)

Flushing (3/233)

Nausea (3/233)

Patients with IRs

All IRs were non-serious, Grades 1 or 2 (mild, moderate), and the majority required no treatment.

Median IR Duration:[1]

LIR: 3.5 days

SIR: 3 days

Local IRs:

- Median symptom size decreased over time
  - Erythema median size from 2.36 to 1.97 in
  - Swelling median size from from 3.94 to 2.76 in

IRs were more frequently reported with the first injection, and no IRs led to treatment discontinuation.

[a]CCOD: December 4, 2023; [b]IRs comprise adverse events with the MedDRA preferred term injection-related reaction and injection site reaction, which occurred during or within 24 hours after OCR SC administration and which were judged by the investigator to be related to the OCR SC injection; [c]Standard-of-care treatment included mostly analgesics (e.g. paracetamol, oral or topical antihistamines) and were used to treat patients with IRs if needed.
CCOD, clinical cut-off date; IR, injection reaction; LIR, local injection reaction; MedDRA, Medical Dictionary for Regulatory Activities; OCR, ocrelizumab; SC, subcutaneous; SIR, systemic injection reaction.
Newsome SD, et al. AAN 2024; Denver, CO; April 13-18, 2024;Poster S31.001. Newsome SD, et al. CMSC 2024; Nashville, TN; May 30, 2024; Presentation DMT06.

1. The median duration of symptoms was 3 days for systemic injection reactions and 3.5 days for local injection reactions. Ocrevus Zunovo [package insert]. Genentech USA Inc.; South San Francisco, CA.

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DEEPER DIVE INTO INJECTION REACTION SAFETY DATA FOR OCRELIZUMAB SC: OCARINA II

SC, subcutaneous

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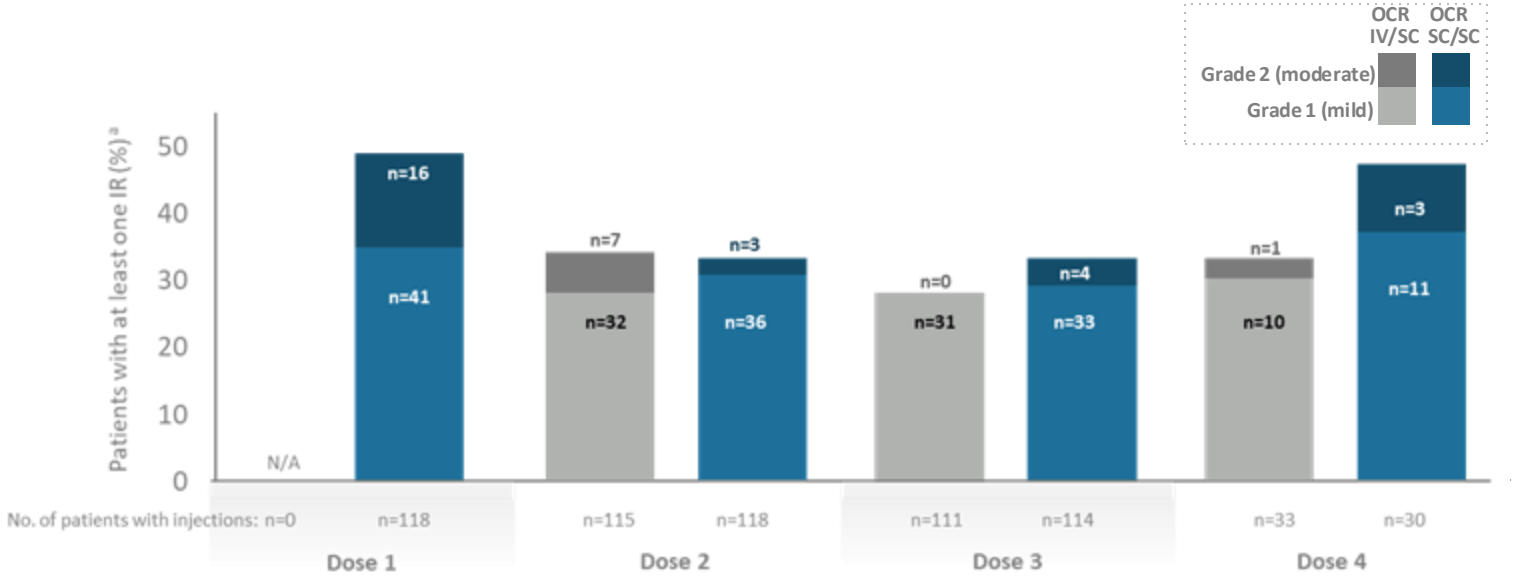
OCARINA II: SEVERITY OF INJECTION REACTIONS BY DOSE



No Grade ≥3 IRs were seen

IR profiles were similar in the IV/SC and SC/SC arms

CCOD: December 4, 2023.

[a]For each injection, in patients with multiple occurrences of IR symptoms, the IR event was counted once, using the symptom with the highest grade of severity; grades were based on National Cancer Institute CTCAE v5.0. Dose 1 corresponds to injection 1 for patients randomized to SC arm, dose 2 corresponds to injection 1 for patients randomized to IV arm and to injection 2 for patients randomized to SC arm; subsequent doses correspond to subsequent injections.

CCOD, clinical cut-off date; CTCAE, Common Terminology Criteria for Adverse Events; IR, injection reaction; OCR, ocrelizumab; IV, intravenous; N/A, not applicable; SC, subcutaneous.

Newsome SD et al. CMSC 2024; Nashville, TN; May 30, 2024; Presentation DMT06 Genentech Data on File

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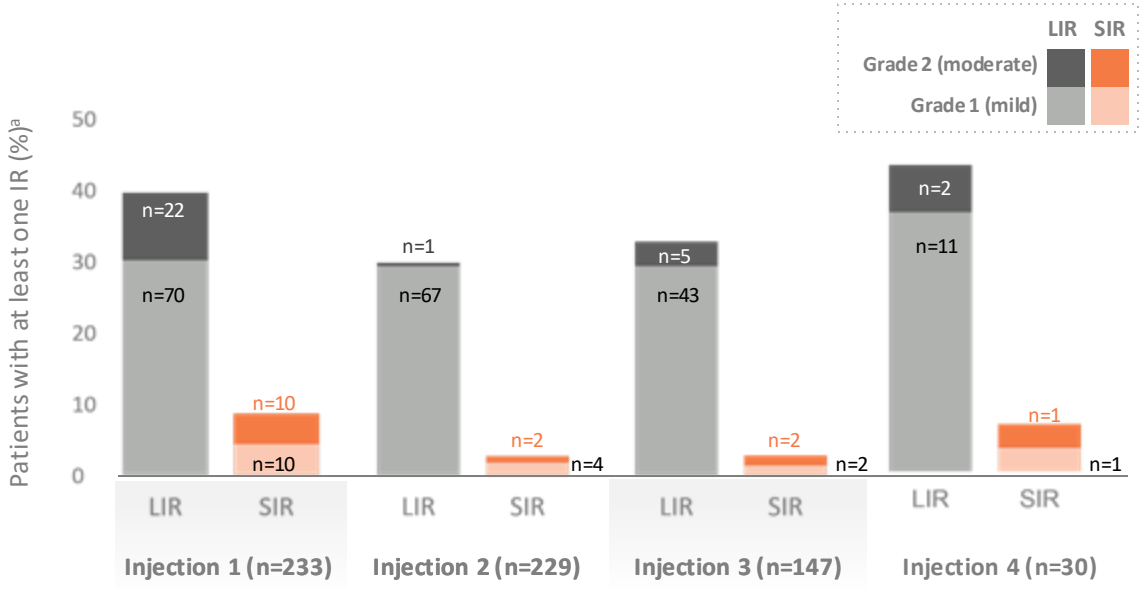
OCARINA II: PERCENTAGE OF PATIENTS WITH LIR AND SIR BY INJECTION



Patients (n/N) with at least one treatment for IR[b]	n= 21 / 233	n= 7 / 229	n= 6 / 147	n= 1 / 30

- **All IRs were nonserious and mild to moderate** (Grades 1 or 2; no Grade ≥3 IRs were reported)
- Most patients did not need treatment for IRs
- Fewer patients required treatment for IRs over time

CCOD: December 4, 2023.

[a]For each injection, in patients with multiple occurrences of IR symptoms, the IR event was counted once, using the symptom with the highest grade of severity; grades were based on National Cancer Institute CTCAE v5.0. Dose 1 corresponds to injection 1 for patients randomized to SC arm, dose 2 corresponds to injection 1 for patients randomized to IV arm and to injection 2 for patients randomized to SC arm; subsequent doses correspond to subsequent injections;[b]Standard of care treatments, such as analgesics (e.g., ibuprofen, paracetamol, oxycodone) and oral or topical antihistamines were administered.

CCOD, clinical cut-off date; CTCAE, Common Terminology Criteria for Adverse Events; IR, injection reaction; IV, intravenous; LIR, local injection reaction; SC, subcutaneous; SIR, systemic injection reaction.

Newsome SD et al. CMSC 2024; Nashville, TN; May 30, 2024; Presentation DMT06; Genentech Data on File

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OCARINA II: LOCAL IR SYMPTOMS DURING AND POST-INJECTION

Timing of local IR			
	10 min[a]	1 h	24 h
Patients with ≥1 local IR symptom, n (%)	n=46/233 (19.7)	n=66/233 (28.3)	n=68/233 (29.2)
Symptoms, n (%)			
Erythema	33 (14.2)	51 (21.9)	40 (17.2)
Pain	17 (7.3)	23 (9.9)	22 (9.4)
Swelling	12 (5.2)	17 (7.3)	10 (4.3)
Pruritus	4 (1.7)	7 (3.0)	8 (3.4)
Bruising	2 (0.9)	5 (2.1)	7 (3.0)

- **The nature of the local IR symptoms did not depend on their time to onset[b]**
- **Most local IRs (90.0%) resolved within 3 days**

CCOD: December 4, 2023.
a 10 min refers to IRs occurring during injection and the duration of the SC injection, which is approximately 10 minutes.
b Except bruising, which occurred >1 hour after injection.
CCOD, clinical cut-off date; IR, injection reaction; SC, subcutaneous.
Newsome SD et al. CMSC 2024; Nashville, TN; May 30, 2024; Presentation DMT06.

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OCARINA II: SYSTEMIC IRs DURING AND POST-INJECTION

Timing of systemic IR			
	10 min[a]	1 h	24 h
Patients with ≥1 systemic IR symptom, n (%)	n=6/233 (2.6)	n=13/233 (5.6)	n=18/233 (7.7)
Symptoms, n (%)			
Flushing	0 (0.0)	0 (0.0)	3 (1.3)
Headache	1 (0.4)	2 (0.9)	3 (1.3)
Fatigue	0 (0.0)	0 (0.0)	2 (0.9)
Nausea	1 (0.4)	1 (0.4)	2 (0.9)
Pain	0 (0.0)	1 (0.4)	2 (0.9)

- **The nature of the systemic IR symptoms did not depend on their time to onset[b]**
- **Most systemic IRs (81.8%) resolved in less than 3 days**

CCOD: December 4, 2023.
a 10 min refers to IRs occurring during injection and the duration of the SC injection, which is approximately 10 minutes.
b Except flushing and fatigue which occurred >1 hour after injection.
CCOD, clinical cut-off date; h, hour; IR, injection reaction; min, minutes.
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KEY TAKEAWAYS

- **Ocrelizumab SC contains** the same monoclonal antibody as the IV formulation, Ocrevus, and is combined with recombinant human **hyaluronidase** PH20 **which facilitates subcutaneous dosing of larger volumes**.[1,2]
- **A PK-bridging approach** can be considered when the same active ingredient of a drug product is used across two different routes of administration (SC/IV) and the clinical profile is already established with one of these routes of administration.[3,5]

In OCARINA II:

- **No clinically significant differences in pharmacokinetic exposures** following the administration of ocrelizumab SC and ocrelizumab IV in MS patients.[1]
- Demonstrated the **comparable exposure** of ocrelizumab SC relative to the IV formulation, which established the **efficacy** of ocrelizumab SC.[1]
- **The injection reactions reported were all non-serious, and mild to moderate**.[4]

IV, intravenous; MS, multiple sclerosis; PK, pharmacokinetic; SC, subcutaneous.

1. Ocrevus Zunovo [package insert]. Genentech USA, Inc.; South San Francisco, CA. 2. Locke K, et al. *Drug Deliv* 2019;26:98-106. 3. FDA. Q5E Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q5e-comparability-biotechnologicalbiological-products-subject-changes-their-manufacturing-process. Accessed May 14, 2024. 4. Newsome SD, et al. AAN 2024; Denver, CO; April 13-18, 2024;Poster S31.001. 5. Xu Z, et al. Clin Pharmacol Ther. 2023;113(5):1011-1029.

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