Trying to help patients with RMS navigate COVID-19?

Discover the data on KESIMPTA®, COVID-19, and vaccination

> "I'm glad there is helpful information for my doctor about KESIMPTA and COVID-19."
>
> Walt: actual KESIMPTA patient since 2021*

RMS=relapsing multiple sclerosis.

*Individual results may vary. Walt was compensated for his time.

INDICATION

KESIMPTA 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.

IMPORTANT SAFETY INFORMATION

Contraindications

KESIMPTA is contraindicated in patients with active hepatitis B virus (HBV) infection, or history of hypersensitivity to ofatumumab, or life-threatening injection-related reaction to KESIMPTA. Hypersensitivity reactions have included anaphylaxis and angioedema.

Warnings and Precautions

Infections

Serious, including life-threatening or fatal, bacterial, fungal, and new or reactivated viral infections have been observed during and following completion of treatment with anti-CD20 B-cell depleting therapies. The overall rate of infections and serious infections in KESIMPTA-treated patients was similar to teriflunomide-treated patients (51.6% vs 52.7%, and 2.5% vs 1.8%, respectively). The most common infections reported by KESIMPTA-treated patients in relapsing MS (RMS) trials included upper respiratory tract infection (39%) and urinary tract infection (10%). Delay KESIMPTA administration in patients with an active infection until resolved.

Consider the potential increased immunosuppressive effects when initiating KESIMPTA after an immunosuppressive therapy or initiating an immunosuppressive therapy after KESIMPTA.

Please see additional Important Safety Information throughout. Click here for full Prescribing Information, including Medication Guide.

Kesimpta® (ofatumumab) 20 mg injection

KESIMPTA and vaccinations*

	Non-live and inactivated vaccines	Live vaccines (eg, live-attenuated vaccines)
For new patients **planning to start KESIMPTA®**[1]	Whenever possible, administer at least **2 weeks** prior to initiation of KESIMPTA.	Administer at least 4 weeks prior to initiation of KESIMPTA.
For patients **already taking KESIMPTA**	• In the pivotal trials, concomitant treatment with non-live vaccines was permitted[2,†] • The use of non-live vaccines is not contraindicated with KESIMPTA therapy[1] • KESIMPTA may interfere with the effectiveness of inactivated vaccines[1,‡]	• The safety of immunization with live or live-attenuated vaccines following KESIMPTA therapy has not been studied[1] • Vaccination with live or live-attenuated vaccines is not recommended during treatment and after discontinuation until B-cell repletion[1,‡]

Currently available COVID-19 vaccines on the market are non-live vaccines.[3]

Vaccination of infants born to mothers treated with KESIMPTA during pregnancy[1‡§]

- In infants of mothers treated with KESIMPTA during pregnancy, do not administer live or live-attenuated vaccines before confirming the recovery of B-cell counts. Depletion of B cells in these infants may increase the risks from live or live-attenuated vaccines[§]
- Inactivated vaccines may be administered, as indicated, prior to recovery from B-cell depletion, but an assessment of vaccine immune responses, including consultation with a qualified specialist, should be considered to determine whether a protective immune response was mounted[§]

RMS=relapsing multiple sclerosis.

*Any vaccine used in patients taking KESIMPTA should be administered in accordance with the KESIMPTA Prescribing Information.
†ASCLEPIOS I and II studied KESIMPTA vs oral Aubagio® (teriflunomide) in patients with RMS (N=927 and N=955, respectively). Primary end point was annualized relapse rate. Maximum duration 120 weeks; median duration 85 weeks. Some patients received non-live vaccines concomitantly with KESIMPTA. However, vaccine response in those patients was not measured during the study and data are not available.[1]
‡Post vaccination, an assessment of vaccine immune responses, including consultation with qualified specialists, should be considered to determine whether a protective immune response was mounted. It is unknown whether KESIMPTA may interfere with vaccine efficacy.[1]
§Data from Studies 1 and 2 indicate a median time to B-cell recovery to either LLN or baseline value of 24.6 weeks post-treatment discontinuation. PK and PD modeling and simulation for B-cell repletion corroborate these data, predicting median time to B-cell recovery to LLN of 23 weeks post-treatment discontinuation.[1]

IMPORTANT SAFETY INFORMATION (cont)

Hepatitis B Virus

Reactivation: No reports of HBV reactivation in patients with MS treated with KESIMPTA. However, HBV reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, has occurred in patients treated with ofatumumab at higher intravenous doses for chronic lymphocytic leukemia (CLL) than the recommended dose in MS and in patients treated with other anti-CD20 antibodies.

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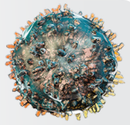
Components of immune function and KESIMPTA[1,4-7]

IgG in the long-term (Phase 3 studies and post hoc analysis)

No decline in IgG was observed at the end of the Phase 3 ASCLEPIOS trials. Mean IgG levels remained stable for up to 3.5 years for KESIMPTA patients in the extension analysis.[1,4,*]



T cells in the body (Phase 2 post hoc analysis)

T cells remained largely unaffected in KESIMPTA patients, as shown by the data from a post hoc analysis of APLIOS, a 12-week, randomized, open-label, multicenter, parallel-group, Phase 2 bioequivalence study conducted in 284 patients with RMS from 41 study centers.[5]

B cells in the spleen (Preclinical data)

Preferential depletion of B cells in the lymph nodes is thought to be promoted by SC administration of KESIMPTA. KESIMPTA may spare B cells in the spleen, which may help maintain immune function, as suggested by preclinical evidence.[6,7]

Interim results of a Phase 4, open-label study assessing the effects of KESIMPTA on humoral immune response to COVID-19 vaccinations in patients with RMS[8]

- Humoral responses to COVID-19 vaccines were seen in 56% (14/25) of patients taking KESIMPTA at first post-vaccination serologic assessment ≥14 days after they received their second or third vaccine dose
- Humoral immune response appears to be increased in patients who received 3 doses compared with those who received 2 doses
  - Overall humoral responses were seen in 78% (7/9) of patients receiving 3 doses vs 44% (7/16) of those receiving 2 doses

The precise mechanism by which KESIMPTA exerts its therapeutic effects is unknown. The clinical relevance of these data is unknown.

Study design: Ongoing open-label, multicenter, single-cohort, prospective study that enrolled RMS patients (aged 18–55) who are currently receiving KESIMPTA for ≥1 month. First post-vaccination serologic assessment occurred ≥14 days after second or third dose followed by a second assessment 90 days thereafter. Patients with prior COVID-19 diagnosis, contraindication to receiving a COVID-19 mRNA vaccine, recent major infections, and prior treatment with S1P receptor modulators or natalizumab <2 months prior to enrollment were excluded. Primary end point: Achieving immune response to non-live COVID-19 mRNA vaccine as defined by a positive SARS-CoV-2 qualitative IgG Ab assay.[8]
Limitations: The population studied was heterogenous and sample size was limited. No conclusions of clinical outcomes can be drawn.

IgG=immunoglobulin G; IgM=immunoglobulin M; mRNA=messenger RNA; S1P=sphingosine 1-phosphate; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; SC=subcutaneous.

*Study design: ALITHIOS, an ongoing open-label, umbrella extension Phase 3b, single-arm, multicenter study evaluating long-term (up to 5 years) safety, tolerability, and effectiveness of KESIMPTA (20 mg SC) in subjects with RMS. The study enrolled 1703 RMS patients from the APLIOS, APOLITOS, and ASCLEPIOS I and II trials who continued KESIMPTA treatment. A long-term safety analysis from ALITHIOS was conducted to evaluate IgM/IgG levels and their association with serious infection for up to 3.5 years.[4]

IMPORTANT SAFETY INFORMATION (cont)

Infection: KESIMPTA is contraindicated in patients with active hepatitis B disease. Fatal infections caused by HBV in patients who have not been previously infected have occurred in patients treated with ofatumumab at higher intravenous doses for CLL than the recommended dose in MS. Perform HBV screening in all patients before initiation of KESIMPTA. Patients who are negative for HBsAg and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], should consult liver disease experts before starting and during KESIMPTA treatment.

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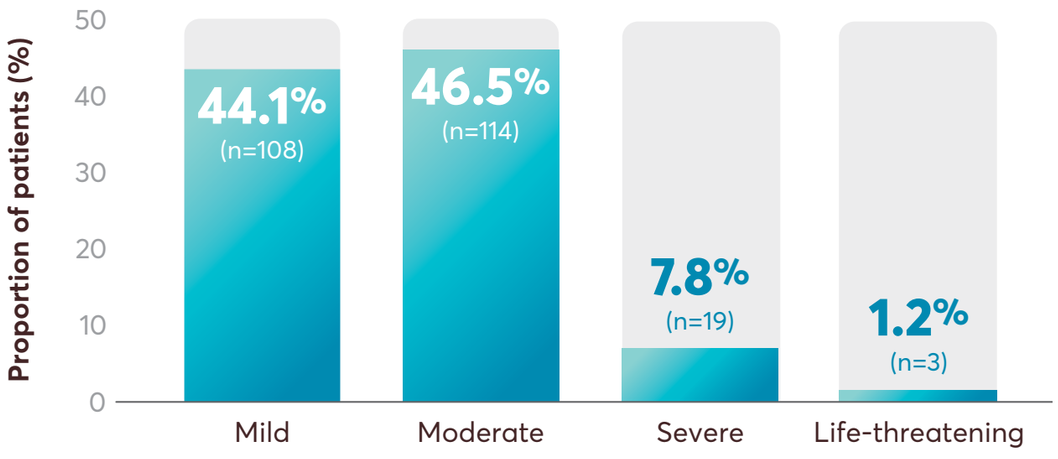
COVID-19 related data from ALITHIOS extension study[9]

ALITHIOS	COVID-19 related data Analysis of data from December 2019 to September 25, 2021
An ongoing, Phase 3B, open-label study evaluating the long-term safety and tolerability of KESIMPTA®	• **245 (14.3%) of the 1703 patients** (as of September 25, 2021) enrolled in ALITHIOS who received KESIMPTA reported that they had contracted COVID-19 • COVID-19 cases with severity, seriousness, outcomes, vaccination status, and breakthrough infections were all included in this analysis • The open-label extension study is not blinded and not controlled. No statistical or clinical conclusion can be made

The majority (222/245) of COVID-19 cases were mild or moderate in severity[9]



- 24 cases were considered serious, with 23 requiring hospitalization
  - 22 patients recovered
  - 2 patients died

IMPORTANT SAFETY INFORMATION (cont)

Progressive Multifocal Leukoencephalopathy

No cases of progressive multifocal leukoencephalopathy (PML) have been reported for KESIMPTA in RMS clinical studies; however, PML resulting in death has occurred in patients being treated with ofatumumab at higher intravenous doses for CLL than the recommended dose in MS. In addition, JC virus infection resulting in PML has also been observed in patients treated with other anti-CD20 antibodies and other MS therapies. If PML is suspected, withhold KESIMPTA and perform an appropriate diagnostic evaluation. If PML is confirmed, KESIMPTA should be discontinued.

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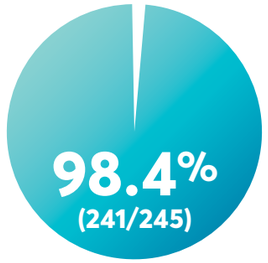
COVID-19 outcomes in KESIMPTA patients

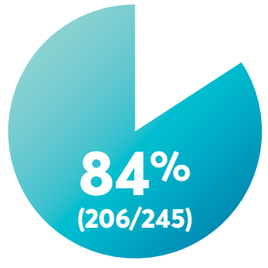


KESIMPTA patients with COVID-19 recovered, were recovering, or recovered with sequelae at study cutoff with no cases of reinfection[9]

2 patients had yet to recover

2 cases had a fatal outcome

- Fatal outcomes (2/245 or 0.8%) due to COVID-19 in KESIMPTA-treated patients were lower than those reported in the general population (2.1%)[9,10]
- The two patients with a fatal outcome were unvaccinated and had underlying comorbidities of diabetes and hypertension in one patient and in another patient who was slightly overweight (BMI of 28.3 kg/m^2)[9]



Patients who were infected with COVID-19 while on KESIMPTA remained on KESIMPTA without interruption[9]

BMI=body mass index.

IMPORTANT SAFETY INFORMATION (cont)

Vaccinations

Administer all immunizations according to immunization guidelines: for live or live-attenuated vaccines at least 4 weeks and, whenever possible at least 2 weeks prior to starting KESIMPTA for inactivated vaccines. The safety of immunization with live or live-attenuated vaccines following KESIMPTA therapy has not been studied. Vaccination with live or live-attenuated vaccines is not recommended during treatment and after discontinuation until B-cell repletion.

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The rate of breakthrough infections in fully vaccinated patients[9]

1.5% of fully vaccinated KESIMPTA patients (n=476) experienced a breakthrough COVID-19 infection*

5 were mild/moderate or non-serious, 1 severe, and 1 life-threatening; all recovered

*559 patients received a COVID-19 vaccination. 476 were fully vaccinated, while 74 were partially vaccinated and 9 received an unspecified COVID-19 vaccination. Breakthrough infections were reported in 7 fully vaccinated and 11 partially vaccinated patients.[9]

IMPORTANT SAFETY INFORMATION (cont)

Vaccinations(cont)

Vaccination of Infants Born to Mothers Treated with KESIMPTA During Pregnancy. For infants whose mother was treated with KESIMPTA during pregnancy, assess B-cell counts prior to administration of live or live-attenuated vaccines. If the B-cell count has not recovered in the infant, do not administer the vaccine as having depleted B-cells may pose an increased risk in these infants.

Injection-Related Reactions and Hypersensitivity Reactions

KESIMPTA can result in systemic injection-related reactions and hypersensitivity reactions, which may be serious or life-threatening. Injection-related reactions with systemic symptoms occurred most commonly within 24 hours of the first injection, but were also observed with later injections. There were no life-threatening injection reactions in RMS clinical studies.

In the post-marketing setting, additional systemic injection-related reactions and hypersensitivity reactions have been reported, including anaphylaxis, angioedema, pruritus, rash, urticaria, erythema, bronchospasm, throat irritation, oropharyngeal pain, dyspnea, pharyngeal or laryngeal edema, flushing, hypotension, dizziness, nausea, and tachycardia. Most cases were not serious and occurred with the first injection. Symptoms of systemic injection-related reactions may be clinically indistinguishable from acute hypersensitivity reactions.

The first injection of KESIMPTA should be performed under the guidance of an appropriately trained health care professional. If systemic injection-related reactions occur, initiate appropriate therapy. Patients who experience symptoms of systemic injection-related reactions or hypersensitivity reactions with KESIMPTA should be instructed to seek immediate medical attention. If local injection-related reactions occur, symptomatic treatment is recommended.

Reduction in Immunoglobulins

As expected with any B-cell depleting therapy, decreased immunoglobulin levels were observed. Monitor the levels of quantitative serum immunoglobulins during treatment, especially in patients with opportunistic or recurrent infections and after discontinuation of therapy until B-cell repletion. Consider discontinuing KESIMPTA therapy if a patient with low immunoglobulins develops a serious opportunistic infection or recurrent infections, or if prolonged hypogammaglobulinemia requires treatment with intravenous immunoglobulins.

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Post-marketing data from Novartis safety database (~4713 patient-treatment years) on COVID-19 and patients taking KESIMPTA[9]

As of September 25, 2021,

90 **patients reported confirmed COVID-19 infections** and 3 suspected cases of COVID-19 were reported to the Novartis safety database for patients with RMS taking KESIMPTA*

- **Most COVID-19 cases were non-serious (88.9% [n=80]), while 11.1% (n=10) were serious:** Serious cases included 1 medically significant case and 9 hospitalizations
- **No fatalities or life-threatening COVID-19 cases were reported** in the post-marketing setting

Characteristics	Confirmed COVID-19 N=90
Seriousness, n (%)	
Non-serious	80 (88.9)
Serious	10 (11.1)
Fatal	0
Hospitalization	9 (0.1)
Life-threatening	0
Medically significant	1 (1.11)
Outcome, n	
Recovered/recovered with sequelae/recovering	30
Condition unchanged	6
Fatal	0
Not reported	54

*Of the 90 confirmed COVID-19 cases, severity of COVID-19 was assessed as mild in 32 patients, moderate in 7 patients, severe in 3 patients, and critical in 1 patient by independent adjudication. In the remaining 47 cases, severity could not be assessed because of the insufficient information provided.

IMPORTANT SAFETY INFORMATION (cont)

Fetal Risk

Based on animal data, KESIMPTA can cause fetal harm due to B-cell lymphopenia and reduce antibody response in offspring exposed to KESIMPTA in utero. Transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 B-cell depleting antibodies during pregnancy. Advise females of reproductive potential to use effective contraception while receiving KESIMPTA and for at least 6 months after the last dose.

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*Individual results may vary. Walt was compensated for his time.

For adults only.

IMPORTANT SAFETY INFORMATION (cont)

Most common adverse reactions

(>10%) are upper respiratory tract infection, headache, injection-related reactions, and local injection-site reactions.

Please see additional Important Safety Information throughout. Click here for full Prescribing Information, including Medication Guide.

References: 1. Kesimpta [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp. **2.** Data on file. OMB157 (ofatumumab) Clinical Study Report ASCLEPIOS I&II. Novartis Pharmaceuticals Corp; East Hanover, NJ. 2019. **3.** Interim clinical considerations for use of COVID-19 vaccines currently authorized in the United States. Centers for Disease Control and Prevention website. Updated March 3, 2021. Accessed March 5, 2021. https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html **4.** Hauser SL, Cross AH, Winthrop K, et al. Safety experience with continued exposure to ofatumumab in patients with relapsing forms of multiple sclerosis for up to 3.5 years. *Mult Scler J*. 2022;1-15. doi:10.1177/13524585221107973 **5.** Wiendl H, Fox E, Goodyear A, et al. Effect of subcutaneous ofatumumab on lymphocyte subsets in patients with RMS: analysis from the APLIOS study. LB129. Poster presented at: 6th Congress of the European Academy of Neurology, May 23-26, 2020; Paris, France; Virtual. **6.** Torres JB, Roodselaar J, Sealey M, et al. Distribution and efficacy of ofatumumab and ocrelizumab in humanized-CD20 mice following subcutaneous or intravenous administration. P2.2-052. Presented at: American Academy of Neurology Annual Meeting; May 4-10, 2019; Philadelphia, PA. **7.** Theil D, Smith P, Huck C, et al. Imaging mass cytometry and single-cell genomics reveal differential depletion and repletion of B-cell populations following ofatumumab treatment in cynomolgus monkeys. *Front Immunol*. 2019;10:1-11. **8.** Cross AH, Chinea A, Hendin B, et al. Interim results of an open-label study to assess humoral response to COVID-19 mRNA vaccine in participants with relapsing multiple sclerosis treated with ofatumumab. P102. Poster presented at: ACTRIMS Forum 2022; February 24-26, 2022; West Palm Beach, FL. **9.** Cross AH, Delgado S, Habek M, et al. COVID-19 outcomes and vaccination in people with relapsing multiple sclerosis treated with ofatumumab. *Neurol Ther*. 2022;1-18. doi.org/10.1007/s40120-022-00341-z **10.** World Health Organization. WHO Coronavirus (COVID-19) Dashboard. Accessed June 29, 2022. https://covid19.who.int/

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