ASCLEPIOS: two identical studies to test how well Kesimpta™ works and its safety in patients with relapsing multiple sclerosis

In total, there were 1882 patients. This was 927 patients in ASCLEPIOS 1 and 955 patients in ASCLEPIOS 2. **Across the two studies ...**

38 years
Average age

8 years
Average time since first symptoms

18-55 years
Wide range of ages

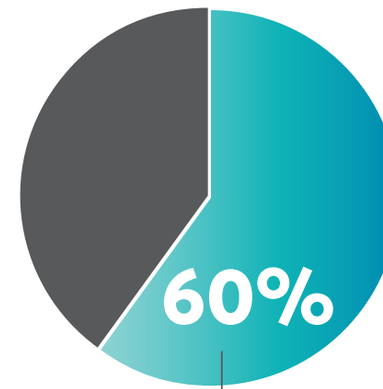
2.9
Average EDSS score

Half of the patients took **KESIMPTA**

This was **946** Patients

Half of the patients took **Teriflunomide**

This was **936** Patients

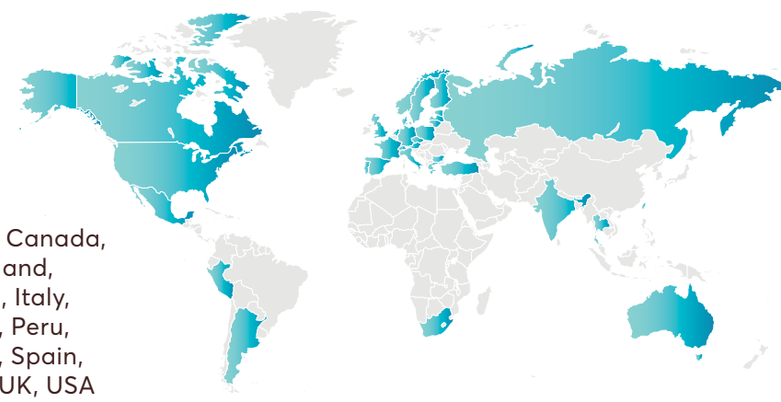


had previously received a DMT

Patients in the studies were from

37
different countries

Argentina, Australia, Austria, Belgium, Bulgaria, Canada, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, India, Israel, Italy, Latvia, Lithuania, Mexico, Netherlands, Norway, Peru, Poland, Portugal, Russia, Slovakia, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, UK, USA



WHAT TYPE OF STUDIES WERE THEY?

Phase 3. This means that the researchers wanted to test if Kesimpta worked better than teriflunomide in a large group of patients with RMS. Other studies are done in smaller or larger groups of patients.

Double-dummy. This means that some of the patients took a pill or an injection that did not have any medicine in it.

- Patients who took Kesimpta also took a placebo pill every day, which was designed to look exactly like teriflunomide, but it did not have any medicine in it.
- Patients who took teriflunomide also took an injection that was designed to look exactly like Kesimpta, but it did not have any medicine in it.

Double-blind. This means that neither the patients nor the researchers knew which medicine each patients took.

Randomized. This means that the patients were put either into the Kesimpta group or the teriflunomide group at random by a computer program. This helped to make sure that the groups were chosen fairly.

WHAT HAPPENED DURING THE STUDIES?

During the studies, the researchers:

- Did a full check of the patients' physical disabilities and abilities, and MS symptoms, every month
- Took MRI scans of the patients' brains every 12 months.

This summary focuses on three main ways that the researchers used to test how well Kesimpta works and its safety in patients with RMS, compared with teriflunomide.

- **Annualized relapse rate, or ARR**
  This is the number of MS relapses, also known as flare-ups or attacks, that the patients had in a year. This is measured as a rate.
- **The average number of gadolinium-enhancing lesions on the patients' MRI brain scans.**
  This is the average number of active lesions patients had developed since the start of the study. A lesion is an area of damage that can be seen on an MRI brain scan. This was measured using a dye called gadolinium to help to make the lesions visible on an MRI image.
- **3- month confirmed disability worsening, or 3-month CDW**
  This is a measure of MS disability progression. This is when MS gets worse over time and people become more and more disabled. A patient had 3-month CDW when their EDSS score was higher than at the start of the study, and was still higher when they checked it 3 months later.

The researchers compared these measurements in the group of patients taking Kesimpta with those in the group taking teriflunomide. The study also measured other ways to tell how well Kesimpta works compared with teriflunomide. These other measures are not reported in this summary.

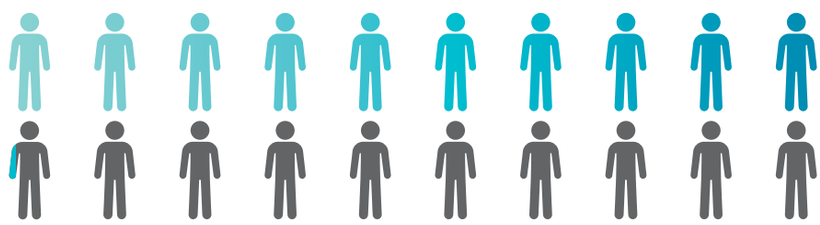
WHAT WERE THE RESULTS OF THE STUDIES?

Annualized relapse rate results

In ASCLEPIOS I, the adjusted annualized relapse rate was 0.11 with Kesimpta. The corresponding rate in ASCLEPIOS II was 0.10. **This is roughly the same as a patient having one MS relapse every 10 years**

In the ASCLEPIOS 1 study, the researchers found that treatment with Kesimpta …

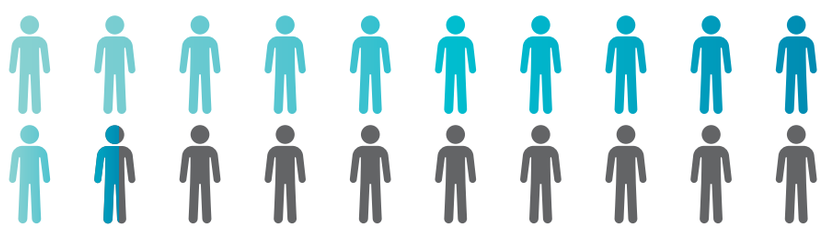
… reduced the number of relapses per year by



50.5%
versus teriflunomide

In the ASCLEPIOS 2 study, the researchers found that treatment with Kesimpta …

… reduced the number of relapses per year by



58.5%
versus teriflunomide

MRI brain scan results

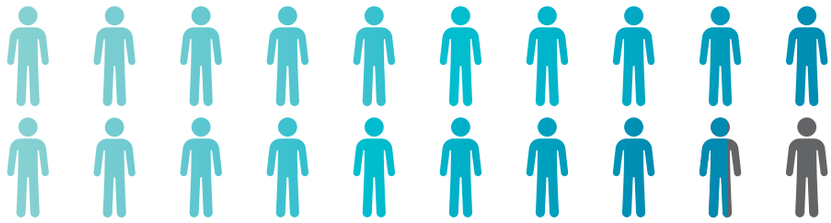
Kesimpta reduced the chance of getting new gadonlinium- enhancing lesions during the study compared with teriflunomide.

In the ASCLEPIOS 1 study, the researchers found that treatment with Kesimpta …

… reduced the chance of new gadonlinium- enhancing lesions lesions by

97.5%
versus teriflunomide

In the ASCLEPIOS 2 study, the researchers found that treatment with Kesimpta …
… reduced the chance of new gadonlinium- enhancing lesions lesions by



93.8 %
versus teriflunomide

MS disability worsening results

Overall, treatment with Kesimpta slowed down MS disability worsening more than treatment with teriflunomide in patients with RMS. The researchers found that across the 2 studies …

… in the patients who took Kesimpta …

9.3%
had 3-month CDW

… in the patients who took teriflunomide …

13.4%
had 3-month CDW

This means that Kesimpta reduced the chance of MS disability worsening by 34.4% compared with teriflunomide after three months.

WHAT WERE THE SIDE EFFECTS DURING THE STUDIES?

Patients may have had medical problems, or negative side effects, during the studies. These may or may not have been related to Kesimpta or teriflunomide. These side effects are known as adverse events.

- Adverse events happened in 83.6% of patients who took Kesimpta. This was 791 out of 946 patients across the two studies.
- Adverse events happened in 84.2% of patients who took teriflunomide. This was 788 out of 936 patients across the two studies.

Researchers expected some adverse events to happen that might be related to how Kesimpta and the placebo for the group taking teriflunomide are injected. These may or may not have been related to Kesimpta or teriflunomide.

Adverse events related to the injection happened in 20.6% of patients who took Kesimpta. This was 189 out of 946 patients across the two studies.

- Adverse events related to the injection happened in 15.3% of patients who took the placebo for the group taking teriflunomide. This was 143 out of 936 patients across the two studies.
  - Most injection-related adverse events happened after the first injection. This happened for 1 4.4% of patients who took Kesimpta and for 7.5% of patients who took the placebo injections.

Some adverse events are considered serious. An adverse event is considered serious when it is life-threatening, causes lasting problems or requires hospital care. These may or may not have been related to Kesimpta or teriflunomide.

- Serious adverse events happened in 9.1% of participants who took Kesimpta.
  This was 195 out of 946 participants across the two studies.
  Serious adverse events happened in 7.9% of participants who took teriflunomide.
  This was 74 out of 936 participants across the two studies.

Kesimpta™ 20 mg/0.4 mL solution for injection

Important note: Before prescribing, consult full prescribing information.

Presentation: 20 mg/0.4 mL Solution for injection in a pre-filled pen
Each pre-filled pen contains 20 mg ofatumumab solution for subcutaneous injection (0.4 mL of 50 mg/mL solution).
Indications: Kesimpta is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS).
Dosage and administration:

Treatment should be initiated by a physician experienced in the management of neurological conditions, including multiple sclerosis.

1.1 Usual dosage

The recommended dose is 20 mg Kesimpta administered by subcutaneous injection at the following intervals:
• initial dosing at weeks 0, 1 and 2 followed by
• subsequent monthly dosing starting at week 4.
To ensure traceability of medicinal products produced using biotechnology, it is recommended that the trade name and batch number be documented at every treatment.

Missed doses

If an injection of Kesimpta is missed, it should be administered as soon as possible without waiting until the next scheduled dose. Subsequent doses should be administered at the recommended intervals.
Special dosage instructions
Elderly patients
No studies have been performed in elderly MS patients. Ofatumumab was studied in patients with relapsing MS (RMS) aged 18 to 55 years. Results from population pharmacokinetics suggest that dose adjustment is not required in elderly patients (see "Pharmacokinetics").

Patients with renal impairment

No specific studies of ofatumumab in patients with renal impairment have been performed.
Patients with mild renal impairment were included in the clinical studies. There is no experience in patients with moderate and severe renal impairment. However, as ofatumumab is not excreted via urine, patients with renal impairment are not expected to require dose modification (see "Pharmacokinetics").

Patients with hepatic impairment

No specific studies of ofatumumab in patients with hepatic impairment have been performed.
Since hepatic metabolism of monoclonal antibodies such as ofatumumab is negligible, hepatic impairment is not expected to impact the pharmacokinetics of this medicinal product. Therefore, patients with hepatic impairment are not expected to require dose modification (see "Pharmacokinetics").

Children and adolescents

The safety and efficacy of Kesimpta in children aged 0 to 18 years have not yet been studied. No data are available.

Contraindications:

• Hypersensitivity to the active substance or any of the excipients • Severely immunocompromised patients
• Presence of an active infection • Known active malignancies. • Treatment initiation during pregnancy.

Warnings and precautions:

• Injection site reaction (local) symptoms observed in clinical studies include erythema, swelling, itching and pain. • Systemic injection-related reactions occurred predominantly with the first injection. Symptoms observed include fever, headache, myalgia, chills and fatigue and were predominantly (99.7%) non-serious and mild to moderate in severity. Inform patients that injection-related reactions generally occur within 24 hours and predominantly following the first injection. • First injection should be performed under the guidance of an appropriately trained healthcare professional. • Kesimpta has the potential for an increased risk of infections. Kesimpta administration should be delayed in patients with active infection until the infection is resolved. • Vigilance is advised for clinical symptoms or MRI findings that may be suggestive of progressive multifocal leukoencephalopathy (PML). If PML is suspected, treatment with Kesimpta should be suspended. • Kesimpta treatment should not be initiated in patients with active hepatitis B (HBV) infection until the infection has been adequately treated. Perform HBV screening in all patients before initiation of treatment with Kesimpta. Patients with positive serology should consult liver disease experts before start of treatment. • Kesimpta must not be administered to patients with severe immunosuppression (e.g. significant neutropenia or lymphopenia). Severely immunocompromised patients must not be treated until the relevant condition resolves • Vaccinations: Administer all required immunizations at least 4 weeks prior to initiation of Kesimpta for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of Kesimpta for inactivated vaccines. Kesimpta may interfere with the effectiveness of inactivated vaccines. Administering live or live-attenuated vaccines to neonates and infants exposed to ofatumumab in utero should be avoided until B-cell recovery occurs. • Patients with existing active malignancies (including patients actively monitored for relapse of a malignancy) must not be treated with ofatumumab. In patients with known risk factors for malignancies the benefit-risk ratio of ofatumumab should be carefully considered and relevant tumour monitoring performed before and during treatment. • In rare cases severe cardiovascular events and severe mucocutaneous reactions have occurred during treatment with other anti-CD20 antibodies. Patients exhibiting a severe mucocutaneous reaction during treatment with Kesimpta should discontinue treatment and seek prompt medical evaluation.
Pregnancy, lactation, females and males of reproductive potential

Pregnancy: There are no or limited amount of data from the use of Kesimpta in pregnant women. Ofatumumab may cause fetal B-cell depletion. **Lactation:** The use of ofatumumab in women during breast-feeding has not been studied. It is unknown whether ofatumumab is transferred into human milk. The developmental and health benefits of breast-feeding should be considered along with the mother's clinical need for Kesimpta and any potential adverse effects on the breast-fed infant from Kesimpta. **Females and males of reproductive potential:** Women of childbearing potential should use effective contraception while receiving Kesimpta and for 6 months after the last treatment of Kesimpta. **Adverse drug reactions:** • **Very common:** upper respiratory tract infections, urinary tract infection, Headache, injection site reactions (local) injection-related reactions (systemic) • **Common:** Oral herpes, Decreased serum immunoglobulin M (IgM) **Interactions:** The risk of additive immune system effects should be considered when coadministering immune-modulating or immunosuppressive therapies with Kesimpta. When switching from drugs with prolonged immune effects, such as ocrelizumab, cladribine, fingolimod, natalizumab, teriflunomide, mitoxantrone or dimethyl fumarate, the duration and mode of action of these drugs should be considered because of potential additive immunosuppressive effects when initiating Kesimpta.

Packs and prices: Country-specific. **Legal classification:** Country-specific. **Leaflet Date:** Jan 2021. **BSS Version:** 1.0

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Kesimpta™ (ofatumumab) 20mg/0.4ml Solution for injection