Novartis Kesimpta® six-year efficacy data show substantial benefits in recently diagnosed treatment-naïve people with relapsing multiple sclerosis

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- Continuous Kesimpta® treatment for up to six years showed sustained efficacy in recently diagnosed (≤3 years) treatment-naïve people living with relapsing multiple sclerosis (RMS) in an analysis of the ALITHIOS open-label extension study[1]
- Similar efficacy outcomes were demonstrated in a separate analysis of continuous Kesimpta treatment for up to six years in the overall ALITHIOS study population[2]
- Switch from teriflunomide to Kesimpta resulted in significant improvements across several efficacy outcomes such as annualized relapse rate and MRI lesion activity in both analyses[1,2]
- Treatment with Kesimpta for up to six years continues to be well tolerated with consistent safety outcomes, supporting the favorable benefit-risk profile of Kesimpta in RMS[2]

EAST HANOVER, N.J., April 17, 2024 -- Novartis today announced data from the ALITHIOS open-label extension study showing sustained efficacy of first-line, continuous Kesimpta® (ofatumumab) treatment for up to six years in recently diagnosed – defined as starting treatment within three years of initial diagnosis – treatment-naïve people living with relapsing multiple sclerosis (RMS).[1] These efficacy outcomes included 44% fewer relapses; 96.4% and 82.7% reductions in MRI lesions (Gd+ T1 and neT2), respectively; and 24.5% and 21.6% fewer 3- and 6-month confirmed disability worsening (CDW) events, respectively, versus those who switched to Kesimpta from teriflunomide.[1] A separate analysis of the overall ALITHIOS population showed similar efficacy with continuous Kesimpta treatment, which was also well-tolerated with a consistent safety profile up to six years.[2] These data will be presented at the American Academy of Neurology (AAN) 2024 Annual Meeting held in Denver, Colorado and virtually on April 13-18, 2024.

"Our analysis of treatment-naïve people who were recently diagnosed with relapsing multiple sclerosis found that first-line use of Kesimpta for up to six years provided long-term benefits, including fewer relapses, profoundly suppressed MRI lesion activity, and fewer disability worsening events," said principal investigator Gabriel Pardo, M.D., Founding Director of the Multiple Sclerosis Center of Excellence at Oklahoma Medical Research Foundation. "While measurable improvements were also seen in patients switching to Kesimpta later on, the delay in irreversible disability worsening was not fully realized in the switch group compared to those starting on Kesimpta first, reinforcing the value of introducing the treatment to patients earlier."

"We are extremely pleased to share the new data from ALITHIOS, which adds to the growing body of evidence of Kesimpta as an efficacious and well-tolerated option for people living with RMS," said Norman Putzki, M.D., Development Unit Head, Neuroscience & Gene Therapy, Development, Novartis Pharmaceuticals Corporation. "Novartis is committed to addressing the biggest challenges for people living with MS through relentless discovery, development, and delivery of potentially transformative medicines with the goal of achieving complete disease control."

Study Results

In the first analysis, the low annualized relapse rate (ARR) experienced by recently diagnosed treatment-naïve (RDTN) people living with RMS receiving continuous Kesimpta during the core Phase III trials was further reduced in the ALITHIOS open-label extension study, from 0.104 to 0.050 (52.0% reduction), corresponding to an adjusted ARR of one relapse per 20 years.[1] Rates of 3- and 6-month progression independent of relapse activity (PIRA) with first-line Kesimpta were also lower versus switch.[1] The observed rapid increase in the proportion of participants with no evidence of disease activity (NEDA-3) with continuous first-line Kesimpta treatment was maintained up to six years.[1]

In RDTN people living with RMS initially randomized to teriflunomide, improvements across several efficacy outcomes were seen after switching to Kesimpta, including significant reductions in ARR (71.3%) and in MRI lesion activity (Gd+ T1: 98.5% reduction; neT2: 93% reduction), and rapid increase in rates of NEDA-3.[1] However, rates of 3- and 6-month CDW events remained higher compared to patients receiving continuous Kesimpta, indicating that the efficacy benefit of first-line Kesimpta on delaying disability worsening was not fully achieved in the switch group.[1] Across both continuous and switch groups, nine out of 10 participants achieved NEDA-3 at Year 6.[1]

Similar results were seen in the second analysis, which looked at the overall ALITHIOS population.[2] Data showed sustained efficacy of continuous Kesimpta up to six years, including low ARR (49.9% reduction between core Phase III trials and extension phase), suppression of MRI lesion activity (Gd+ T1: 56.7% reduction; neT2: 89.3% reduction), sustained reduction of 6-month CDW events (14.1%, relative to the switch group), lower rates of 6-month PIRA, and sustained high rates of NEDA-3.[2] People switching from teriflunomide to Kesimpta experienced reductions in ARR (73.8%) and MRI lesion activity (Gd+ T1: 97.7% reduction; neT2: 91.8% reduction) and a rapid increase in NEDA-3 rates during the extension period.[2] Six-month CDW rates remained higher compared to patients receiving continuous Kesimpta, again highlighting an efficacy benefit of first-line Kesimpta on delaying disability worsening that was not fully achieved in the switch group.[2] At Year 6, NEDA-3 status was achieved in nine out of 10 participants in both the continuous and switch groups.[2]

The study also found that treatment with Kesimpta for up to six years was well-tolerated with no unexpected safety signals identified.[2] The rates of adverse events (AEs), serious AEs, serious infections, and malignancies remained stable with no increased risks over six years.[2]

The overall rates of AEs and serious AEs up to six years of Kesimpta treatment were consistent between the core Phase III trials and the ALITHIOS extension study.[2] The most common AEs were infections (COVID-19 [34.3%], nasopharyngitis [20.6%], upper respiratory tract infection [14.9%], and urinary tract infection [14.4%]).[2] The incidence of serious infections remained stable over time and did not increase with Kesimpta treatment up to six years.[2]

Mean serum immunoglobulin G (IgG) levels remained stable up to six years of treatment and the majority of patients (97.2%) had IgG levels above the lower limit of normal (LLN).[2] Mean serum immunoglobulin M (IgM) levels decreased over time but remained above the LLN for the majority of patients (65.9%).[2] No clinically meaningful association was observed between IgG/IgM levels below the LLN and risk of serious infections.[2]

About Multiple Sclerosis

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system characterized by myelin destruction and axonal damage in the brain, optic nerves and spinal cord.[3] MS, which affects around 2 million people worldwide, can be characterized into four main types: clinically isolated syndrome (CIS), relapsing-remitting (RRMS), secondary progressive (SPMS) and primary progressive (PPMS).[4,5] The various forms of MS can be distinguished based on whether a patient experiences relapses (clearly defined acute inflammatory attacks of worsening neurological function), and/or whether they experience progression of neurologic damage and disability from the onset of the disease.[3]

About Kesimpta® (ofatumumab)

Kesimpta is a targeted, precisely dosed and delivered B-cell therapy that provides the flexibility of self-administration for adults with relapsing forms of multiple sclerosis (RMS).

Kesimpta is the first fully human anti-CD20 monoclonal antibody (mAb) self-administered by a once-monthly injection, delivered subcutaneously (SC) in RMS.[6, 7, 8]

The treatment regimen was designed and tested to enhance safety and tolerability and minimize the risk of systemic injection-related reactions.[6] Initial doses of Kesimpta are at Weeks 0, 1 and 2, with the first injection performed under the guidance of a healthcare professional. Monthly Kesimpta 20 mg doses are associated with rapid reduction and near-complete peripheral B-cell depletion, with no significant effect on pharmacokinetics due to body weight.[6] As shown in preclinical studies, Kesimpta is thought to work by binding to a distinct epitope on the CD20 molecule inducing potent B-cell lysis and depletion.[9] The selective mechanism of action and SC administration of Kesimpta allows precise delivery to the lymph nodes, where B-cell depletion in MS is needed, and preclinical studies have shown that it may preserve the B-cells in the spleen.[10]

Data from the ASCLEPIOS I/II core studies demonstrate Kesimpta's efficacy and favorable safety and tolerability profile in RMS participants and the ALITHIOS open-label extension study provides additional support with up to 6 years of data.[2,11] The at-home administration of Kesimpta by monthly doses of 20 mg/0.4mL with an autoinjector (Sensoready®) also matches the preferences of many people living with MS due to its ease of use and supports patients to be compliant with, and persistent on the therapy over time.[6] Kesimpta was originally developed by Genmab and licensed to GlaxoSmithKline; Novartis obtained rights for ofatumumab from GlaxoSmithKline in all indications, including RMS, in December 2015.[12]

Kesimpta has been approved for the treatment of relapsing forms of multiple sclerosis in over 90 countries worldwide with more than 100,000 patients treated as of March 2024.

Novartis in Neuroscience
At Novartis, in Neuroscience, we are committed to understanding and solving some of the most burdensome neurological conditions to improve the quality of life for patients and their caregivers, and to make a positive impact on society. We aim to lead the discovery, development and delivery of innovative medicines to create a transformational impact for people living with severe neurological conditions by changing the course of disease progression.

Through innovation, partnerships and community engagement, we have been tackling neurological conditions for >80 years, launching transformative treatments which have made meaningful differences to millions of people worldwide. We continue to collaborate on the development of industry-leading innovative medicines for multiple sclerosis, and in the areas of neuroimmunology, neurodegeneration, and neuromuscular/rare diseases.

To ensure patients everywhere can benefit from these life-changing therapies, we work closely with key stakeholders across the world to ensure rapid access and sustainable accessibility to our medicines, with the aim of providing the best treatment choices for each person's unique journey.

KESIMPTA

Indication
KESIMPTA is a prescription medicine used to treat adults with relapsing forms of multiple sclerosis (MS) including clinically isolated syndrome (CIS), relapsing-remitting disease, and active secondary progressive disease.

It is not known if KESIMPTA is safe or effective in children.

Important Safety Information
Who should not take KESIMPTA?
Do NOT take KESIMPTA if you:

- have an active hepatitis B virus (HBV) infection.
- have had an allergic reaction to ofatumumab or life-threatening injection-related reaction to KESIMPTA.

What is the most important information I should know about KESIMPTA?
KESIMPTA can cause serious side effects such as:

- Infections. Serious infections, which can be life-threatening or cause death, can happen during treatment with KESIMPTA. If you have an active infection, your health care provider (HCP) should delay your treatment with KESIMPTA until your infection is gone. KESIMPTA taken before or after other medicines that weaken the immune system may increase your risk of getting infections. Tell your HCP right away if you have any infections or get any symptoms including painful and frequent urination, nasal congestion, runny nose, sore throat, fever, chills, cough, or body aches.
- HBV reactivation. If you have ever had HBV infection, it may become active again during or after treatment with KESIMPTA (reactivation). If this happens, it may cause serious liver problems including liver failure or death. Before starting KESIMPTA, your HCP will do a blood test to check for HBV. They will also continue to monitor you during and after treatment with KESIMPTA for HBV. Tell your HCP right away if you get worsening tiredness or yellowing of your skin or the white part of your eyes.
- Progressive Multifocal Leukoencephalopathy (PML). PML may happen with KESIMPTA. PML is a rare, serious brain infection caused by a virus that may get worse over days or weeks. PML can result in death or severe disability. Tell your HCP right away if you have any new or worsening neurologic signs or symptoms. These may include weakness on one side of your body, loss of coordination in arms and legs, vision problems, changes in thinking and memory, which may lead to confusion and personality changes.
- Weakened immune system. KESIMPTA taken before or after other medicines that weaken the immune system could increase your risk of getting infections.

Before you take KESIMPTA, tell your HCP about all your medical conditions, including if you:

- Have or think you have an infection including HBV or PML.
- Have ever taken, currently take, or plan to take medicines that affect your immune system. These medicines could increase your risk of getting an infection.
- Have had a recent vaccination or are scheduled to receive any vaccinations.
    - You should receive any required 'live' or 'live-attenuated' vaccines at least 4 weeks before you start treatment with KESIMPTA. You should not receive 'live' or 'live-attenuated' vaccines while you are being treated with KESIMPTA and until your HCP tells you that your immune system is no longer weakened.
    - Whenever possible, you should receive any 'non-live' vaccines at least 2 weeks before you start treatment with KESIMPTA.
    - Talk to your HCP about vaccinations for your baby if you used KESIMPTA during your pregnancy.
- Are pregnant, think that you might be pregnant, or plan to become pregnant. It is not known if KESIMPTA will harm your unborn baby. Females who can become pregnant should use birth control (contraception) during treatment with KESIMPTA and for 6 months after your last treatment. Talk with your HCP about what birth control method is right for you during this time.
- Are breastfeeding or plan to breastfeed. It is not known if KESIMPTA passes into your breast milk. Talk to your HCP about the best way to feed your baby if you take KESIMPTA.

Tell your HCP about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I use KESIMPTA?
See the detailed Instructions for Use that comes with KESIMPTA for information about how to prepare and inject a dose of KESIMPTA and how to properly throw away (dispose of) used KESIMPTA Sensoready pens or prefilled syringes.

- Use KESIMPTA exactly as your HCP tells you to use it.
- Your HCP will show you how to prepare and inject KESIMPTA the right way before you use it for the first time.

- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with moles, scars, or stretch marks.

KESIMPTA may cause serious side effects including:

- Injection-related reactions. Injection-related reactions are a common side effect of KESIMPTA. Injecting KESIMPTA can cause injection-related reactions that can happen within 24 hours (1 day) following the first injections and with later injections. There are two kinds of reactions:
  - at or near the injection site: redness of the skin, swelling, itching, and pain. Talk to your HCP if you have any of these signs and symptoms.
  - that may happen when certain substances are released in your body: fever, headache, pain in the muscles, chills, tiredness, rash, hives, trouble breathing, swelling of the face, eyelids, lips, mouth, tongue and throat, and feeling faint, or chest tightness. Contact your HCP right away if you experience any of these signs and symptoms, especially if they become worse or you have new severe signs of reactions after subsequent injections. It could be a sign of an allergic reaction, which can be serious.
- Low immunoglobulins. KESIMPTA may cause a decrease in some types of antibodies. Your HCP will do blood tests to check your blood immunoglobulin levels.

The most common side effects of KESIMPTA include:

- Upper respiratory tract infection, with symptoms such as sore throat and runny nose, and headache.
- Headache.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full Prescribing Information including Medication Guide.

Disclaimer

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About Novartis

Novartis is an innovative medicines company. Every day, we work to reimagine medicine to improve and extend people's lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach more than 250 million people worldwide.

Reimagine medicine with us: Visit us at https://www.novartis.com and https://www.novartis.us and connect with us on LinkedIn, LinkedIn US, Facebook, X/Twitter, X/Twitter US and Instagram.

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