Novartis presents new four-year data on efficacy and safety of Kesimpta® (ofatumumab) in people living with relapsing multiple sclerosis

Apr 12, 2022

- *Phase 3 ASCLEPIOS I/II trials and the ALITHIOS open-label extension demonstrated the efficacy and safety of continuous Kesimpta® (ofatumumab) treatment and in those switched from teriflunomide, with no new safety risks identified over the treatment period*[1,2,3]
- *Data showed that continuous treatment with Kesimpta for up to four years was associated with fewer relapses as well as reduced risk of three-month and six-month confirmed disability worsening and less lesion activity versus those who switched*[1]
- *Interim analysis data from the ongoing KYRIOS open-label, prospective study showed that people living with relapsing multiple sclerosis vaccinated during stable Kesimpta treatment can mount an immune response to the COVID-19 mRNA vaccines, as soon as one week after initial vaccination*[4]
- *An analysis of injection-related reactions associated with subcutaneous administration of Kesimpta showed they were 99% mild to moderate in severity, with no life-threatening reactions*[5]

East Hanover, April 5, 2022 — Novartis today announced new long-term data from the Phase 3 ASCLEPIOS I/II trials and the ALITHIOS open-label extension that demonstrated long-term efficacy and safety of Kesimpta® (ofatumumab), with continued reduced risk of disability worsening, for people living with relapsing multiple sclerosis following up to four years of treatment.[1] Kesimpta maintained a similar safety profile as seen in the pivotal Phase 3 trials up to four years of treatment, with no new safety risks identified over the treatment period.[1,2] The data will be presented at the American Academy of Neurology (AAN) Annual Meeting being held on April 2–7, 2022 in Seattle, USA and virtually on April 24–26, 2022.

In addition to demonstrating efficacy up to four years of continuous treatment with Kesimpta, participants who switched from teriflunomide to Kesimpta in the extension phase demonstrated pronounced reductions in relapses and MRI lesions. In those receiving Kesimpta for up to four years, immunoglobulin G (IgG) levels remained stable and mean immunoglobulin M (IgM) levels decreased yet remained above the lower limit of normal, and no association between Ig levels and serious infection was observed. The overall rates of adverse events (AEs), serious AEs and overall rate of serious infections were consistent with those observed in the Phase 3 ASCLEPIOS I/II trials and did not increase with treatment up to four years despite the COVID-19 pandemic.[1,6]

Data from the ongoing KYRIOS open-label, prospective study showed that people living with multiple sclerosis on Kesimpta can mount an immune response to the COVID-19 mRNA vaccines.[4] All participants in the study who were vaccinated during continuous Kesimpta treatment developed an immune response as soon as one week after initial vaccination. Immune response in participants who received a booster during treatment was similar to those who received a booster before treatment. In a study examining injection-related reactions (IRRs) associated with subcutaneous administration of Kesimpta in the ALITHIOS trial and from post-marketing reports, IRRs were mostly mild to moderate in severity (99%) with no medically confirmed fatal or

life-threatening IRRs identified with Kesimpta.[5] These findings were consistent with those from the Phase 3 ASCLEPIOS I/II trials.[6]

“We are pleased to share long-term data of up to four years that support Kesimpta as an efficacious and well-tolerated, first-choice option for people living with relapsing multiple sclerosis. The sustained reductions in disability progression and lesion activity observed in patients receiving continuous Kesimpta versus those who switched later from teriflunomide highlight the value of earlier treatment initiation with Kesimpta,” said Lykke Hinsch Gylvin, Neuroscience Global Medical Franchise Head, Novartis Pharmaceuticals. “In addition to these safety and efficacy data, we have presented findings that suggest people taking Kesimpta can mount an immune response to COVID-19 vaccination. During this pandemic, it is critical for people living with multiple sclerosis to have access to safe and efficacious treatments that do not interfere with their vaccine doses. Novartis is committed to continued research in multiple sclerosis with regards to COVID-19 vaccination and these data mark an additional milestone in this commitment.”

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.[7] MS, which affects approximately 2.3 million people worldwide[8], can be characterized into four main types: clinically isolated syndrome (CIS), relapsing-remitting (RRMS), secondary progressive (SPMS) and primary progressive (PPMS).[9] 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.[10]

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). It is an anti-CD20 monoclonal antibody (mAb) self-administered by a once-monthly injection, delivered subcutaneously.[11,12] Initial doses of Kesimpta are at Weeks 0, 1 and 2, with the first injection performed under the guidance of a healthcare professional. 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.[13] The selective mechanism of action and subcutaneous 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.[14] Once-monthly dosing of Kesimpta differs from other anti-CD20 therapies as it allows faster repletion of B-cells, offering more flexibility in MS management.[10] Ofatumumab was originally developed by Genmab and licensed to GlaxoSmithKline. Novartis obtained rights for ofatumumab from GlaxoSmithKline in all indications, including RMS, in December 2015.[15]

Kesimpta has been approved for the treatment of relapsing forms of multiple sclerosis in the United States, European Union, United Kingdom, Canada, China, Switzerland, Singapore, Australia, Japan, Argentina, United Arab Emirates, Albania, and India.

Novartis in Neuroscience

At Novartis Neuroscience, we have been tackling neurological conditions for more than 80 years, launching transformative treatments which have made meaningful differences to millions of people worldwide. We continue to collaborate on industry-leading treatments in multiple sclerosis, pediatric neurology, neurodegeneration and neuropsychiatry because we know through innovation, partnership and community engagement early on, we can improve the standard of care.

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

KESIMPTA

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
Contraindication: KESIMPTA is contraindicated in patients with active hepatitis B virus infection.

Warnings and Precautions
Infections: An increased risk of infections has been observed with other anti-CD20 B-cell depleting therapies. KESIMPTA has the potential for an increased risk of infections including serious bacterial, fungal, and new or reactivated viral infections; some have been fatal in patients treated with other anti-CD20 antibodies. 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.

Hepatitis B Virus: *Reactivation:* No reports of hepatitis B virus (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.

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.

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.

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.

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: 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.

The first injection of KESIMPTA should be performed under the guidance of an appropriately trained health care professional. If 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.

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.

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

Please see full Prescribing Information, including Medication Guide.

Disclaimer

This media update contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “seek,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this media update, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that the investigational or approved products described in this media update will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general

political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this media update as of this date and does not undertake any obligation to update any forward-looking statements contained in this media update as a result of new information, future events or otherwise.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs nearly 15,000 people in the United States. For more information, please visit https://www.novartis.us.

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