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

Apr 20, 2023

- The ALITHIOS open-label extension study showed continuous treatment with Kesimpta® (ofatumumab) for up to five years in relapsing multiple sclerosis (RMS) patients was associated with reduced risk of disability progression versus those who switched later from teriflunomide to Kesimpta[1]
- Outcomes related to both disability progression and brain volume change up to five years favored earlier initiation of Kesimpta in people living with RMS[1]
- A separate ALITHIOS analysis showed consistent safety profile of Kesimpta treatment for up to five years in people with RMS and in those switched from teriflunomide[2]
- Treatment with Kesimpta continued to be well tolerated with no new safety signals identified over the treatment period[2]

EAST HANOVER, N.J., April 20, 2023 -- Novartis today announced new long-term data from the ALITHIOS open-label extension study showing that up to five years, patients treated earlier and continuously with Kesimpta® (ofatumumab) had fewer disability worsening events and low brain volume change versus those who started on teriflunomide and were later switched to Kesimpta[1]. A separate analysis showed that treatment with Kesimpta for up to five years was well-tolerated, with no new or increased safety risks identified[2]. These data will be presented at the American Academy of Neurology (AAN) Annual Meeting held in Boston and virtually on April 22-27, 2023.

"With continuous Kesimpta treatment, key indicators of disability progression and brain volume change showed that most patients remained free from disease progression up to five years," said principal investigator Jeffrey A. Cohen, MD, of the Neurological Institute at Cleveland Clinic. "Outcomes favored earlier, compared with later, initiation of treatment with Kesimpta. Along with the five-year safety analysis, these data support this treatment as a well-tolerated, efficacious treatment option for people living with relapsing multiple sclerosis."

In people with RMS who continued in the ALITHIOS study for up to five years, earlier treatment with Kesimpta was associated with fewer confirmed disability worsening (CDW) events, including progression independent of relapse activity and relapse associated worsening, versus those who switched later from teriflunomide1. More than 80% of patients remained free of six-month CDW over the same five-year period[1].

Additionally, brain volume change remained low (less than 1.5% loss) with Kesimpta treatment over five years, and overall, patients initially randomized to Kesimpta had lower levels of brain volume loss at year five than those initially randomized to teriflunomide[1]. Annual rate of brain volume change (ABVC) in the core Phase III trials for continuous Kesimpta was -0.34%/year and in the switch group, -0.42%/year (P=0.115). In the extension, ABVC in the Kesimpta group was -0.27%/year and in the switch group, -0.28%/year (P=0.666)[1].

"These longer-term data continue to reinforce the favorable safety profile of Kesimpta, as well as its ability to slow disease progression, supporting its earlier use in people with relapsing multiple sclerosis," said Victor Bultó, President, Innovative Medicines US, Novartis Pharmaceuticals Corporation. "Novartis remains committed to the multiple sclerosis community in our continued study of Kesimpta and to supporting those living with MS and their families throughout their journey."

The separate analysis of the ALITHIOS extension data showed consistent safety results of Kesimpta for people with RMS following up to five years of treatment[2]. The overall rates of adverse events (AEs) and serious AEs were consistent with the core Phase III trials[2,3]. The most common AEs were infections (COVID-19 [30.3%], nasopharyngitis [19%], upper respiratory tract infection [12.8%] and urinary tract infection [12.7%])[2]. Most COVID-19 cases were mild to moderate in severity (93.9%) and non-serious (92.3%), and 98.6% of patients treated with Kesimpta recovered, recovered with sequalae, or were recovering from COVID-19[2]. Most (90.3%) infections resolved without discontinuing Kesimpta treatment[2].

The overall rate of serious infections also remained stable with no increased risk over five years (106 patients, or 5.38%, experienced serious infection in the core Phase III plus extension trials)[2]. Mean serum immunoglobulin G (IgG) levels remained stable up to five years of treatment and the majority of patients (98%) 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 (69.4%)[2]. There was no association between reduction in Ig levels and risk of serious infections[2]. Treatment interruption/discontinuation was reported in three (0.2%)/four (0.2%) patients due to low IgG; and 202 (10.3%)/71 (3.6%) patients due to low IgM[2]. There were six fatal cases due to serious infections (five were COVID-19-related and one was due to pneumonia and septic shock)[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[4] MS, which affects around 2 million people worldwide[5], can be characterized into four main types: clinically isolated syndrome (CIS), relapsing-remitting (RRMS), secondary progressive (SPMS) and primary progressive (PPMS)[6]. 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[4].

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[7,8]. 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[9]. 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[10]. Data from the ALITHIOS open-label extension study for up to 5 years and the ASCLEPIOS I/II core studies show Kesimpta's efficacy and favorable safety and tolerability profile in RMS participants[1,2] 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[11]. Ofatumumab has been approved

for the treatment of relapsing forms of multiple sclerosis in over 80 countries worldwide with more than 40,000 patients treated.

Novartis in Neuroscience
At Novartis Neuroscience, we have been tackling neurological conditions for >80 years, launching transformative treatments which have made meaningful differences to millions of people worldwide now and in the future. We continue to collaborate on industry-leading treatments in multiple sclerosis and neuroimmunology, neurodegeneration, psychiatry and neuromuscular/rare diseases. We know that through innovation, partnerships and community engagement early on, we can understand and treat some of the most burdensome neurological conditions to help patients maintain their quality of life longer and make a positive impact on society.

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 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 press release 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," "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 press release, 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 press release 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 press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release 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. We deliver high-value medicines that alleviate society's greatest disease burdens through technology leadership in R&D and novel access approaches. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs nearly 14,500 people in the United States. For more information, please visit https://www.novartis.us

Novartis and Novartis US is on Twitter. Sign up to follow @Novartis at https://twitter.com/novartisnews and @NovartisUS at https://twitter.com/NovartisUS.
For Novartis multimedia content, please visit https://www.novartis.com/news/media-library.
For questions about the site or required registration, please contact media.relations@novartis.com.

References

1. Cohen JA, Hauser SL, Zielman R, et al. Effect of Longer-term Ofatumumab Treatment on Disability Worsening and Brain Volume Change. Oral presentation at the American Academy of Neurology (AAN) 2023; April 22-27, 2023; Boston, MA.
2. Cohen JA, Hauser SL, Cross AH, et al. Five-Year Safety of Ofatumumab in People Living With Relapsing Multiple Sclerosis. Poster presentation at the American Academy of Neurology (AAN) 2023; April 22-27, 2023; Boston, MA.
3. Hauser SL, Bar-Or A, Cohen JA, et al. Ofatumumab versus Teriflunomide in Multiple Sclerosis. N Engl J Med. 2020;383(6):546-557. doi:10.1056/NEJMoa1917246
4. Guthrie EW. Multiple sclerosis: A primer and update. Adv Studies Pharm. 2007;4(11):313-317.
5. Multiple Sclerosis International Federation. Atlas of MS 2013-Mapping Multiple Sclerosis Around the World. Accessed August 12, 2020. http://www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf
6. National MS Society. Types of MS. Accessed January 18, 2023. https://www.nationalmssociety.org/What-is-MS/Types-of-MS
7. Kesimpta Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corp; August 2020.
8. Bar-Or A, Fox E, Goodyear A, et al. Onset of B-cell depletion with subcutaneous administration of

ofatumumab in relapsing multiple sclerosis: results from the APLIOS bioequivalence study. Poster presentation at: ACTRIMS; February 2020; West Palm Beach, FL.
9. Smith P, Kakarieka A, Wallstroem E. Ofatumumab is a fully human anti-CD20 antibody achieving potent B-cell depletion through binding a distinct epitope. Poster presentation at: ECTRIMS; September 2016; London, UK.
10. Smith P, Huck C, Wegert V, et al. Low-dose, subcutaneous anti-CD20 therapy effectively depletes B-cells and ameliorates CNS autoimmunity. Poster presentation at: ECTRIMS; September 2016; London, UK.
11. Genmab Press Release: Genmab announces completion of agreement to transfer remaining ofatumumab rights. December 21, 2015. Accessed January 18, 2023. https://ir.genmab.com/static-files/9d491b72-bb0b-4e46-a792-dee6c29aaf7d

###

Novartis Media Relations

E-mail: media.relations@novartis.com

North America

Julie Masow +1 862 579 8456

Marlena Abdinoor +1 617 335 9525

Novartis Investor Relations

E-mail:

investor.relations@novartis.com

North America

Sloan Simpson +1 862 778 5052

SOURCE Novartis Pharmaceuticals Corporation

List of links present in page

1. https://prod1.novartis.com/us-en/us-en/news/media-releases/novartis-presents-new-five-year-data-disability-outcomes-and-safety-kesimpta-ofatumumab-people-living-relapsing-multiple-sclerosis
2. https://www.novartis.us/sites/www.novartis.us/files/kesimpta.pdf
3. https://www.novartis.us
4. https://twitter.com/novartisnews
5. https://twitter.com/NovartisUS
6. https://www.novartis.com/news/media-library
7. mailto:media.relations@novartis.com
8. http://www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf
9. https://www.nationalmssociety.org/What-is-MS/Types-of-MS
10. https://ir.genmab.com/static-files/9d491b72-bb0b-4e46-a792-dee6c29aaf7d
11. mailto:media.relations@novartis.com
12. mailto:investor.relations@novartis.com