Novartis presents data at ACTRIMS-ECTRIMS for Kesimpta® (ofatumumab) in newly diagnosed treatment-naïve adults with relapsing multiple sclerosis

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- New post hoc data from Phase III ASCLEPIOS trials showed newly diagnosed, treatment-naïve patients experienced reductions in annualized relapse rates and MRI lesion activity and prolonged time to disability worsening when treated with Kesimpta vs teriflunomide(1)
- Additional safety data in over 1,800 patients who continued Kesimpta treatment or switched therapy from previous studies reinforce the favorable safety profile of Kesimpta in patients with relapsing forms of multiple sclerosis (RMS)(2)
- Baseline serum neurofilament light chain (NfL) levels in the ASCLEPIOS trials demonstrated a prognostic value for disease activity and worsening in all patients, including newly diagnosed, treatment-naïve patients(3)
- Kesimpta is the first and only FDA-approved, self-administered, targeted B-cell therapy for adults with RMS(4)

EAST HANOVER, N.J., Sept. 11, 2020 /PRNewswire/ -- Novartis announced today new post hoc data showing the efficacy and safety of Kesimpta® (ofatumumab), a targeted B-cell therapy, in patients with relapsing forms of multiple sclerosis (RMS) who are newly diagnosed as well as ongoing safety study findings. These data—presented at the MSVirtual2020: 8th Joint ACTRIMS-ECTRIMS Meeting taking place on September 11–13, 2020—further support Kesimpta as a first-choice treatment option for adults with RMS.

"These encouraging data show that newly diagnosed and treatment-naïve patients may benefit from lower disease activity when treated with Kesimpta," said Dr. Amit Bar-Or, University of Pennsylvania.

A post hoc analysis from the Phase III ASCLEPIOS I and II trials (n=615) evaluated the efficacy and safety profile of treatment with Kesimpta in a subgroup of patients with early RMS (newly diagnosed and treatment-naïve). Baseline characteristics of the newly diagnosed (within three years before screening), treatment-naïve (no prior disease-modifying therapy use) subgroup were typical of early MS patients (median age and MS duration since diagnosis were 36 and 0.35 years, respectively). The study results showed Kesimpta significantly reduced the annualized relapse rate (ARR) by 50.3% (0.09 vs 0.18) compared with teriflunomide (P<.001). Kesimpta significantly reduced the mean number of both gadolinium-enhancing (Gd+) T1 lesions by 95.4% (0.02 vs 0.39; P<.001) and new or enlarging T2 lesions by 82.0% (0.86 vs 4.78; P<.001) compared with teriflunomide. Kesimpta also showed a relative risk reduction of 38% (P=.065) in 3-month confirmed disability worsening (CDW) and a significant relative risk reduction of 46% (P=.044) in 6-month CDW. Overall, Kesimpta had a similar safety profile to teriflunomide. Adverse events (AEs) occurred in 84.7% ofatumumab vs 86.0% teriflunomide-treated patients; serious AEs (SAEs) were reported in 7.0% and 5.3%, respectively. Infection rates were comparable between ofatumumab (56.1%) and teriflunomide (56.5%); serious infections rates were 1.9% and 0.7%, respectively, and no opportunistic infections were reported. An additional post hoc analysis presented in the same poster at MSVirtual2020 showed that the odds of achieving no evidence of disease

activity (NEDA-3; no relapses, no MRI lesions, and no disability worsening combined) with Kesimpta versus teriflunomide in the same newly diagnosed, treatment-naïve subgroup were >3-fold higher at the first year (47.0% vs 24.7% of patients; P<.001) and >14-fold higher at the second year of treatment (92.1% vs 46.8% of patients, P<.001).[1]

A separate safety analysis (n=1,873) of the ongoing Phase IIIb ALITHIOS trial reported on the extended exposure of Kesimpta in patients with RMS. The ALITHIOS trial included patients who either continued on Kesimpta treatment from the Phase III ASCLEPIOS trials or the Phase II APLIOS trial (continuous) or switched from teriflunomide in the ASCLEPIOS trials to Kesimpta (newly-switched). The results showed no new safety signals, highlighting that the safety profile of Kesimpta in RMS patients remains consistent with data reported in the core studies. In this analysis, 71.4% of patients (continuous: 82%; newly-switched: 51%) experienced at least one AE; most were mild-to-moderate. AEs led to ofatumumab discontinuation in 3.0% of patients. SAEs were observed in 6.2% of patients. Incidence of infections was 38.5% (continuous: 49.3%, newly-switched: 18.0%). Serious infections occurred in 1.8% of patients. Incidence of systemic injection-related reactions (IRRs) was 23.2% (continuous: 24.4%; newly-switched: 21.0%); most IRRs were non-serious and non treatment-limiting.[2]

"Collectively, these data add to the body of evidence that shows Kesimpta to be a powerful B-cell therapy with a favorable safety profile for people living with RMS, including those who are newly diagnosed or previously treated," said Krishnan Ramanathan, Neuroscience Global Program Head at Novartis. "Novartis is committed to reimagining care and bringing innovative treatment options for people living with this disease."

In addition, another analysis of the pooled ASCLEPIOS trials presented indicated the prognostic value of serum neurofilament light chain (NfL) in assessing future course of disease in RMS.[3] The value of measuring serum NfL is also supported by findings from the APLIOS study that demonstrate a clear association of NfL with disease activity, either in the form of new Gd+ T1 lesions or relapses.[5]

All abstracts will be published in the Multiple Sclerosis Journal following the meeting.

In August, the US Food and Drug Administration approved Kesimpta as an injection for subcutaneous use for the treatment of RMS, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Kesimpta is the first and only targeted B-cell therapy that can be self-administered once monthly at home via the Sensoready® autoinjector pen.[4]

Novartis is committed to bringing Kesimpta to patients around the world and additional regulatory filings are currently underway across the world, with regulatory approval for Kesimpta in Europe expected by Q2 2021.

About Kesimpta® (ofatumumab)

Kesimpta is a targeted, precisely dosed and delivered B-cell therapy that provides the flexibility of self-administration for adults with RMS. It is an anti-CD20 monoclonal antibody (mAb) self-administered by a once-monthly injection, delivered subcutaneously.[4,6] Initial doses of Kesimpta are given 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.[7] 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.[8] Once-monthly dosing of Kesimpta also allows rapid repletion of B-cells and offers more flexibility.[9] 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.[10]

About ASCLEPIOS I and II studies

The ASCLEPIOS I and II studies are twin, identical design, flexible duration (up to 30 months), double-blind, randomized, multi-center Phase III studies evaluating the safety and efficacy of Kesimpta 20 mg monthly subcutaneous injections versus teriflunomide 14 mg oral tablets taken once daily in adults with RMS. The ASCLEPIOS I and II studies enrolled 1,882 patients with MS, between the ages of 18 and 55 years, with an Expanded Disability Status Scale (EDSS) score between 0 and 5.5.[4] The studies were conducted in over 350 sites in 37 countries.[11] Kesimpta demonstrated a significant reduction in ARR by 51% (0.11 vs 0.22) and 59% (0.10 vs 0.25) compared with teriflunomide (P<.001 in both studies) in ASCLEPIOS I and II, respectively (primary endpoint). Kesimpta also showed a relative risk reduction of 34.4% (P=.002) in 3-month CDP compared with teriflunomide in a pre-specified meta-analysis, as defined in ASCLEPIOS.[4]

Kesimpta showed significant reduction of both Gd+ T1 lesions and new or enlarging T2 lesions. It significantly reduced the mean number of both Gd+ T1 lesions (98% and 94% relative reduction in ASCLEPIOS I and II, respectively, both P<.001) and new or enlarging T2 lesions (82% and 85% relative reduction in ASCLEPIOS I and II, respectively, both P<.001) vs teriflunomide.[4]

Kesimpta had a similar safety profile to teriflunomide, with the frequency of serious infections and malignancies also being similar across both treatment groups. Upper respiratory tract infection, headache, injection-related reactions, and local injection site reactions were the most commonly observed adverse reactions with Kesimpta (incidence greater than 10%).[4]

A separate post hoc analysis demonstrated that the odds of achieving no evidence of disease activity (NEDA-3; no relapses, no MRI lesions, and no disability worsening combined) with Kesimpta versus teriflunomide were >3-fold higher at Months 0–12 (47.0% vs 24.5% of patients) and >8-fold higher at Months 12–24 (87.8% vs 48.2% of patients).[12]

Overall Kesimpta, an antibody targeting CD20 positive B-cells, delivered superior efficacy and demonstrated a safety profile with infection rates similar to teriflunomide.[4]

About ALITHIOS study

The ALITHIOS study is an ongoing open-label, single arm, multi-center extension Phase III study evaluating the long-term safety, tolerability and effectiveness of ofatumumab in subjects with RMS who have participated in a Novartis ofatumumab clinical MS study. The primary endpoint is the number of patients that experience an adverse event or abnormal laboratory, vital and/or ECG results and positive suicidality outcomes. Secondary endpoints include number of relapse rates per year, 3- and 6-month CDW, 6-, 12- and 24-month confirmed disability improvement and improvement until end of study. This study includes a vaccination sub-study investigating the effects of ofatumumab on the development of antibody responses to selected vaccines and keyhole limpet hemocyanin (KLH) neo-antigen in subjects with RMS.[13]

About APLIOS study

The APLIOS study is a 12-week, open-label, Phase II bioequivalence study to determine the onset of B-cell depletion with Kesimpta subcutaneous monthly injections and the bioequivalence of subcutaneous administration of Kesimpta via a prefilled syringe—as used in ASCLEPIOS I and II—and a Sensoready pen in patients with RMS. Patients were randomized according to injection device and site including the abdomen and the thigh. B-cell depletion was measured nine times over 12 weeks and Gd+ lesion counts were assessed

at baseline and at Weeks 4, 8 and 12. Regardless of injection device or site, Kesimpta 20 mg subcutaneous monthly injections resulted in rapid, close to complete and sustained B-cell depletion; the proportion of patients with B-cell concentrations of <10 cells/µL was >65% after the first injection by Day 7, 94% by Week 4, and sustained >95% at all following injections. Kesimpta treatment reduced the mean number of Gd+ lesions from baseline (1.5) to 0.8, 0.3 and 0.1 by Weeks 4, 8 and 12, respectively; the proportion of patients free from Gd+ lesions at the corresponding time points were 66.5%, 86.7% and 94.1%, respectively.[6]

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.[14] MS, which affects approximately 2.3 million people worldwide,[15] can be characterized into four main types of MS: clinically isolated syndrome (CIS), relapsing remitting (RRMS), secondary progressive (SPMS) and primary progressive (PPMS).[16] 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.[14]

Novartis in Neuroscience

Novartis has a strong ongoing commitment to neuroscience and to bringing innovative treatments to patients suffering from neurological conditions where there is a high unmet need. We are committed to supporting patients and physicians in multiple disease areas, including MS, migraine, Alzheimer's disease, Parkinson's disease, epilepsy and attention deficit hyperactivity disorder, and have a promising pipeline in MS, Alzheimer's disease, spinal muscular atrophy and specialty neurology.

Indication

What is KESIMPTA (ofatumumab) injection?

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 active hepatitis B virus (HBV) infection.

What is the most important information I should know about KESIMPTA?

KESIMPTA can cause serious side effects such as:

- Infections. Serious infections can happen during treatment with KESIMPTA. If you have an active infection, your healthcare 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. Talk with your HCP if you have any of these signs and symptoms:
    - at or near the injection site: redness of the skin, swelling, itching, and pain or
    - that may happen when certain substances are released in your body: fever, headache, pain in the muscles, chills, and tiredness.
- 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.

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 about 15,000 people in the United States. For more information, please visit https://www.novartis.us.

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