

MEDIA & INVESTOR RELEASE

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

- *New post hoc data from Phase III ASCLEPIOS trials showed newly diagnosed, treatment-naïve patients experienced reductions in annualized relapse rates, MRI lesion activity and reductions in time to disability worsening when treated with Kesimpta vs teriflunomide¹*
- *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 patients³*
- *Kesimpta is the first and only FDA-approved, self-administered, targeted B-cell therapy for adults with RMS⁴*

Basel, September 11, 2020 — 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. 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, $P < .001$). Overall, Kesimpta had a similar safety profile to teriflunomide¹.

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 studies².

“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 RMS³. 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 relapses⁵.

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 pen⁴.

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 depletion⁷. 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 spleen⁸. Once-monthly dosing of Kesimpta also allows faster repletion of B-cells and offers more flexibility⁹. Ofatumumab was originally developed by Genmab and licensed to GlaxoSmithKline. Novartis obtained rights for ofatumumab from GlaxoSmithKline in all indications, including RMS, in December 2015¹⁰.

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 5.5⁴. The studies were conducted in over 350 sites in 37 countries¹¹. 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 pre-specified meta-analysis, as defined in ASCLEPIOS⁴.

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 teriflunomide⁴.

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 Kesimpta may halt new disease activity in RMS patients. It showed the odds of achieving NEDA-3 with ofatumumab versus teriflunomide were >3-fold higher at Months 0–12 (47.0% vs 24.5% of patients; $P<.001$) and >8-fold higher at Months 12–24 (87.8% vs 48.2% of patients; $P<.001$)¹².

Overall Kesimpta, an antibody targeting CD20 positive B-cells, delivered superior efficacy and demonstrated a safety profile with infection rates similar to teriflunomide⁴.

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 RMS¹³.

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/ μ L 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%, respectively⁶.

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 cord¹⁴. MS, which affects approximately 2.3 million people worldwide¹⁵, 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 disease¹⁴.

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.

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About Novartis

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 products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 109,000 people of more than 145 nationalities work at Novartis around the world. Find out more at

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