Novartis pivotal data show children and adolescents with relapsing MS had an 82% lower relapse rate with fingolimod vs. interferon beta-1a

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- - PARADIGMS data also show fingolimod-treated patients had significantly fewer new brain lesions vs. those on intramuscular interferon beta-1a injections(1)
- - Currently there are no disease-modifying therapies specifically approved for children and adolescents with MS, a population that often experiences more frequent relapses than adults with early MS(2)
- - Novartis is committed to advancing care for young people with relapsing MS

EAST HANOVER, N.J., Oct. 28, 2017 /PRNewswire/ -- Novartis today announced results from the Phase III PARADIGMS study, investigating the safety and efficacy of fingolimod vs. interferon beta-1a, in children and adolescents (ages 10 to <18) with relapsing multiple sclerosis (MS). Treatment with oral fingolimod resulted in an 82% reduction in the rate of relapses (annualized relapse rate) in this patient population over a period of up to two years, compared to interferon beta-1a intramuscular injections ($p < 0.001$)[1]. PARADIGMS is the first completed randomized, controlled clinical trial specifically designed for children and adolescents with relapsing MS. The results have been presented at the 7th Joint European and Americas Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS-ACTRIMS) meeting on October 28, 2017 in Paris, France.

"There are currently no FDA-approved MS therapies for the pediatric population," said Dr. Tanuja Chitnis, Principal Investigator for PARADIGMS and Director of the Partners Pediatric Multiple Sclerosis Center, Massachusetts General Hospital, Boston, US, and Scientist, Ann Romney Center, Brigham and Women's Hospital, Boston, US. "We are encouraged by the reduction in the annualized relapse rate we've seen with fingolimod in this study. PARADIGMS was designed specifically for pediatric patients, who oftentimes have more frequent relapses than adults with early MS."

Additional data from the study demonstrated:

- Secondary endpoints showed a significant reduction in the number of new / newly enlarging T2 lesions and Gd-T1 lesions in the brain in fingolimod-treated patients compared to those treated with interferon beta-1a, as measured by magnetic resonance imaging (MRI)[1].
- The safety profile of fingolimod in this study was overall consistent with that seen in previous clinical trials in adults. In this study, while more adverse events (AEs) were reported in the interferon beta-1a group, severe AEs were reported at a higher frequency in fingolimod-treated patients[3].
- An exploratory analysis found individuals treated with fingolimod had significantly less brain volume loss (measured by MRI), compared to those treated with interferon beta-1a[1].

"Gilenya has been shown to improve outcomes for adults with relapsing MS. We're proud of having completed this head-to-head trial in children and adolescents with relapsing MS and are encouraged by the findings," said Fabrice Chouraqui, President of Novartis Pharmaceuticals Corporation. "The study reflects our ongoing commitment to the MS community."

Fingolimod, also known as Gilenya® in the US, is approved to treat relapsing forms of MS in adults. Gilenya is not currently approved for children and adolescents with relapsing MS. Novartis is working on submission with health authorities worldwide for pediatric patients.

About the Phase III PARADIGMS study

The Phase III PARADIGMS study (NCT01892722) is a double-blind, randomized, multi-center study to evaluate the safety and efficacy of oral fingolimod compared to interferon beta-1a in children and adolescents with a confirmed diagnosis of relapsing multiple sclerosis (MS), over a period of up to two years, followed by a five-year open label extension phase[4]. The study enrolled 215 children and adolescents with MS, between the ages of 10 and <18 years with an Expanded Disability Status Scale (EDSS) score between 0 and 5.5[4]. Patients were randomized to receive once-daily oral fingolimod (0.5 mg or 0.25 mg, dependent on patients' body weight) or intramuscular interferon beta-1a once weekly[4].

The primary endpoint of the study was the frequency of relapses in patients treated up to 24 months (annualized relapse rate)[4]. Secondary endpoints included the number of new or newly enlarged T2 lesions, Gadolinium enhancing T1 lesions, safety and the pharmacokinetic properties of fingolimod, all measured throughout the treatment period[4]. Brain volume loss (measured by MRI) was an exploratory endpoint, for which the study was not powered[4].

The Phase III PARADIGMS study was conducted in 87 sites over 25 countries, and was designed in partnership with the US Food and Drug Administration, European Medicines Agency and the International Pediatric Multiple Sclerosis Study Group.

About Multiple Sclerosis

Multiple sclerosis (MS) is a chronic disorder of the central nervous system (CNS) that disrupts the normal functioning of the brain, optic nerves and spinal cord through inflammation and tissue loss[5]. In adults, there are three types of MS: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS) and primary progressive MS (PPMS)[6]. In children, RRMS accounts for nearly all cases (approximately 98 percent)[7].

The evolution of MS results in an increasing loss of both physical and cognitive (e.g., memory) function. This has a substantial negative impact on the lives of the approximately 2.3 million people worldwide affected by MS, of which between three and five percent are estimated to be children[8,9].

About Gilenya® (fingolimod) in adults

Gilenya was the first once-a-day pill approved to treat relapsing multiple sclerosis (MS). Approved for first-line use, Gilenya is a disease-modifying therapy (DMT) that offers freedom from injections, which may fit many patients' lifestyles. Gilenya helps slow down the physical problems caused by RRMS and decreases the frequency of MS flare-ups (relapses).

Gilenya is the most prescribed oral once-daily DMT. In the US, approximately 73,000 patients have been exposed to Gilenya. Worldwide, Gilenya has been used to treat approximately 213,000 patients in both clinical trials and the post-marketing setting, with approximately 453,000 years of patient experience[3].

Indication

Gilenya is a prescription medicine used to treat relapsing forms of multiple sclerosis (MS) in adults. Gilenya can decrease the number of MS flare-ups (relapses). Gilenya does not cure MS, but it can help slow down the physical problems that MS causes.

Important Safety Information

You should not take Gilenya if in the last 6 months you experienced heart attack, unstable angina, stroke or warning stroke, or certain types of heart failure. Do not take Gilenya if you have an irregular or abnormal heartbeat (arrhythmia), including a heart finding called prolonged QT as seen on an ECG, or if you take medicines that change your heart rhythm. Do not take Gilenya if you are allergic to fingolimod or any of the other ingredients.

Gilenya may cause side effects such as:

- Slow heart rate, especially after first dose. You will be monitored by a health care professional for at least 6 hours after your first dose. Your pulse and blood pressure will be checked hourly. You'll get an ECG before and 6 hours after your first dose. If any heart problems arise or your heart rate is still low, you'll continue to be monitored. If you have any serious side effects, especially those that require treatment with other medicines, or if you have certain types of heart problems, or if you're taking medicines that can affect your heart, you'll be watched overnight. If you experience slow heart rate, it will usually return to normal within 1 month. Call your doctor, or seek immediate medical attention if you have any symptoms of slow heart rate, such as feeling dizzy or tired or feeling like your heart is beating slowly or skipping beats. Symptoms can happen up to 24 hours after the first dose. Do not stop taking Gilenya without consulting with your doctor. Call your doctor if you miss 1 or more doses of Gilenya—you may need to repeat the 6-hour monitoring.
- Increased risk of serious infections. Gilenya lowers the number of white blood cells (lymphocytes) in your blood. This will usually go back to normal within 2 months of stopping Gilenya. Your doctor may do a blood test before you start Gilenya. Gilenya may decrease the way vaccines work in your body, especially the chicken pox vaccine. Increased risk of infection was seen with doses higher than the approved dose (0.5 mg). Two patients died who took higher-dose Gilenya (1.25 mg) combined with high-dose steroids. Call your doctor right away if you have fever, tiredness, body aches, chills, nausea, vomiting, or headache accompanied by fever, neck stiffness, sensitivity to light, nausea, and/or confusion. These may be symptoms of meningitis.
- Progressive multifocal leukoencephalopathy (PML). PML is a rare brain infection that usually leads to death or severe disability. If PML happens, it usually happens in people with weakened immune systems. It is important that you call your doctor right away if you have any new or worsening medical problems that have lasted several days, including problems with thinking, eyesight, strength, balance, weakness on 1 side of your body, or using your arms and legs.
- Macular edema, a vision problem that can cause some of the same vision symptoms as an MS attack (optic neuritis), or no symptoms. If it happens, macular edema usually starts in the first 3 to 4 months after starting Gilenya. Your doctor should test your vision before you start Gilenya; 3 to 4 months after you start Gilenya; and any time you notice vision changes. Vision problems may continue after macular edema has gone away. Your risk of macular edema may be higher if you have diabetes or have had an inflammation of your eye (uveitis). Call your doctor right away if you have blurriness, shadows, or a blind spot in the center of your vision; sensitivity to light; or unusually colored vision.
- Swelling and narrowing of the blood vessels in your brain. A condition called PRES (Posterior reversible encephalopathy syndrome) has occurred rarely in patients taking Gilenya. Symptoms of PRES usually get better when you stop taking Gilenya. However, if left untreated, it may lead to a stroke. Call your doctor right away if you experience any symptoms, such as sudden headache, confusion, seizures, loss of vision, or weakness.
- Breathing problems. Some patients have shortness of breath. Call your doctor right away if you have trouble breathing.
- Liver problems. Your doctor should do blood tests to check your liver before you start Gilenya. Call your doctor right away if you have nausea, vomiting, stomach pain, loss of appetite, tiredness, dark urine, or if your skin or the whites of your eyes turn yellow.

- Increases in blood pressure (BP). BP should be monitored during treatment.
- A type of skin cancer called basal cell carcinoma (BCC). Talk to your doctor if you notice any skin nodules (shiny, pearly nodules), patches or open sores that do not heal within weeks. These may be signs of BCC.

Gilenya may harm your unborn baby. Talk to your doctor if you are pregnant or planning to become pregnant. Women who can become pregnant should use effective birth control while on Gilenya, and for at least 2 months after stopping. If you become pregnant while taking Gilenya, or within 2 months after stopping, tell your doctor right away. Women who take Gilenya should not breastfeed, as it is not known if Gilenya passes into breast milk. A pregnancy registry is available for women who become pregnant during Gilenya treatment. For more information, contact the Gilenya Pregnancy Registry by calling Quintiles at 1-877-598-7237, by e-mailing gpr@quintiles.com, or by going to www.gilenyapregnancyregistry.com.

Tell your doctor about all your medical conditions, including if you had or now have an irregular or abnormal heartbeat; heart problems; a history of repeated fainting; a fever or infection, or if you are unable to fight infections due to a disease or are taking medicines that lower your immune system, including corticosteroids, or have taken them in the past; eye problems; diabetes; breathing or liver problems; or uncontrolled high blood pressure. Also tell your doctor if you have had chicken pox or have received the chicken pox vaccine. Your doctor may test for the chicken pox virus, and you may need to get the full course of the chicken pox vaccine and wait 1 month before starting Gilenya.

If you take too much Gilenya, call your doctor or go to the nearest hospital emergency room right away.

Tell your doctor about all the medicines you take or have recently taken, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Tell your doctor if you have been vaccinated within 1 month before you start taking Gilenya. You should not get certain vaccines, called live attenuated vaccines, while taking Gilenya and for at least 2 months after stopping Gilenya treatment.

The most common side effects with Gilenya were headache, abnormal liver tests, diarrhea, cough, flu, sinusitis, back pain, abdominal pain, and pain in arms or legs.

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 at http://www.pharma.us.novartis.com/product/pi/pdf/gilenya.pdf.

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Located in East Hanover, NJ Novartis Pharmaceuticals Corporation is an affiliate of Novartis which provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 119,000 full-time-equivalent associates. Novartis products are available in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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References

1. Chitnis T, Arnold DL, Banwell B, et al. PARADIGMS: A Randomised Double-blind Study of Fingolimod Versus Interferon β-1a in Paediatric Multiple Sclerosis. Abstract no. 276. Oral presentation at 7th Joint ECTRIMS-ACTRIMS Meeting, Paris, France, October 25-28, 2017.
2. National Multiple Sclerosis Society. Pediatric MS. http://www.nationalmssociety.org/What-is-MS/Who-Gets-MS/Pediatric-MS. Accessed October 17, 2017.
3. Novartis data on file.
4. ClinicalTrials.gov. Safety and Efficacy of Fingolimod in Pediatric Patients With Multiple Sclerosis. NCT01892722. https://clinicaltrials.gov/ct2/show/NCT01892722. Accessed October 17, 2017.
5. PubMed Health. Multiple Sclerosis (MS). https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0024311/. Accessed October 17, 2017.
6. Multiple Sclerosis Society. Types of MS. https://www.mssociety.org.uk/what-is-ms/types-of-ms. Accessed October 17, 2017.
7. Waldman A, Ness J, Pohl D, et al. Pediatric multiple sclerosis: Clinical features and outcome. Neurology 2016;87 (Suppl 2):S74-S81.
8. Patel Y, Bhise V, Krupp L. Pediatric multiple sclerosis. Annals of Indian Academy of Neurology. 2009;12(4):238-245.
9. Multiple Sclerosis International Federation. Atlas of MS 2013. https://www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf. Accessed October 17, 2017.

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