Novartis data finds relapsing MS patients on Gilenya® had greater treatment retention and satisfaction rates vs. injectable DMTs

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- - In a well-controlled, randomized, open-label study, Gilenya patients had higher treatment retention rates at one year, 81.3% vs. those on injectable DMTs, 29.2%
- - Throughout the study almost 10 times more patients switched from injectable DMTs to Gilenya vs. Gilenya to injectable DMTs (90.5% vs. 9.5%, respectively)
- - At the end of randomized treatment, patients on Gilenya had higher treatment satisfaction and less brain volume loss vs. patients on injectable DMTs
- - In a separate post hoc subgroup analysis of African-American patients, treatment retention was greater with Gilenya vs. injectable DMTs

EAST HANOVER, N.J., Sept. 16, 2016 /PRNewswire/ -- Novartis announced new data today from the Prospective, Randomized, active-controlled, open-label study to Evaluate patient retention of Fingolimod 0.5 mg vs. approved first-line injectable disease-modifying therapies (interferon ß or glatiramer acetate), over a period of 12 months in adults with Relapsing-remitting Multiple Sclerosis (PREFERMS). PREFERMS included 875 patients and is the largest, prospective, randomized, active-controlled, open-label study to evaluate patient retention in relapsing-remitting multiple sclerosis (RRMS) patients. These data, which included findings from a pre-planned analysis of the impact of treatment switches and a post hoc analysis of the study's African-American patient subgroup, were presented at the annual Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in London, UK, September 14-17, 2016.

Throughout the study, patients were given the opportunity to switch treatments, and a substantial number of patients, nearly 10 times as many patients, who were randomized to injectable disease-modifying therapies (DMTs), switched treatment to Gilenya® (fingolimod) (90.5%, n=257) than from Gilenya to injectable DMTs (9.5%, n=27). It's important to note the study was not powered to detect the treatment difference in the secondary efficacy endpoints or treatment effects related to switching study medication.

End of Randomized Treatment Results
In the pre-planned analysis at the end of randomized treatment (when patients either switched or discontinued randomized treatment), significantly more patients were satisfied with treatment in the Gilenya group compared to the group receiving injectable DMTs, 77.4% vs. 47.7%, respectively ($p<0.0001$). Gilenya also reduced brain volume loss compared with injectable DMTs. At the end of randomized treatment, the exposure-adjusted mean percentage of brain volume loss in the Gilenya compared to the injectable DMT group was 0.48% vs. 0.75%, respectively ($p<0.001$).

At the end of randomized treatment, the between-group differences in patient satisfaction and brain volume loss favored Gilenya over injectable DMTs. By the end of the study, a high number of patients switched from injectable DMTs to Gilenya (90.5%, n=257) and the between-group differences became similar. This is potentially due to the high number of patients who switched from the injectable DMT group to Gilenya.

"These additional analyses from our large well-controlled study demonstrate our ongoing commitment to help improve patient outcomes in MS and address some of the key challenges healthcare providers face on a day-to-day basis," said Marcia Kayath, MD, Vice President and Head of US Clinical Development and Medical Affairs, Novartis Pharmaceuticals Corporation. "As a leader in neuroscience, Novartis is committed to advancing research in MS to increase understanding of our current medicines and bring additional innovative therapies to patients and physicians."

Safety Results

Among the patients who changed therapy from injectable DMTs to Gilenya, the rates of overall adverse events (AEs)/per patient-year decreased from 10.854 at end of randomization to 6.438 at end of study; rates for AEs/per patient-year leading to discontinuation (1.652 vs. 0.657) and rates of serious AEs/per patient year remained similar (0.06). Overall, the Gilenya safety profile was consistent with data from previous studies.

African-American Patient Subgroup Analysis

While rates of MS are generally low among African-Americans, the disease course can be aggressive. PREFERMS had the largest African-American cohort of any RRMS study with 136 of 875 patients or 16% of the overall study population. In a separate post hoc analysis of this African-American patient subgroup, the treatment retention rate for Gilenya was 80.6% (54 of 67 patients) compared with 30.4% (21 of 69 patients) for injectable DMTs ($p<0.0001$) at the end of randomized treatment. Proportionately more patients expressed satisfaction with Gilenya than with injectable DMTs, 80.6% vs. 49.3% ($p<0.0001$).

Study Design

PREFERMS was a 12-month, Phase IV, open-label, active-controlled, randomized, multicenter study conducted at 117 sites in the US. At enrollment, patients with RRMS were treatment-naïve or had received only one injectable DMT class (IFNβ-1a, IFNβ-1b or glatiramer acetate). In the study a total of 875 patients were randomized (1:1) to Gilenya 0.5 mg (n=433) or to a pre-selected injectable DMT (n=428), and followed up quarterly for 12 months. After a minimum of 3 months of treatment, a single on-study treatment switch was allowed, however, switches due to efficacy or safety were allowed (based on patient-doctor consultation) at any month following randomization. The primary endpoint was to compare the patient retention on randomized treatment over 12 months. This study was powered for the primary endpoint (retention rate). The study was not powered to detect the treatment difference in the secondary efficacy endpoints or treatment effects related to switching study medication.

About Multiple Sclerosis

Multiple sclerosis, a chronic disease of the central nervous system, affects around 400,000 people in the US. Approximately 85 percent of people with MS have relapsing-remitting MS, where the immune system attacks healthy tissue. This form of MS is a potentially debilitating condition characterized by relapses with worsening neurological function, followed by periods of remission where patients partially or fully recover, during which the disease remains stable.

About Gilenya

Gilenya was the first once-a-day pill approved to treat relapsing forms of multiple sclerosis (RRMS). 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, more than 64,000 patients have been exposed to Gilenya. Worldwide, Gilenya has been used to treat approximately 155,000 patients in both clinical trials and the post-marketing setting, with approximately 343,000 years of patient experience.

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.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as "potentially," "commitment," "committed," "may," "innovative," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Gilenya, potential marketing approvals for any investigational therapies for MS being developed at Novartis, or regarding potential future revenues from Gilenya and such investigational therapies for MS. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management 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

Gilenya will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Neither can there be any guarantee that any investigational therapies for MS being developed at Novartis will be submitted or approved for sale in any market, or at any particular time. Nor can there be any guarantee that Gilenya or any investigational therapies for MS being developed at Novartis will be commercially successful in the future. In particular, management's expectations regarding Gilenya and such investigational therapies for MS could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected safety, quality or manufacturing issues, 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

Novartis Pharmaceuticals Corporation offers a broad range of medicines for cancer, cardiovascular disease, endocrine disease, inflammatory disease, infectious disease, neurological disease, organ transplantation, psychiatric disease, respiratory disease and skin conditions.

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, 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, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit http://www.novartis.com.

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