Post-Hoc Data Show Daily Activity Participation, Independence and Sleep Quality Improved in Adults with Moderate to Severe Rheumatoid Arthritis After Treatment with ORENCIA® (Abatacept)

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- Data presented at American College of Rheumatology Annual Congress -

BOSTON--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced the results of three post-hoc analyses from two Phase III pivotal trials that showed ORENCIA® (abatacept) improved daily activity participation, such as work or household chores, physical and social-role independence and sleep quality in adult rheumatoid arthritis (RA) patients who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate (MTX) or tumor necrosis factor (TNF) antagonists.

These data are from post-hoc analyses of two Phase III pivotal trials investigating ORENCIA: AIM (Abatacept in Inadequate responders to Methotrexate) and ATTAIN (Abatacept Trial in Treatment of Anti-TNF Inadequate Responders).

"The chronic nature of RA can have a significant impact on a person's health-related quality of life, including independence, ability to perform daily activities and sleep quality," said George Wells, M.Sc., Ph.D., Professor of the Department of Epidemiology and Community Medicine, University of Ottawa.

About the Data

Poster presentations of these analyses of the AIM (n=433 for ORENCIA plus MTX; n=219 for placebo plus MTX) and ATTAIN (n=258 for ORENCIA plus DMARDs; n=133 for placebo plus DMARDs) studies evaluating health-related quality of life improvement in daily activity participation, independence and sleep quality in RA patients treated with ORENCIA® (abatacept) were presented last week at the ACR Annual Scientific Meeting in Boston, MA.

An analysis of the AIM and ATTAIN studies presented by Li, et al, looked at RA patients' ability to participate in daily usual activities using a validated activity participation questionnaire. Patients who were treated with ORENCIA were compared with those in the placebo group. This questionnaire was used to assess the number of days in the past 30 days that a patient was unable to perform his or her usual daily activities, defined as paid or unpaid work, household chores or personal care, due to RA. A change of four days in activity participation was deemed to be clinically meaningful.

The percent of patients demonstrating an ability to participate in daily activities in AIM was 61 percent for ORENCIA vs. 46 percent for placebo at one year, and in ATTAIN was 53 percent vs. 32 percent, respectively, at six months. The study found that activity gain was correlated to clinical aspects, physical function and health-related quality of life. In a multi-regression analysis, it was determined that key contributors to activity levels included joint counts, patient global assessment, fatigue, physical function and the physical domains as measured by the Short-Form (SF-36).

A separate analysis of the ATTAIN trial presented by Hassett, et al, examined the incidence of improvement in social role functioning and decreased need for help from others at six months for the ORENCIA group compared to placebo. This was assessed using a multidimensional scale for independence that was derived from validated measures (including the Health Assessment Questionnaire [HAQ], SF-36 and activity participation questionnaire) in which patient physical and social independence were evaluated. After a final analysis, this scale was constructed of two factors: socio-emotional role independence (including SF-36 role-physical, role-emotional, social functioning domains and days with activity limitation) and physical independence (including HAQ items on reach help, care help and ambulating help). Interviews with 20 RA patients confirmed the concept of measuring independence using a multidimensional scale that included these two factors.

Change in mean score on Factor 1 (socio-emotional role independence) was 0.921 for the ORENCIA group and 0.169 for the placebo group (p-value less than 0.0001). Change in mean score on Factor 2 (physical independence) was 0.499 for the ORENCIA group and 0.078 for the placebo group (p-value equals 0.0029). The study concluded that the multi-dimensional assessment of independence based on items from commonly used measurement tools (Disease Activity Score 28, Health Assessment Questionnaire Disability Index and SF-36) is viable.

An analysis of the AIM and ATTAIN studies, presented by Wells, et al, examined several different aspects of sleep in RA patients. Sleep quality was assessed using the validated Medical Outcomes Study sleep questionnaire (MOS- sleep). The treatment groups were compared on the seven derived MOS-sleep scales: awakened short of breath or with headache,
snoring, sleep adequacy, sleep disturbance, drowsiness, and sleep problems Index I and Index II. Sleep problems Index I and II are summary scores based on the mean of several sleep-related issues, and a higher score indicates more severity in sleep problems. In addition, the study compared sleep duration and optimal sleep based on the MOS-sleep module.

There was an 18 percent improvement in optimal sleep scores in the ORENCIA® (abatacept) group versus -12 percent in the placebo group for the ATTAIN study (p-value less than 0.0001) at six months and a 16 percent improvement in optimal sleep scores in the ORENCIA group versus 5 percent in placebo group for the AIM study (p-value equals 0.0214) at 12 months. Sleep quantity was not significantly different. In the ATTAIN study, measurement of sleep adequacy was 9.0 in the ORENCIA group and 6.6 in the placebo group (p-value equals 0.0028), sleep disturbance was -11.3 in the ORENCIA group and -2.9 in the placebo group (p-value equals 0.0005), drowsiness was -10.5 in the ORENCIA group and -1.6 in the placebo group (p-value less than 0.0001) sleep problems Index I was -9.5 in the ORENCIA group and -1.4 in the placebo group (p-value less than 0.0001) and Index II was -9.8 in the ORENCIA group and -2.1 in the placebo group (p-value less than 0.0001). MOS-sleep scales measuring awoken short of breath or with headache and snoring were not significantly different in the ATTAIN group. In the AIM study, measurement of sleep disturbance in the ORENCIA group was -13.0 and -8.9 in the placebo group (p-value equals 0.0197), sleep problems Index I was -9.4 in the ORENCIA group and -6.7 in the placebo group (p-value equals 0.0476) and Index II was -10.4 in the ORENCIA group and -7.3 in the placebo group (p-value equals 0.0173). MOS-sleep scales measuring awoken short of breath or with headache, snoring, adequacy or drowsiness were not significantly different in the AIM group.

About AIM and ATTAIN

AIM was a Phase III multi-center, randomized, double-blind, placebo-controlled trial with 652 patients treated at baseline who had active RA despite MTX therapy (638 included in efficacy analyses). The study was double-blind through one year, followed by an ongoing, open-label, long-term extension study. A total of 376 (from the original 424) patients in the group treated with ORENCIA® (abatacept) entered the long-term extension study. Additional DMARDs, non-steroidal anti-inflammatory drugs (NSAIDs), and aspirin were added and/or adjusted at the discretion of the investigator in the long-term extension study. Primary reasons for discontinuation in the long-term extension studies were adverse events, withdrawal of consent, and lack of efficacy.

Primary endpoints were ACR 20 at six months ORENCIA vs. placebo (67.9 percent vs. 39.7 percent, respectively; p-value less than 0.001), clinically significant improvement in HAQ-DI at one year (63.7 percent vs. 39.3 percent, respectively; p-value less than 0.001), erosion score at one year (mean change from baseline 0.61 vs. 1.47, respectively; p-value less than 0.01). Secondary endpoints included ACR 20, 50, and 70 over time; major clinical response (45 percent for ORENCIA plus MTX), DAS at one year (42.5 percent vs. 9.9 percent, respectively; p-value less than 0.001), joint space narrowing (mean change from baseline 0.46 vs. 0.97, respectively; p-value less than 0.01), total Sharp scores at one year (mean change from baseline 1.07 vs. 2.43, respectively; p-value less than 0.01), and SF-36 through one year (mean change from baseline 8.44 vs. 5.28, respectively; p-value less than 0.001).

ATTAIN was a Phase III multi-center, randomized, double-blind, placebo-controlled trial with 391 patients treated at baseline who had active RA despite anti-TNF therapy (389 included in efficacy analyses). The study was double-blind through six months, followed by an ongoing, open-label, long-term extension study. A total of 217 (from the original 256) patients in the group treated with ORENCIA entered the long-term extension study. Additional DMARDs, NSAIDs, and aspirin were added and/or adjusted at the discretion of the investigator in the long-term extension study. Primary reasons for discontinuation in the long-term extension studies were adverse events and lack of efficacy.

Primary endpoints were ACR 20 at six months ORENCIA vs. placebo (50.4 placebo vs. 19.5 percent, respectively; p-value less than 0.001) and improvement in HAQ-DI at six months (47.3 percent vs. 23.3 percent, respectively; p-value less than 0.001). Secondary endpoints were ACR 20, 50, and 70 over time, DAS28 at six months (DAS28 less than or equal to 3.2, 18 percent and DAS28 less than 2.6; 11.1 percent) and SF-36 at six months (55.6 percent vs. 31.6 percent, respectively; p-value less than 0.001). In five clinical trials, the most serious adverse reactions were serious infections (3 percent ORENCIA® (abatacept) vs. 1.9 percent placebo) and malignancies (1.3 percent ORENCIA vs. 1.1 percent placebo). The most commonly reported acute infusion-related AEs (one to two percent) were dizziness, headache, and hypertension with fewer than one percent of patients discontinuing ORENCIA due to infusion-related events.

About ORENCIA

ORENCIA® is indicated in the United States for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adults with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more DMARDs, such as methotrexate or TNF antagonists. ORENCIA may be used as monotherapy or concomitantly with DMARDs other than TNF antagonists. ORENCIA should not be administered concomitantly with TNF antagonists and is not recommended for use concomitantly with anakinra.

Dosing and Administration

ORENCIA® is administered by a healthcare professional as a 30-minute intravenous infusion at a fixed dose based on body weight range approximating 10 mg/kg at day 0, 2 weeks, 4 weeks, and every 4 weeks thereafter. Acute infusion-related reactions were experienced in nine percent of people treated with ORENCIA® and in six percent of people treated with placebo. According to the full prescribing information, the most frequently reported infusion-related adverse events (1 percent to 2 percent) were dizziness, headache, and hypertension. In pivotal studies, premedications were not required. However, appropriate medical support measures for the treatment of hypersensitivity reactions should be available for immediate use in the event of a reaction.

Important Safety Information about ORENCIA

Before receiving treatment with ORENCIA® individuals should tell their doctor if they are taking a TNF blocker (e.g., Enbrel®, Humira®, Remicade®) to treat rheumatoid arthritis (RA). ORENCIA should not be taken with these medications because of a higher chance of getting a serious infection. Individuals should also tell their doctor if they are taking Kineret® to treat RA. ORENCIA should not be taken with Kineret. People taking ORENCIA should notify their doctor if they are taking any other medications including hormones, over-the-counter medicines, vitamins, supplements or herbal products.
Individuals should let their doctor know if they have any kind of infection including an infection that is in only one place of the body (such as an open cut or sore) or an infection that is in the whole body (such as the flu). Having an infection could increase the risk for serious side effects from ORENCIA® (abatacept). It is also important for individuals to let their doctor know if they have an infection that won’t go away or a history of infections that keep coming back.

People who have had tuberculosis (TB), a positive skin test for TB, recent close contact with someone who has had TB or develop any of the symptoms of TB (a dry cough that doesn’t go away, weight loss, fever, night sweats) should call their doctor right away. Before starting treatment with ORENCIA, a doctor may examine the individual for TB or perform a skin test.

In addition, individuals should let their doctor know if they are scheduled to have surgery or any vaccination or have recently received a vaccination. People should inform their doctor if they have a history of chronic obstructive pulmonary (lung) disease (COPD). Taking ORENCIA may cause COPD symptoms to get worse.

People who have diabetes and use a blood glucose monitor to check their sugar levels should tell their doctor. The infusion of ORENCIA contains maltose, a sugar that can give falsely high blood glucose readings with some monitors on the day the infusion is received. The doctor may recommend a different monitor.

Women who are pregnant, planning to become pregnant or are thinking about becoming pregnant should tell their doctor. It is not known if ORENCIA can harm an unborn baby. Women who are breast feeding should also inform their doctor. They will need to decide to either breast-feed or receive treatment with ORENCIA, but not both.

Like all medicines that affect your immune system, ORENCIA can cause serious side effects. The possible serious side effects include serious infections and allergic reactions. Also, rare cases of certain kinds of cancers have been reported.

People taking ORENCIA are at increased risk for developing infections including pneumonia, and other infections caused by viruses, bacteria, or fungi. Individuals should call their doctor immediately if they feel sick or get any infection during treatment with ORENCIA.

Allergic reactions are usually mild or moderate, generally occur within the first 24 hours of an infusion, and include hives, swollen face, eyelids, lips, tongue, throat, or trouble breathing. There have been some serious allergic reactions reported after receiving an infusion of ORENCIA.

There have been rare cases of certain kinds of cancer. The role of ORENCIA® (abatacept) in the development of cancer is not known.

The more common side effects with ORENCIA are headache, upper respiratory tract infection, sore throat, and nausea.

For Full Prescribing Information, please visit http://www.orencia.com/ or http://www.bms.com/

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*Sleep problems Index I includes the following sleep-related issues: feeling rested upon waking in the morning, awakening short of breath or with a headache, having trouble falling asleep, awakening during sleep time and having trouble falling asleep again, having trouble staying awake during the day and getting the amount of sleep needed. Sleep problems Index II includes the following sleep-related issues: amount of time taken to fall sleep, feeling that sleep is not quiet, feeling rested upon waking in the morning, awakening short of breath or with a headache, feeling drowsy or sleepy during the day, having trouble falling asleep, awakening during sleep time and having trouble falling asleep again, having trouble staying awake during the day and getting the amount of sleep needed.

SOURCE: Bristol-Myers Squibb Company

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