C-AXSPAND

A **52-Week** Randomized Placebo-Controlled Phase 3 Trial of Certolizumab Pegol **(CZP)**, an Anti-TNF Therapy, in Non-Radiographic Axial Spondyloarthritis **(nr-axSpA)**

UNMET NEED

As many as 3.3 million individuals in the U.S. live with axSpA.[1,2] Of these, approximately half meet the criteria for nr-axSpA.[3] The FDA recently approved CIMZIA (certolizumab pegol) to treat adults with active nr-axSpA with objective signs of inflammation. This milestone provides an important new treatment option for patients living with this often undiagnosed, chronic, painful and debilitating disease.

C-AXSPAND IS THE FIRST RANDOMIZED, PLACEBO-CONTROLLED STUDY TO FOLLOW ADULT PATIENTS WITH NR-AXSPA OVER 52 WEEKS

PRIMARY ENDPOINT

The proportion of patients achieving major improvement in the Ankylosing Spondylitis Disease Activity Score (ASDAS-MI), **defined as ≥2.0 point decrease from baseline**.[4]

FIRST SECONDARY ENDPOINT

assessment of SpondyloArthritis International Society **40% response criteria** (ASAS40) was evaluated at Weeks 12 and 52.[4]

317 PATIENTS: RANDOMIZED 1:1 TO RECEIVE

- Placebo+**common background medications**
- **CZP+common background medications (CZP 400 mg at Weeks 0, 2 and 4, followed by CZP 200 mg every two weeks)**
- Parallel-group, double-blind design

COMMON BACKGROUND MEDICATIONS INCLUDE

- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Corticosteroids
- Analgesics (opioid and non-opioid)
- Slow-acting anti-rheumatic drugs

RESULTS

The study MET THE PRIMARY ENDPOINT, with significantly more CZP-treated patients demonstrating ASDAS-MI after 52 weeks compared to placebo-treated patients[4]

CZP PATIENTS **47%**

PLACEBO PATIENTS **7%**

The study MET THE FIRST SECONDARY ENDPOINT of ASAS40 at Week 12[4]

CZP PATIENTS **48%**

PLACEBO PATIENTS **11%**

C-AXSPAND indicates that nr-axSpA may not improve on its own and patients do not typically experience relief with existing medications, demonstrating the potential value of new treatment options. The safety profile was consistent with previous clinical trials of CIMZIA. The first 52 weeks of the study have been completed and an additional two years of safety follow-up are ongoing. By week 52 of the study, 60% of placebo-treated patients switched to open-label treatments, compared to 12% of CZP-treated patients demonstrating the need for more effective treatment for the patients with nr-axSpA with inadequate response to NSAIDs.

Please see below for Important Safety Information.

For full prescribing information, please visit UCB-USA.com.

***ABOUT ASDAS-MI**

The ASDAS-MI is a validated, highly discriminatory composite index to assess patient disease activity in axSpA through objective evidence of systemic inflammation and patient-reported outcomes. The ASDAS-MI is a more rigorous measure than the more commonly used ASAS20 or ASAS40.

IMPORTANT SAFETY INFORMATION ABOUT CIMZIA® IN THE US

CONTRAINDICATIONS

CIMZIA is contraindicated in patients with a history of hypersensitivity reaction to certolizumab pegol or to any of the excipients. Reactions have included angioedema, anaphylaxis, serum sickness, and urticaria.

SERIOUS INFECTIONS

Patients treated with CIMZIA are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Discontinue CIMZIA if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before CIMZIA use and during therapy. Initiate treatment for latent TB prior to CIMZIA use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.**

Carefully consider the risks and benefits of treatment with CIMZIA prior to initiating therapy in the following patients: with chronic or recurrent infection; who have been exposed to TB; with a history of opportunistic infection; who resided in or traveled in regions where mycoses are endemic; with underlying conditions that may predispose them to infection. Monitor patients closely for the development of signs and symptoms of infection during and after treatment with CIMZIA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

- Do not start CIMZIA during an active infection, including localized infections.
- Patients older than 65 years, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants may be at greater risk of infection.
- If an infection develops, monitor carefully and initiate appropriate therapy.

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which CIMZIA is a member. CIMZIA is not indicated for use in pediatric patients.

- Consider the risks and benefits of CIMZIA treatment prior to initiating or continuing therapy in a patient with known malignancy.
- In clinical trials, more cases of malignancies were observed among CIMZIA-treated patients compared to control patients.
- In CIMZIA clinical trials, there was an approximately 2-fold higher rate of lymphoma than expected in the general U.S. population. Patients with rheumatoid arthritis, particularly those with highly active disease, are at a higher risk of lymphoma than the general population.
- Malignancies, some fatal, have been reported among children, adolescents, and young adults being treated with TNF blockers. Approximately half of the cases were lymphoma, while the rest were other types of malignancies, including rare types associated with immunosuppression and malignancies not usually seen in this patient population.
- Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers, including CIMZIA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases have occurred in patients with Crohn's disease or ulcerative colitis, and the majority were in adolescent and young adult males. Almost all of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. Carefully assess the risks and benefits of treating with CIMZIA in these patient types.
- Cases of acute and chronic leukemia were reported with TNF blocker use.

HEART FAILURE

- Worsening and new onset congestive heart failure (CHF) has been reported with TNF blockers. Exercise caution and monitor carefully.

HYPERSENSITIVITY

- Angioedema, anaphylactoid reaction, dyspnea, hypotension, rash, serum sickness, and urticaria have been reported following CIMZIA administration. If a serious allergic reaction occurs, stop CIMZIA and institute appropriate therapy. The needle shield inside the removable cap of the CIMZIA prefilled syringe contains a plastic derivative of natural rubber latex which may cause an allergic reaction in individuals sensitive to latex.

HEPATITIS B VIRUS REACTIVATION

- Use of TNF blockers, including CIMZIA, may increase the risk of reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases have been fatal.
- Test patients for HBV infection before initiating treatment with CIMZIA.
- Exercise caution in patients who are carriers of HBV and monitor them before and during CIMZIA treatment.
- Discontinue CIMZIA and begin antiviral therapy in patients who develop HBV reactivation. Exercise caution when resuming CIMZIA after HBV treatment.

NEUROLOGIC REACTIONS

- TNF blockers, including CIMZIA, have been associated with rare cases of new onset or exacerbation of central nervous system and peripheral demyelinating diseases, including multiple sclerosis, seizure disorder, optic neuritis, peripheral neuropathy, and Guillain-Barré syndrome.

HEMATOLOGIC REACTIONS

- Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia has been infrequently reported with CIMZIA.
- Consider stopping CIMZIA if significant hematologic abnormalities occur.

DRUG INTERACTIONS

- Do not use CIMZIA in combination with other biological DMARDS.

AUTOIMMUNITY

- Treatment with CIMZIA may result in the formation of autoantibodies and, rarely, in development of a lupus-like syndrome. Discontinue treatment if symptoms of a lupus-like syndrome develop.

IMMUNIZATIONS

- Patients on CIMZIA should not receive live or live-attenuated vaccines.

ADVERSE REACTIONS

- The most common adverse reactions in CIMZIA clinical trials (≥8%) were: upper respiratory infections (18%), rash (9%), and urinary tract infections (8%).

References:

1. Reveille JD, et al. Prevalence of axial spondylarthritis in the United States: estimates from a cross-sectional survey. *Arthritis Care Res*. 2012;64(6):905-910.
2. United States Census. US and World Population Clock. https://www.census.gov/popclock/. Accessed June 26, 2018.
3. Baraliakos X, Braun J. Non-radiographic axial spondyloarthritis and ankylosing spondylitis: what are the similarities and differences? *RMD Open*. 2015;1 (Suppl 1): e000053. doi: 10.1136/rmdopen-2015-000053.
4. CIMZIA U.S. Prescribing Information. Available at https://www.ucb-usa.com/_up/ucb_usa_com_kopie/documents/Cimzia_PI.pdf. Accessed March 2019.

March 2019

US-P-CZ-nraxp-1900001