Annual European Congress of Rheumatology (EULAR) 2017

Madrid, Spain, 14-17 June 2017

CONTINUING ANTI-TNF TREATMENT WITH CZP FOR RA DURING PREGNANCY: NO OR NEGLIGIBLE PLACENTAL TRANSFER

Highly sensitive assay confirms no or negligible placental transfer of certolizumab pegol in women with rheumatoid arthritis

Madrid, Spain, 14 June 2017: The results of a pharmacokinetic study presented today at the Annual European Congress of Rheumatology (EULAR) 2017 showed no or negligible placental transfer of the anti-TNF drug certolizumab pegol (CZP) from mothers to infants during pregnancy.[1]

These results suggest a developing baby is not being exposed to a meaningful concentration of CZP in the uterus, which in turn suggests that the continuation of this specific anti-TNF treatment throughout pregnancy might be safe.[1]

There is a need for effective and safe treatment during pregnancy in women affected by chronic active inflammatory diseases, such as rheumatoid arthritis. Adequate disease control is crucial to ensure the best foetal and maternal health, and reduce adverse pregnancy outcomes.[2]

“For rheumatologists, the management of RA patients wishing to become pregnant involves balancing the need to withdraw certain drugs, while at the same time keeping disease activity under control. Anti-TNFs are an effective treatment option in RA and spondyloarthritis but, because most cross the placenta, they are often stopped during pregnancy,” said lead author Professor Xavier Mariette from University Hospitals of Paris-Sud, France.

“The results of this study support the continuation of CZP treatment during pregnancy when considered necessary to control disease activity. We therefore believe that these data will have a significant impact on clinical practice by providing robust information for women who need treatment to keep their disease under control during pregnancy. “However, there will of course still be the risk of the typical adverse effects associated with an anti-TNF treatment, such as infection or an immune reaction, which could affect the outcome of the pregnancy,” he cautioned.

Using a highly sensitive assay, to accurately measure the potential level of placental transfer of CZP from mothers to infants, CZP levels were below 0.032 µg / mL, the Lower Limit of Quantification (LLOQ)* of this assay, in 13 out of 14 infant blood samples at birth. Just 1 infant had a minimal CZP level of 0.042 µg / mL at birth (infant / mother plasma ratio: 0.09%); none of the infants had quantifiable levels at Weeks 4 and 8.

From the umbilical cord blood samples taken at birth, only 3/15 had quantifiable CZP levels (maximum: 0.048 µg / mL). No anti-CZP antibodies were detected in mothers, umbilical cords, or infants. The infants of CZP-exposed mothers had a safety profile consistent with that of unexposed similar-age infants.

Active transfer of an anti-TNF drug across the placenta involves binding of its Fc-region to the neonatal Fc receptor, which in turn may result in adverse foetal or neonatal effects. In contrast to other anti-TNFs, CZP lacks this Fc-region. Ex-vivo studies using a human placental transfer model had previously shown that this unique structure of CZP limits its transfer through the placenta to the foetus.[3]

CRIB was a pharmacokinetic study of pregnant women (≥30 weeks gestation) receiving a maintenance dose of CZP for an approved indication. The last dose of CZP was within 35 days of delivery. Of 21 CZP-treated pregnant women screened; 16 entered the study. Blood samples were collected from the mothers, umbilical cords, and infants at delivery, and infants again at 4 and 8 weeks post-delivery.

CZP concentration was measured with a sensitive, CZP-specific electrochemiluminescence immunoassay, with an LLOQ of 0.032 µg / mL, which is 10-times lower (more sensitive) than the assay used in prior CZP pharmacokinetic studies.

Maternal CZP plasma levels at delivery were within the expected therapeutic range (median [range]: 24.4 [5.0–49.4] µg / mL).

Abstract Number: OP0017

-ENDS-

* LLOQ represents the lowest concentration of CZP that can be detected within the validated quantitative range of the assay

NOTES TO EDITORS:

For further information on this study, or to request an interview with the study lead, please do not hesitate to contact the EULAR congress Press Office in the Goya Room at the IFEMA, Madrid during EULAR 2017 or on:

Email: eularpressoffice@cohnwolfe.com
Onsite tel: +44 (0)7786 171 476 / +34 91722 3115
Twitter: @EULAR_Press
Youtube: Eular Press Office

About Rheumatic and Musculoskeletal Diseases

Rheumatic and musculoskeletal diseases (RMDs) are a diverse group of diseases that commonly affect the joints, but can also affect the muscles, other tissues and internal organs. There are more than 200 different RMDs, affecting both children and adults. They are usually caused by problems of the immune system, inflammation, infections or gradual deterioration of joints, muscle and bones. Many of these diseases are long term and worsen over time. They are typically painful and limit function. In severe cases, RMDs can result in significant disability, having a major impact on both quality of life and life expectancy.

About 'Don't Delay, Connect Today!'

'Don't Delay, Connect Today!' is a EULAR initiative that unites the voices of its three pillars, patient (PARE) organisations, scientific member societies and health professional associations - as well as its international network - with the goal of highlighting the importance of early diagnosis and access to treatment. In Europe alone, over 120 million people are currently living with a rheumatic disease (RMD), with many cases undetected. The 'Don't Delay, Connect Today' campaign aims to highlight that early diagnosis of RMDs and access to treatment can prevent further damage, and also reduce the burden on individual life and society as a whole.

About EULAR

The European League Against Rheumatism (EULAR) is an umbrella organisation which represents scientific societies, health professional associations and organisations for people with rheumatic and musculoskeletal diseases throughout Europe. EULAR aims to reduce the burden of rheumatic and musculoskeletal diseases on individuals and society and to improve the treatment, prevention and rehabilitation of rheumatic and musculoskeletal diseases. To this end, EULAR fosters excellence in education and research in the field of rheumatology. It promotes the translation of research advances into daily care and fights for the recognition of the needs of people with musculoskeletal diseases by the governing bodies in Europe through advocacy action.

To find out more about the activities of EULAR, visit: www.eular.org

References

[1] Mariette X, Flynn A, Förger F, *et al*. Lack of placental transfer of certolizumab pegol during pregnancy: results from CRIB, a prospective, postmarketing, multicenter, pharmacokinetic study. EULAR 2017; Madrid: Abstract OP0017
[2] de Man YA, Hazes JM, van der Heide H, *et al*. Association of higher rheumatoid arthritis disease activity during pregnancy with lower birth weight: results of a national prospective study. *Arthritis Rheum*. 2009; 6(11): 3196-206
[3] Porter C, Armstrong-Fisher S, Kopotsha T, *et al*. Certolizumab pegol does not bind the neonatal Fc receptor (FcRn): Consequences for FcRn-mediated in vitro transcytosis and ex vivo human placental transfer. *J Reprod Immunol*. 2016; 116: 7-12