MedicalXpress

Continuing anti-TNF treatment with CZP for RA during pregnancy: No or negligible placental transfer

June 15 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.

These results suggest developing babies are 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.

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.

"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.

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 four and eight 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).

Provided by European League Against Rheumatism