Reported congenital malformations after exposure to non-tumour necrosis factor inhibitors: a retrospective comparative study in EudraVigilance

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Abstract

Aim To evaluate the number and nature of reported congenital malformations (CMs) after intrauterine exposure to non-tumour necrosis factor inhibitors (non-TNFis) compared to certolizumab pegol (CZP) Material and methods A retrospective comparative study was conducted in the EudraVigilance (EV) database. EV is a pharmacovigilance database, which can be used for detecting safety signals and generating hypotheses on possible relations between drugs and adverse events. A supposedly safe biologic (CZP) was considered as the reference group. Pregnancy-reports of non-TNFis and CZP were extracted. Odds ratios (ORs) for CMs were calculated for each non-TNFi, versus CZP (quantitative assessment). Then, CM patterns were compared to CZP in consultation with a clinical geneticist (qualitative assessment). Results ORs were not statistically significant except for belimumab and vedolizumab (similar in magnitude). Although qualitative analyses did not show any specific patterns for belimumab but three cases of corpus callosum agenesis (CCA) were identified for vedolizumab (versus null in CZP and other investigated non-TNFis). Two of the CCA cases were associated with other neurological CMs (one cerebral ventriculomegaly with microcephaly and one polymicrogyria). This may indicate that these CCAs are related to undiagnosed genetic alterations or are associated with the underlying maternal disease, although a definite relationship with vedolizumab exposure cannot be ruled out. Conclusion No special safety signal was identified regarding the occurrence of CMs after exposure to non-TNFis, except for vedolizumab. Based on available information, no firm conclusions can be made regarding observed CCAs in the vedolizumab group (it warrants further research)

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