Live attenuated vaccination after *in utero* exposure to TNF inhibitors: real-world experience from a tertiary centre

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Dear Editor,

The management of live attenuated vaccines (LAVs) in infants exposed *in utero* to TNF inhibitors (TNFi) has evolved considerably in recent years. Earlier European recommendations advised avoiding all LAVs during the first 6 months of life following prenatal exposure to biologic agents. However, the updated 2024 EULAR recommendations now support routine rotavirus vaccination after exposure to any TNFi. Furthermore, they state that certolizumab pegol does not require infant vaccination schedule modifications due to its minimal placental transfer[1]. Conversely, BCG vaccination remains a concern after exposure to monoclonal TNFi with significant transplacental transfer during the second half of pregnancy, such as adalimumab, infliximab and golimumab[1,2]. Preconception counselling may facilitate treatment optimisation before and during pregnancy in women with inflammatory rheumatic diseases, contributing to improved maternal and fetal outcomes[3].

We conducted a short exploratory study to describe the real-world outcomes of infants exposed to TNFi during pregnancy who received LAVs within the first 6 months of life in routine clinical practice. We retrospectively reviewed children born between 2021 and 2024 to mothers with immune-mediated rheumatic diseases treated with TNFi during pregnancy at our tertiary centre. Vaccination data were collected according to the Portuguese National Immunization Programme, and medical records were reviewed for vaccine-related adverse events and infectious complications.

Of the twenty-nine infants exposed to biologic agents *in utero*, 18 (62%) received at least one live attenuated vaccine before 6 months of age. Among these 18 infants, 12 (67%) were exposed to certolizumab and 6 (33%) to adalimumab. Certolizumab pegol was continued throughout pregnancy in all exposed pregnancies, whereas adalimumab was discontinued at a median gestational age of 22 weeks (range 12–28 weeks). Rotavirus vaccination was administered to 17 infants, and 5 received BCG vaccination (including 4 who received both). Of the 5 infants who received BCG, 3 were exposed to certolizumab and 2 to adalimumab (maternal adalimumab was discontinued at 27 and 28 weeks' gestation, respectively). Notably, the single infant exposed to etanercept received BCG vaccination at 8 months of age. No vaccine-related adverse events, serious infections or hospitalisations were observed.

Our findings are consistent with the recently updated EULAR recommendations, which support routine rotavirus vaccination after exposure to any TNFi and unrestricted vaccination schedules after certolizumab exposure[1]. The most clinically relevant aspect of our cohort concerns the two infants exposed to adalimumab until late second trimester who subsequently received BCG vaccination without complications. This remains a grey area in clinical practice because current EULAR guidance recommends delaying BCG vaccination for 6 months in infants exposed to TNFi with relevant transplacental transfer after gestational week 20, largely based on historical, rare reports of disseminated fatal BCG infection associated mainly with infliximab exposure[1-4].

Although limited by the retrospective design and small sample size, our data provides additional reassuring real-world evidence supporting a nuanced, agent-specific approach to LAV administration after *in utero* TNFi exposure. National registries such as Reuma.pt could facilitate the prospective collection of data on maternal treatment exposure, pregnancy outcomes and the safety of infant vaccination[5]. Larger prospective studies are needed to better quantify the safety margins of BCG vaccination following late pregnancy exposure to monoclonal TNFi agents.

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