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**Psoriasis and pregnancy outcomes in biological therapies: a real-life, multi-center experience.**

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Sir,

We performed a retrospective study including 307 psoriatic women of childbearing age treated with biologics in 5 Dermatologic Center of University Hospitals (Modena, Bologna, Reggio Emilia, Parma, Ferrara) from 2004 to 2019.

We defined the pregnancy exposed to biological drugs if the woman had at least one administration during pregnancy: we identified 14 pregnancies in 12 women.

Patients has been treated with a biological drug since 35 ± 24 months at time of conception. None of them experienced AE during treatment.

BMI of pregnant women was 25.85 ± 6.2, duration of disease was 8 ± 5.0 years (drug and therapy duration are specified in Tab.1)

All patients discontinued the therapy when they discovered to be pregnant. Only a woman, after discontinuation of treatment with infliximab biosimilar, because of a very severe form of psoriasis and psoriatic arthritis, resumed the therapy and started certolizumab pegol, continued during all pregnancy.

In 8 women psoriasis worsened during pregnancy.

Ten healthy children were delivered, 1 pregnancy is actually in progress (6 month), 2 women chose elective abortion and 1 woman had a spontaneous abortion (tab 1).

Due to severe clinical condition, 1 woman breastfeed her child during the therapy with certolizumab pegol. The other women had no problem in breastfeeding and resumed the biological therapy after the end of this period.

In 9 cases women had spontaneous delivery, only 1 had cesarean delivery, but all children had a normal weight at birth. No congenital abnormalities and no cognitive disorders or other diseases were observed in children, including psoriasis.

Our case series describes 10 healthy children with a completely normal growth.

Data reported show that conception during biologics therapy is safe; if psoriasis is well controlled, it is recommended to suspend the therapy. In case of flare, it is preferable to use certolizumab pegol.

During pregnancy, the maternal immune system shows a shifting from the Th1 to the Th2 direction, allowing the tolerance to the fetus, moreover the stimulation of immunity mediated by B lymphocytes and the inhibition of immunity mediated by T lymphocytes cause a greater secretion of Th2 cytokines. [1]

Also, Th17 and T-reg lymphocytes show a change in their balance during pregnancy. [2]

During the first trimester of gestation, the maternal-fetal transport of IgG is poor due to their dimension > 100 kDa. Infliximab and adalimumab are IgG1 monoclonal. They are actively

transported from mother to the fetus trough placenta, via Fc receptor that appear after week 14 of gestation.[3] Etanercept shows considerably less transport than other anti-TNFα because of its different size and its shorter half-life.[4] Infliximab and adalimumab may preferentially be stopped before 20 weeks, and etanercept before week 30–32 of pregnancy.[5] Certolizumab pegol is an IgG1 antibody without Fc portion, and it does not cross the placental barrier nor the breast milk. Regarding ustekinumab, an IgG1 antibodies against IL12/23, there are few case series without AE.[6]

Secukinumab is an anti IL17 antibody and an IgG1 molecule that crosses placenta from the third trimester. Data available regarding pregnancy occurred in mother treated with secukinumab provide reassurance in cases of conception in mother exposed, because of there is no evidence of adverse pregnancy outcomes.[7] No data are available for ixekizumab in pregnancy.

A systematic review describes how the adverse pregnancy outcomes were statistically significant in women affected by psoriasis.[8]

Only few studies followed-up for a long period the children born from mother treated with biological therapy during pregnancy.[9]

Italian guidelines suggest using biologics only in high-need situations and to stop the therapy with infliximab and adalimumab in the last trimester.[10]

Further larger prospective studies are warranted for women affected by psoriasis receiving biological therapy.

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**Tab. 1:** the table shows the age of woman at pregnancy, drug taken at time of conception, the value of PASI before, during and after pregnancy, last week of administration, pregnancies outcomes. PASI T1: PASI at last administration of biologic; PASI T2: PASI at the end of pregnancy; PASI T3: PASI after resume of biological therapy.

| Patient | Age at pregnancy (years) | Biological treatment | PASI (baseline) | PASI T1 | Last drug administration (week of gestation) | Treatment during pregnancy | PASI T2 | Psoriasis worsening during pregnancy | Biologic resumed after pregnancy (months) | PASI T3 | Age of child | Child growth and physiological development |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 32 | secukinumab | 12 | 0 | 4 | none | 5 | yes | not yet | 2 | 5 years | normal |
| 2 | 30 | infliximab | 8 | 2 | 3 | none | 8 | yes | yes | 4 | 4 years | normal |
| 3 | 27 | secukinumab | 12 | 0 | 5 | none | 6 | yes | 7 | 2 | 2 years | normal |
| 4 | 16 | infliximab | 14.5 | 5 | 6 | / | / | / | 1 | / | / | elective abortion |
| 5 | 31 | infliximab | 10.5 | 3 | 6 | none | 10 | yes | 2 | 0 | 12 years | normal |
| 5 | 37 | ustekinumab | 10.5 | 1 | 11 | none | 11 | yes | 1 | 0 | 5 years | normal |
| 6 | 32 | infliximab (CT-P13) | 16 | 22 | 6 | switch to certolizumab pegol | 5 | yes (improved after switch to certolizumab pegol) | never interrupted | never interrupted | 1 years | normal |
| 7 | 27 | etanercept | 13.5 | 3 | 6 | none | 3 | no | therapy not resumed | therapy not resumed | 10 years | normal |
| 8 | 30 | ustekinumab | 12 | 0 | 5 | none | 4 | yes | therapy not resumed | therapy not resumed | 1 years | normal |
| 9 | 36 | adalimumab | 14 | 1 | 5 | none | 6 | yes | 4 | 8 | 2 months | normal |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 | 26 | ustekinumab | 10 | 0 | 8 | none | 12 | yes | 4 | 10 | 2 years | normal |
| 10 | 28 | ustekinumab | 10 | 0 | 6 | / | / | / | 1 | / | / | spontaneous abortion |
| 11 | 35 | ustekinumab | 12 | 0 | 6 | / | / | / | 1 | / | / | elective abortion |
| 12 | 30 | ustekinumab | 11 | 2 | 4 | none | in progress | no | / | / | / | / |

PASI T1: PASI at last administration of biologic; PASI T2: PASI at the end of pregnancy; PASI T3: PASI after biological retrieve