

Supplementary Table S7. Follow up of children\* exposed to immunosuppressive medications in 2<sup>nd</sup> and/or 3<sup>rd</sup> trimester of pregnancy,

SLR period 2006-2015

Maternal medication in pregnancy	Type of publication in numbers	References	Number of children	Mean follow up time and range: years (yrs)	Number of children vaccinated <sup>1</sup> / children with normal vaccination response	Rate of serious infection <sup>2</sup> in 1 <sup>st</sup> year of life compared to non-exposed children	Physical development: Number of children normal/impaired	Cognitive development: Number of children normal /impaired	Comments
<b>Infliximab</b>	<b>2 cohorts (2 abstracts)</b> 2 case-controls 7 case-reports	[1-11]	269	1.1 (4 mo.-3yrs)	49/48	Not increased	57/0	22/0	1 child died after BCG vaccination at 3 months of age
<b>Adalimumab</b>	<b>2 cohorts (2 abstracts)</b> 2 case-controls 3 case-reports	[1,4,7-9,12,13]	136	1.2 (5 mo.-2.2 yrs)	3/3	Not increased	15/1	3/0	
<b>Certolizumab</b>	<b>2 cohorts (2 abstracts)</b>	[7,8]	99	1.0	Not reported	Not increased	10/0	Not studied	
<b>Rituximab</b>	9 case-reports	[1,14-21]	8	1.4 (6 mo.-4.5yrs)	5/5	Not reported	8/0	2/0	Transient B cell depletion in children exposed in 2 <sup>nd</sup> and 3 <sup>rd</sup> trimester
<b>Ciclosporin</b>	<b>1 cohort</b>	[22]	39	Mean not reported. (7 mo.-3 yrs)	Not reported	Not reported	Not reported	39/0	
<b>Azathioprine</b>	<b>1 cohort</b> 2 case-controls	[23-25]	58	4.5 yrs (6 mo.-9.2 yrs)	45/45	Not increased	45/0	58/7	
<b>Dexamethason</b>	<b>2 cohorts</b>	[26,27]	27	6 (1.8-11 yrs)	Not reported	Not reported	11/0	27/0	

\*Included only if total number of children exposed to a medication > 5

<sup>1</sup>According to National vaccination programs, including measles, mumps, rubella, pertussis, tetanus, diphtheria, hepatitis B, poliomyelitis. In some countries live vaccines BCG vaccine is given at 3 months and rotavirus at 2,4, and 6 months of age

<sup>2</sup>Serious infection defined as requiring intravenous treatment or hospitalization

## REFERENCES

1. Bortlik, M, Duricova, D, Machkova, N, *et al.* Impact of anti-tumor necrosis factor alpha antibodies administered to pregnant women with inflammatory bowel disease on long-term outcome of exposed children. *Inflamm Bowel Dis* 2014;20:495-501.
2. Cheent, K, Nolan, J, Shariq, S, *et al.* Case Report: Fatal case of disseminated BCG infection in an infant born to a mother taking infliximab for Crohn's Disease. *Journal of Crohn's and Colitis* 2010;4:603-05.
3. Correia, LM, Bonilha, DQ, Ramos, JD, *et al.* Inflammatory bowel disease and pregnancy: Report of two cases treated with infliximab and a review of the literature. *Eur J Gastroenterol Hepatol* 2010;22:1260-64.
4. Fritzsche, J, Pilch, A, Mury, D, *et al.* Infliximab and adalimumab use during breastfeeding. *J Clin Gastroenterol* 2012;46:718-9.
5. Guiddir, T, Fremond, ML, Triki, TB, *et al.* Anti-TNF-alpha therapy may cause neonatal neutropenia. *Pediatrics* 2014;134:e1189-93.
6. Kane, S, Ford, J, Cohen, R, *et al.* Absence of infliximab in infants and breast milk from nursing mothers receiving therapy for Crohn's disease before and after delivery. *J Clin Gastroenterol* 2009;43:613-6.
7. Mahadevan, U, Martin, CF, Chambers, C, *et al.* Achievement of developmental milestones among offspring of women with inflammatory bowel disease: The piano registry. [abstract]. *Gastroenterology* 2014;1(Suppl 5):S1.
8. Mahadevan, U, Martin, CF, Dubinsky, M, *et al.* Exposure to anti-TNFalpha therapy in the third trimester of pregnancy is not associated with increased adverse outcomes: Results from the piano registry. [abstract]. *Gastroenterology* 2014;1(Suppl 5):S170.
9. Seirafi, M, de Vroey, B, Amiot, A, *et al.* Factors associated with pregnancy outcome in anti-TNF treated women with inflammatory bowel disease. *Aliment Pharmacol Ther* 2014;40:363-73.
10. Steenholdt, C, Al-Khalaf, M, Ainsworth, MA, *et al.* Therapeutic infliximab drug level in a child born to a woman with ulcerative colitis treated until gestation week 31. *Journal of Crohn's and Colitis* 2012;6:358-61.
11. Stengel, JZ, Arnold, HL. Is infliximab safe to use while breastfeeding? *World J Gastroenterol* 2008;14:3085-87.
12. Coburn, LA, Wise, PE, Schwartz, DA. The successful use of adalimumab to treat active Crohn's disease of an ileoanal pouch during pregnancy. *Dig Dis Sci* 2006;51:2045-7.
13. Jurgens, M, Brand, S, Filik, L, *et al.* Safety of adalimumab in Crohn's disease during pregnancy: case report and review of the literature. *Inflamm Bowel Dis* 2010;16:1634-6.

14. Decker, M, Rothermundt, C, Hollander, G, *et al.* Rituximab plus CHOP for treatment of diffuse large B-cell lymphoma during second trimester of pregnancy. *Lancet Oncol* 2006;7:693-4.
15. Friedrichs, B, Tiemann, M, Salwender, H, *et al.* The effects of rituximab treatment during pregnancy on a neonate. *Haematologica* 2006;91:1426-7.
16. Klink, DT, van Elburg, RM, Schreurs, MW, *et al.* Rituximab administration in third trimester of pregnancy suppresses neonatal B-cell development. *Clin Dev Immunol* 2008;2008:271363.
17. Martinez-Martinez, MU, Baranda-Candido, L, Gonzalez-Amaro, R, *et al.* Modified neonatal B-cell repertoire as a consequence of rituximab administration to a pregnant woman. *Rheumatology (Oxford)* 2013;52:405-6.
18. Ojeda-Uribe, M, Afif, N, Dahan, E, *et al.* Exposure to abatacept or rituximab in the first trimester of pregnancy in three women with autoimmune diseases. *Clin Rheumatol* 2013;32:695-700.
19. Pellkofer, HL, Suessmair, C, Schulze, A, *et al.* Course of neuromyelitis optica during inadvertent pregnancy in a patient treated with rituximab. *Mult Scler* 2009;15:1006-8.
20. Ponte, P, Lopes, MJ. Apparent safe use of single dose rituximab for recalcitrant atopic dermatitis in the first trimester of a twin pregnancy. *J Am Acad Dermatol* 2010;63:355-6.
21. Ton, E, Tekstra, J, Hellmann, PM, *et al.* Safety of rituximab therapy during twins' pregnancy. *Rheumatology (Oxford)* 2011;50:806-8.
22. Nulman, I, Sgro, M, Barrera, M, *et al.* Long-term neurodevelopment of children exposed in utero to ciclosporin after maternal renal transplant. *Paediatr Drugs* 2010;12:113-22.
23. Angelberger, S, Reinisch, W, Messerschmidt, A, *et al.* Long-term follow-up of babies exposed to azathioprine in utero and via breastfeeding. *J Crohns Colitis* 2011;5:95-100.
24. de Meij, TG, Jharap, B, Kneepkens, CM, *et al.* Long-term follow-up of children exposed intrauterine to maternal thiopurine therapy during pregnancy in females with inflammatory bowel disease. *Aliment Pharmacol Ther* 2013;38:38-43.
25. Marder, W, Ganser, MA, Romero, V, *et al.* In utero azathioprine exposure and increased utilization of special educational services in children born to mothers with systemic lupus erythematosus. *Arthritis Care Res (Hoboken)* 2013;65:759-66.
26. Brucato, A, Astori, MG, Cimaz, R, *et al.* Normal neuropsychological development in children with congenital complete heart block who may or may not be exposed to high-dose dexamethasone in utero. *Ann Rheum Dis* 2006;65:1422-6.
27. Kelly, EN, Sananes, R, Chiu-Man, C, *et al.* Prenatal anti-Ro antibody exposure, congenital complete atrioventricular heart block, and high-dose steroid therapy: impact on neurocognitive outcome in school-age children. *Arthritis Rheumatol* 2014;66:2290-6.