**Table 2. Study characteristics and outcomes for the outcome measure immunogenicity**

| First author, year | Vaccine | Patients | Medication used[a] | Follow-up | Result | Effect of medication on results |
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| **DPT** | | | | | | |
| Brunner, 2020 | DT | IG: n=29 JIA patients<br>CG: n=17 JIA patients not vaccinated | 29 ABT, 22 MTX, 3 LD-GC | 24 months | 100% SP tetanus, 90% SP diphtheria 2 m post vaccine. | All patients had protective antibody levels to tetanus after ≥2 months of abatacept treatment and 26/29 (89.7%) patients had protective antibody levels to diphtheria. |
| Ingelman-Sundberg, 2016[b] | DTP | IG: n=50 in total, 46 JIA patients<br>CG: n=31 HC | 10 NSAID, 8 MTX, 32 MTX+TNFi | Not applicable | IgG-TT reduced in MTX+TNFi group. | Patients treated with any DMARD had lower tetanus serum IgG compared to healthy controls and NSAID-treated patients. |
| Heijstek, 2012[b] | DT | IG: n=400 JIA patients<br>CG: n=2176 HC | 93 MTX, 8 TNFi, 28 GC 10 mg/day | Not applicable | Reduced SP and GMT for tetanus. | Methotrexate use and glucocorticosteroid use did not have any effect on pathogen-specific GMT or seroprotection rates. |
| **HPV** | | | | | | |
| Heijstek, 2014 | HPV-b(Cervarix vaccine) | IG: n=68 JIA patients<br>CG: n=55 HC | 24 MTX, 9 TNFi, 6 other DMARD | 12 months | Equal SC and GMT in JIA and HC. | Methotrexate did not affect HPV16 or HPV18 antibodies. No difference in antibody concentrations in patient with anti-TNF, but the sample size was too small to draw definite conclusions. |
| Esposito, 2014 | HPV-b (Cervarix vaccine) | IG: n=21 JIA patients<br>CG: n=55 HC | 10 NSAID, 5 MTX, 6 TNFi | 7 months | 100% SC. Reduced titers 1 month post 3th vaccine in JIA vs HC. No effect of medication. | No effect on immune response of NSAIDs, methotrexate, and etanercept. |
| **HBV/HAV** | | | | | | |
| Çakmak, 2022 | Hepatitis B | IG: n=262 JIA patients<br>CG: n=274 HC | Not reported | Not applicable | Anti-Hbs antibody:<br>JIA patients: 59.1%<br>Control: 72.9%, p=0.002.<br><br>HbsAG positivity: N=0 in both groups | Four patients were negative for anti-Hbs and were receiving DMARDs (methotrexate=1, sulfasalazine=1) and biological agents (etanercept=1, adalimumab=1) |

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| | | | | | Median anti-HBs titers<br>JIA patients: 14 (range 0-1000) IU/L<br>Control: 43.3 (range 0-1000) IU/L, p=0.01<br><br>Anti-nuclear antibody positivity<br>JIA patients: 27.1%. Among these, anti-Hbs antibody seropositivity rate was 69.1% (n=49) while this rate was 56.2% (n=104) in the remaining ANA negative cases (n=185) (p=0.04). | |
| Erguven, 2010 | Hepatitis A | IG: n=47 JIA patients<br>CG: n=67 HC | 4 anti-TNF, 5 NSAIDs, 29 MTX, 12 prednisolone, 19 salazopyrine, 11 MTX-prednisolone | 2 months after second dose | Positive anti-HAV IgG (n (%)):<br>JIA: 43 (91.5%)<br>Control: 67 (100%) | Four patients (3.5%) had negative titers, these were all male patients with active systemic JIA and using anti-TNF. |
| **MenC** | | | | | | |
| Stoof, 2014 | MenC conjugate (NeisVac-C) vaccine | IG: n=127 JIA patients<br>CG: n=1527 HC | 42 MTX, 66 pre-MTX, 7 NA bDMARD, 53 pre-, 4 GC, 10 pre-GC | Not applicable | Equal SP 4 years post vaccine JIA vs HC. MenC-IgG decrease over time. | Starting methotrexate treatment did not affect the decline of MenC-specific IgG concentrations. However, starting biological treatment induced a trend towards accelerated decay in MenC-specific antibodies, with a faster predicted decay rate in 92.6% of patients. |
| **PCV/PPV** | | | | | | |
| Aikawa, 2015 | PPV23 | IG: n=17 JIA patients pre-etanercept<br>CG: n=10 JIA patients using MTX | IG: MTX HD 2 weeks before ETA<br>CG: 10 LD MTX | 12 months | Equal SC at 2 (53 vs. 30%) and 12 months (36 vs. 40%) in JIA with and without TNFi. | Adequate vaccine response was similar between patients with anti-TNF and without anti-TNF. |
| **Influenza** | | | | | | |
| Aikawa, 2012 | H1N1 | IG: n=237 in total, 93 JIA patients<br>CG: n=91 HC | 90 GC, MTX 74, 43 AZA, 23 CYC, 13 MMF, 6 LEF, 3 Cy | 21 days | Subgroup analysis: N=93<br>Before immunization, % | Not reported |

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| | | | | | (95%CI) 20.4 (12.2–28.6) After immunization, % (95%CI) 88.2 (81.6–94.8) Seroconversation rate, % (95%CI) 82.8 (75.1–90.5) (p<0.05) | |
| Aikawa, 2013 | H1N1 | IG: n=95 JIA patients<br>CG: n=91 HC | 16 TNFi, 63 DMARD(s) | 3 weeks | Equal SP and GMT.<br>Reduced SC in pts, irresp.of TNF/MTX | No difference in immunogenicity between patients with and without immunosuppressive drugs, and with and without MTX and with and without TNF blockers. |
| Carvalho, 2013 | Influenza (H1N1, H3N2, B/Florida) | IG: n=44 JIA patients<br>CG: n=10 healthy controls | IS, DMARDs, or anti-TNFα ranging from 55.7% to 70% | 180 days | Equal SP & SC in JIA and HC. TNFi lower SP and SC for H1N1 but SP for h3N2 &B/Florida was normal (N = not reported). | Patients on anti-TNFα drugs presented lower seroconversion (p = 0.03) and seroprotection (60%) responses to H1N1 strain, but the seroprotection above the cut-off levels to the other strains: H3N2 (100%) and B/Florida (80%). |
| Toplak, 2012 | Influenza (H1N1, H3N2, Influenza B) | IG: n=31 JIA patients<br>CG: n=14 HC and n=31 not vaccinated JIA patients | 18 NSAID, 2 DMARD, 7 DMARD + GC, 4 TNF | 6 months | Equal SP pts and HC | GMTs for all vaccine viruses were significantly elevated 1 months after vaccination in patients using DMARDs. The group of 4 children with anti-TNF treatment did not respond significantly to any of the vaccine viruses.<br><br>After 6 months, all 4 children with anti-TNF had protective titers but did not respond significantly as a group.<br><br>Compared to the GMTs before vaccination, the values after 6 months were still significantly |

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| | | | | | | elevated for the Influenza B vaccine virus in both study groups including children treated with DMARDs, but not<br>in a subgroup of 4 children also receiving anti-TNF-α therapy. |
| Woerner, 2011 | Influenza (H1N1, H3N2, H1N1 MDCK cell adapted, H3N2 MDCK adapted, and influenza B MDCK adapted) | IG: n=34 in total, of which n=25 JIA patients<br>CG: n=16 HC | 18 MTX, 10 TNFi, 8 MTX+TNFi | 4-8 weeks after single dose or after the second of two doses. | Equal SP pts vs. HC, reduced GMT. | Subgroup analysis for immunosuppressive medication (MTX vs. TNFα inhibitors vs. MTX and TNFα inihibitors) showed no significant differences between the treatment groups in seroprotection, seroconversion or post-vaccination GMTs.<br><br>Treatment with TNFα inhibitors showed a trend toward a lower relative change between pre-vaccination and post-vaccination titers in comparison to treatment with MTX (p 0.06 resp. 0.66). |
| Dell'Era, 2012 | Influenza (M59 adjuvanted, with H1N1, H3N2, and influenza B) | IG: n=60 JIA patients<br>CG: n=30 HC | 30 DMARD vs. 30 aTNF (Etanercept) | 3 months | Equal SP & SC in JIA and HC. TNFi lower H1N1-GMT & more rapid decline in H3N2-GMT | All, except in one, 100% seroconversation and seroprotection in JIA patients treated with etanercept and DMARDs after follow-up.<br><br>There was no difference in the B antigen immunogenicity endpoints between the DMARD-treated JIA patients and HC |
| Camacho-Lovillo, 2017 | Influenza (H1N1, H3N2, B) | IG: n=25 JIA patients<br>CG: n=6 healthy siblings | 15 anti-TNFα (11 etanercept and 4 adalimumab), | 1 year | SP after 4–8 weeks: 97.8% H1N1, 95.6% H3N2, 91.1% B. | No differences were observed in the short-time and long-time (after 1 year) antibody response |

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| | | | 4 anti-IL-1R (anakinra), 6 anti-IL-6R (tocilizumab) | | | and postvaccination seroprotection, GMT, and seroconversion rates to vaccination based on treatment.<br>No difference in seroprotection or antibody titers in patients with biological treatment and concomitant systemic steroids (n=2), compared with patients with biological treatment with no steroids |
| **MMR (live-attenuated vaccine)** | | | | | | |
| Heijstek, 2013 | MMR (MMR-NVI and M-M-RVAXPRO) | IG: n=68 vaccinated JIA patients<br>CG: n=69 unvaccinated JIA patients | 60 MTX, 15 biologicals, 3 GC | 12 months | SP and GMT higher in vacc. vs. controls | Revaccinated patients taking biologics at the time of revaccination were seroprotected.<br><br>One patient was taking methotrexate, 9.3 mg/m2 per week, at the time of vaccination and showed a small increase in mumps-specific antibodies at 3 months, but antibodies dropped below seroprotection levels at 12 months. Another patient using methotrexate was started just after vaccination, followed by etanercept at 9 months. This patient was seronegative for measles, mumps, and rubella at baseline and failed to produce a serologic response to mumps, whereas measles-specific antibodies increased 17-fold and rubella-specific antibodies 179-fold. |
| Heijstek, 2012[b] | MMR | IG: n=400 JIA patients<br>CG: n=2176 HC | 93 MTX, 8 TNFi, 28 GC 10 mg/day | Not applicable | Reduced SP and GMT for mumps, rubella, but not measles. | Methotrexate use and glucocorticosteroid use did not have any |

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| | | | | | | effect on pathogen-specific GMT or seroprotection. |
| Ingelman-Sundberg, 2016[b] | MMR | IG: n=50 in total, 46 JIA patients<br>CG: n=31 HC | 10 NSAID, 8 MTX, 32 MTX+TNFi | Not applicable | Equal IgG titers MV and RV, IgG-TT reduced in MTX+iTNF group. Vacc.-spec. mem. B cells preserved in patients with booster | No difference in measles and rubella titers rates between patients using DMARDs and patients using NSAIDs and HC. |
| **VZV (live-attenuated vaccine)** | | | | | | |
| Groot, 2017 | VZV (Oka strain, Varilrix as second dose) | IG: n=49 in total, 39 JIA patients<br>CG: n=18 HC | 49 MTX, 16 GCs, 3 biologics | 4-6 weeks after vaccination | Equal GMT in pts & HC, more VZV-spec. T cells. | Type of immunosuppressive drug did not have a significant effect on humoral response (p = 0.203) but patients who used biologics at time of vaccination of the first vaccination (n = 3) did not show an increase in antibody concentrations after vaccination. Of the two patients who used biologics and received two vaccines, one (using etanercept) responded to the second vaccine and one (using abatacept) did not. |

**AB, antibody; ABT, abatacept; ADA, adalimumab; AE, ad verse event;ANR, Anakinra; AZA, azathioprine; bDMARD, biological disease modifying anti-rheumatic drugs;CAM, canakinumab; CG, control group; Cy, cyclophosphamide; CYC, cyclosporine; DTP, diphtheria tetanus pertussis; ETN, etanercept; GC, glucocorticosteroids; GMT, geometric mean titer; HAV, hepatitis A virus; HBV, hepatitis B virus; HC, healthy controls; IBD, inflammatory bowel disease; IFX, infliximab; IG, intervention group; IgG, immunoglobulin G; HCQ, hydroxychloroquine; IRD, immune rheumatic diseases; IS, immunosuppression; IVIG, intravenous immunoglobulines; JIA, juvenile idiopathic arthritis; LEF, leflunomide; MMF, mycophenolic acid; MMR(/V), measles mumps rubella (/varicella); 6-MP, 6-mercaptopurine; MTX, methotrexate; MV, measles vaccine; NSAID, non-steroid anti-inflammatory drug; pts, patients; RAI, relative avidity index; RD, rheumatic diseases; RTX, rituxim; SAE, severe adverse event; SC, seroconversion; SFU, spot forming units; SP, seroprotection; TBE, tick-borne-encephalitis; TBEV, tick-borne-encephalitis virus; TCZ, tocilizumab; Thiopur, thiopurine; TNFi, tumor necrosis factor inhibitor; TT, tetanus toxoid; vacc, vaccine; VZV, varicella zoster virus**

**[a]Medication used in the intervention group, unless reported different. Numbers represent amount of patients using that medication.**

**[b] Studies are reported twice due to use of two different vaccines**