Rheumatoid arthritis - biological DMARDs

AB0420 MATERNAL AND NEONATAL ANTIBODY LEVELS UPON PERTUSSIS VACCINATION IN PREGNANT WOMEN ON IMMUNE-MODULATING THERAPY FOR RHEUMATIC DISEASE

Keywords: Vaccination/Immunization, bDMARD, Pregnancy and reproduction

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Background: While protection against pertussis following maternal tetanus-diphtheria-and-acellular-pertussis (Tdap) vaccination has been demonstrated in term-born infants from healthy mothers[1], no evidence is available on Tdap vaccination in combination with immune-modulating therapy during pregnancy.
Objectives: In this pilot-study, we explored whether treatment with Tumor Necrosis Factor alpha inhibitors (TNFis) in pregnant patients with rheumatic disease interferes with Tdap vaccine responses and/or affects maternal IgG antibody concentrations against the relevant antigens in the newborns.
Methods: Patients included by a rheumatologist during pregnancy received a Tdap vaccination in their late-second or early-third trimester. Blood samples were drawn during the first trimester, three months after delivery and from the umbilical cord. IgG antibody levels against Tdap-included antigens were measured using a bead-based multiplex immunoassay. Findings on patients exposed to TNFis were compared with those from TNFi-unexposed patients and with data from a historical comparator study among healthy Tdap vaccinated mother-infant-pairs (n=53). [2]
Results: 66 patients (46 exposed and 20 unexposed to TNFIs) were enrolled. No differences in IgG antibody levels against Tdap-included antigens were observed between TNFi-exposed and unexposed patients before and after Tdap vaccination (Figure 1). In cord sera however, antibody levels against pertussis toxin were significantly lower after TNFi-treatment (35.94IU/mL, 95%CI 20.68-62.45) compared with no TNFis (94.61IU/mL, 95%CI 48.89-183.07) and with cord blood from the comparison cohort of healthy women-infant-pairs (125.12IU/mL, 95%CI 90.75-172.50). We observed similar differences for filamentous hemagglutinin, pertactin, tetanus toxoid, and diphtheria toxoid.
Conclusion: These preliminary data indicate no reduced IgG antibody response upon maternal Tdap vaccination in pregnant women following immune-modulating treatment, although our findings suggest that TNFis during pregnancy induce lower maternal antibody levels against Tdap-included antigens in newborns.
REFERENCES:

[1] Byrne L, Campbell H, Andrews N, Ribeiro S, Amirthalingam G. Hospitalisation of preterm infants with pertussis in the context of a maternal vaccination programme in England. Arch Dis Child. 2018;103(3):224-9.
[2] Barug D, Pronk I, van Houten MA, Versteegh FGA, Knol MJ, van de Kassteele J, et al. Maternal pertussis vaccination and its effects on the immune response of infants aged up to 12 months in the Netherlands: an open-label, parallel, randomised controlled trial. Lancet Infect Dis. 2019;19(4):392-401.

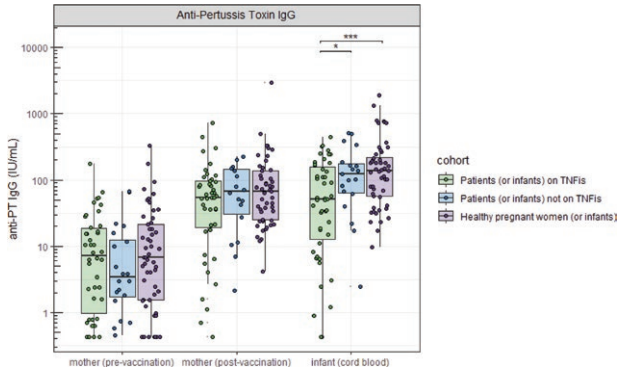

Figure 1. Anti-Pertussis toxin (anti-PT IgG) concentrations (IU/mL) before and after vaccination and in cord sera, represented for women exposed or unexposed to TNFis, or healthy pregnant women, including their offspring. X-axis: type and time-point of blood sample draw. Y-axis: IgG antibody concentration against pertussis toxin (IU/mL). Significance *p<0.05, **p<0.01, ***p<0.001.

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AB0421 REAL-WORLD EFFECTIVENESS OF UPADACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Real-world evidence

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Background: The Janus Kinase (JAK) inhibitor Upadacitinib (UPA) has shown efficacy in rheumatoid arthritis (RA) in trials, yet real-world evidence is lacking.
Objectives: We aimed to assess short-term effectiveness of UPA for standard of care for RA.
Methods: Data from participants included in the electronic platform "Tool for Administrative Reimbursement Drug Information Sharing" (TARDIS) were analysed. TARDIS collects data from all Belgian RA patients on advanced therapy during submissions of reimbursement requests for drug initiation or prolongation. Patients initiating UPA between 01/11/2020-31/12/2021, ≥18 years and DAS28>3.7 were included. Effectiveness was based on drug retention, proportion of patients achieving remission (DAS-28 <2.6), low disease activity (LDA, DAS-28 ≤3.2), HAQ-DI≤0.25 (HAQ25), HAQ-DI≤0.50 (HAQ50) as well as a clinical meaningful HAQ-DI-decrease (MCID_HAQ) since baseline of 0.22 at the first follow-up moment at 3 months. Sensitivity analyses by 1st, 2nd or 3rd+-line advanced therapy were performed.
Results: From 13 175 patients in TARDIS in the relevant time period, 996 patients on UPA could be included. Table 1 details this population. Of 871 patients with drug information at next follow-up, 783 (90%) continued UPA, and 42 (5%), 22 (3%), and 18 (2%) changed to a TNFi, non-TNFi and other JAKi respectively. In other effectiveness analyses, 705/996 (71%) patients were included. Remission and LDA were reached in 60% (421/705) and 74% (521/705) of patients respectively. HAQ25, HAQ50 and MCID_HAQ were reached in 11% (78/705), 26% (183/705) and 67% (475/705) of patients. Effectiveness slightly decreased with increasing line of therapy (Figure 1).

Table 1. Baseline characteristics of TARDIS patients on UPA

	Total UPA population
Number	996
Age (mean ±SD, years)	57.5 ±12.7
Disease duration (mean ±SD, years)	9.3 ±9.5
ESR (mean ±SD, mm/hour)	24.3 ±19.9
CRP (mean ±SD, mg/L)	13.1 ±15.5
SJC28 (mean ±SD)	6.5 ±4.5
TJC28 (mean ±SD)	9.2 ±5.4
DAS28 (mean ±SD, years)	5.0 ±0.8
HAQ-DI (mean ±SD, 0-3)*	1.3 ±0.8
PGA (mean ±SD, 0-100)	67.5 ±18.3
Advanced treatment naïve (yes)	434/996 (43.6%)
Advanced treatment Experienced (yes)	562/996 (56.4%)
2nd line	247/562 (24.8%)
3th line +	315/562 (31.6%)
Previous advanced treatment type**	
TNFi,	268/562 (48.2%)
Non-TNFi,	177/562 (31.8%)
JAKi	111/562 (20.0%)

Legend: Numbers given are mean ± SD or number, proportion. TNFi = tumour necrosis factor inhibitor, JAKi = Janus Kinase inhibitor, HAQ= health assessment questionnaire, PGA= Patient Global assessment; CRP= C-reactive protein; ESR= erythrocyte sedimentation rate; TJC= tender joint count; SJC= Swollen joint Count; DAS28 = disease activity score based on the 28joints. *Missing HAQ(0-3) scores were imputed by regression using age and HAQ(0-60) scores. **for 6 patients this was undefined.

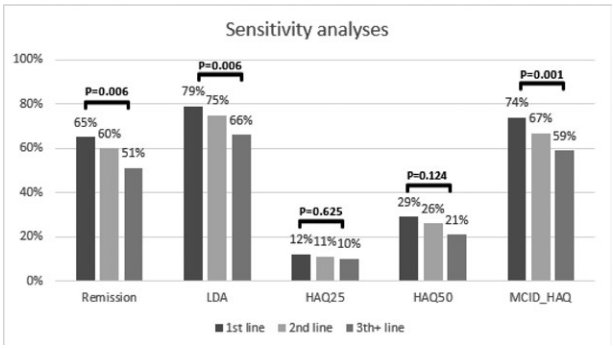

Figure 1. Effectiveness outcomes at 3 months of UPA per treatment line. remission (DAS-28 <2.6), LDA - low disease activity (DAS-28 ≤3.2), HAQ-DI≤0.25 (HAQ25), HAQ-DI≤0.50 (HAQ50) and minimum HAQ-DI-decrease (MCID_HAQ) since baseline of 0.22

Conclusion: Most patients continued UPA treatment. UPA improved clinical outcomes after 3 months in patients with moderately to severely active RA in a real-world setting, even in 3rd line of advanced therapy.

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AB0422 THE EFFECTS OF CONCOMITANT USE OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SARILUMAB

Keywords: Real-world evidence, Rheumatoid arthritis, bDMARD

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Background: Sarilumab was launched the second interleukin 6 receptor inhibitor (IL-6Ri) as a treatment for patients with rheumatoid arthritis (RA) in Japan. Tocilizumab, that was known as first IL-6Ri, showed excellent therapeutic effect without methotrexate (MTX) for RA. However, it was unknown that the effect on concomitant use of MTX in RA patients treated with sarilumab.

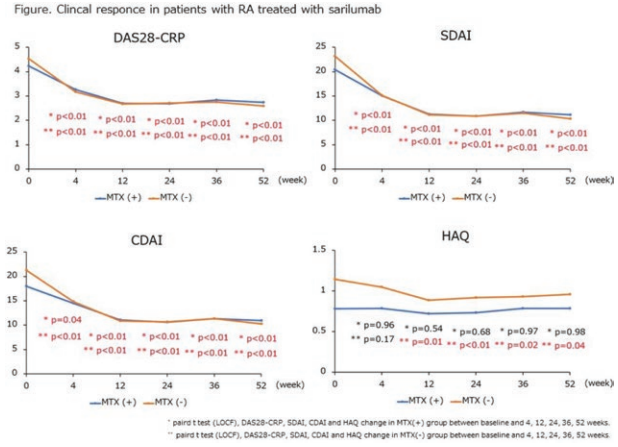
Objectives: We evaluated the effect on concomitant use of MTX in RA patients treated with sarilumab.

Methods: This study used a multicenter database included 673 RA patients treated with b/tsDMARDs. We finally analyzed 72 RA patients treated with sarilumab. Thirty-three RA patients were combined with MTX (MTX group) and 39 RA patients were not combined with MTX (non-MTX group). The continuation rate and efficacy at 52 weeks after sarilumab treatment in each group was evaluated.

Results: Non-MTX group was older, longer disease duration, and lower eGFR than MTX group (Table 1). The continuation rate at 52 weeks was not different between MTX group and non-MTX group (56.4 vs 74.4%, p=0.08). DAS28-CRP, SDAI, CDAI were decreased at 4, 12, 24, 36, 52 weeks after sarilumab treatment compared to baseline in both MTX group and non-MTX group (Figure 1). Improvement rate of DAS28-CRP, SDAI and CDAI at 4, 12, 24, 36, 52 weeks after sarilumab treatment were not different between groups (DAS28-CRP: p=0.36, p=0.53, p=0.56, p=0.46, p=0.29; SDAI: p=0.58, p=0.93, p=0.90, p=0.63, p=0.56; CDAI: p=0.65, p=0.98, p=0.99, p=0.61, p=0.47; respectively). HAQ was not improved in MTX group, but improved in non-MTX group during 52 weeks sarilumab treatment (MTX group, p=0.98; non-NTX group, p=0.04). In all patients, 49 RA patients were treated sarilumab as 2nd and more line biological/ targeted synthetic disease-modifying anti rheumatic dugs (b/tsDMARDs). DAS28-CRP, SDAI and CDAI at baseline in RA patients treated with sarilumab as 2nd and more line b/tsDMARDs were 4.1, 18.9, 16.4 in MTX group (n=23), and 4.6, 24.3, 22.6 in non-MTX group (n=26). DAS28-CRP, SDAI and CDAI were decreased at 4, 12, 24, 36, 52 weeks after sarilumab as 2nd and more line treatment compared to baseline in both MTX group (DAS28-CRP: 3.0, 2.5, 2.5, 2.7, 2.7, p<0.01, respectively; SDAI: 12.5, 9.6, 9.3, 10.6, 10.3, p<0.01, respectively; CDAI: 12.2, 9.4, 9.0, 10.2, 10.1, p<0.01, respectively) and non-MTX group (DAS28-CRP: 3.3, 2.8, 2.8, 2.8, 2.6, p<0.01, respectively; SDAI: 15.6, 11.5, 11.4, 11.1, 9.9, p<0.01, respectively; CDAI: 15.2, 11.1, 11.1, 11.0, 9.7, p<0.01, respectively). Improvement rate of DAS28-CRP, SDAI and CDAI at 4, 12, 24, 36, 52 weeks after sarilumab as 2nd and more line treatment were not different between groups (DAS28-CRP: p=0.99, p=0.96, p=0.83, p=0.94, p=0.53; SDAI: p=0.10, p=0.65, p=0.79, p=0.87, p=0.68; CDAI: p=0.95, p=0.72, p=0.76, p=0.74, p=0.53; respectively).

Table 1. Baseline characteristics of RA patients treated with sarilumab

	MTX (+) group (n=33)	MTX (-) group (n=39)	p
Age (years)	61.51 ± 13.68	69.51 ± 13.12	< 0.01
Male/ Female ratio	10/23	8/31	0.5
Disease durations (years)	9.30 ± 10.22	17.39 ± 11.33	< 0.01
RF positive ratio (%)	81.82	79.49	1.0
CCP positive ratio (%)	77.42	82.86	0.85
CRP (mg/dl)	2.44 ± 2.82	1.90 ± 2.06	0.65
MMP-3 (ng/ml)	271.57 ± 314.38	342.34 ± 327.87	0.047
eGFR	79.78 ± 27.50	58.22 ± 27.52	<0.01
DAS28-CRP	4.23 ± 1.31	4.53 ± 1.0	0.26
SDAI	20.41 ± 12.07	23.17 ± 9.66	0.17
CDAI	17.97 ± 10.71	21.27 ± 9.25	0.08
HAQ	0.78 ± 0.78	1.14 ± 0.88	0.02
MTX (mg/week)	8.58 ± 3.58	0 ± 0	<0.01
Glucocorticoid use (%)	18.18 (6/33)	38.46 (15/39)	0.1
Glucocorticoid dose (mg/day)	7.17 ± 3.19	5.83 ± 3.24	0.37
Number of past use of b/tsDMARD			
0 (%)	30.3	33.3	
1 (%)	51.5	33.3	
2 (%)	12.1	15.4	
3(%)	6.1	10.3	
4 (%)	0	5.1	
5 (%)	0	2.6	
Interstitial pneumonia	2/33	7/39	0.17



Conclusion: Sarilumab improved disease activity in patients with RA regardless of concomitant use of MTX.

REFERENCES: NIL.

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Disclosure of Interests: None Declared.

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AB0423 IMPROVEMENT OF ULTRASONOGRAPHIC FINDINGS IN JAK INHIBITOR TREATED JAPANESE RHEUMATOID ARTHRITIS PATIENTS COMPARISON WITH TNF INHIBITOR THERAPY

Keywords: Rheumatoid arthritis, Ultrasound, bDMARD

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Background: JAK inhibitor (JAKi) and TNF inhibitor (TNFi) are the important therapeutic agent for the treatment of rheumatoid arthritis (RA). However there is still few studies of improvement of ultrasonographic findings in RA treats comparison with JAKi and TNFi.

Objectives: To evaluate the improvement of ultrasonographic findings in JAKi treated RA patients comparison with TNFi.