POS0693

IMPACT OF UPADACITINIB VERSUS ABATACEPT ON INDIVIDUAL DISEASE OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSES TO BIOLOGIC DMARDS

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Background: The phase 3 SELECT-CHOICE trial of patients with rheumatoid arthritis (RA) and prior inadequate response to biologic DMARD(s) (bDMARD-IR) demonstrated superiority of the JAK inhibitor upadacitinib (UPA) vs abatacept (ABA) in the mean change from baseline (BL) in DAS28(CRP) and in the proportion achieving DAS28(CRP) <2.6 at week (wk) 12, with higher incidence of serious adverse events reported in the UPA treatment group.

Objectives: To evaluate the impact of UPA vs ABA on individual components of composite measures of disease activity in SELECT-CHOICE.

Methods: In SELECT-CHOICE, a double-blind phase 3 trial, bDMARD-IR patients were randomly assigned to UPA 15 mg once daily or ABA, each with background conventional synthetic DMARDs, for 24 wks. For this post hoc analysis, the proportions of patients achieving improvement from BL through wk 24 in ACR core variables (including SJC, TJC, Patient Global Assessment [PtGA], Physician Global Assessment [PhGA], pain, HAQ-DI, and hsCRP) and Boolean remission criteria were evaluated. Differences in the cumulative distributions of CDAI, DAS28(hsCRP), SDAI, and ACR-n (the lowest of percent change in TJC, percent change in SJC, or median of the other 5 ACR components) were determined using the Kolmogorov-Smirnov test and are reported as observed. For all other variables, non-responder imputation was applied for missing data. Nominal *P* values are provided throughout.

Results: A total of 616 bDMARD-IR patients with moderate to severe RA were randomized in SELECT-CHOICE (UPA 15 mg, n=303; ABA, n=309). BL demographic and disease characteristics were generally comparable between treatment groups, with a mean disease duration of approximately 12 years and mean CDAI of 39.6. At wk 12, more patients receiving UPA vs ABA achieved ≥50% improvements from BL in TJC68, PtGA, and hsCRP, with comparable proportions observed between UPA and ABA for the remaining ACR components (Figure 1). At wk 24, similar proportions of patients receiving UPA and ABA achieved ≥50% improvements in all but the hsCRP component. Overall, 15% and 26% of patients on UPA compared with 6% and 15% on ABA demonstrated ≥50% improvements across all ACR components at wks 12 and 24, respectively. At wks 12 and 24, Boolean remission was achieved by 6% and 14% of patients on UPA vs 2% and 10% of patients on ABA, respectively; the proportion of patients in both treatment groups achieving the individual Boolean components were also reported (Table 1). While comparable at BL, cumulative distributions of CDAI, SDAI, DAS28(hsCRP), and ACR-n were improved on UPA vs ABA at wk 12 (all nominal *P* <0.05); differences persisted for most measures at wk 24.

Table 1. Proportions of Patients Achieving Boolean Remission and Its Components at Week 12 and 24 (NRI)

	Week 12		Week 24	
	UPA 15 mg	ABA	UPA 15 mg	ABA
n (%)	(N=303)	(N=309)	(N=303)	(N=309)
Boolean Remission	19 (6)***	5 (2)	42 (14)*	30 (10)
PtGA ≤10	54 (18)***	29 (9)	80 (26)*	66 (21)
TJC ≤1	89 (29)***	64 (21)	134 (44)*	115 (37)
SJC ≤1	127 (42)**	106 (34)	169 (56)*	152 (49)
hsCRP ≤1 mg/dL	257 (85)***	209 (68)	244 (81)***	199 (64)

Nominal ***P <.001, **P <.01, *P <.05 for UPA vs ABA. ABA, abatacept; PtGA, Patient's Global Assessment of disease severity; UPA, upadacitinib.

Conclusion: In this post hoc analysis of bDMARD-IR RA patients, improvements in components of disease measures were reported for both UPA and ABA through 24 weeks, with numeric differences noted for several components. Nominally higher attainment of Boolean remission and its components were observed for UPA over ABA.

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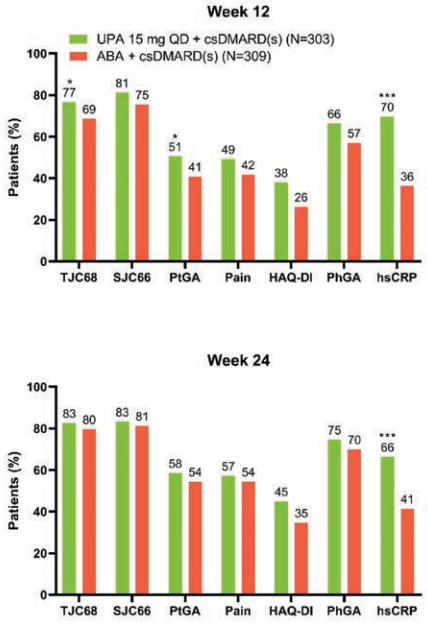
Figure. Proportions of Patients Receiving UPA vs ABA Who Achieved at Least 50% Improvement From Baseline in Each of the ACR Components at Week 12 and 24 (NRI)



Nominal ***P <.001, **P <.01, *P <.05 for UPA vs ABA. P values were calculated using the Cochran-Mantel-Haenszel test, with adjustment for the main stratification factor of previous failed biologic DMARD. ABA, abatacept; ACR, American College of Rheumatology; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire–Disability Index; hsCRP, high sensitivity C-reactive protein; NRI, non-responder imputation; PhGA, Physician's Global Assessment of disease severity; PtGA, Patient's Global Assessment of disease severity; QD, daily; SJC66, Swollen Joint Count based on 66 joints; TJC68, Tender Joint Count based on 68 joints; UPA, upadacitinib.

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WHAT TREATMENT GIVES THE BEST CLINICAL RESPONSE AFTER CESSATION OF JAKI THERAPY IN PATIENTS WITH RA? DATA OF THE TARDIS-RA REGISTRY, A NATIONWIDE BELGIAN BIOLOGIC REGISTRY

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Background: JAKi represent a new important class in Rheumatoid Arthritis (RA) treatment options. It is unknown which specific bDMARD or mode of action should be selected after stopping a JAKi.

Objectives: To study if clinical response differs between advanced therapies that are initiated after stopping a JAKi.
Methods: Patients were included from the electronic platform "Tool for Administrative Reimbursement Drug Information Sharing" (TARDIS). Data from all Belgian RA patients on biologic and targeted therapy are collected here for drug reimbursement. Patients were selected for this analysis if they had stopped JAKi therapy and initiated a subsequent therapy. Patients were grouped by TNFi, T/B cell therapy, IL6i or JAKi therapy. The DAS28 response and proportion of patients in remission at the first follow-up (between 3 and 6 months) were compared between groups. Remission was defined as DAS28<2.6. Analyses were repeated in patients who were prescribed the stopped JAKi as first-line or as subsequent line therapy. Data were compared via χ^2, Anova and t-tests.
Results: In total, 1238 patients who had stopped JAKi therapy were included. TNFi, T/B cell therapy, IL6i or JAKi therapy was initiated in 36% (441/1238), 19% (233/1238), 18% (227/1238) and 27% (337/1238) respectively. Most baseline demographic and clinical characteristics differed between groups (Table 1).

Table 1.

	TNFi	B/T cell	IL6i	JAKi	p-value
Number	441 (36%)	233 (19%)	227 (18%)	337 (27%)	
Age (years)	**55 ± 14**	**57 ± 13**	**55 ± 14**	**59 ± 12**	**<0.001**
Gender (women)	323 (73%)	177 (76%)	186 (82%)	257 (76%)	0.100
Weight (kg)	74 ± 15	79 ± 17	75 ± 15	75 ± 15	0.111
Disease duration (years)	**9 ± 8**	**10 ± 9**	**11 ± 9**	**11 ± 9**	**0.002**
HAQ (0-3)	1.6 ± 0.7	1.8 ± 0.6	1.5 ± 0.7	1.5 ± 0.8	0.353
PGA (0-100)	**65 ± 20**	**68 ± 21**	**67 ± 21**	**57 ± 24**	**<0.001**
CRP (mg/l)	**10 ± 16**	**14 ± 20**	**16 ± 28**	**11 ± 17**	**0.003**
ESR (mm/h)	22 ± 21	24 ± 19	27 ± 21	25 ± 22	0.117
TJC28	**8 ± 6**	**8 ± 6**	**9 ± 6**	**7 ± 6**	**0.001**
SJC28	**5 ± 4**	**6 ± 5**	**6 ± 4**	**5 ± 5**	**0.006**
DAS28	**4.7 ± 1.1**	**4.8 ± 1.1**	**4.9 ± 1.2**	**4.4 ± 1.3**	**<0.001**
2nd line of therapy after initial JAKi therapy	**211 (48%)**	**56 (24%)**	**52 (23%)**	**112 (33%)**	**<0.001**

Numbers given are mean ± SD or number, proportion. TNFi = tumour necrosis factor inhibitor, ts= targeted synthetic, 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

The clinical response could be studied in 577 patients. Patients on rituximab were excluded as these were retreated on flare, following Belgian reimbursement criteria. TNFi, Tcell therapy, IL6i or JAKi therapy was initiated in 37% (211/577), 13% (76/577), 18% (102/577) and 33% (188/577) of these patients respectively. DAS28 decreased on average with 1.7 ± 1.5, 1.6 ± 1.4, 2.4 ± 1.6* and 1.3 ± 1.6 for patients on TNFi, T cell therapy, IL6i or JAKi therapy respectively (*p<0.001). Remission was reached in 42%, 41%, 56%* and 39% for patients on TNFi, T cell therapy, IL6i or JAKi therapy respectively (*p=0.045).
Before switching, JAKi therapy was the first advanced therapy in 35% (204/577). In this "naïve" subgroup, DAS28 decreased on average with 1.9 ± 1.5, 1.9 ± 1.3, 2.4 ± 1.8 and 1.0 ± 1.7* for patients on TNFi, Tcell therapy, IL6i or JAKi therapy respectively (*p=0.001). Remission was reached in 44%, 48%, 58% and 35% for patients on TNFi, Tcell therapy, IL6i or JAKi therapy respectively (p=0.279).
In the "experienced" subgroup, who started JAKi therapy as subsequent line therapy in 65% (373/577), DAS28 decreased on average with 1.5 ± 1.6, 1.5 ± 1.4, 2.3 ± 1.6* and 1.4 ± 1.6 for patients on TNFi, Tcell therapy, IL6i or JAKi therapy respectively (*p<0.001). Remission was reached in 40%, 38%, 55% and 41% for patients on TNFi, Tcell therapy, IL6i or JAKi therapy respectively (p=0.118).
Conclusion: Our results show clearly that IL6 inhibitors have a better clinical response after JAKi cessation compared to other mode of actions, including other JAKi. However, considerable baseline differences existed, that could influence our results.
Disclosure of Interests: None declared
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POS0695 EFFECT OF METHOTREXATE AND FOLIC ACID CO-ADMINISTRATION IN ARTHRITIS

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Background: Methotrexate (MTX) is the recommended first-line treatment for rheumatoid arthritis. Adjuvant-induced arthritis (AIA) rat is a robust model with a high prevalence of arthritis used to investigate arthritis. MTX reduces inflammation, but associated with adverse events, such as gastrointestinal, hepatic, and hematology toxicity (1). To reduce these side effects, folic acid (FA) is administrated at distance to MTX with no defined recommendation for its dosing (5-25mg/week) or time point of administration (2) (1-3 days after MTX application). Whether the complicated therapeutic regimen with MTX once a week and FA at another time point affects compliance is an open question. MTX is metabolized in polyglutamates derivates (MTX-PG), which is a biomarker of MTX efficacy as its half-life (1-4 weeks) is longer than MTX (4h) (3).
Objectives: The aim of this study was to assess efficacy and tolerance of co-administration of MTX and FA compared to MTX with FA applied one day after MTX in the AIA.
Methods: Female Lewis rat were randomly divided in three groups and received an injection of Mycobacterium butyricum defining day (D) 0 to induce arthritis. An historic AIA group was used as control. Treatment began on D9, one day before arthritis onset in this model. The first group rats were treated with MTX only (n=13), the second group received MTX and FA at the same day (n=14), and the third group received FA one day after MTX administration (n=14). MTX was administrated intraperitoneally (IP) at 1 mg/kg every 3 days (4) and FA was delivered IP at 0.17 mg/kg. Arthritic index (AI) and ankle circumference (AC) were monitored to assess arthritis. Microcomputed tomography of the ankle was performed to assess bone loss. Moreover, complete blood count, transaminases, and MTX-PG were assessed.
Results: Arthritis developed at D10 in all groups. AI and AC were similar in MTX groups at the various time points. At D17, arthritis severity was lower in MTX groups (AI (mean and standard deviation): 1.4 ± 1.6; AC: 35 ± 7 mm) compared to AIA historical group (AI: 3.3 ± 0.6; AC: 42 ± 4 mm). Bone erosion and bone loss parameters were similar in all groups. Cortical porosity was around 0.40% ± 0.15 and bone volume / total volume was around 0.22% ± 0.13. MTX-PG1 was found at similar levels in MTX groups and correlated negatively with AI in MTX alone or MTX and FA at the same day groups (p<0.05 and p<0.01, respectively). Finally, white and red blood cells, platelets, hemoglobin, mean corpuscular volume, transaminases, and creatinine were found at a similar level in MTX groups.
Conclusion: Co-administration of MTX with FA on the same day is effective compared to FA application one day after MTX. MTX metabolism was not affected, as demonstrated by the MTX-PG concentrations. The biological tolerance between the protocols was comparable. Thus, co-administration of MTX and FA seems to be possible and may be more convenient to the patients and improve compliance at the end.
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POS0696 DOES PREDNISONE USE DURING PREGNANCY IN WOMEN WITH RHEUMATOID ARTHRITIS INDUCE INSULIN RESISTANCE IN THE OFFSPRING?

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Background: The use of long-term corticosteroids during pregnancy has been growing over the past decades[1]. Corticosteroids can be given when an auto-inflammatory disease like rheumatoid arthritis (RA) is too active. Several studies have shown that long-term corticosteroids use in pregnancy is associated with maternal and fetal adverse outcomes, like preeclampsia, shorter gestational age, lower birth weight and rapid catch-up growth [1-3]. These last two outcomes could influence the insulin resistance later in life[4].