THU0174

CHARACTERIZATION OF REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH UPADACITINIB OR COMPARATORS

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Background: Across all phase 3 studies, treatment with upadacitinib (UPA), a JAK1-selective inhibitor, was associated with significantly higher remission (REM) rates, compared to placebo (PBO) or active comparators, in RA patients (pts) who were methotrexate (MTX)-naïve, had inadequate response to conventional synthetic (csDMARD-IR) or had inadequate response or intolerance to biologic DMARDs (bDMARD-IR).

Objectives: REM definitions are based on composite scores of various individual assessments of disease activity. To determine the response to UPA on REM and component assessments, we assessed the proportions of pts achieving REM using multiple REM definitions, and the improvement in their respective individual components, compared to PBO or active comparators, in 3 different RA pt populations spanning a range of RA pt populations.

Methods: Three phase 3 studies included pts who were MTX naïve (SELECT EARLY, n=945), MTX-IR (SELECT COMPARE, n=1629) and bDMARD-IR (SELECT BEYOND, n=498). The proportion of pts achieving REM at Week (Wk) 12 by 4 definitions (DAS28-CRP<2.6; CDAI ≤2.8; SDAI ≤3.3 and Boolean, defined as ≤1 for TJC, SJC, patient's global assessment of disease activity [PGA], and CRP ≤1 mg/L) were determined. For each definition of REM, the mean change in each of the respective component scores was also assessed. Binary endpoints are based on Non-responder imputation (NRI), and continuous endpoints on mixed-effect model repeat measurement (MMRM). Comparisons were made between UPA-treated groups vs respective control arms (MTX, adalimumab [ADA] or PBO).

Results: Pt demographics and disease characteristics have been previously reported. ¹⁻³ At 12 wks, in EARLY and COMPARE, a significantly greater proportion of pts receiving UPA 15 mg or 30 mg QD achieved REM by all 4 definitions vs MTX, PBO or ADA (Table). In BEYOND, a refractory population many of whom had inadequate response to multiple bDMARDs, a significantly greater proportion of pts receiving UPA 30mg achieved all REM definitions vs PBO within the first 12 wks, with significantly greater proportions on UPA 15mg achieving DAS28-CRP<2.6 and Boolean REM (Table). Rates of REM in BEYOND further increased through Wk 24 for both dose groups.¹ Compared to respective control groups, pts receiving UPA 15 or 30 mg QD had significantly greater improvements in each REM disease component (except for PhGA vs ADA in COMPARE). Significantly more pts receiving UPA also achieved the required cutoffs on the individual components of Boolean REM compared to respective controls.

Conclusion: Significantly greater proportions of pts receiving UPA 15 or 30mg achieved REM by multiple definitions at 12 wks compared to PBO, MTX or ADA. All disease activity components of each REM definition were significantly improved in pts receiving UPA compared to MTX or PBO, and all Boolean components were significantly improved in pts receiving UPA 15mg compared to ADA.

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Abstract THU0174 –Table 1.

Parameter at 12 weeks	SELECT EARLY (MTX-naïve)			SELECT COMPARE (MTX-IR)			SELECT BEYOND (bDMARD-IR)		
	MTX n=324	UPA 15 mg QD n=327	UPA 30 mg QD n=334	PBO n=551	ADA 40 mg QD n=557	UPA 15 mg QD n=551	PBO n=189	UPA 15 mg QD n=184	UPA 30 mg QD n=185
Proportion of patients achieving REM by various criteria (NRI), (%)									
DAS28-CRP	14	30***	41***	6	18	20***	10	20***	24***
CDAI	6	10***	21***	3	8	13***	5	8	12*
SDAI	6	10***	22***	3	7	12***	5	8	13*
Boolean	6	13**	15***	2	4	10***	2	7*	8**
Mean Change from BL (mmHg)									
TJC8	-7.3	-8.0***	-8.9***	-7.3	-8.0***	-8.6	-7.8***	-8.6	-9.5***
SJC8	-8.2	-10.1***	-10.7***	-8.5	-9.7***	-10.0	-9.3***	-10.0***	-10.5***
PhGA	-24.6	-34.0***	-38.0***	-25.2	-33.6	-30.4***	-25.0	-28.0***	-29.2***
PGA	-35.1	-45.0***	-47.0***	-35.6	-43.8***	-40.5***	-35.3	-38.8***	-40.3***
CRP	-10.6	-17.5***	-18.4***	-10.7	-16.4	-13.3***	-11.3	-11.0***	-12.5***
Proportion of patients achieving individual components of the Boolean REM criteria (NRI), (%)									
PGA SDO	13	25***	30***	7	12	20***	8	15*	19**
TJC8 S1	22	38***	37***	13	25	33***	13	30***	26**
SJC8 S1	22	40***	40***	19	32	42***	23	38***	33*
PhCRP S1	42	84***	83***	50	69	76***	49	82***	79***

* For continuous endpoints, results are based on MMRM.

For EARLY: **p<.05, ***p<.001; for COMPARE: **p<.05, ***p<.001 for UPA 15 mg vs PBO, **p<.05, ***p<.001 for UPA 15 mg vs ADA. Comparison not indicated for ADA vs PBO.

For BEYOND: **p<.05, ***p<.001 for UPA 15 mg or 30 mg vs PBO.

DAS28-CRP, 28-joint disease activity score using C-reactive protein; CDAI, clinical disease activity index; SDAI, simplified disease activity index; TJC8, swollen joint count of 28 joints; SJC8, tender joint count of 28 joints; PGA, patient's global assessment of disease activity; PhGA, physician's global assessment of disease activity; CRP, high-sensitivity C-reactive protein.

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THU0175

DOSE-DEPENDENT RISK OF METHOTREXATE FOR RENAL IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is a mainstay in the therapy of rheumatoid arthritis (RA). It is recommended that MTX should be rapidly

escalated to the maximum tolerated dose (16 - 30 mg/week) and tapering MTX can be considered after a persistent remission¹⁾. Renal impairment is one of the major concerns in treatment with high dose MTX for malignancy, but it is still unclear whether low dose MTX administration in RA cause the renal impairment or not.

Objectives: The purpose of this study is to elucidate the association between MTX dosage and a one-year change of estimate glomerular filtration rate (eGFR) in RA patients.

Methods: Of outpatients with RA in Okayama university hospital between 2006 and 2017, 497 patients who had continued the administration of MTX for more than one year were enrolled. All patients fulfilled the ACR/EULAR 2010 Classification Criteria for RA. Patients who had nephrotic syndrome, unilateral kidney or other rheumatic disorders other than secondary Sjögren's syndrome were excluded. The primary outcome was the change of eGFR during the most recent one year in each patient. The revised Japanese equation of Modification of Diet in Renal Disease²⁾ was used to calculate eGFR. MTX dosage was defined as an average dosage of MTX during the observational period. We evaluated the association between MTX dosage and the primary outcome using univariate and multivariate analysis.

Results: Median (IQR) age was 64 (54 - 72) years, 78% were female, and median disease duration was 73 (31 - 160) months. The median dosage of MTX was 8 mg/week (6 - 10.1) and biological agents were used in 28% of the patients. The eGFR (mean $\pm$ SD) decreased by 1.2 ± 8.3 ml/min/1.73m² in one year and MTX dosage was associated with the change of eGFR significant inversely ($p < 0.0001$). The eGFR in patients treated with MTX < 8 mg/week ($n=185$), ≥ 8 and < 10 ($n=131$), ≥ 10 and < 12 ($n=86$), ≥ 12 ($n=95$) decreased 0.2 ± 0.6 , 0.6 ± 0.7 , 1.0 ± 0.9 , and 4.6 ± 0.8 ml/min/1.73m²/year, respectively. After adjusting possible confounding factors such as sex, age, concomitant use of NSAIDs, hypertension, and C reactive protein (CRP) using multiple linear regression analysis, MTX dosage was still an independent risk factor for the decrease of eGFR (beta-coefficient: -0.4, 95% confidence interval -0.12 - -0.61, $p=0.003$).

Conclusion: Careful monitoring of renal function should be required in long-time treatment for RA patients with MTX.

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THU0176

COMPARISON OF ADHERENCE TO MONOTHERAPY VERSUS COMBINED THERAPY IN RHEUMATOID ARTHRITIS

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Background: Treatment adherence in Rheumatoid Arthritis (RA) patients vary from 30 to 80% (1). It is important to identify the associated factors to a low adherence, so clinicians can make interventions to obtain better therapeutic results. Adherence to treatment has been described to be affected by several factors, such as access to healthcare facilities, education, socioeconomic status, quality of communication between physician and patient, among others (2). There are no previous studies that investigate if the number of drugs received in RA patients affects this adherence. REPAIR[®] is a program designed with the purpose of improve data collection and medical practice in our outpatient clinic.

Objectives: To compare the adherence to synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) among RA patients prescribed with monotherapy and combined therapy.

Methods: Cross sectional, observational, comparative study. This study was conducted in the outpatient rheumatology clinic of University Hospital in Monterrey, México. Consecutive patients with RA, were approached

during their normal routine rheumatology appointments, in the March 2018 to December 2018 period. They were asked how many days of the last month they forgot or took their DMARDs (self-report). We classified the adherence rate in 2 categories based on the days of the last month they took the indicated medication; adequate: 75%-100% (> 21 days), inadequate $< 75\%$ (< 21 days). When adherence was inadequate we interrogated about the cause. Data was obtained from REPAIR[®] (internal electronic patient record). The Kolmogorov Smirnov test was used to determine normal distribution. Categorical variables are expressed as total number and percentage (%), and numerical variables as median and the 25th-75th percentiles (q25-q75). Chi square and Mann Whitney U test were used to compare groups and considered significant if $p < 0.05$. Data was analyzed with the statistical package SPSS version 24 (New York, USA).

Results: A total of 959 patients were included. When comparing adherence to treatment and gender between groups, no statistically significant difference was found. The main cause of inadequate adherence in the monotherapy group was the economic (30.3%) and own decision in the combined therapy group (29.1%).

Table 1:

	Monotherapy (n=346)	Combined therapy (n=613)	p
Age (years), median (q25-q75)	54 (44-63)	53 (43-59)	0.018
Women, n (%)	317 (91.6)	575 (93.8)	0.362
Inadequate adherence to treatment, n (%)	52 (15)	102 (16.6)	0.514
Adequate adherence to treatment, n (%)	294 (85)	511 (83.4)	

Conclusion: Patients with combined therapy had the same percentage of inadequate adherence as patients with monotherapy. These results may indicate that number of drugs prescribed not necessarily affects adherence to treatment. The principal causes for an inadequate adherence to treatment were: economic for monotherapy group and own decision for combined therapy group. However, long-term studies are needed to evaluate the persistence of treatment in these groups of patients.

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THU0177

TREATMENT PATTERNS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH A BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUG OR JAK INHIBITOR: A NATION-WIDE STUDY IN KOREA

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Background: Limited data are available on whether patients with rheumatoid arthritis (RA) are treated with conventional disease-modifying anti-rheumatic drugs (cDMARDs) according to the current recommendations before they initiate biologic DMARDs (bDMARDs) or JAK inhibitors (JAKis).

Objectives: We examined the treatment patterns among Korean RA patients who received bDMARDs or JAKis in a real world setting, using the 2002-2016 Korean National Health Insurance Service database that covers the entire Korean population.

Methods: We identified RA patients who initiated bDMARDs (TNF inhibitor, abatacept, rituximab and tocilizumab) or JAKis (tofacitinib). Their treatment patterns during 1 year after RA diagnosis (defined as free of any RA diagnosis or any DMARD use for one year before the diagnosis) and prior to the initiation of index drugs (bDMARDs or JAKis) were examined regarding: initial cDMARD used, dose and parenteral use of methotrexate (MTX), use and time to combination therapy of cDMARDs, and steroid use.