were seen at 1 month after bari treatment. These either remained flat or improved 3 months after treatment. An increase from baseline in creatinine was also seen. These tendencies continued to the final observation. Moving forward, these items should be monitored for long-term evaluation.

Abstract THU0196 –Table 1.

Table 1. Patients' background		(mean ± SD)	
	Bio naïve	Bio experienced	
Age (years old)	66.4 ± 9.0	69.8 ± 11.2	
Disease duration (years)	3.81 ± 3.50	4.57 ± 3.13	
Male / Female	3 / 16	4 / 9	
RF positive / ACPA positive (%)	68.4 / 73.7	84.6 / 76.9	
Stage (I/II/III/IV) / Class (I/II/III/IV)	(10/5/4/0) / (4/8/4/3)	(5/4/3/1) / (2/5/4/2)	
MTX dose (mg/week)	8.94 ± 9.23	6.67 ± 7.10	
PSL dose (mg/day)	1.41 ± 1.87	1.33 ± 2.06	

Table 2. Change of clinical assessments		(mean ± SD)		
(Bio naïve)	baseline	1 month	3 months	6 months
SJC	7.06 ± 2.54	1.68 ± 1.70 [§]	0.75 ± 1.29 [§]	0.66 ± 0.85 [§]
TJC	7.68 ± 3.18	2.19 ± 1.94 [§]	1.13 ± 1.50 [§]	0.98 ± 1.05 [§]
CRP (mg/dl)	2.00 ± 1.50	0.67 ± 0.93 [§]	0.17 ± 0.25 [§]	0.15 ± 0.24 [§]
CDAI	24.92 ± 7.26	7.11 ± 4.84 [§]	3.87 ± 4.31 [§]	2.94 ± 3.13 [§]
Pain VAS	50.3 ± 21.4	21.4 ± 16.8 [§]	15.3 ± 13.8 [§]	12.0 ± 9.8 [§]
PGA	49.9 ± 18.6	21.2 ± 17.6 [§]	11.5 ± 13.8 [§]	9.8 ± 12.5 [§]
HAQ-DI	0.76 ± 0.33	0.43 ± 0.24 [§]	0.30 ± 0.18 [§]	0.28 ± 0.17 [§]

Table 2. Change of clinical assessments		(mean ± SD)		
(Bio experienced)	baseline	1 month	3 months	6 months
SJC	7.78 ± 5.65	2.22 ± 1.92 [*]	0.78 ± 1.09 [*]	0.75 ± 1.49 [*]
TJC	8.67 ± 4.82	2.22 ± 1.79 [*]	1.78 ± 1.72 [*]	1.62 ± 1.84 [*]
CRP (mg/dl)	4.40 ± 4.51	0.82 ± 1.45 ^{**}	0.78 ± 1.00 [*]	0.72 ± 1.10 [*]
CDAI	28.77 ± 12.30	9.06 ± 6.82 [*]	6.23 ± 6.16 [*]	6.28 ± 6.50 [*]
Pain VAS	59.0 ± 28.0	29.1 ± 27.5 [*]	23.8 ± 25.0 [*]	21.3 ± 27.9 [*]
PGA	66.6 ± 25.2	25.4 ± 24.3 [*]	20.6 ± 26.3 [*]	21.6 ± 25.4 [*]
HAQ-DI	1.04 ± 0.56	0.68 ± 0.57 [*]	0.56 ± 0.47 [*]	0.50 ± 0.54 [*]

Table 3. Adverse events		(mean ± SD)	
Barigroup + TNFi group	N (%)		
Pneumonia	2 (6.3)		
Herpes zoster	1 (3.1)		
upper respiratory tract infection	5 (15.6)		
nasopharyngitis	3 (9.3)		
Laboratory data abnormality	15 (46.9)		

[§]p < 0.01 vs baseline

^{*}p < 0.01 vs baseline

[§]p < 0.01 vs baseline

^{*}p < 0.01 vs baseline

Conclusion: These data showed that bari has a favorable benefit-risk balance in a real-world clinic and thus may be considered as a good treatment option for Japanese RA patients who have an inadequate response to csDMARDs or bDMARDs.

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THU0197

MONOTHERAPY WITH UPADACITINIB IN MTX-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 48 WEEKS FROM THE SELECT-EARLY STUDY

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Background: Upadacitinib (UPA), a JAK1-selective inhibitor, was efficacious as monotherapy upto 24 weeks (wks) in MTX-naïve patients (pts) with active RA.¹

Objectives: To assess safety and efficacy of UPA through 48 wks in an ongoing extension of the ph 3 SELECT-EARLY RCT.

Methods: SELECT-EARLY had a 48-wk double-blind active comparator-controlled period. Pts were initially randomized to monotherapy (mono) with UPA 15 or 30 mg or MTX (titrated up to Wk8). Rescue therapy was offered if pts met the following: (1) From Wk 12-24, pts without ≥20% improvement from BL (Δ) in both TJC and SJC at 2 consecutive visits continued blinded study drug with optimized background RA medications. (2) At Wk26, pts with CDAI ≤2.8 continued their original study drug; in pts with CDAI >2.8 and <20% Δ in TJC and SJC, for those on MTX, UPA15/30mg was added; for those on UPA15/30mg, MTX was added. For pts with CDAI ≤2.8 but ≥20%Δ in TJC and SJC, background medications were optimized. Background csDMARDs could be initiated after Wk26. After Wk48, pts could continue in a long-term extension. Efficacy data up to the Wk48 visit are reported based on initial randomized treatment. For binary non-radiographic endpoints, NRI was used for missing data and rescue handling; for continuous non-radiographic endpoints, LOCF was used for rescue handling. Radiographic analyses are based on linear extrapolation for missing data imputation and rescue handling. Adverse events (AE) per 100 pt yrs (PY) are summarized up to a cut-off date of Aug 16 2018.

Results: Of 945 pts randomized and treated, 747(79%) completed Wk48 treatment, 163 (17.2%) discontinued (D/C) study drug prior to Wk48, 35

pts (4%) had not completed the Wk48 treatment as of this analysis. Primary reasons for D/C were AEs for 62 pts (6.5%), and lack of efficacy in 20 pts (2.1%). At Wk26, UPA15/30 was added for 37 (12%) of pts on MTX; MTX was added for 19 (6%) and 9 (3%) of pts on UPA15 and UPA30, respectively. Cumulative exposures to MTX mono, UPA15 mono and UPA30 mono were 314.4, 343.1 and 336.7 PYs, respectively. Through Wk48, pts on UPA15 and 30 vs MTX continued to have significantly greater improvements in clinical, functional and pt-reported outcomes (except FACIT-F for UPA15, p=.058 vs MTX) (Table 1). At Wk 48, CDAI Remission (REM) was achieved by 33% and 40% of pts on UPA15 and 30 respectively vs 17% on MTX; 28% and 33% vs 13% achieved Boolean REM. At Wk48, ΔmTSS were significantly less on UPA15 and UPA30 vs MTX. The safety profile of UPA15 and UPA30 mono was generally similar to MTX, except for total AEs and herpes zoster, which were higher with UPA15 and 30 vs MTX (Table 2). There were 11 deaths (including 3 non-treatment emergent deaths) due to varied causes.

Abstract THU0197 –Table 1.

Table 1. Efficacy Endpoints at Week 48			
	MTX N=314	UPA 15 MG N=317	UPA 30 MG N=314
ACR20, %	57	74***	75***
ACR50, %	43	63***	68***
ACR70, %	29	51***	53***
DAS28-CRP LDA (≤3.2), %	39	59***	66***
DAS28-CRP <2.6, %	29	49***	53***
CDAI LDA, (≤10), %	43	60***	64***
CDAI REM, (≤2.8), %	17	33***	40***
Boolean REM, %	13	28***	33***
Change in HAQ-DI	-0.74	-0.96***	-1.04***
Change in FACIT-F	8.5	10.1*	11.6***
Change in mTSS [§]	1.00	0.03***	0.14***

Results are based on NRI (binary endpoints), LOCF for rescue (change in HAQ-DI, FACIT-F), or linear extrapolation (change in mTSS); ***, p<.001 vs MTX; *, p=.058;

Boolean REM: TJC ≤1, SJC ≤1, CRP ≤1 mg/dl, PGA ≤1 (0–10 scale)

[§]mTSS from 2nd reading session of radiographs at Wk48

Abstract THU0197 –Table 2.

Table 2. Treatment emergent adverse event (AE) summary; E/100PY in Patients on monotherapy (censored at time of change to combination exposure of UPA+MTX/csDMARD)			
	MTX MONO N=314, PY=314.4	UPA 15 MONO N=317 PY=343.1	UPA 30 MONO N=314 PY=336.7
Any Adverse Event	303.1	345.4	358.2
Serious AE	11.8	14.3	15.4
AE Leading To D/C Of Study Drug	8.9	11.4	10.7
Serious Infection	2.9	4.1	5.0
Herpes Zoster [†]	1.3	6.4	4.8
Hepatic disorder [‡]	19.7	18.7	15.7
Any Malignancy (excluding NMSC) [§]	1.0	1.2	0.6
MACE (adjudicated) [¶]	0.6	0.9	1.2
VTE (adjudicated) [¶]	0.6	0	0.3
Deaths [‡]	0.3	1.2	1.8

[†]Herpes zoster: most involved a single dermatome and were non-serious. No cases of CNS involvement.

[‡]Hepatic disorders: majority were asymptomatic transaminase elevations.

[§]Malignancies excl. NMSC: MTX: 1 malignant neoplasm of ovary, 1 pt with gall bladder adenocarcinoma and hepatic cancer;

UPA15: 1 malignant neoplasm progression, 1 metastatic malignant melanoma, 1 squamous cell carcinoma of lung, 1 uterine carcinoma in situ;

UPA30: 1 cervix cell carcinoma, 1 uterine cancer

[¶]MACE (includes cardiovascular [CV] death, non-fatal Myocardial infarction [MI], non-fatal stroke):

MTX: 1 CV death, 1 non-fatal stroke; UPA15: 1 CV death, 1 pt had 2 adjudicated events: a non-fatal MI, followed by CV death (due to hypoxic encephalopathy, not MI); UPA30: 3 CV deaths, 1 non-fatal MI

[‡]VTE: MTX: 1 pt with PE; 1 pt with DVT and PE; UPA30: 1 DVT

[‡]Deaths (includes non-treatment emergent [NTE] deaths): MTX: 1 due to acute MI; UPA15: 2 due to MI (1 was NTE), 1 due to malignant melanoma and malignant neoplasm (NTE), 1 non-CV death; UPA30: 1 due to pneumonia/sepsis, 1 fatal MI, 2 CV deaths, 1 due to peritonitis, 1 CV death due to other causes (NTE); 1 death due to meningitis was reported on combination of UPA30+csDMARDs

Conclusion: UPA15 and 30 monotherapy continued to show significant improvements in RA signs and symptoms and inhibition of structural damage vs MTX through 48 wks. Only a small proportion of pts required MTX addition to UPA mono at Wk26 to achieve and maintain response. The safety profile based on all exposure remained consistent with ph 2 and 3 RCTs in RA, although an integrated safety analysis of UPA across the full ph 3 RA program will provide a more comprehensive understanding of the benefit:risk profile of UPA in RA.

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THU0198

EFFECTIVENESS OF REMISSION-INDUCTION STRATEGIES FOR EARLY RHEUMATOID ARTHRITIS (RA): A SYSTEMATIC LITERATURE REVIEW

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Background: Several trials studied initiation of therapy in early RA patients with a more intensive strategy than the standard disease modifying anti-rheumatic drug (DMARD) strategy according to current guidelines, with the aim of rapidly inducing clinical remission (remission-induction strategies).

Objectives: To establish in early RA patients the effectiveness of remission-induction strategies compared to standard DMARD strategies according to current guidelines.

Methods: A systematic literature review was performed, searching Embase and Medline October 2018 for RCTs and other comparative studies in

early RA patients, published the past 5 years. Induction therapy was defined as initiating treatment with a biological (b)DMARD or a targeted small molecule (ts)DMARD, both with or without a conventional synthetic (cs)DMARD, or initiating a csDMARD with moderately-high dosed glucocorticoids (GCs), with delayed tapering (not 'bridging therapy') or starting ≥ 2 csDMARDs. Standard DMARD strategy was defined as starting monotherapy with a csDMARD, with or without GCs as bridging therapy.

The outcome was remission according to a validated disease activity index or the Boolean definition.¹ Numbers of patients were extracted from all studies and relative risks (RR) for achieving remission with 95% confidence intervals (95%CI) per study were calculated. Subgroup analyses were performed for different definitions of remission, the use of a b/tsDMARD as part of the induction therapy strategy (yes/no) and the use of concomitant GC bridging therapy (yes/no) in standard DMARD strategies.

Results: Included were 22 clinical studies, involving 4435 patients in induction strategies and 3314 in standard DMARD strategies. For remission, 17 studies applied the criterion of DAS28 < 2.6 , 12 the Boolean remission definition, 7 CDAI ≤ 2.8 and 10 studies SDAI ≤ 3.3 . Remission had to be present during 6 to 12 months in all studies. Heterogeneity in study design prohibited providing an overall pooled effect estimate, but for subgroups pooled estimates were given for descriptive purposes.

In the figure we provide results for studies applying the DAS28 remission definition. Of those studies, 13/17 (76%) showed a statistically significant effect in favour of induction therapy. The pooled RR of achieving remission for strategies initiating bDMARDs was 1.73 [95%CI 1.59 to 1.88] versus the standard DMARD strategy without GC bridging, and it was 1.20 [95%CI 1.03 to 1.40] for induction strategies without bDMARD versus standard DMARD strategies without GC bridging. No superior effect of any induction strategy was found compared to that of standard DMARD strategies with GC bridging (pooled RR 1.06, 95%CI 0.83 to 1.35).

When using other remission definitions, all induction strategy studies with Boolean/CDAI/SDAI outcomes applied a b/tsDMARD, and 63%, 100% and 78%, respectively found a statistically significantly superior effect compared to standard DMARD strategies without GC bridging; however, compared to standard DMARD strategies with GC bridging, only trends in the same direction were found.

Figure 1 Outcomes of the individual studies using DAS28 based remission outcome.

*Nam 2014a: bDMARD used in induction therapy strategy and GC bridging in standard care.

Abstract THU0198 – Figure 1

Conclusion: Induction therapy strategies initiated in early RA patients are more effective in achieving remission compared to standard DMARD strategies. However, their benefit compared to that of a standard DMARD strategy with GC bridging seems to be limited.

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