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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Acknowledgement: AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barretto, PhD, of AbbVie, Inc.

Disclosure of Interests: Stephen Hall Grant/research support from: AbbVie Inc, BMS, Lilly, Janssen, Pfizer, UCB, and Novartis, Consultant for: AbbVie Inc, BMS, Lilly, Janssen, Pfizer, UCB, and Novartis, Tsutomu Takeuchi Grant/research support from: Astellas Pharma Inc, Chugai Pharmaceutical Co, Ltd., Daiichi Sankyo Co., Ltd., Takeda Pharmaceutical Co., Ltd., AbbVie GK, Asahikasei Pharma Corp., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Eisai Co., Ltd., AYUMI Pharmaceutical Corporation, Nipponkayaku Co. Ltd., Novartis Pharma K.K., Grant/research support from: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Grant/

research support from: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., AbbVie GK, Nipponkayaku Co.Ltd, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Taiho Pharmaceutical Co. Ltd., Chugai Pharmaceutical Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., GlaxoSmithKline K.K., UCB Japan Co. Ltd., Consultant for: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Consultant for: Astra Zeneca K.K., Eli Lilly Japan K.K., Novartis Pharma K.K., Mitsubishi Tanabe Pharma Co., Asahi Kasei Medical K.K., AbbVie GK, Daiichi Sankyo Co., Ltd., Bristol Myers Squibb, and Nipponkayaku Co. Ltd., Speakers bureau: Astellas Pharma Inc., Bristol Myers Squibb, Chugai Pharmaceutical Co., Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc., Santen Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., AbbVie GK, Asahi Kasei Pharma Corp., Taisho Toyama Pharmaceutical Co., Ltd., SymBio Pharmaceuticals Ltd., Janssen Pharmaceutical K.K., Celltrion Inc., Nipponkayaku Co. Ltd., and UCB Japan, Speakers bureau: AbbVie, Asahi Kasei, Astellas, AstraZeneca, AYUMI, Bristol-Myers Squibb, Chugai, Daiichi Sankyo, Eisai, Eli Lilly Japan, Janssen, Mitsubishi Tanabe, Nippon Kayaku, Novartis, Pfizer Japan Inc, Taiho, Taisho Toyama, Takeda, Teijin, Speakers bureau: AbbVie GK, Bristol-Myers K.K., Chugai Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Co., Pfizer Japan Inc, Astellas Pharma Inc, Daiichi Sankyo Co. Ltd., Eisai Co. Ltd., Sanofi K.K., Teijin Pharma Ltd., Takeda Pharmaceutical Co. Ltd., Novartis Pharma K.K., Glen Thomson Grant/research support from: AbbVie, Consultant for: Amgen, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead, Samsung, Sandoz and Lilly, Bernard Combe Consultant for: AbbVie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB, Andrea Everding: None declared, Karel Pavelka: None declared, Yanna Song Shareholder of: AbbVie, Employee of: AbbVie, Tim Shaw Shareholder of: AbbVie Inc, Employee of: AbbVie Inc, Alan Friedman Shareholder of: AbbVie, Employee of: AbbVie, In-Ho Song Shareholder of: AbbVie Inc, Employee of: AbbVie Inc, Eduardo Mysler Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Pfizer, Novartis, Janssen, Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc, and Roche, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc, and Roche, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Pfizer, Novartis, Janssen, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc, and Roche

Abstract THU0174 –Table 1.

Parameter at 12 weeks	SELECT EARLY (MTX-naïve)			SELECT COMPARE (MTX-IR)			SELECT BEYOND (bDMARD-IR)		
	MTX n=924	UPA 15 mg QD n=937	UPA 30 mg QD n=934	PBO n=551	ADA 40 mg QD n=557	UPA 15 mg QD n=551	PBO n=551	UPA 15 mg QD n=551	UPA 30 mg QD n=551
Proportion of patients achieving REM by various criteria (NRI), (%)									
DAS28-CRP <2.6	14	30***	41***	6	18	20***	10	29***	24***
CDAI ≤2.8	6	10***	21***	3	8	13***	5	8	12*
SDAI ≤3.3	6	10***	22***	3	7	12***	5	8	13*
Boolean	6	13**	15***	2	4	10***	2	7*	8**
Mean Change from Baseline (mmHg)									
TJC8	-7.3	-8.0***	-8.9***	-7.3	-8.0***	-8.6	-7.8***	-8.9***	-9.5***
SJC8	-8.2	-10.1***	-10.7***	-8.5	-9.7***	-10.0	-10.0***	-10.7***	-11.5***
PhGA	-26.6	-34.0***	-38.0***	-25.2	-33.6	-30.4***	-25.0	-38.0***	-39.2***
PGA	-35.1	-45.0***	-47.0***	-35.6	-43.6	-40.4***	-35.3	-45.0***	-46.3***
CRP	-10.6	-17.5***	-18.4***	-10.7	-16.4	-13.3***	-11.3	-17.0***	-17.5***
Proportion of patients achieving individual components of the Boolean REM criteria (NRI), (%)									
PGA SDO	13	25***	30***	7	12	20***	8	15*	10**
TJC8 S1	22	38***	37***	13	25	33***	13	30***	26**
SJC8 S1	12	48***	48***	10	32	42***	23	58***	58***
PhGA S1	62	84***	83***	50	69	76***	40	87***	79***

* For continuous endpoints, results are based on MMRM.

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

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

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

DAS28-CRP, 28-joint disease activity score using C-reactive protein; CDAI, clinical disease activity index; SDAI, simplified disease activity index; PGA, swollen joint count of 28 joints; TJC8, tender joint count of 8 joints; PhGA, patient's global assessment of disease activity; PGA, physician's global assessment of disease activity; CRP, high-sensitivity C-reactive protein.

DOI: 10.1136/annrheumdis-2019-eular.2003

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