Title

OP0128 INTEGRATED LABORATORY ABNORMALITY PROFILES OF UPADACITINIB WITH UP TO 4.5 YEARS OF EXPOSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED IN THE SELECT PHASE 3 PROGRAM

Journal

Annals of the Rheumatic Diseases, 80(Suppl 1)

ISSN

0003-4967

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Publication Date

2021-06-01

DOI

10.1136/annrheumdis-2021-eular.1815

Peer reviewed

Results: Of the 398 pooled PLC patients, 285 continued their MTX and 113 had no MTX (or other background csDMARDs). Baseline characteristics were similar (Table 1).

Table 1. Baseline characteristics

	Placebo without background csDMARD	Placebo + continued MTX
n	113	285
Age (years) *	56 (48-64)	56 (45-64)
Female (%)	95 (84.1%)	236 (82.8%)
Disease duration (years)	8.4±5.2	8.8±7.5
ACPA positive (%)	88 (77.9%)	214 (75.1%)
RF positive (%)	90 (79.6%)	211 (74%)
SJC 66 (0-66)	15.9±9.9	16.2±10.8
TJC 68 (0-68)	29.1±16.8	26.7±15.7
PGA (VAS 0-10)	6.8±2.2	6.5±2.1
EGA (VAS 0-10)	6.4±1.8	6.1±1.9
Pain (VAS 0-10)	7.0±1.9	6.6±2.1
HAQ-DI (0-3)	1.6±0.7	1.6±0.6
CRP (mg/dL) *	1.2 (0.5-3.5)	1.0 (0.4-2.6)
CDAI	39.4±13.5	38.5±12.8
Concomitant GC intake (%)	67 (59.3%)	174 (61.1%)
Concomitant MTX (%)	0 (0%)	285 (100%)
MTX dosage ≥12.5mg (%)	0 (0%)	222 (77.9%)
MTX dosage <12.5mg (%)	0 (0%)	63 (22.1%)

Data is shown as mean (± standard deviation) or n (%) unless stated otherwise* median (IQR)

At wk 16, an ACR20 response was achieved by 72/285 (25.3%) of PLC+c-MTX and 14/113 (12.4%) receiving PLC only patients (p=0.005); for ACR50 these numbers were 25/285 (8.4%) vs. 1/113 (0.9%; p=0.003); and for ACR70 they were 8/285 (2.8%) vs. 0/113 (0%; p=0.112). Also, significantly more PLC+cMTX patients achieved a CDAI LDA at wk 16 (25/285, 8.8%) compared to PLC only treated patients (2/113; 1.8%; p=0.013). Results between the two arms were numerically or statistically different already from week 4 (for ACR 20) or week 8 (ACR 50, CDAI LDA) onwards (Figure 1).

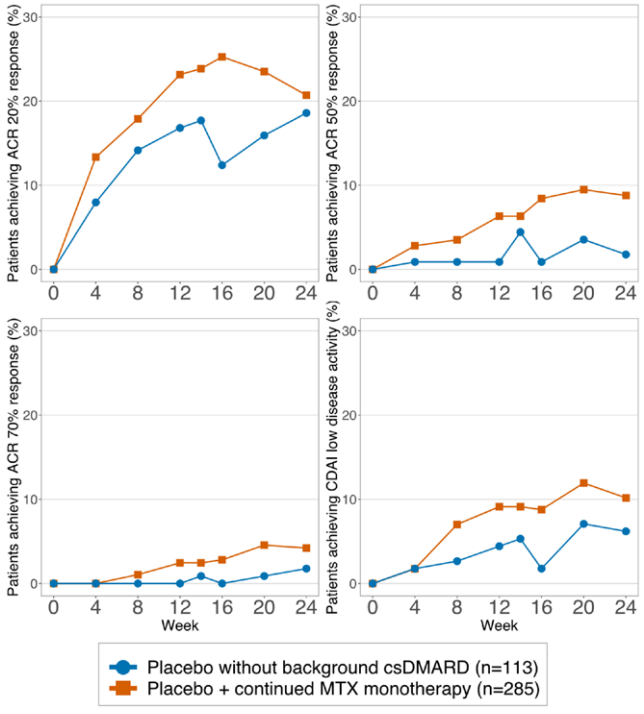

Figure 1. ACR 20/50/70 and CDAI LDA responses of PLC patients with continued MTX vs. PLC patients without csDMARD background therapy.

Conclusion: In patients randomized to placebo therapy, continued MTX background therapy increases clinical responses and achievement of good clinical states. These findings imply that pre-existing and putatively insufficient background therapy should be effectively optimized before enrollment into a clinical trial protocol.

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[2] Aletaha D *et al. Lancet* 2017; **389**: 1206–1217.

Acknowledgements: This study, carried out under YODA Project # 2018-3704, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C. The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C.

Disclosure of Interests: Andreas Kerschbaumer Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli-Lilly, Gilead, Merck Sharp and Dohme, Novartis and Pfizer, Paid instructor for: Celgene, Zaida Iasha Rivai: None declared, Josef S. Smolen Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO Pharma, Janssen, Lilly, Merck Sharp & Dohme, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, and UCB, Consultant of: AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Gilead, ILTOO Pharma, Janssen, Lilly, Merck Sharp & Dohme, Novartis-Sandoz, Pfizer, Roche, Samsung, Sanofi, and UCB, Grant/research support from: Abbvie, AstraZeneca, Janssen, Lilly, Merck Sharpe & Dohme, Pfizer, and Roche, Daniel Aletaha Speakers bureau: Abbvie, Amgen, Lilly, Merck, Novartis, Pfizer, Roche, Sandoz, Consultant of: Abbvie, Amgen, Lilly, Merck, Novartis, Pfizer, Roche, Sandoz, Grant/research support from: Abbvie, Amgen, Lilly, Novartis, Roche, SoBi, Sanofi

DOI: 10.1136/annrheumdis-2021-eular.1532

OP0128

INTEGRATED LABORATORY ABNORMALITY PROFILES OF UPADACITINIB WITH UP TO 4.5 YEARS OF EXPOSURE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED IN THE SELECT PHASE 3 PROGRAM

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Background: Upadacitinib (UPA) is an oral Janus kinase inhibitor approved for rheumatoid arthritis (RA). The safety and efficacy of UPA has been evaluated across a spectrum of patients (pts) with RA in the phase 3 SELECT clinical program.[1,2]

Objectives: To describe long-term laboratory profiles (cutoff date: June 30, 2020) associated with exposure to UPA, adalimumab (ADA), and methotrexate (MTX) in pts with RA treated in the SELECT trials.

Methods: Data were analyzed from 6 randomized controlled UPA RA trials.[1,2] The proportions of pts experiencing potentially clinically significant laboratory changes at a single time point were summarized for the following groups: pooled UPA 15 mg once daily (QD; UPA15; 6 trials), pooled UPA 30 mg QD (UPA30; 4 trials), ADA 40 mg every other week (EOW; 1 trial), and MTX monotherapy (1 trial). Pts received UPA with/without background conventional synthetic disease-modifying antirheumatic drugs. Treatment-emergent adverse events are reported as exposure-adjusted event rates (events/100 pt-years [E/100 PY]). Toxicity was graded per OMERACT criteria, or NCI CTCAE for creatine phosphokinase (CPK) and creatinine.

Results: 4413 pts received ≥1 dose of UPA (UPA15, n=3209; UPA30, n=1204). Exposures were comparable between treatment groups (Table). Proportions of pts with Grade (Gr) 3 and 4 decreases in hemoglobin were highest with UPA30 and MTX (Table). Rates of anemia, as reported by the investigator, were comparable between UPA15, ADA, and MTX groups (Figure); the frequency of UPA-treated pts who discontinued due to anemia was low in all arms. Gr 3 and 4 decreases in neutrophils and lymphocytes with UPA were dose-dependent and higher vs ADA or MTX. Discontinuations due to neutropenia and lymphopenia were rare (<0.1%). Transaminase elevations were more frequent with UPA and MTX vs ADA; however, the proportion of pts who discontinued due to increases in alanine (ALT) or aspartate aminotransferase (AST) were comparable between UPA15 and ADA, and numerically higher with UPA30 and MTX. CPK elevations were more frequent with UPA (Figure). Most events were asymptomatic, and the 1 case of rhabdomyolysis in the UPA30 group was unrelated to study drug (attributed to influenza).

Table 1. Pts with potentially clinically significant laboratory changes

Variable, n (%)	MTX monotherapy (n=314; 637.4 PY)	ADA 40 mg EOW (n=579; 1051.8 PY)	UPA 15 mg QD (n=3209; 7023.8 PY)	UPA 30 mg QD (n=1204; 3091.6 PY)
Mean (SD) exposure, weeks	106 (67)	95 (70)	114 (64)	134 (66)
Median (range) exposure, weeks	144 (1, 221)	118 (2, 231)	136 (0, 232)	160 (0, 231)
Hemoglobin, g/L				
Gr 3 (70–<80 or decreased 21–<30)	28[a] (9.0)	24[b] (4.2)	254[d] (7.9)	169[f] (14.2)
Gr 4 (<70 or decreased ≥30)	16[a] (5.1)	16[b] (2.8)	101[d] (3.2)	78[f] (6.5)
Neutrophils, 10^9/L				
Gr 3 (0.5–<1.0)	3[a] (1.0)	3[b] (0.5)	40[d] (1.2)	37[g] (3.1)
Gr 4 (<0.5)	1[a] (0.3)	1[b] (0.2)	10[d] (0.3)	5[g] (0.4)
Lymphocytes, 10^9/L				
Gr 3 (0.5–<1.0)	74[a] (23.7)	53[b] (9.2)	802[d] (25.1)	423[g] (35.5)
Gr 4 (<0.5)	5[a] (1.6)	3[b] (0.5)	75[d] (2.3)	47[g] (3.9)
ALT, U/L				
Gr 3 (3.0–8.0 × ULN)	26[a] (8.3)	13[c] (2.3)	152[e] (4.8)	71[h] (5.9)
Gr 4 (>8.0 × ULN)	5[a] (1.6)	4[c] (0.7)	26[e] (0.8)	10[h] (0.8)
AST, U/L				
Gr 3 (3.0–8.0 × ULN)	15[a] (4.8)	9[c] (1.6)	101[e] (3.2)	36[h] (3.0)
Gr 4 (>8.0 × ULN)	1[a] (0.3)	5[c] (0.9)	18[e] (0.6)	8[h] (0.7)
CPK, U/L				
Gr 3 (>5.0–10.0 × ULN)	2[a] (0.6)	3[c] (0.5)	65[e] (2.0)	36[i] (3.0)
Gr 4 (>10.0 × ULN)	0[a] (0)	3[c] (0.5)	27[e] (0.8)	15[i] (1.3)
Creatinine, µmol/L				
Gr 3 (>3.0–6.0 × ULN)	0[a] (0)	1[c] (0.2)	3[e] (<0.1)	2[j] (0.2)
Gr 4 (>6.0 × ULN)	0[a] (0)	4[c] (0.7)	8[e] (0.3)	1[j] (<0.1)

[a]n=312. [b]n=576. [c]n=577. [d]n=3201. [e]n=3199. [f]n=1193. [g]n=1192. [h]n=1195. [i]n=1196. [j]n=1197ULN, upper limit of normal

Conclusion: This long-term analysis of UPA-treated pts with RA showed dose-dependent relationships for several laboratory abnormalities. Incidences of these with UPA15 were typically higher than with ADA but similar to MTX, except for increased CPK elevations. Treatment discontinuations due to laboratory abnormalities were infrequent and similar across all treatment groups.

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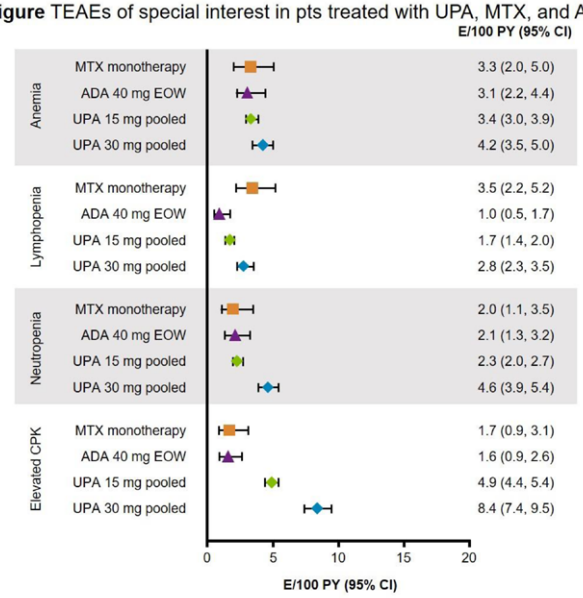
Acknowledgements: AbbVie funded this study; contributed to its design; participated in data collection, analysis, and interpretation of the data; and participated in the writing, review, and approval of the abstract. No honoraria or payments were made for authorship. Medical writing support was provided by Russell Craddock, PhD, of 2 the Nth (Cheshire, UK), and was funded by AbbVie.

Figure TEAEs of special interest in pts treated with UPA, MTX, and ADA[a]



MTX: n=314, PY=637.4; ADA 40 mg EOW: n=579, PY=1051.8; UPA 15 mg pooled: n=3209, PY=7023.8; UPA 30 mg pooled: n=1204, PY=3091.6

[a]Pts who switched from placebo, ADA, or MTX to UPA were included in the UPA analysis set from the start of UPA, while those who switched from UPA to ADA were included in the ADA analysis set from the start of ADA, and were censored at time of switch. MTX monotherapy was censored at time of rescue to combination therapy (addition of UPA)

ADA, adalimumab; CI, confidence interval; CPK, creatine phosphokinase; E/100 PY, events/100 pt-years; EOW, every other week; MTX, methotrexate; pt, patient; PY, pt-years; TEAE, treatment-emergent adverse event; UPA, upadacitinib

Disclosure of Interests: Christina Charles-Schoeman Consultant of: AbbVie, Gilead, Pfizer, and Sanofi/Regeneron, Grant/research support from: AbbVie, Bristol-Myers Squibb, and Pfizer, Jon T Giles Consultant of: AbbVie, Bristol-Myers Squibb, Eli Lilly, Gilead, Pfizer, and UCB, Grant/research support from: Pfizer, Nancy Lane Consultant of: Amgen, Mallinckrodt, Pfizer, and Roche, Ernest Choy Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Chugai, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer, Regeneron, Roche, Sanofi, and UCB, Consultant of: AbbVie, Amgen, Biocon, Biogen, Chugai, Eli Lilly, Gilead, Janssen, Merck Serono, Novartis, Pfizer, Regeneron, Roche, R-Pharm, and Sanofi, Grant/research support from: Bio-Cancer, Biogen, Novartis, Pfizer, Roche, Sanofi, and UCB, Daniel Furst Speakers bureau: AbbVie, Continuing Medical Education, and Novartis, Consultant of: Actelion, Amgen, Bristol-Myers Squibb, Corbus, Galapagos, Novartis, and Pfizer, Grant/research support from: Actelion, Amgen, Bristol-Myers Squibb, Corbus, Galapagos, GSK, NIH, Novartis, Pfizer, Roche/Genentech, and Sanofi, Jiří Vencovský Speakers bureau: AbbVie, Biogen, MSD, Pfizer, Roche, Sanofi, and UCB, Consultant of: AbbVie, Boehringer Ingelheim, Eli Lilly, Gilead, and Octapharma, Anthony G Wilson: None declared, Gerd Rüdiger Burmester Speakers bureau: AbbVie, Eli Lilly, Gilead, Janssen, MSD, Pfizer, Roche, and UCB, Consultant of: AbbVie, Eli Lilly, Gilead, Janssen, MSD, Pfizer, Roche, and UCB, Tim Shaw Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Yanna Song Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Heidi Camp Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Nasser Khan Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Jillian Yee Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Samuel Anyanwu Shareholder of: May own stock or options in AbbVie, Employee of: AbbVie, Iain McInnes Consultant of: AbbVie, Celgene, Janssen, Novartis, and UCB, Grant/research support from: Celgene, Janssen, Novartis, Pfizer, Roche, and UCB
DOI: 10.1136/annrheumdis-2021-eular.1815