Women's Hospital and Harvard Medical School, Boston, United States of America; [5]*Dept of Rheumatology, W China Hospital, Sichuan Univ, Sichuan, China*; [6]*Dept of Nephrology and Rheumatology, Kyorin Univ School of Medicine, Tokyo, Japan*; [7]*Dept of Rheumatology and Connective Tissue Diseases, 2nd Univ Hospital, Bydgoszcz, Poland*; [8]*Facultad de Medicina, Univ Autonoma de Chihuahua, Chihuahua, Mexico*; [9]*Goethe Univ and Fraunhofer IME-TMP, Frankfurt, Germany*

Background: Upadacitinib (UPA) is an oral, reversible, JAK inhibitor approved for treatment of rheumatoid arthritis (RA) and currently under evaluation for treatment of psoriatic arthritis (PsA).
Objectives: To assess the efficacy and safety of UPA vs placebo (PBO) and adalimumab (ADA) in patients (pts) with PsA and prior IR or intolerance to ≥1 non-biologic DMARD (non-bDMARD).
Methods: Pts with active PsA (≥3 swollen and ≥3 tender joints), active or historical psoriasis, and on ≤2 non-bDMARDs were randomized 1:1:1:1 to once daily UPA 15mg (UPA15), UPA 30mg (UPA30), ADA 40mg every other week, or PBO. The primary endpoint was the proportion of pts achieving ACR20 for UPA vs PBO at Wk 12. Multiplicity controlled secondary endpoints for each dose of UPA vs PBO included change in HAQ-DI, FACIT-F, and SF-36 PCS (Wk 12); static Investigator Global Assessment of Psoriasis of 0 or 1, PASI75, and change in Self-Assessment of Psoriasis Symptoms (Wk 16); change in modified Sharp/van der Heijde Score (mTSS), proportion of pts achieving MDA, and resolution of enthesitis (LEI=0) and dactylitis (LDI=0) (Wk 24). For each dose of UPA, the multiplicity-controlled analysis also included non-inferiority and superiority vs ADA for ACR20 and superiority for HAQ-DI and pt's assessment of pain NRS (Wk 12). ACR50/70 at Wk 12 and ACR20 at Wk 2 were additional secondary endpoints. Treatment-emergent adverse events (TEAEs) through 24 wks are reported for pts who received ≥1 dose of study drug.
Results: 1705 pts were randomized; 1704 received study drug (53.2% female, mean age 50.8 yrs, mean duration of PsA diagnosis 6.1 yrs). 82% were on ≥1 concomitant non-bDMARD, of whom 84% received MTX +/- another non-bDMARD. At Wk 12, ACR20 rates were 70.6% with UPA15 and 78.5% with UPA30 vs 36.2% with PBO ($p < .001$ for UPA15/30 vs PBO) and 65.0% with ADA (non-inferiority, $p < .001$ for UPA15/30 vs ADA; superiority, $p < .001$ for UPA30 vs ADA). A greater proportion of pts achieved ACR50/70 with UPA15/30 vs PBO and UPA30 vs ADA. Improvements were observed with UPA15/30 vs PBO for all multiplicity controlled secondary endpoints and for UPA 15/30 vs ADA for HAQ-DI and UPA 30 vs ADA for improvement in pain (**Figure 1A-1B**). At Wk 24, change in mTSS was 0.25 for PBO, -0.04 for UPA15, 0.03 for UPA30, and 0.01 for ADA ($p < 0.001$ for UPA15/30 vs PBO). The rates of TEAEs and serious AEs, including serious infections, were similar in the PBO, UPA15, and ADA arms and higher with UPA30 (**Figure 2**). The rate of herpes zoster was similar for PBO and UPA15/30. No MACE was reported with UPA. One malignancy occurred in each of the PBO and UPA15 arms, and 3 malignancies were reported in each of the UPA30 and ADA arms. VTE were reported in 1 pt on PBO, 1 pt on UPA30, and 2 pts on ADA. One death occurred in the PBO arm.
Conclusion: In this non-bDMARD-IR PsA population, treatment with UPA15/30 demonstrated improvement in musculoskeletal symptoms, psoriasis, physical function, pain, and fatigue and inhibited radiographic progression; improvements were observed by Wk 2. At Wk 12, UPA15/30 were non-inferior to ADA for ACR20, with superiority demonstrated for UPA30. Greater percentages of UPA vs PBO pts achieved stringent measures of disease control (MDA, ACR50/70, sIGA 0/1). No new safety signals were identified compared with the safety profile observed in RA.

Figure 1. Efficacy Outcomes

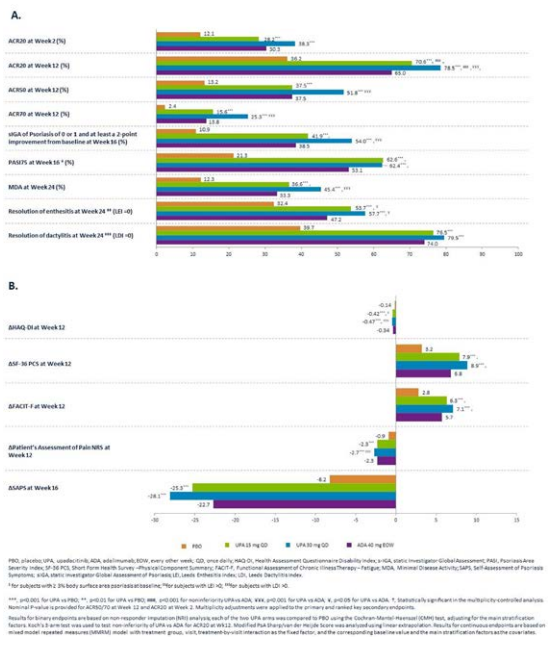
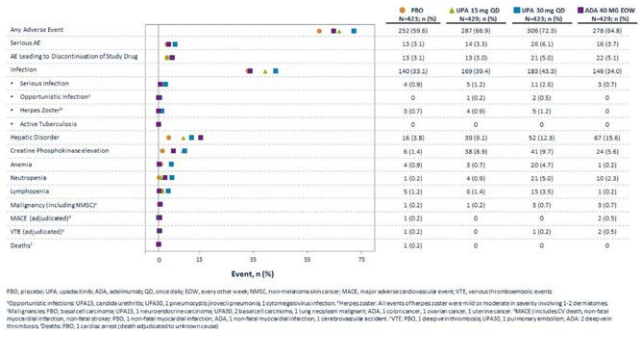


Figure 2. Safety Summary Through Week 24



PBO, placebo; UPA, upadacitinib; ADA, adalimumab; QD, once daily; EOW, every other week; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event; VTE, venous thromboembolic events

†Opportunistic infections: UPA15, candida urethritis; UPA30, 1 pneumocystis jirovecii pneumonia, 1 cytomegalovirus infection. ‡Herpes zoster: All events of herpes zoster were mild or moderate in severity involving 1-2 dermatomes. §Malignancies: PBO, basal cell carcinoma; UPA15, 1 neuroendocrine carcinoma; UPA30, 2 basal cell carcinoma, 1 lung neoplasm malignant; ADA, 1 colon cancer, 1 ovarian cancer, 1 uterine cancer. ¶MACE (includes CV death, non-fatal myocardial infarction, non-fatal stroke): PBO, 1 non-fatal myocardial infarction; ADA, 1 non-fatal myocardial infarction, 1 cerebrovascular accident. #VTE: PBO, 1 deep vein thrombosis; UPA30, 1 pulmonary embolism; ADA: 2 deep vein thrombosis. ‖Deaths: PBO, 1 cardiac arrest (death adjudicated to unknown cause)

Disclosure of Interests: Iain McInnes: None declared, Jaclyn Anderson Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Marina Magrey Grant/research support from: Amgen, AbbVie, and UCB Pharma, Consultant of: Novartis, Eli Lilly, Pfizer, and Janssen, Joseph F. Merola Consultant of: Merck, Abbvie, Dermavant, Eli Lilly, Novartis, Janssen, UCB, Celgene, Sanofi, Regeneron, Arena, Sun Pharma, Biogen, Pfizer, EMD Sorono, Avotres and Leo Pharma, Yi Liu: None declared, Mitsumasa Kishimoto Consultant of: bbVie, Eli Lilly, Celgene, Pfizer, Gilead, Janssen, and UCB Pharma, Speakers bureau: AbbVie, Eisai, Celgene, Pfizer, Novartis, Eli Lilly, Tanabe-Mitsubishi, Ayumi, Janssen, Astellas, and UCB Pharma, Sławomir Jeka Speakers bureau: AbbVie, Pfizer, Roche, Novartis, MSD, Sandoz, Eli Lilly, Egis, UCB, Celgene, Cesar Francisco Pacheco Tena: None declared, xin wang Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Liang Chen Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Patrick Zueger Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Aileen Pangan Shareholder of: AbbVie Inc., Employee of: AbbVie Inc., Frank Behrens Grant/research support from: Pfizer, Janssen, Chugai, Celgene and Roche, Consultant of: Pfizer, AbbVie, Sanofi, Lilly, Novartis, UCB, Genzyme, Boehringer, Janssen, MSD, Celgene, Roche and Chugai
DOI: 10.1136/annrheumdis-2020-eular.6727

Biological DMARDs in RA I

OP0018

A MULTICENTER RANDOMIZED STUDY IN EARLY RHEUMATOID ARTHRITIS TO COMPARE ACTIVE CONVENTIONAL THERAPY VERSUS THREE BIOLOGICAL TREATMENTS: 24 WEEK EFFICACY RESULTS OF THE NORD-STAR TRIAL

M. L. Hetland[1], E. A. Haavardsholm[1], A. Rudin[1], D. Nordström[1], M. Nurmohamed[1], B. Gudbjornsson[1], J. Lampa[1], K. Hørslev-Petersen[1], T. Uhlig[1], G. Gröndal[1], M. Østergaard[1], M. Heiberg[1], J. Twisk[1], S. Krabbe[1], K. Lend[1], I. Olsen[1], J. Lindqvist[1], A. K. H. Ekwall[1], K. L. Grøn[1], M. C. Kapetanovic[1], F. Faustini[1], R. Tuompo[1], T. Lorenzen[1], G. Cagnotto[1], E. Baecklund[1], O. Hendricks[1], D. Vedder[1], T. Sokka-Isler[1], T. Husmark[1], M. K. A. Ljosa[1], E. Brodin[1], T. Ellingsen[1], A. Soderbergh[1], M. Rizk[1], Å. Reckner[1], P. Larsson[1], L. Uhrenholt[1], S. A. Just[1], D. Stevens[1], T. B. Laurberg[1], G. Bakland[1], R. Van Vollenhoven[1]. [1]*Denmark, Finland, Iceland, Netherlands, Norway, Sweden*

Background: The optimal first-line treatment of patients (pts) with early rheumatoid arthritis (RA) is yet to be established.
Objectives: The primary aim was to assess and compare the proportion of pts who achieved remission with active conventional therapy (ACT) and with three different biologic therapies after 24 wks. Secondary aims were to assess and compare other efficacy measures.
Methods: The investigator-initiated NORD-STAR trial (NCT01491815) was conducted in the Nordic countries and Netherlands. In this multicenter, randomized, open-label, blinded-assessor study pts with treatment-naïve, early RA with DAS28>3.2, and positive RF or ACPA, or CRP >10mg/L were randomized 1:1:1:1. Methotrexate (25 mg/week after one month) was combined with: 1) (ACT): oral prednisolone (tapered quickly); *or*: sulphasalazine, hydroxychloroquine and mandatory intra-articular (IA) glucocorticoid (GC) injections in swollen joints <wk 20; 2) certolizumab 200 mg EOW SC (CZP); 3) abatacept 125 mg/wk SC (ABA); tocilizumab 162 mg/wk SC (TCZ). IA GC was allowed in all arms <wk 20. Primary outcome was clinical disease activity index remission (CDAI≤2.8) at wk 24. Secondary outcomes included CDAI remission over time and other remission criteria. Dichotomous outcomes were analyzed by adjusted logistic regression with non-responder imputation (NRI). Non-inferiority analyses had a pre-specified margin of 15%.
Results: 812 pts were randomized. Age was 54.3±14.7 yrs (mean±SD), 31.2% were male, DAS28 5.0±1.1, 74.9% were RF and 81.9% ACPA positive. Fig 1 shows the adjusted CDAI remission rates over time with 95% CI. Table shows crude remission and response rates and absolute differences in adjusted

Table. Primary and key secondary outcomes at 24 weeks (ITT)

	Active conventional therapy (ACT)	Certolizumab +MTX	Abatacept +MTX	Tocilizumab +MTX
No of pts (ITT)	200	203	204	188[§]
		Crude remission and response rates		
CDAI remission	**42.0%**	**47.8%**	**52.5%**	**41.0%**
ACR/EULAR Boolean remission	34.0%	38.4%	37.3%	31.4%
DAS28 remission	63.5%	68.5%	69.6%	63.3%
SDAI remission	41.5%	49.8%	51.5%	42.6%
EULAR good response	71.5%	76.9%	79.9%	71.3%
		Difference (95% CI) in rates with Arm 1 as reference (adjusted)		
CDAI remission	**Ref**	**4% (-5 to 13%)**	**9% (0.1 to 19%)**	**-1% (-10 to 9%)**
ACR/EULAR Boolean remission	Ref	4% (-6 to 13%)	5% (-5 to 14%)	-4% (-13 to 6%)
DAS28 remission	Ref	3% (-6 to 11%)	5% (-4 to 13%)	-1% (-10 to 8%)
SDAI remission	Ref	6% (-3 to 18%)	9% (-0.3 to 18%)	1% (-8 to 11%)
EULAR good response	Ref	4% (-4 to 14%)	8% (-2 to 18%)	0.4% (-10 to 11%)

[§]17 patients allocated to Tocilizumab did not receive it due to its unavailability and were excluded from ITT.

remission and response rates (superiority analysis). Differences in remission and response rates with CZP and TCZ, but not with ABA, remained within the pre-defined non-inferiority margin versus ACT, Fig 2.

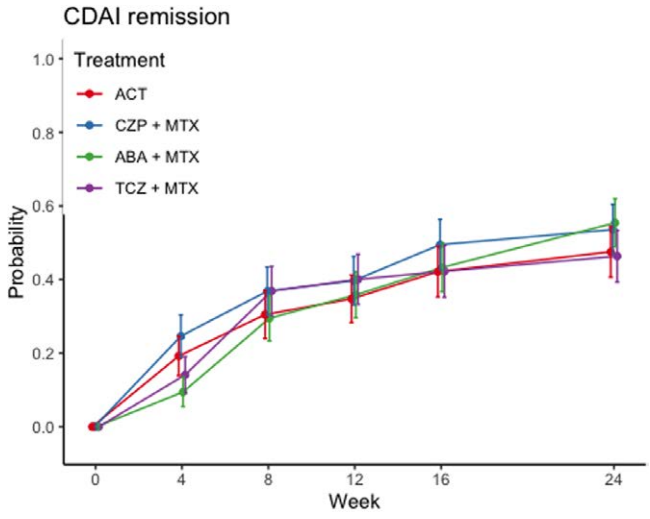
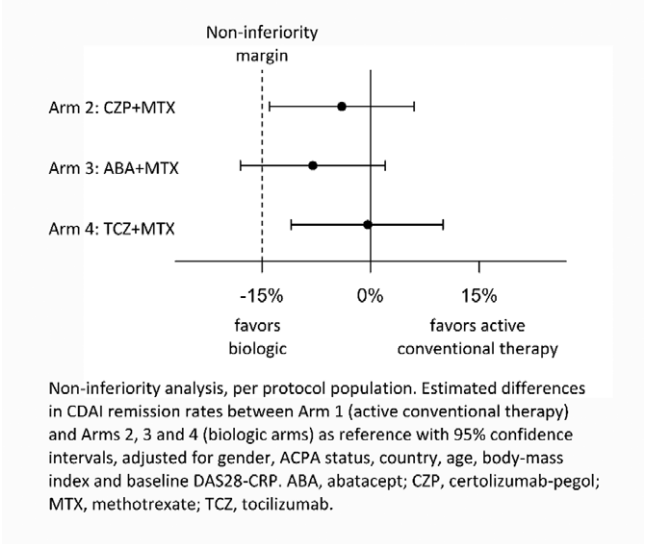


Figure 1. CDAI remission over time (adj. estimates with 95% CI)



Non-inferiority analysis, per protocol population. Estimated differences in CDAI remission rates between Arm 1 (active conventional therapy) and Arms 2, 3 and 4 (biologic arms) as reference with 95% confidence intervals, adjusted for gender, ACPA status, country, age, body-mass index and baseline DAS28-CRP. ABA, abatacept; CZP, certolizumab-pegol; MTX, methotrexate; TCZ, tocilizumab.

Figure 2. Non-inferiority analysis of protocol population. Estimated differences in CDAI remission rates between Arm 1 (active conventional therapy) and Arms 2, 3, and 4 (biologic arms) as reference with 95% confidence intervals, adjusted for gender, ACPA status, country, age, body-mass index and baseline DAS28-CRP. ABA, abatacept; CZP, certolizumab-pegol; MTX, methotrexate; TCZ, tocilizumab.

Conclusion: High remission rates were found across all four treatment arms at 24 wks. Higher CDAI remission rate was observed for ABA versus ACT (+9%) and for CZP (+4%), but not for TCZ (-1%). With the predefined 15% margin, ACT was non-inferior to CZP and TCZ, but not to ABA. This underscores the efficacy of active conventional therapy based on MTX combined with glucocorticoids and may guide future treatment strategies for early RA.

Acknowledgments: Manufacturers provided CZP and ABA.

Disclosure of Interests: Merete L. Hetland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen and Pfizer, Consultant of: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck and Samsung Bioepis, Espen A Haavardsholm Grant/research support from: AbbVie, UCB Pharma, Pfizer Inc, MSD Norway, Roche Norway, Consultant of: Pfizer, AbbVie, Janssen-Cilag, Gilead, UCB Pharma, Celgene, Lilly, Paid instructor for: UCB Pharma, Speakers bureau: Pfizer, AbbVie, UCB Pharma, Celgene, Lilly, Roche, MSD, Anna Rudin Consultant of: Astra/Zeneca, Dan Nordström Consultant of: Abbvie, Celgene, Lilly, Novartis, Pfizer, Roche and UCB., Speakers bureau: Abbvie, Celgene, Lilly, Novartis, Pfizer, Roche and UCB., Michael Nurmohamed Grant/research support from: Not related to this research, Consultant of: Not related to this research, Speakers bureau: Not related to this research, Björn Gudbjornsson Speakers bureau: Novartis and Amgen, Jon Lampa Speakers bureau: Pfizer, Janssen, Novartis, Kim Hørslev-Petersen: None declared, Till Uhlig Consultant of: Lilly, Pfizer, Speakers bureau: Grünenthal, Novartis, Gerdur Gröndal: None declared, Mikkel Østergaard Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Merck, and Novartis, Consultant of: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Roche, Sandoz, Sanofi, and UCB, Marte Heiberg: None declared, Jos Twisk: None declared, Simon Krabbe: None declared, Kristina Lend: None declared, Inge Olsen: None declared, Joakim Lindqvist: None declared, Anna-Karin H Ekwall Consultant of: AbbVie, Pfizer, Kathrine L. Grøn Grant/research support from: BMS, Meliha C Kapetanovic: None declared, Francesca Faustini: None declared, Riitta Tuompo: None declared, Tove Lorenzen: None declared, Giovanni Cagnotto: None declared, Eva Baecklund: None declared, Oliver Hendricks Grant/research support from: Pfizer, MSD, Daisy Vedder: None declared, Tuulikki Sokka-Isler: None declared, Tomas Husmark: None declared, Maud-Kristine A Ljosa: None declared, Eli Brodin: None declared, Torkell Ellingsen: None declared, Annika Soderbergh: None declared, Milad Rizk Speakers bureau: AbbVie, Åsa Reckner: None declared, Per Larsson: None declared, Line Uhrenholt Speakers bureau: Abbvie, Eli Lilly and Novartis (not related to the submitted work), Søren Andreas Just: None declared, David Stevens: None declared, Trine Bay Laurberg Consultant of: UCB Pharma (Advisory Board), Gunnstein Bakland Consultant of: Novartis, UCB, Ronald van Vollenhoven Grant/research support from: BMS, GSK, Lilly, UCB, Pfizer, Roche, Consultant of: AbbVie, AstraZeneca, Biogen, Biotest, Celgene, Gilead, Janssen, Pfizer, Servier, UCB, Speakers bureau: AbbVie, Pfizer, UCB

DOI: 10.1136/annrheumdis-2020-eular.689

OP0019

STABLE VERSUS TAPERED AND WITHDRAWN TREATMENT WITH TUMOR NECROSIS FACTOR INHIBITOR IN RHEUMATOID ARTHRITIS REMISSION (ARCTIC REWIND): A RANDOMISED, OPEN-LABEL, PHASE 4, NON-INFERIORITY TRIAL

S. Lillegraven[1], N. P. Sundlisæter[1], A. B. Aga[1], J. Sexton[1], I. Olsen[2], Å. Lexberg[3], T. M. Madland[4], H. Fremstad[5], C. A. Høili[6], G. Bakland[7], C. Spada[8], H. Haukeland[9], I. M. Hansen[10], E. Moholt[1], T. Uhlig[1], D. Solomon[11], D. Van der Heijde[1,12], T. K. Kvien[1], E. A. Haavardsholm[1]. *[1]Diakonhjemmet Hospital, Oslo, Norway; [2]Oslo Univ. Hosp., Oslo, Norway; [3]Vestre Viken HF, Drammen, Norway; [4]Haukeland Univ. Hosp., Bergen, Norway; [5]Ålesund Hosp.,*