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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 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 pts 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

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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

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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 (25mg/week after one month) was combined with: 1) (ACT): oral prednisolone (tapered quickly); or: 2) sulphasalazine, hydroxychloroquine and mandatory intra-articular (IA) glucocorticoid (GC) injections in swollen joints <wk 20; 3) certolizumab 200mg EOW SC (CZP); 4) abatacept 125mg/wk SC (ABA); tocilizumab 162mg/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 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 [§]
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) **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.

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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

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