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, 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 comitant non-bDMARD, of whom 48% 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 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.


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Biological DMARDs in RA

**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-asseressor study pts with treatment-naive, early RA with DAS28>3.2, and positive RF or ACCP, 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 sulphasalazine, hydroxychloroquine and mandatory intra-articular (IA) glucocorticoid (GC) injections to all <wk 20.3) certolizumab 200mg EOW SC (CZP); 3) abatacept 125mg/wk SC (CZP); 4) 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 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 remisision and response rates and absolute differences in adjusted
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 2 (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 golituzumab and may guide future treatment strategies for early RA.

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

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Active conventional therapy (ACT)</th>
<th>Certolizumab +MTX</th>
<th>Abatacept +MTX</th>
<th>Tocilizumab +MTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of pts (ITT)</td>
<td>200</td>
<td>203</td>
<td>204</td>
<td>188</td>
</tr>
<tr>
<td>CDAI remission</td>
<td>42.0%</td>
<td>47.8%</td>
<td>52.5%</td>
<td>41.0%</td>
</tr>
<tr>
<td>ACR/EULAR Boolean remission</td>
<td>34.0%</td>
<td>38.4%</td>
<td>37.3%</td>
<td>31.4%</td>
</tr>
<tr>
<td>DAS28 remission</td>
<td>63.5%</td>
<td>68.5%</td>
<td>69.6%</td>
<td>63.3%</td>
</tr>
<tr>
<td>SDAI remission</td>
<td>41.5%</td>
<td>49.8%</td>
<td>51.6%</td>
<td>42.6%</td>
</tr>
<tr>
<td>EULAR good response</td>
<td>71.5%</td>
<td>79.9%</td>
<td>79.9%</td>
<td>71.3%</td>
</tr>
</tbody>
</table>

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% (-4 to 14%) -4% (-13 to 6%)
DAS28 remission Ref 3% (-6 to 11%) 5% (1.2 to 9%) 1% (-8 to 11%)
SDAI remission Ref 6% (-3 to 18%) 9% (0.1 to 19%) -1% (-10 to 9%)
EULAR good response Ref 4% (-4 to 14%) 8% (2 to 18%) 0.4% (-10 to 11%)

AbbVie, Bristol-Myers Squibb, Celgene, Merck, and Novartis. Consultant of: AbbVie, Bristol-Myers Squibb, Boehringer Ingeheim, 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 Consultant/research support from: BMS, Melia C Kapetanovic: None declared, Francesca Faustini: None declared, Raffa Tuompo: None declared, Tove Lorenzen: None declared, Giovanni Cagnotto: None declared, Eva Baeklund: None declared, Oliver Hendricks Consultant/research support from: Pfizer, MSD, Daisy Vedder: None declared, Tuulikki Sokska-Iseri: None declared, Tomas Husmark: None declared, Maud-Kristine A Lipso: None declared, Eli Brodin: None declared, Torkell Ellingsen: None declared, Anni Reinalder: None declared, Maud 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 Consultant/research support from: BMS, GSK, Lilly, UCB, Pfizer, Roche, Consultant of: AbbVie, AstraZeneca, Biogen, Biocyt, Celgene, Gilead, Janssen, Pfizer, Servier, UCB, Speakers bureau: AbbVie, Pfizer, UCB

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OP0019 STABLE VERSUS TAPERED AND WITHDRAWN TREATMENT WITH TUMOR NECROSIS FACTOR INHIBITOR IN RHEUMATOID ARTHRITIS REMISSION (ARTICL REWIND): A RANDOMISED, OPEN-LABEL, PHASE 4, NON-INFERIORITY TRIAL

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