Objectives: To assess the impact of adalimumab on disease activity and patient-reported outcomes among adalimumab- vs. nbDMARD/NSAID-treated patients over 24 months.
Methods: Patients were enrolled between July 2011 and December 2017 and followed for up to 24 months. Treatment was per routine care and all analyses were perfomed using the intent-to-treat (ITT) approach. Between-group differences for change in patient-reported disease activity (BASDAI), morning stiffness (minutes/day), functional limitation (BASFI), quality of life (QoL: SF-12), depression (BDI-II), and work productivity (WLQ) were assessed with repeated measures models for overall treatment effect; baseline-adjusted estimates (least square means [LSM]) for each visit were produced. Achievement of, and time to the following endpoints were assessed: 50% improvement from baseline in BASDAI (BASDAI50); minimum clinically important improvements (MCIIs) in BASDAI ($\Delta \geq 1.1$); BASFI ($\Delta \geq 0.6$); SF-12 physical component score (PCS; $\Delta \geq 4.4$) and mental component score (MCS; $\Delta \geq 3.1$); and low disease activity for BASDAI (<4) and BASFI (<3.8).
Results: A total of 452 adalimumab-treated patients and 187 nbDMARD/NSAID-treated patients were enrolled in the study and included in the analyses. At baseline, mean (SD) BASDAI [6.4 (1.8) vs. 5.0 (1.8); p<0.001] and BASFI [5.5 (2.4) vs. 3.7 (2.4)] were however significantly (p<0.001) higher among adalimumab-treated patients compared to nbDMARD/NSAID-treated patients, respectively. Over 24 months, adalimumab-treated patients had significantly lower overall BASDAI scores compared to nbDMARD/NSAID-treated patients [estimate (95% CI): -0.7 (-1.2, -0.3); p=0.007]. BASFI scores were also significantly lower among adalimumab-treated patients over the course of the study [estimate (95% CI): -0.4 (-0.8, 0.0); p=0.013]. Both groups had statistically comparable outcomes for morning stiffness, BDI-II, WLQ, and SF-12.
Adalimumab-treated patients were also at significantly higher odds of achieving therapeutic response thresholds, including BASDAI50 [OR (95% CI): 1.7 (1.2-2.3)], BASDAI<4 [1.8 (1.2-2.7)], MCII for BASDAI [1.9 (13.-2.9)], and MCII for BASFI [1.6 (1.1-1.2)]. Time to achievement of each threshold was significantly shorter among adalimumab-treated patients for BASDAI50 [HR (95% CI): 1.8 (1.1-2.8)], BASDAI<4 [1.7 (1.6-3.6)], and MCII for BASDAI [1.5 (1.0-2.3)]. Time to achievement of MCII for BASFI was not statistically different between groups; for BASFI<3.8 and MCII for both SF-12 PCS and MCS, both odds of, and time to achievement, were also statistically comparable.
At month 24, baseline-adjusted BASDAI and BASFI was comparable (p>0.05): LSM (95%CI) 3.5 (3.3, 3.8) vs. 3.6 (3.2-4.0), and 2.9 (2.6-3.1) vs. 3.3 (2.9-3.7), respectively, for adalimumab-treated vs. nbDMARD/NSAID-treated patients.
Conclusion: Among Canadian patients with active AS, adalimumab-treated patients reported a greater overall reduction in disease burden related to both self-reported disease activity and functional capacity compared to nbDMARD/NSAID-treated patients, along with higher odds and shorter time to achieving therapeutic response thresholds. Despite the overall beneficial effects observed with adalimumab, residual disease burden, however, is observed for Canadian AS patients even after 24 months of treatment.
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OP0144

EFFICACY AND SAFETY OF UPADACITINIB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: 1-YEAR RESULTS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY WITH OPEN-LABEL EXTENSION

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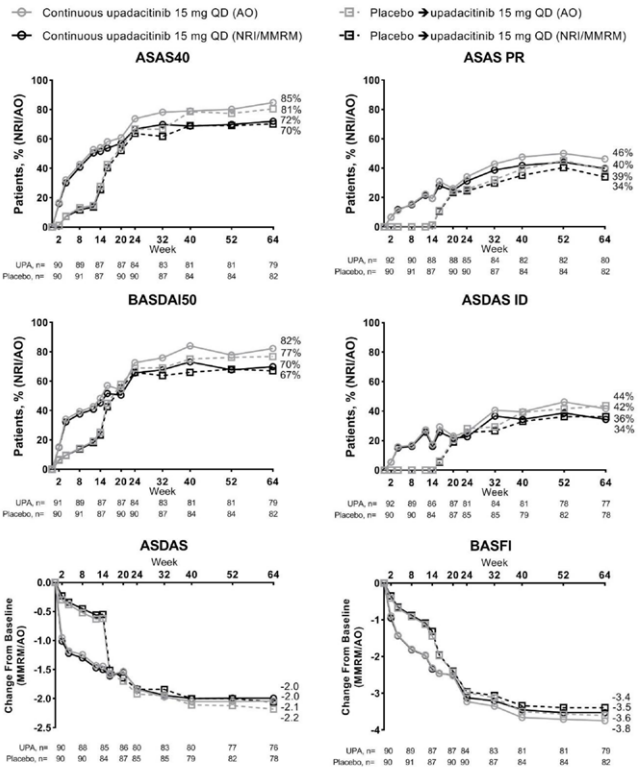
Background: Upadacitinib (UPA) was efficacious and well tolerated vs placebo (PBO) during the first 14 weeks (wks) of the phase 2/3 SELECT-AXIS 1 study in patients (pts) with active ankylosing spondylitis (AS) who had an inadequate response to NSAIDs.[1]
Objectives: To report efficacy and safety of UPA through 1 year in the SELECT-AXIS 1 study.
Methods: In SELECT-AXIS 1 (NCT03178487) pts were randomized 1:1 to UPA 15 mg once daily (QD) or PBO; at wk 14, pts continued in the 90-wk open-label extension and received UPA 15 mg QD; reported here are data up to wk 64. The study enrolled pts (≥18 y) with active AS (defined as BASDAI ≥4 and pt assessment of back pain ≥4 [numeric rating scale, 0–10] at screening and baseline [BL]) who had inadequate response to ≥2 NSAIDs or intolerance to or contraindication for NSAIDs and were biologic DMARD naive. Efficacy assessments included percentage of pts with Assessment of SpondyloArthritis international Society (ASAS) 20/40 response, ASAS partial remission, BASDAI50, AS Disease Activity Score (ASDAS) and change from BL in ASDAS and BASFI. Data are reported as observed and by using non-responder imputation (NRI). Treatment-emergent adverse events (TEAEs) were reported as events per 100 patient-years (PY) up to January 31, 2020.
Results: Of 187 pts, 178 pts (each n=89 for UPA and PBO arms) completed wk 14 on study drug and entered the open-label extension; 160 pts completed wk 64. Efficacy was maintained or continued to improve throughout the study in the continuous UPA group: 85% (95% CI, 77%–93%) of pts achieved ASAS40 at wk 64 in the as-observed analysis and 72% (63%–81%) in the NRI analysis (Figure). Pts who switched from PBO to UPA at wk 14 showed similar speed of onset and magnitude of response vs pts

Figure. Efficacy Endpoints Over Time



AO, as observed; ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Scores; ID, inactive disease; MMRM, mixed-effect model repeated measures; NRI, non-responder imputation; PR, partial remission; QD, once daily; UPA, upadacitinib.
Dashed line: all patients randomized to placebo received open-label UPA starting from week 14.
N's below the graphs are for as observed analysis. N's for NRI analysis were 94 for placebo to upadacitinib and 93 for continuous upadacitinib.
160 patients completed week 64; lack of efficacy (n=10) and adverse events (n=4) were the most common reasons for discontinuation between weeks 14 and 64.

initially randomized to UPA: 81% (95% CI, 72%–89%) in the as-observed analysis and 70% (61%–80%) in the NRI analysis achieved ASAS40 at wk 64 (Figure). Similar results were observed for other efficacy endpoints (Figure). Among all 182 pts receiving UPA, 618 AEs were reported. AEs leading to discontinuation and serious AEs were low (Table). No serious infections, active tuberculosis, venous thromboembolic events, gastrointestinal perforation, major adverse cardiovascular events, renal dysfunction, or deaths were reported.

Table 1. TEAEs per 100 PYs

Events/(E/100 PY)	UPA 15 mg QD N=182 (237.6 PY)
Any AE	618 (260.1)
Serious AE	14 (5.9)
AE leading to discontinuation	15 (6.3)
Infections	205 (86.3)
Opportunistic infection*	2 (0.8)
Herpes zoster†	5 (2.1)
Creatine phosphokinase elevation‡	28 (11.8)
Hepatic disorder§	24 (10.1)
Neutropenia‖	7 (2.9)
Anemia‖	3 (1.3)
Lymphopenia‖	2 (0.8)
Malignancy¶	1 (0.4)
Death	0

AE, adverse event; PY, patient-year; QD, once daily; TEAE, treatment-emergent AE; UPA, upadacitinib.*Two non-serious events of esophageal candidiasis in the same patient.†Five events in 4 patients; all non-serious and limited to 1 dermatome.‡All events were non-serious and none led to study drug discontinuation; majority were asymptomatic.§Majority based on asymptomatic alanine aminotransferase/aspartate aminotransferase elevations; all were non-serious and none led to study drug discontinuation.‖All events were non-serious and none led to study drug discontinuation.¶Squamous cell carcinoma of tongue in 61-year-old male former smoker; no reasonable possibility to be study drug related per investigator.

Conclusion: UPA 15 mg QD showed sustained and consistent efficacy over 1 year. Pts who switched from placebo to UPA at wk 14 showed a similar efficacy response compared with pts who received continuous UPA. No new safety findings were observed compared with safety data from the UPA clinical development program in other indications.[2]

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[2] Cohen, et al. *Arthritis Rheumatol*. 2019;71(suppl 10).

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Diagnostics and imaging procedures

OP0145 **DIFFERENTIAL DIAGNOSIS OF RA AND PSA USING NEURAL NETWORKS ON THREE-DIMENSIONAL BONE SHAPE OF FINGER JOINTS**

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Background: Early diagnosis and reliable differentiation between rheumatic diseases (RMDs) are crucial to start an adequate therapy and prevent irreversible damage. Since finger joints are commonly affected in rheumatoid arthritis (RA) and psoriatic arthritis (PsA), imaging of the peripheral skeleton is an essential step of diagnosis at a rheumatologist. High resolution peripheral quantitative computed tomography (HR-pQCT) allows an even more detailed and three-dimensional (3D) illustration of the peripheral bone than conventional radiographs. Segmented scans contain further information, such as the density, microstructure, and shape of the bones, which can be further analyzed by neural networks.
Objectives: We hypothesize that, based on the shape of the second metacarpophalangeal (MCP) joint from HR-pQCT images, a neural network can be trained to differentiate between RA, PsA, and healthy controls and to reveal regions in the bone shape characteristic for the diseases.
Methods: HR-pQCT images of MCP joints from patients with classified CCP positive RA, classified PsA, and healthy controls with low motion artifacts and appropriate scan region were selected as reported previously [3]. Scans were performed as part of the clinical routine and patients gave their informed consent to use pseudonymized data (Ethics approval 334_16B). Based on the assumption that pathognomonic changes develop over time, only images were used, where the period between classification and imaging exceeded one year.
Based on previous work [4], a pixel-wise mask of the second metacarpal bone was generated using a neural network based on the HR-pQCT scans of patients. Supervised auto-encoder [1] networks were used to predict the correct class given the bone mask only. For the neural network experiment, the patient scans were split on a patient-level into training (70%), validation (20%), and testing (10%). Guided backpropagation [2] was used as a method to investigate the regions influencing the class prediction most.
Results: In total, images of 331 patients were included in the experiments. The evaluation of the model on the 33 test cases yielded a high accuracy for the healthy control with 94%, RA patients with 84%, and PsA patients with 89%. An area under the receiver operator curve of 91% could be achieved. The regions of the bone mask influencing the network´s decision most are highlighted exemplary in Figure 1.

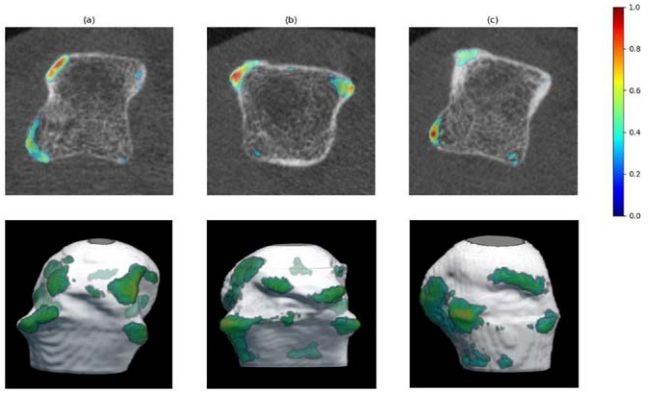

Figure 1. Visualization of the HR-pQCT slices with gradient maps. Higher values (red) represent regions that had a stronger contribution to the classification result. The HR-pQCT images are displayed for reference only. (a) Healthy patient, (b) RA diagnosed patient, and (c) PsA diagnosed patient. The first row shows the single slices with the highest values corresponding to the 3D bone masks in the second row.

Conclusion: For the first time, a neural network-based approach successfully provides a differential diagnosis of RA and PsA based only on the shape of the second MCP in HR-pQCT images. The evaluation of the test set suggests that high curvatures of the bone surface in the joint region significantly influence the prediction of the network, suggesting an in-depth investigation of these regions