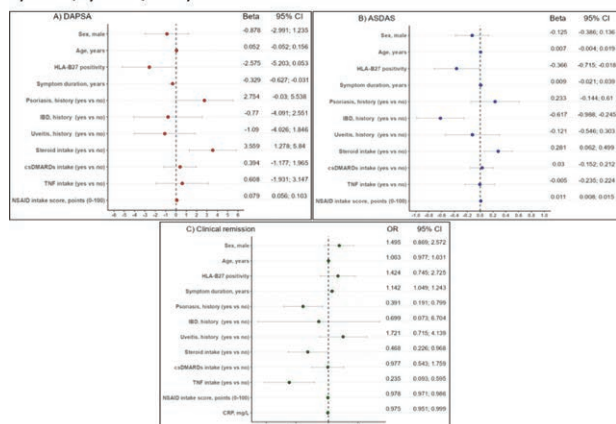


**Figure. Multivariable GEE analyses show associations between parameters and outcomes A) DAPSA, B) ASDAS, and C) Clinical remission.**



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OP0058

## PREDICTION OF LOW DISEASE ACTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH SECUKINUMAB IN REAL WORLD – DATA FROM THE GERMAN AQUILA STUDY

**Keywords:** Real-world evidence, Spondyloarthritis, Artificial Intelligence

A. Vodencarevic<sup>1</sup>, J. Brandt-Juergens<sup>2</sup>, D. Peterlik<sup>1</sup>, B. Gmeiner<sup>1</sup>, U. Kiltz<sup>3</sup>.

<sup>1</sup>Novartis, Novartis Pharma GmbH, Nürnberg, Germany; <sup>2</sup>Rheumatologie, Schwerpunktpraxis, Berlin, Germany; <sup>3</sup>Rheumazentrum Ruhrgebiet, Herne und Ruhr-Universität Bochum, Herne, Germany

**Background:** Secukinumab (SEC) proved to be an effective treatment for patients suffering from ankylosing spondylitis (AS) in randomized clinical trials [1]. There is only limited knowledge on prediction of low disease activity (LDA) and treatment strategy in AS patients under SEC treatment in routine clinical care.

**Objectives:** Using real-world data from the German non-interventional study AQUILA [2], the main objectives were (1) to predict LDA in individual AS patients treated with SEC through machine learning methods and (2) to identify the most important predictors and their influence on the prediction using explainable artificial intelligence (XAI).

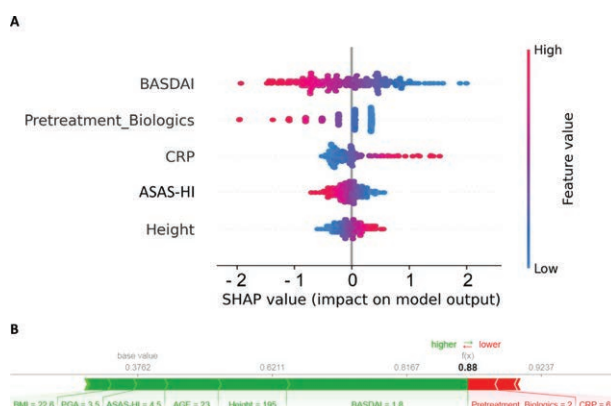
**Methods:** Data of 580 AS patients from the AQUILA study were used. Thirty-two demographic, clinical and treatment parameters at baseline (BL) served as input data to develop prediction models. LDA was defined as Bath ankylosing spondylitis disease activity index (BASDAI)  $\leq 2.0$  at week (w) 16 (+/- 6 w). Samples were divided into training (70%) and validation (30%) cohorts. Ten different prediction models were applied and compared. Model performance was measured using area under the receiver operating characteristic curve (AUROC) which represents the probability that a randomly selected patient with LDA will have higher prediction to achieve LDA than a patient with moderate/high disease activity. Additionally, sensitivity and specificity of the prediction model were computed and express the proportion of correctly identified patients who reach or don't

reach LDA at w16, respectively. Shapley XAI estimated importance and impact of each predictor based on how it affected the change in individual prediction [3]. **Results:** The most influencing predictor was BASDAI at BL, followed by the number of pretreatments with biologics, C-reactive protein (CRP), assessment of spondyloarthritis international society health index (ASAS-HI) and patient height (Figure 1 A). AUROC of the best performing prediction model was 0.84. Sensitivity and specificity were 0.87 and 0.67, respectively. Applied XAI approach showed that the lower the BL values of BASDAI, ASAS-HI and number of pretreatments with biologics were, the higher the probability of reaching LDA at w16 was. The opposite was the case for BL values of CRP and body height (Figure 1 A). The approach also provided visual explanations of patient-individual predictions: Variables with values shown in green color increased probability of reaching LDA at w16, whereas red ones showed the opposite effect (Figure 1 B).

**Conclusion:** A promising prediction model accuracy of LDA in AS patients treated with SEC could be reached and validated. Identified main predictors at BL, such as BASDAI and number of pretreatments with biologics, and their direction of influence on the prediction of LDA mostly match the existing clinical knowledge [4]. The analysis showed that XAI can provide useful clinical insights into patient-individual predictions, potentially guiding AS treatment decisions in future.

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**Figure 1. Main results**

**A:** Main predictors at baseline and their direction of influence based on Shapley values [3]

**B:** Explanation of patient-individual prediction of 88% using baseline data

Assessment of spondyloarthritis international society health index (ASAS-HI), Bath ankylosing spondylitis disease activity index (BASDAI), body mass index (BMI), C-reactive protein (CRP), patient global assessment (PGA), Shapley Additive exPlanations (SHAP)

**Acknowledgements:** NIL.

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OP0059

## EFFECT OF SECUKINUMAB VERSUS ADALIMUMAB BIOSIMILAR ON RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: A RANDOMISED PHASE IIIB STUDY

**Keywords:** Randomized control trial, Spondyloarthritis, Clinical Trials

X. Baraliakos<sup>1,2</sup>, M. Østergaard<sup>3</sup>, D. Poddubnyy<sup>4</sup>, D. Van der Heijde<sup>5</sup>, A. Deodhar<sup>6</sup>, P. Machado<sup>7</sup>, V. Navarro-Compán<sup>8</sup>, K. G. Hermann<sup>9</sup>, M. Kishimoto<sup>10</sup>, E. Y. Lee<sup>11</sup>, L. S. Gensler<sup>12</sup>, U. Kiltz<sup>1,2</sup>, M. Eigenmann<sup>13</sup>,

P. Pertel<sup>13</sup>, A. Readie<sup>14</sup>, H. Richards<sup>13</sup>, B. Porter<sup>14</sup>, J. Braun<sup>1,2</sup>. <sup>1</sup>Rheumazentrum Ruhrgebiet, Rheumatology, Herne, Germany; <sup>2</sup>Ruhr-Universität Bochum, Rheumatology, Bochum, Germany; <sup>3</sup>Copenhagen University Hospital Rigshospitalet, Center for Rheumatology and Spine Diseases, Center of Head and Orthopedics, Glostrup, Denmark; <sup>4</sup>Charité - Universitätsmedizin Berlin and German Rheumatism Research Centre, Rheumatology, Berlin, Germany; <sup>5</sup>Leiden University Medical Centre, Department of Rheumatology, Leiden, Netherlands; <sup>6</sup>Oregon Health & Science University, Division of Arthritis and Rheumatic Diseases, Portland, United States of America; <sup>7</sup>University College London, Centre for Rheumatology & Department of Neuromuscular Diseases, London, United Kingdom; <sup>8</sup>University Hospital La Paz, IdiPaz, Department of Rheumatology, Madrid, Spain; <sup>9</sup>University Hospital Charité - Campus Mitte, Charitéplatz 110117, Department of Radiology, Berlin, Germany; <sup>10</sup>Kyoto University School of Medicine, Department of Nephrology and Rheumatology, Tokyo, Japan; <sup>11</sup>Seoul National University College of Medicine, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea); <sup>12</sup>University of California, San Francisco, Department of Medicine, Division of Rheumatology, California, United States of America; <sup>13</sup>Novartis Pharma AG, Immunology, Basel, Switzerland; <sup>14</sup>Novartis Pharmaceuticals Corporation, East Hanover, Immunology, New Jersey, United States of America

**Background:** Limited data exist on the effect of biologics in slowing radiographic progression in patients (pts) with radiographic axial spondyloarthritis (r-axSpA). Two-year data from MEASURE 1 showed low radiographic progression with secukinumab (SEC).[1]

**Objectives:** To compare the effect of SEC vs adalimumab biosimilar (SDZ-ADL) on spinal radiographic progression from SURPASS.[2,3] the first head-to-head study in r-axSpA.

**Methods:** In this phase IIIb study, bio-naïve pts with active r-axSpA with a BASDAI  $\geq 4$ , spinal pain score  $\geq 4$  (range 0–10), total back pain score  $\geq 40$  mm (range 0–100 mm), and with hs-CRP  $\geq 5$  mg/L or  $\geq 1$  syndesmophyte(s) on spinal radiograph were randomised (1:1:1) to SEC (150/300 mg; dose-blinded) or SDZ-ADL (40 mg; open label). Radiographs and MRIs were reviewed by 3 independent central readers (no adjudication performed) blinded to treatment and chronology of images. Primary endpoint was the proportion of pts with no radiographic progression (change from baseline [CFB] in modified Stoke AS Spinal Score [mSASSS]  $\leq 0.5$ ) on SEC vs SDZ-ADL at week (wk) 104 (superiority testing). Secondary endpoints included CFB-mSASSS at wk 104, proportion of pts with  $\geq 1$  syndesmophyte(s) at baseline (BSL) with no new syndesmophytes(s) at wk 104, CFB-MRI Berlin sacroiliac joint (SIJ) inflammation score, CFB-AS Spine MRI-activity (ASpiMRI-a) Berlin modification score, and safety.

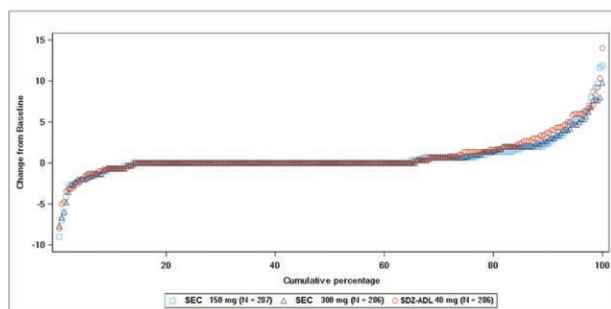
**Results:** Overall, 859 pts received SEC 150 mg (n=287), 300 mg (n=286), or SDZ-ADL (n=286). With 78.5% male, mean age 42.1 years, mSASSS 16.6, BASDAI 7.1, hsCRP 20.4 mg/L, and 73% with  $\geq 1$  syndesmophyte(s), this population had high risk of radiographic progression. At wk 104, cumulative distribution of CFB-mSASSS was similar across arms (Figure 1). Proportion of pts with no radiographic progression was 66.1%, 66.9%, and 65.6% (P=ns, both SEC doses) while mean CFB-mSASSS was 0.54, 0.55, and 0.72 with SEC 150 mg, 300 mg, and SDZ-ADL. Overall, 56.9%, 53.8%, and 53.3% of pts in SEC 150 mg, 300 mg, and SDZ-ADL arms, with a BSL  $\geq 1$  syndesmophyte(s) did not develop new syndesmophyte(s) by wk 104 (Table 1). In the MRI sub-set (N=418), mean SIJ scores at BSL and wk 16 were 2.54 and 0.98 (SEC 150 mg), 1.96 and 0.92 (SEC 300 mg), and 1.59 and 0.38 (SDZ-ADL); corresponding spine scores were 3.50 and 1.79, 2.56 and 1.25, and 3.00 and 0.71.

**Conclusion:** Spinal radiographic progression over 2 years was low with no significant difference between SEC and SDZ-ADL arms. No new safety signals were identified.

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Figure 1. Probability plot of change from BSL in mSASSS at wk 104



mSASSS, modified Stoke Ankylosing Spondylitis Spinal Score; SDZ-ADL, adalimumab biosimilar; SEC, secukinumab

Table 1. Radiographic assessments at wk 104

| No radiographic progression* | Treatment group        | n          | No progression rate (%)                     | Estimated mean (95% CI) | Marginal difference (95% CI)†         | Nominal P-value     |
|------------------------------|------------------------|------------|---|-------------------------|---------------------------------------|---------------------|
| Change from BSL in mSASSS#   | SEC 150 mg             | 283        | 66.1  | 66.63 (60.73, 72.54)    | 1.51 (-6.63, 9.64)                    | 0.716               |
|                              | SEC 300 mg             | 280        | 66.9  | 66.80 (60.45, 73.14)    | 1.67 (-6.61, 9.95)                    | 0.693               |
|                              | SDZ-ADL 40 mg          | 283        | 65.6  | 65.13 (58.77, 71.49)    | -                                     | -                   |
|                              | <b>Treatment group</b> | <b>n</b>   | <b>Within treatment</b>                     |                         | <b>Treatment contrast in LS mean†</b> |                     |
|                              |                        |            | <b>LS mean (SE)</b>                         |                         | <b>LS mean (SE)</b>                   | <b>95% CI</b>       |
|                              | SEC 150 mg             | 283        | 0.54 (0.18)                                 |                         | -0.18 (0.24)                          | -0.65, 0.29         |
| No new syndesmophytes*‡      | SEC 300 mg             | 280        | 0.55 (0.18)                                 |                         | -0.16 (0.24)                          | -0.64, 0.32         |
|                              | SDZ-ADL 40 mg          | 283        | 0.72 (0.18)                                 |                         | -                                     | -                   |
|                              | <b>Treatment group</b> | <b>n</b>   | <b>Pts with no new syndesmophyte(s) (%)</b> |                         | <b>Estimated mean (95% CI)</b>        |                     |
|                              |                        |            |   |                         | <b>Marginal difference (95% CI)†</b>  |                     |
|                              | SEC 150 mg             | 211 (73.5) | 56.9  |                         | 57.22 (50.16, 64.28)                  | 4.32 (-5.62, 14.27) |
|                              | SEC 300 mg             | 204 (71.3) | 53.8  |                         | 53.98 (46.19, 61.78)                  | 1.09 (-9.13, 11.31) |
| No new syndesmophytes*‡      | SDZ-ADL 40 mg          | 212 (74.1) | 53.3  |                         | 52.89 (45.54, 60.24)                  | -                   |

SEC 150 mg, N=287; SEC 300 mg, N=286; SDZ-ADL 40 mg, N=286.

\*Estimated mean, marginal difference, 95% CI, and p-value are from logistic regression model with treatment as a factor and BSL mSASSS score/count of vertebral corners with syndesmophyte as covariate using marginal standardisation method.

†LS Mean and 95% CI are from ANCOVA model with treatment as a factor and BSL mSASSS score as covariate.

‡Comparison vs SDZ-ADL 40 mg.

‡pts with syndesmophyte(s) at BSL

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and UCB, Grant/research support from: AbbVie, Biocad, Biogen, Chugai, Eli Lilly, Fresenius, GSK, Grünenthal, Hexal, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Marco Eigenmann Shareholder of: Novartis, Employee of: Novartis, Patricia Pertel Shareholder of: Novartis, Employee of: Novartis, Aimee Readie Shareholder of: Novartis, Employee of: Novartis, Hanno Richards Shareholder of: Novartis, Employee of: Novartis, Brian Porter Shareholder of: Novartis, Employee of: Novartis, Juergen Braun Consultant of: Personal fees from: Abbvie, Amgen, Boehringer, Celltrion, MSD, Novartis, UCB, and Eli Lilly.

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OP0060

# CLINICAL CONSEQUENCES OF INFLIXIMAB IMMUNOGENICITY AND THE IMPACT OF THERAPEUTIC DRUG MONITORING: SECONDARY ANALYSES OF A RANDOMISED CLINICAL TRIAL

**Keywords:** Rheumatoid arthritis, bDMARD, Spondyloarthritis

M. K. Brun<sup>1,2</sup>, K. H. Bjørlykke<sup>2,3</sup>, J. E. Gehin<sup>4</sup>, D. J. Warren<sup>4</sup>, R. A. Klaasen<sup>4</sup>, J. Sexton<sup>1</sup>, Ø. Sandanger<sup>5</sup>, T. K. Kvien<sup>1,2</sup>, C. Mørk<sup>6</sup>, J. Jahnsen<sup>2,3</sup>, N. Bolstad<sup>4</sup>, K. K. Jørgensen<sup>3</sup>, E. A. Haavardsholm<sup>1,2</sup>, G. L. Goll<sup>1</sup>, S. W. Syversen<sup>1</sup>. <sup>1</sup>Diakonhjemmet Hospital, Center for Treatment of Rheumatic and Musculoskeletal Diseases (REMEDY), Oslo, Norway; <sup>2</sup>University of Oslo, Institute of Clinical Medicine, Oslo, Norway; <sup>3</sup>Akershus University Hospital, Department of Gastroenterology, Lorenskog, Norway; <sup>4</sup>Norwegian Radium Hospital, Department of Medical Biochemistry, Oslo, Norway; <sup>5</sup>Oslo universitetssykehus HF, Rikshospitalet, Section of Dermatology, Oslo, Norway; <sup>6</sup>Akershus Dermatologist Center, Akershus Dermatologist Center, Akershus, Norway

**Background:** Neutralising anti-drug antibodies (ADAb) are a problem in treatment with TNF-inhibitors (TNFi). Prospective data are needed to better understand how ADAb formation impacts safety and treatment outcomes of TNFi. Proactive therapeutic drug monitoring (TDM) allows for timely detection of ADAb and this strategy may have a role in reducing the negative clinical consequences of ADAb.

**Objectives:** To explore the temporal relation between anti-infliximab antibody formation and treatment outcomes and adverse events, and to assess the impact of TDM as a strategy to reduce these consequences.

**Methods:** Patients with immune mediated inflammatory diseases on infliximab therapy (n=615; 181 spondyloarthritis, 120 rheumatoid arthritis, 72 psoriatic arthritis, 114 ulcerative colitis, 83 Crohns disease and 45 psoriasis) were included in the Norwegian Drug Monitoring (NOR-DRUM) trials (1, 2) and randomised to TDM or standard infliximab therapy. Patients were followed for 30 and 52 weeks in the NOR-DRUM A (induction therapy) and NOR-DRUM B (maintenance therapy) trials, respectively. Neutralising ADAb were assessed with a drug sensitive automated fluorescence assay at each infusion. In this sub-study, we assessed the risk of; failure to achieve remission (analysis A), disease worsening during maintenance therapy (analysis B), treatment discontinuation (analysis C) and adverse events (analysis D) in patients developing ADAb compared to patients without ADAb using logistic- or cox regression and Kaplan-Meier survival analyses, stratified by TDM or standard therapy. Regression analyses were adjusted for potential confounders (Table 1). Remission and disease worsening were defined by disease specific composite scores (1, 2).

**Results:** ADAb were detected in 147/615 (24 %) patients. Patients with ADAb had higher risk of not achieving remission 30 weeks after initiating infliximab therapy (odds ratio (OR) 2.4, 95 % confidence interval (CI) 1.3-4.2, P<0.01) (Table 1, Figure 1A) and of having a disease worsening during 52 weeks of infliximab maintenance therapy (hazard ratio (HR) 2.1, CI 1.4-3.3, P<0.001) (Figure 1B). ADAb formation was not significantly associated with adverse events in general, but the risk of infusion reactions was highly increased in patients with ADAb (HR 29, CI 11-78, P<0.001). The risk of infliximab treatment discontinuation was increased in ADAb positive patients (HR 6.5, CI 4.7-8.9, P<0.001). Patients developing ADAb in the TDM group had lower risk of disease worsening or an infusion reaction than patients with ADAb in the standard infliximab therapy group (Table 1, Figure 1B and C). Patients with ADAb discontinued infliximab treatment more often in the TDM group than in the control group (Table 1, Figure 1D).

**Conclusion:** Formation of ADAb led to poorer clinical outcomes both during induction and maintenance therapy with infliximab and increased the risk of infusion reactions. Early detection of ADAb by proactive TDM reduced the negative consequences of ADAb, both on infliximab effectiveness and safety, highlighting the role of proactive TDM in optimising TNFi therapy.

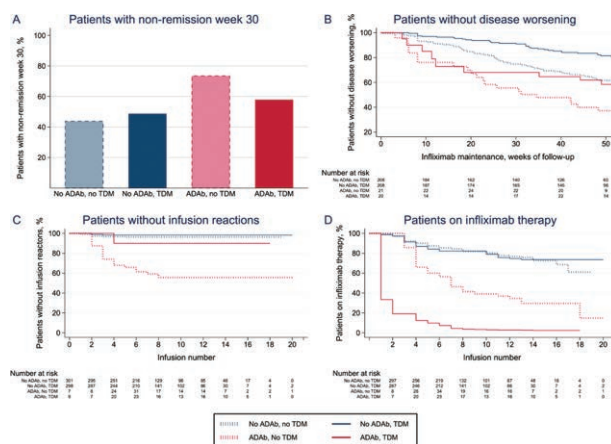
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**Table 1. Treatment and safety outcomes related to ADAb formation and TDM**

| Analysis A) Non-remission             | OR (CI)       | P      |
|---------------------------------------|---------------|--------|
| ADAb                                  | 2.4 (1.3-4.2) | <0.01  |
| TDM                                   | 1.0 (0.7-1.5) | 0.9    |
| Analysis B) Disease worsening         | HR (CI)       | P      |
| ADAb                                  | 2.1 (1.4,3.2) | <0.01  |
| TDM                                   | 0.4 (0.3-0.6) | <0.001 |
| Analysis C) Infusion reaction         | HR (CI)       | P      |
| ADAb                                  | 29 (11-78)    | <0.001 |
| TDM                                   | 0.3 (0.1-0.7) | <0.01  |
| Analysis D) Treatment discontinuation | HR (CI)       | P      |
| ADAb                                  | 6.5 (4.7-8.9) | <0.001 |
| TDM                                   | 1.4 (1.0-1.8) | 0.03   |

Results from multivariable logistic (A)- or cox (B-D) regression models including the covariates: ADAb, TDM, age, sex, diagnosis, comedication. Results shown in table are risk of A) non-remission week 30, B) disease worsening during 52 weeks of maintenance therapy, C) infusion reactions and D) infliximab treatment discontinuation for patients developing ADAb and for patients in the TDM group.



**Figure 1.**

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# DEVELOPMENT OF EXTRA-MUSCULOSKELETAL MANIFESTATIONS IN UPADACITINIB-TREATED PATIENTS WITH PSORIATIC ARTHRITIS, ANKYLOSING SPONDYLITIS, OR NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS

**Keywords:** Uveitis, Safety, Spondyloarthritis

D. Poddubnyy<sup>1</sup>, B. Parikh<sup>2</sup>, D. Elewaut<sup>3</sup>, V. Navarro-Compán<sup>4</sup>, S. Siebert<sup>5</sup>, M. Paley<sup>6</sup>, D. Coombs<sup>2</sup>, R. Mccaskill<sup>2</sup>, A. Biljan<sup>2</sup>, P. Wung<sup>2</sup>, E. Lubrano<sup>7</sup>. <sup>1</sup>Charité Universitätsmedizin, Department of Gastroenterology, Infectious Diseases and Rheumatology, Berlin, Germany; <sup>2</sup>AbbVie Inc., Immunology, North Chicago, United States of America; <sup>3</sup>Ghent University Hospital and VIB