Short running head: CanSpA_Secukinumab in AxSpA

Title: Real-world Retention and Clinical Effectiveness of Secukinumab for Axial Spondyloarthritis: Results from the CanSpA Research Network

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Conflict of interest:

Dr. Robert Inman has received consulting fees from Abbvie, Janssen, Lilly, Novartis, and Sandoz. Dr. Denis Choquette has received research grant support from Abbvie, Amgen, Eli Lilly, Fresenius-Kabi, Novartis, Pfizer, Sandoz, Celltrion, Teva Pharmaceuticals, and Sanofi-Genzyme, and consulting or speaker fees from Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Celltrion, and Teva Pharmaceuticals. Dr. Majed Khraishi has received consulting fees from Abbvie, Amgen, Gilead, Novartis, Pfizer and UCB. Dr. Dafna Gladman has received research grant support from Abbvie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, and consulting fees from Abbvie, Amgen, Celgene, Eli Lilly, Galapagos, Gilead, Janssen, Novartis, Pfizer and UCB. Patrick Leclerc and Shamiza Hussein are employees of Novartis Pharmaceuticals Canada Inc. Drew Neish is an employee of IQVIA. IQVIA received consulting fees from the sponsor, Novartis Pharmaceuticals Canada Inc., for the study.

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Statement of ethics and consent:

Ethics approval was received from the following review boards for this study: UNH Research Ethics Board (#20-5991, UHN) and Advara (#Pro00045670, Rhumadata). A waiver of consent was granted for this

study, as the study was a secondary analysis of deidentified patient data that posed no more than minimal risk to participants.

ABSTRACT

Objective: Axial spondyloarthritis (axSpA) is a chronic, immune-mediated, inflammatory condition consisting of two clinical subsets: non-radiographic axSpA (nr-axSpA) and ankylosing spondylitis (AS), the latter having an estimated prevalence of 0.2 to 1% in Canada. Secukinumab received Health Canada approval in 2016 for the treatment of adults with axSpA who have responded inadequately to conventional treatment, and has demonstrated efficacy and safety through extensive clinical trials. However, there is limited evidence on its real-world use in Canada. The objective of this study was to use the Canadian Spondyloarthritis (CanSpA) Research Network to describe real-world retention and effectiveness of secukinumab in the Canadian axSpA population.

Methods: This was an observational cohort study of Canadian axSpA patients ages 18-65 years within the CanSpA network that had received treatment with secukinumab. Patients were indexed on first date of secukinumab initiation. Retention and clinical effectiveness were assessed at 12-months post-index. Clinical effectiveness was measured as proportion in remission and change in disease activity using multiple clinical indices.

Results: 146 patients were included. Overall retention was estimated at 62.9%. Low disease activity (BASDAI <4) was achieved in 29.2% of patients, and 2.0% had achieved ASDAS-based remission. BASMI scores improved by >60% from baseline to 12-months.

Conclusion: The results of this real-world study of Canadian axSpA patients, one of the first of its kind, support the effectiveness of secukinumab for treatment of axSpA. The CanSpA network presents an opportunity to continue building and improving the real-world evidence base for treatment of Canadian patients with SpA.

INTRODUCTION

Spondyloarthritis (SpA) refers to a group of immune-mediated, inflammatory diseases characterized by inflammation of the joints and spine, and in severe cases, structural damage and disability.[1] Axial spondyloarthritis (axSpA) is just one subtype of SpA where chronic spondyloarthritis symptoms present primarily in the axial skeleton, including the spine and/or sacroiliac joints.[2] AxSpA consists of two clinically defined subsets: non-radiographic axSpA (nr-axSpA), where chronic symptoms are present but no structural damage is visible on X-ray imaging, and ankylosing spondylitis (AS), which is characterized by chronic symptoms as well as structural damage of the spine and/or sacroiliac joints visible on X-rays.[2] Prevalence estimates in Canada have been mostly limited to diagnosis of AS rather than nr-axSpA or axSpA more broadly, and it is estimated that up to 1% of Canadians are living with AS.[3,4] The Canadian Rheumatology Association (CRA) published guidelines on the treatment of spondylarthritis (SpA) in 2014[5], and more recent recommendations from the Assessment in AS (ASAS) working group/European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) were published in 2016 and 2019, respectively.[6,7] Among treatment-naïve axSpA patients, recommended first-line treatment consists of continuous treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and local corticosteroid injections or methotrexate for peripheral arthritis.[5–8] If axSpA is active despite first-line treatment, guidelines recommend treatment with biologic disease-modifying antirheumatic drugs (bDMARDs), typically tumour necrosis factor inhibitors (TNFis), and other bDMARDs such as interleukin-17 inhibitors (IL-17is).[5–7]

Secukinumab is an IL-17 inhibitor bDMARD that received Health Canada approval in 2016 for the treatment of adult patients with axSpA who have responded inadequately to conventional treatment.[9] The recommended maintenance dose for axSpA is monthly 150mg subcutaneous injections. If AS disease activity persists at the 150mg dose, a monthly maintenance dosage of 300mg can be considered. Secukinumab suppresses inflammatory immune response and has demonstrated clinical efficacy and safety through extensive clinical trials, where AS and nr-axSpA patients showed significant improvements in signs and symptoms up to five years after start of treatment.[10–12] Safety and clinical effectiveness of secukinumab has also been demonstrated in a real-world setting. A registry-based study from the European Spondyloarthritis (EuroSpA) research network collaboration found that 72% of axSpA patients in the study were retained on secukinumab and 51% had achieved low-disease activity (BASDAI <4) 12 months after initiation.[13] The prospective observational study SERENA, also conducted in Europe, found that

approximately 79% of AS patients were retained on secukinumab two years after enrollment.[14] Similar retention rates were observed in a Canadian retrospective study of Patient Support Program (PSP) data, though 12-month retention was lower among AS patients with previous experience on a biologic relative to those that were biologic-naïve at secukinumab initiation (61.6% versus 76.8%).[15] However, there is minimal additional evidence on the real-world use of secukinumab in Canada for the treatment of axSpA.

The Canadian Spondyloarthritis (CanSpA) research collaboration network was created to maximize collaboration between several independent Canadian SpA registries. The aim of the CanSpA research network is to generate comprehensive real-world SpA evidence to answer questions for which a larger sample size and broader landscape coverage represent an advantage. It also creates opportunities for expansion in both the number of stakeholders involved and the scope of data collected for the performance of follow up analyses. This particular study pooled data on patients with SpA, including nr-axSpA and AS, collected during routine clinical care from multiple Canadian SpA registries. Its aim was to use data from the CanSpA network to describe real-world retention to secukinumab and its clinical effectiveness among Canadian patients with axSpA in their first year of secukinumab treatment.

METHODS

CanSpA Research Collaboration Network

This was a retrospective, registry-based real-world study of axSpA patients in Canada within the CanSpA network, who were newly prescribed secukinumab as part of routine clinical care. The CanSpA network includes multiple SpA patient registries in Canada, each of which contributes data collected through routine clinical practice from multiple rheumatology clinics.

Data sources

This study used the deidentified patient-level data of patients with axSpA extracted from one of two participating registries in the CanSpA network: University Health Network (UNH) in the province of Ontario, and Rhumadata in the province of Quebec. Variables for data extraction were pre-specified in a protocol and statistical analysis plan, and deidentified data was securely transferred to a common server where source data was then pooled and synthesized for analysis. All final analyses were conducted on the final pooled anonymized dataset. Ethics approval was received from the following review boards for this study: UNH Research Ethics Board (#20-5991, UHN) and Advara (#Pro00045670, Rhumadata). A waiver of consent was

granted for this study, as the study was a secondary analysis of deidentified patient data that posed no more than minimal risk to participants.

Patient population

To be eligible for inclusion, patients must have had a documented diagnosis of axSpA and received treatment with secukinumab at any point between secukinumab availability in Canada (including availability through clinical trials) and at least six months prior to date of data extraction (November 2021). Patients also had to be 18 to 65 years of age at secukinumab initiation, with a minimum of 6 months of follow-up since the start of secukinumab treatment, regardless of treatment status and outcomes. No additional exclusion criteria were applied.

Study variables

The primary outcome of the study was retention at 12 months. Secondary outcomes included clinical effectiveness 12 months after secukinumab initiation, and reasons for discontinuation of secukinumab.

Retention was defined as the time from secukinumab initiation to secukinumab discontinuation and was reported as the Kaplan-Meier-estimate of the probability of retention on secukinumab 12 months after initiation.

Clinical effectiveness was assessed using several clinical indices: Ankylosing Spondylitis Disease Activity Score (ASDAS) using C-reactive protein (ASDAS-CRP) and erythrocyte sedimentation rate (ASDAS-ESR); Bath Ankylosing Spondylitis Disease Activity Index (BASDAI); Bath Ankylosing Spondylitis Functional Index (BASFI); Bath Ankylosing Spondylitis Metrology Index (BASMI); Physician Global Assessment (PhysGA); Patient Global Assessment (PatGA); Tender joint count using a 68 and 28 joint denominator (TJC68 and TJC28, respectively); and Swollen joint count using a 66 and 28 joint denominator (SJC66 and SJC28, respectively).

Clinical effectiveness was reported as the proportion of patients with inactive disease at 12 months, as well as clinical response (i.e., change in clinical score) from baseline to 12 months. Remission was calculated as the proportion of patients falling below an index-specific threshold by 12 months. The thresholds were <1.3 for ASDAS-CRP inactive disease and <4 for BASDAI low-disease activity. ASDAS-CRP and BASDAI rates were reported both unadjusted and LUNDEX-adjusted based on the proportion of patients retained on secukinumab at 12 months.[16] Clinical response was calculated as the mean percentage change in clinical index score from baseline to 12 months for patients with a score recorded at both timepoints.

In addition to the above outcomes, baseline demographics, clinical characteristics, and treatment history at baseline were also measured and reported.

Statistical analysis

The primary outcome, retention at 12 months, was reported as the Kaplan-Meier estimate of the probability of being retained on secukinumab 12 months after initiation. Retention was reported overall and stratified by prior b/tsDMARD experience (experienced or naïve), sex (male or female), and duration of disease (0 – 3 years, 4 – 9 years, or 10+ years). Comparison of retention between strata was performed using the Log-rank test.

All variables were also summarized descriptively. Descriptive statistics for continuous variables are reported as mean and standard deviation (SD), or median and interquartile range (IQR), and categorical variables are described as counts and proportions (%). All analyses were performed using SAS® (SAS-Institute, Cary, NC, USA).

RESULTS

Of the 218 patients identified in the CanSpA network who had a documented diagnosis of axSpA and had been prescribed secukinumab, 146 were between 18 and 65 years of age at secukinumab initiation with at least 6 months of follow-up and comprised the full analysis set (Figure 1). The mean age of the cohort at secukinumab initiation was 43.3 (11.0) years, and 79 (54.1%) patients were male. The average BMI in the cohort was 27.9 kg/m^2 (6.0), and 37 (25.3%) patients were smokers. Psoriasis and iritis were present in 42 (28.8%) and 20 (13.7%) patients, respectively. At baseline, 34 (23.3%) patients were b/tsDMARD-naïve versus 112 (76.7%) with prior b/tsDMARD-experience; among those with prior b/tsDMARD-experience, the average number of prior biologics used was 2.6 (1.6). The average time since axSpA diagnosis was 5.0 (4.8) years. A diagnosis of AS was reported for 124 (84.9%) patients, while the remaining 22 (15.1%) were nr-axSpA (Table 1), though it should be noted that imaging data was not extracted to confirm AS diagnosis in this study.

12-month retention

At 12 months post-initiation 92 patients remained on secukinumab, with a KM-estimated retention rate of 62.9% (Figure 2). KM-estimated retention was 55.7% (19 of 34 patients) among b/tsDMARD-naïve patients versus 65.0% (73 of 112 patients) among b/tsDMARD-experienced, though this difference was not

statistically significant (p= .73). There was also no significant difference in retention rates between males (65.8%; 51 of 79 patients) and females (59.4%; 41 of 67 patients) (p= .27). Retention was also similar across disease durations, with a retention rate of 63.9% (46 of 72 patients) for those with disease duration of zero to three years, 59.2% (30 of 52 patients) for those with disease duration of four to nine years, and 68.2% (16 of 22 patients) for those with disease duration of ten years or longer (p= .76).

Clinical remission and response

At 12 months, one out of 51 (2.0%) patients with an ASDAS-CRP score had achieved ASDAS-based inactive disease. The LUNDEX-adjusted ASDAS inactive disease rate was 1.2%. Twenty-eight out of 96 (29.2%) patients with BASDAI scores had achieved BASDAI-based low disease activity (BASDAI <4), with a LUNDEX-adjusted rate of 18.4% (Table 2).

Patients showed an overall trend of improvement in clinical scores from baseline to 12 months. Among patients with a score recorded both at baseline and 12 months, ASDAS-CRP and ASDAS-ESR improved, on average, by 6.1% (from 3.5 to 3.3) and 4.7% (from 3.4 to 3.2), respectively, from baseline to 12 months. BASDAI and BASFI showed similar improvements, dropping by 16.5% (from 6.3 to 5.3) and 9.5% (from 5.5 to 5.0), respectively. BASMI improved by 60.2%, dropping from 3.4 at baseline to 1.3 at 12 months. The largest improvements were seen for TJC68 and SJC66, improving by 66.5% (from 2.2 to 0.7) and 70.4% (from 0.7 to 0.2), respectively, from baseline to 12 months. Full results for all captured clinical indices are described in Figure 3.

Reasons for discontinuation

Of the 146 patients that had initiated secukinumab at baseline, 52 (35.6%) had discontinued secukinumab by 12 months (i.e., had a documented discontinuation date before 12 months or before being lost to follow-up). Of these 52 patients, 34 (65.4%) cited lack or loss of effectiveness as their reason for discontinuation, with 19 (36.5%) discontinuing at or before six months, and 15 (28.8%) discontinuing after six months of secukinumab treatment. Other reasons for discontinuation included adverse events (10 patients; 19.2%) or patient preference (1 patient; 1.9%), with no reason provided from the remaining 7 (13.5%) patients (Table 3).

DISCUSSION

This registry-based real-world study is the first in Canada to use multiple rheumatology registries to study the effectiveness of secukinumab among axSpA patients and adds to existing real-world evidence on the use of secukinumab for the treatment of axSpA. The results of this analysis showed that approximately 63% of axSpA patients remained on secukinumab up to 12 months after initiation, with the majority of discontinuers ceasing treatment due to lack or loss of effectiveness. These estimates of retention are somewhat lower than other real-world studies internationally, where 12-month secukinumab retention has been estimated from approximately 66% to more than 85% across all axSpA or AS patients.[13,14,17] However, previous literature consistently indicates that biologic-naïve axSpA patients tend to show better retention to treatment with a biologic than those with prior failure on biologics, and retention results are often stratified by prior biologic treatments based on this baseline difference in the risk of discontinuation. This pattern has been previously shown in other Canadian real-world populations; a retrospective analysis of 1,913 patients enrolled in a PSP in Canada found that AS patients previously naïve to biologics showed 12-month retention rates of 76.8% relative to 61.6% among those with prior biologic use before initiating secukinumab.[18] We attempted to perform the same stratification in the current study, and found that when we limited the current results only to patients with prior b/tsDMARD experience we observed a 12-month retention rate of 65%. This retention rate aligns more closely to other real-world b/tsDMARD-experienced axSpA cohorts reporting similar retention rates of 60 – 66%.[13,18,19] In comparison, b/tsDMARD-naïve cohorts from the same studies report retention rates of 73 – 80%.[13,18,19] Interestingly, this same trend was not seen in the current study, and it appears the lower overall retention rate observed is actually being driven by the b/tsDMARD-naïve patients, among whom the 12-month retention rate was 55.7%. Although no significant difference was detected between the b/tsDMARD-naïve versus experienced patients, directionally these results diverge from clinical expectations and the trends just described from other real-world retention studies, including a Canadian report on the use of secukinumab in 1,913 AS patients.[18] That said, the sample size of b/tsDMARD-naïve patients was small, with just 34 patients at baseline and 19 patients retained at 12 months. Thus, it is possible that this small sample does not adequately represent typical behaviours of biologic-naïve or biologic experienced patients. Furthermore, while the pooling of data across multiple registries and clinics offers the advantage of bolstering sample sizes for study, it simultaneously presents the dilemma of potentially masking important differences between patient populations and clinical practice settings when pooled. It is possible

that variability in practice and treatment access across clinics, and variability in patient populations, such as the proportion with prior b/tsDMARD experience, could have impacted treatment outcomes differentially, as has been shown in other real-world studies of secukinumab use.[13] The impact of differences in care setting in Canada were beyond the scope of this study, however, and remains an area for future research. Nevertheless, the rates of retention observed here and in other cohorts indicate that secukinumab treatment shows benefit justifying continued treatment for at least 12 months in the majority of axSpA patients.

With respect to clinical effectiveness, patients showed an improvement in scores from baseline to 12 months across all clinical indices reported, supporting the 12-month retention rates observed. However, the proportion of patients achieving remission was slightly lower than clinical trials where remission rates ranged from 17.6% (ASDAS) to 22.3% (BASDAI)[20], as well as other real-world studies reporting around 11% in remission (ASDAS) and 51% with low disease activity (BASDAI, threshold of 4). In comparison, over 12 months we observed a rate of 2% for ASDAS inactive disease, and 27% for BASDAI low-disease activity. That said, one expects treatment effectiveness observed in clinical trials to be optimal relative to a real-world setting, given the use of strict inclusion criteria and treatment protocols that serve to improve baseline probability of treatment adherence and success. Variations in methodology between real-world studies, though, are less consequential than those between real-world studies and clinical trials, and differences in outcomes observed between real-world cohorts are less easily explained. However, differences in population and baseline characteristics can still exist despite similar methodologies, and in that regard, there are a few potential explanations for differences observed between CanSpA and other real-world studies. First, b/tsDMARD-experienced patients are typically less likely to experience treatment success than patients who are naïve to b/tsDMARD at treatment initiation[13,18], and 77% of the patients in CanSpA were b/tsDMARD-experienced with an average of more than two prior biologics, relative to proportions as low as 55% in other real-world cohorts[14], which could have resulted in lower clinical response in the cohort overall. It was not feasible to stratify the current remission and response results by prior b/tsDMARD experience due to small sample sizes, but it would be interesting to see how clinical remission and response compared between these two groups in the broader Canadian population. Further, it should be noted that 79.3% of axSpA patients were on a 150mg Q4W dose at baseline relative to only 14.1% on the higher 300mg Q4W dose, and by 12 months there were still 52.9% on the 150mg dose relative to 18.4% on 300mg. Additional dosing instructions for secukinumab were approved in October 2020 recommending that the maintenance dose be

escalated to 300mg for AS patients that are not experiencing adequate response at the 150mg dose, and indeed the Canadian retrospective study of PSP data found that 34% of patients escalated up from the 150 mg dose within 12 months and experienced a corresponding reduction in disease activity.[15] As patients in the CanSpA cohort may have been treated before the recommended escalation to 300mg was added to the product label in 2020, it is possible that AS patients in the current study were not optimally escalated on secukinumab which may have contributed to suboptimal clinical response and premature discontinuation.

This study represents one of the first studies in Canada to describe real-world retention and clinical effectiveness of secukinumab in Canadian patients with axSpA. Real-world data enhances the evidence base for a therapeutic area beyond what is available in clinical trials and provides insight into how treatment performs in a more naturalistic setting and with a more heterogenous sample that better represents the broader patient population. CanSpA presents an opportunity to continue building and improving the real-world evidence base for research questions that benefit from a larger landscape coverage and for which a larger sample size is required. It also represents an opportunity to guide data capture and extraction for novel research questions. However, use of real-world data does confer some usual limitations. First, imaging data was not extracted to confirm AS diagnosis, therefore it was not possible to confirm that patients diagnosed with AS had received radiographic confirmation. However, as differences between AS and nr-axSpA were not a primary focus of this analysis, and previous literature suggests the disease burden associated with each is comparable[21], this was not considered a major limitation. Second, up to 60 patients were excluded from the analysis for not having a minimum of six months clinic follow-up post-index date, which could create selection bias in the final analysis if non-responders are more or less likely to return to the clinic at least six months after treatment initiation. That said, clinically speaking we would expect non-responders to be more likely to receive ongoing clinical management, not less, in order to address symptoms and amend treatment, suggesting this limitation may lead to an under-estimate of retention and effectiveness rather than over-estimate. Third, due to variability in data collection across the clinics contributing to CanSpA there was substantial data missingness across the datasets, particularly for clinical indices. Although missingness is, at times, unavoidable due to the minimally invasive nature of real-world studies, this missingness could still serve to bias results if data is more likely to be missing for patients showing a certain response. Furthermore, the small sample size of the study may have resulted in a cohort that is less generalizable to the spectrum of axSpA patients than a larger cohort would be, especially when performing stratification according to

biologic status, and limited our ability to conduct meaningful sub-group analyses and further investigate counter-intuitive findings. Lastly, this study uses retrospective data primarily collected in the context of clinical practice, for which rigorous data collection via protocols and validation practices were unlikely. This is often an unavoidable limitation of real-world data; that is, it could introduce artefactual inconsistencies in the data and uncertainty about results. Despite all of these limitations, this study has begun to fill an important knowledge gap in Canada focusing first on the real-world use and effectiveness of secukinumab for axSpA. Plans to broaden the CanSpA initiative are already underway, and future studies within the CanSpA network will aim to improve upon the limitations discussed above and continue addressing real-world evidence needs in Canada.

REFERENCES

1. American College of Rheumatology. Spondyloarthritis [Internet. Accessed August 18, 2022.] Available from: https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Spondyloarthritis

2. Sieper J, Poddubnyy D. Axial spondyloarthritis. Lancet. 2017;390:73–84.

3. Wang R, Ward MM. Epidemiology of axial spondyloarthritis: An update. Curr Opin Rheumatol. 2018;30:137–43.

4. Haroon NN, Paterson JM, Li P, Haroon N. Increasing proportion of female patients with ankylosing spondylitis: a population-based study of trends in the incidence and prevalence of AS. BMJ Open. 2014;4:e006634.

5. Rohekar S, Chan J, Tse SML, et al. 2014 Update of the Canadian Rheumatology Association/Spondyloarthritis Research Consortium of Canada treatment recommendations for the management of spondyloarthritis. Part I: Principles of the management of spondyloarthritis in Canada. J Rheumatol. 2015;42:654–64.

6. Heijde D van der, Ramiro S, Landewé R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017;76:978–91.

7. Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. Arthritis Care Res. 2019;71:1285–99.

8. Ganapati A, Gowri M, Antonisamy B, Danda D. Combination of methotrexate and sulfasalazine is an efficacious option for axial spondyloarthritis in a resource-limited, real-world clinical setting: a prospective cohort study. Clin Rheumatol. 2021;40:1871–9.

9. American College of Rheumatology. Secukinumab (Cosentyx). [Internet. Accessed August 18, 2022.] Available from: https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Treatments/Secukinumab-Cosentyx

10. Baeten D, Sieper J, Braun J, et al. Secukinumab, an interleukin-17A inhibitor, in ankylosing spondylitis. New Engl J Med. 2015;373:2534–48.

11. Marzo-Ortega H, Sieper J, Kivitz AJ, et al. 5-year efficacy and safety of secukinumab in patients with ankylosing spondylitis: end-of-study results from the phase 3 MEASURE 2 trial. Lancet Rheumatol. 2020;2:e339–46.

12. Deodhar A, Blanco R, Dokoupilová E, et al. Improvement of signs and symptoms of nonradiographic axial spondyloarthritis in patients treated with secukinumab: Primary results of a randomized, placebo-controlled phase III study. Arthritis Rheumatol. 2021;73:110–20.

13. Michelsen B, Lindström U, Codreanu C, et al. Drug retention, inactive disease and response rates in 1860 patients with axial spondyloarthritis initiating secukinumab treatment: Routine care data from 13 registries in the EuroSpA collaboration. RMD Open. 2020;6:e001280.

14. Kiltz U, Sfikakis P, Gullick N, et al. Secukinumab retention and safety in patients with active psoriatic arthritis or ankylosing spondylitis: 2 year interim results of the observational SERENA study [abstract]. Ann Rheum Dis. 2021;80(Suppl 1):337.1-338.

15. Aydin SZ, Inman R, Masetto A, et al. Secukinumab dose escalation for the treatment of ankylosing spondylitis in Canada: Retrospective analysis using real world data from the XPOSE patient support program. Paper presented at: CRA & AHPA Annual Scientific Meeting; 2021 Feb 24; Virtual.

16. Kristensen LE, Saxne T, Geborek P. The LUNDEX, a new index of drug efficacy in clinical practice: results of a five-year observational study of treatment with infliximab and etanercept among rheumatoid arthritis patients in southern Sweden. Arthritis Rheum. 2006;54:600–6.

17. Kiltz U, Peterlik D, Winkelmann V, Tony HP. AQUILA study in Germany – Real world adherence and persistence of secukinumab treatment in ankylosing spondylitis and psoriatic arthritis patients – An interim analysis [abstract]. Ann Rheum Dis. 2019;78(Suppl 2):1814–5.

18. Aydin S, Rahman P, Chan J, Wang CA, Chen YH, Tian H, et al. Real-world effectiveness of secukinumab in the treatment of ankylosing spondylitis in Canada: Retrospective analysis using data from the patient support program. Paper presented at: CRA & AHPA Annual Scientific Meeting; 2020 Feb 26-29. Victoria, Canada.

19. Kiltz U, Brandt-Juergens J, Kastner P, Riechers E, Peterlik D, Tony HP. How Do TNF-alpha-Inhibitors in medical history affect patient reported outcomes and retention in ankylosing spondylitis patients treated with secukinumab in real world? – German observational study [abstract]. Paper presented at: Arthritis Rheumatol. 2020;72(Suppl 10)

20. Baraliakos X, Van den Bosch F, Machado PM, et al. Achievement of remission endpoints with secukinumab over 3 years in active ankylosing spondylitis: Pooled analysis of two phase 3 studies. Rheumatol Ther. 2021;8:273–88.

21. Bedaiwi M, Sari I, Thavaneswaran A, Ayearst R, Haroon N, Inman RD. Fatigue in ankylosing spondylitis and nonradiographic axial spondyloarthritis: Analysis from a longitudinal observation cohort. J Rheumatol. 2015;42:2354–60.

Table and Figure legends

Table 1: Baseline demographics and clinical characteristics.

*Unless otherwise specified, age, sex, smoking status, comorbidities, and medication history were documented if they were captured at any time in the patient's history. All other baseline variables must have been captured within the 8 months prior to secukinumab initiation. **Percentages are calculated as a proportion of the patients with non-missing values for each variable. ^12-month dose reported only among the 92 patients retained on secukinumab at 12-months.

Abbreviations: SD= standard deviation; IQR= interquartile range; BMI= body mass index; axSpA= axial spondyloarthritis; csDMARD= conventional synthetic disease-modifying antirheumatic drug; b/tsDMARD= biologic/targeted synthetic disease-modifying antirheumatic drug; HLA B27= human leukocyte antigen B27; CRP= c-reactive protein; ESR= erythrocyte sedimentation rate

Table 2: Inactive or low disease activity status at 12 months.

*12-month clinical outcome scores were recorded as the value recorded closest to the date 12 months after secukinumab initiation and had to occur within 4 months of the 12-month date. **Percentages are calculated as a proportion of the patients with non-missing values for each variable.

Abbreviations: ASDAS= ankylosing spondylitis disease activity score; BASDAI= Bath ankylosing spondylitis disease activity index

Table 3: Reasons for discontinuation among those discontinuing secukinumab by 12 months.

Figure 1: Patient selection flowchart.

Abbreviations: axSpA= axial spondyloarthritis

Figure 2: Kaplan Meier-estimated retention to secukinumab from secukinumab initiation up to 12 months post-initiation.

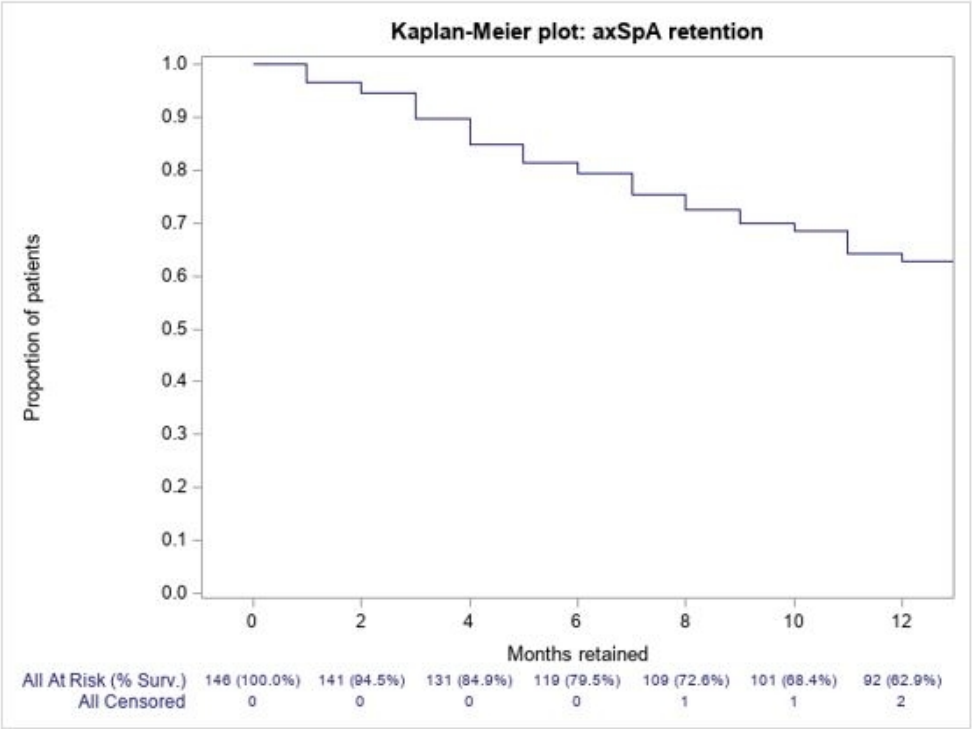
Figure 3: Mean clinical response from baseline to 12 months for patients with both a baseline and 12-month score recorded.

*12-month clinical outcome scores were recorded as the value recorded closest to the date 12 months after secukinumab initiation and had to occur within 4 months of the 12-month date. **In order to calculate change from baseline to 12 months and be considered "non-missing", patients had to have a score recorded at both baseline and 12 months.

Abbreviations: ASDAS= ankylosing spondylitis disease activity score; CRP= c-reactive protein; ESR= erythrocyte sedimentation rate; BASDAI= Bath ankylosing spondylitis disease activity index; BASFI= Bath ankylosing spondylitis functional index; BASMI= Bath ankylosing spondylitis metrology index; PatGA= patient global assessment; PhysGA= physician global assessment; TJC= tender joint count; SJC= swollen joint count

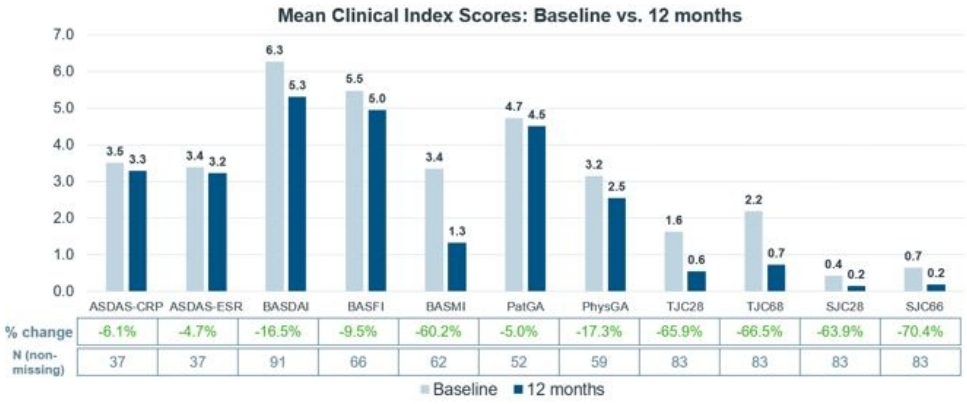
Patient selection flowchart.

85x91mm (144 x 144 DPI)



Kaplan Meier-estimated retention to secukinumab from secukinumab initiation up to 12 months post-initiation.

100x75mm (144 x 144 DPI)



Mean clinical response from baseline to 12 months for patients with both a baseline and 12-month score recorded.

120x51mm (144 x 144 DPI)

Table 1: Baseline demographics and clinical characteristics.

Characteristics, **n (%), mean (SD), or median (IQR)**	**Total** **(N=146)**
Index age, N (missing)	146 (0)
Mean (SD), years	43.3 (11.0)
Sex, N (missing)	146 (0)
Male, n (%)	79 (54.1%)
Smoking status, N (missing)	141 (5)
Smoker, n (%)	37 (26.2%)
BMI, N (missing)	115 (31)
Mean (SD), years	27.9 (6.0)
Diagnosis, N (missing)	146 (0)
Ankylosing spondylitis, n (%)	124 (84.9%)
Non-radiographic axSpA, n (%)	22 (15.1%)
Comorbidities, N (missing)	146 (0)
Cancer	7 (4.8%)
Depression	13 (8.9%)
Anxiety	3 (2.1%)
Medication history, N (missing)	146 (0)
Concomitant csDMARD within 30 days of index	14 (9.6%)
b/tsDMARD naive	34 (23.3%)
Years since diagnosis, N (missing)	146 (0)
Mean (SD), years	5.0 (4.8)
HLA-B27 status, N (missing)	140 (6)
Positive, n (%)	100 (71.4%)
CRP, N (missing)	114 (32)
Mean (SD), mg/L	9.1 (15.7)

ESR, N (missing)	107 (39)
Mean (SD), mm/h	14.7 (18.1)
Dactylitis count, N (missing)	128 (18)
Mean (SD)	0.0 (0.2)
Enthesitis count, N (missing)	128 (18)
Count > 1, n (%)	29 (22.7%)
Nail lesions, N (missing)	146 (0)
Present, n (%)	6 (4.1%)
Iritis, N (missing)	93 (53)
Present, n (%)	20 (13.7%)
Psoriasis, N (missing)	146 (0)
Present, n (%)	42 (28.8%)
Baseline dose, N (missing)	135 (11)
150mg Q4W, n (%)	107 (79.3%)
300mg Q4W, n (%)	19 (14.1%)
150mg Q2W, n (%)	6 (4.4%)
Other, n (%)	3 (2.2%)
12-month dose, N (missing)^	86 (6)
150mg Q4W, n (%)	46 (52.9%)
300mg Q4W, n (%)	16 (18.4%)
150mg Q2W, n (%)	17 (19.5%)
Other, n (%)	7 (9.2%)

*Unless otherwise specified, age, sex, smoking status, comorbidities, and medication history were documented if they were captured at any time in the patient's history. All other baseline variables must have been captured within the 8 months prior to secukinumab initiation. **Percentages are calculated as a proportion of the patients with non-missing values for each variable. ^12-month dose reported only among the 92 patients retained on secukinumab at 12-months.

Abbreviations: SD= standard deviation; IQR= interquartile range; BMI= body mass index; axSpA= axial spondyloarthritis; csDMARD= conventional synthetic disease-modifying antirheumatic drug; b/tsDMARD= biologic/targeted synthetic disease-modifying antirheumatic drug; HLA B27= human leukocyte antigen B27; CRP= c-reactive protein; ESR= erythrocyte sedimentation rate

Table 2: Inactive or low disease activity status at 12 months.

Clinical index (Non-missing N)	**Achieved remission status, N (%), [LUNDEX adjusted]**
ASDAS (51)	1 (2.0%), [1.2%]
BASDAI (96)	28 (29.2%), [18.4%]

*12-month clinical outcome scores were recorded as the value recorded closest to the date 12 months after secukinumab initiation and had to occur within 4 months of the 12-month date. **Percentages are calculated as a proportion of the patients with non-missing values for each variable.

Abbreviations: ASDAS= ankylosing spondylitis disease activity score; BASDAI= Bath ankylosing spondylitis disease activity index

Table 3: Reasons for discontinuation among those discontinuing secukinumab by 12 months.

Reasons for Discontinuation	**N (%)**
Discontinued secukinumab before 12 months	54 (100%)
Efficacy-related, ≤ 6 months	19 (35.2%)
Efficacy-related, > 6 months	15 (27.8%)
Adverse event	10 (18.5%)
Patient preference	1 (1.8%)
Missing	9 (16.7%)