THU0369 SECUKINUMAB 150MG PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS OF ACTIVE ANKYLOSING SPONDYLITIS WITH HIGH RETENTION RATE: 3-YEAR RESULTS FROM PHASE III TRIAL, MEASURE 2

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Background: Secukinumab improved signs and symptoms of ankylosing spondylitis (AS) over 2 years in the MEASURE 2 study (NCT01649375).[1,2]
Objectives: To report the efficacy and safety of secukinumab over 3 years from the MEASURE 2 study.
Methods: 219 patients (pts) with active AS were randomised to subcutaneous secukinumab 150mg (72 pts), 75mg (73 pts) or placebo (PBO, 74 pts). At Week (Wk) 16, PBO treated pts were re-randomised 1:1 to secukinumab 150mg or 75mg, irrespective of clinical response. Pts initially randomised to secukinumab and those who switched from PBO to secukinumab at Wk 16 were included in the analysis (secukinumab 150mg, N=106 and secukinumab 75mg, N=105). Outcome measures at Wk 156 included ASAS20 and 40, ASDAS-CRP inactive disease, ASAS5/6, BASDAI, SF-36 PCS and ASAS partial remission. Data are reported as observed. Safety analyses included all pts who received ≥1 dose of secukinumab.
Results: At 156 wks, the completion rates for secukinumab 150mg was 81.1% (86/106) and 72.4% (76/105) for 75mg. Higher discontinuation rates for 75mg were in part due to lack of efficacy or patient/guardian decision. Efficacy observed across endpoints from Wks 52 to 156 are summarised in the Table. Higher responses were observed in the 150mg group (Table and Figure). Over the entire study period, the mean exposure [±SD] to secukinumab was 914.3±315.5 days. The exposure-adjusted incidence rates with Any secukinumab for infections/infestations, Crohn's disease, malignant/unspecified tumours and major adverse cardiovascular events were 1.5, 0.6, 0.6 and 0.6 per 100 pt-years, respectively.
Conclusions: Secukinumab 150mg provided sustained improvement in the signs & symptoms along with physical functions with over 80% retention rate through 3 years in pts with AS. Safety profile remained favourable and was consistent with previous reports.[1,2]
References:
[1] Baeten et al. N Engl J Med. 2015;373:2534–48.
[2] Marzo-Ortega et al. Ann Rheum Dis. 2016;75:812–3.
Disclosure of Interest: H. Marzo-Ortega Grant/research support from: Janssen and Pfizer, Consultant for: Abbvie, Celgene, Janssen, Novartis and UCB, Speakers bureau: Abbvie, Celgene, Janssen and UCB, C. Legerton Grant/research support from: AbbVie, Ablynx, Acerta, Amgen, AstraZeneca, Celgene, GSK, Janssen, E. Lilly, BMS, Pfizer, Novartis, Sandoz, UCB, Daiichi Sankyo, ChemoCentryx, Boehringer Ingelheim, Speakers bureau: Novartis, Celgene and Amgen, J. Sieper Grant/research support from: AbbVie, Pfizer and Merck, Consultant for: AbbVie, Pfizer, Merck, UCB and Novartis, Speakers bureau: AbbVie, Pfizer, Merck and UCB, A. Kivitz Consultant for: AbbVie, Pfizer, Genentech, UCB and Celgene, Speakers bureau: AbbVie, Pfizer, Genentech, UCB and Celgene, R. Blanco: None declared, M. Cohen Consultant for: Abbvie, Amgen, BMS, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi and UCB, Speakers bureau: Abbvie, Amgen, BMS, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi and UCB, E. M. Delicha Employee of: Novartis, S. Rohrer Shareholder of: Novartis, Employee of: Novartis, H. Richards Shareholder of: Novartis, Employee of: Novartis
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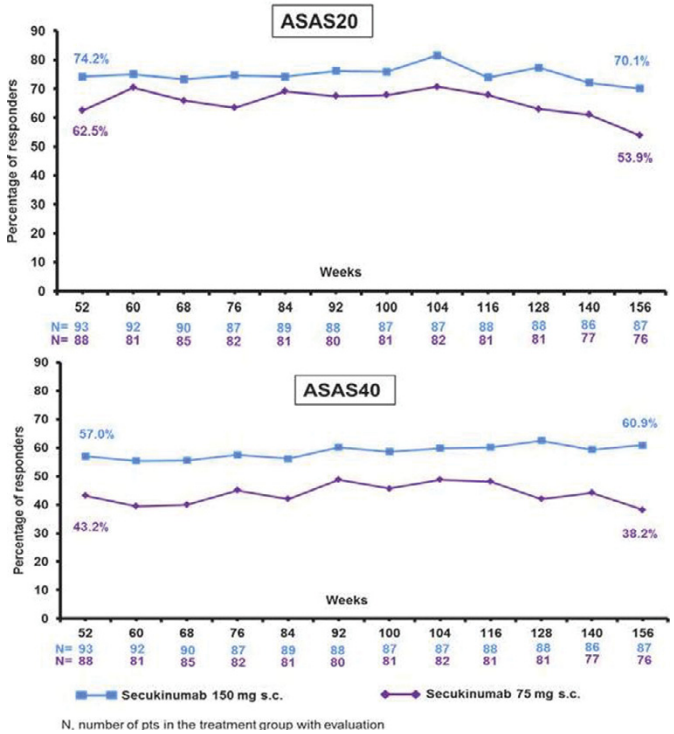
Table 1. Summary of Efficacy Results at Wks 52 and 156

Variable	Wk	Secukinumab	
		150mg	75mg
ASAS20, % responders (n/N)	52	74.2 (69/93)	62.5 (55/88)
	156	70.1 (61/87)	53.9 (41/76)
ASAS40, % responders (n/N)	52	57.0 (53/93)	43.2 (38/88)
	156	60.9 (53/87)	38.2 (29/76)
ASDAS-CRP Inactive Disease, % pts (n/N)	52	19.4 (18/93)	17.2 (15/87)
	156	25.6 (22/86)	12.0 (9/75)
ASAS 5/6, % responders (n/N)	52	61.3 (57/93)	49.4 (44/89)
	156	58.6 (51/87)	40.8 (31/76)
±SD (N)	52	-3.2±2.3 (93)	-2.5±2.2 (89)
	156	-3.3±2.5 (87)	-2.5±2.3 (76)
±SD (N)	52	7.6±7.7 (94)	6.4±7.3 (85)
	156	6.3±9.8 (84)	4.5±9.7 (72)
ASAS partial remission, % pts (n/N)	52	24.7 (23/93)	18.0 (16/89)
	156	32.2 (28/87)	11.8 (9/76)

ASAS, Assessment of Spondyloarthritis International Society criteria; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; hsCRP, high sensitivity C-reactive protein; n, number of responders; N, number of pts in the treatment group with evaluation SD, standard deviation; SF-36 PCS, Short Form-36 physical component summary.

Figure: ASAS20/40 response rate through Week 156



N, number of pts in the treatment group with evaluation

THU0370 INCREASED INTERLEUKIN-17A CONCENTRATION REMAINS HIGH IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH TUMOR NECROSIS α INHIBITORS WITHIN THE YEAR

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Background: Ankylosing spondylitis (AS) is associated with changes in the serum cytokines concentrations. During the treatment cytokines profile could change in different manner.
Objectives: The aim of the study was to evaluate the changes in concentration of interleukin-17A (IL-17A) in patients with AS, treated with tumor necrosis factor α inhibitors (anti-TNFα) during the year.
Methods: 30 patients with AS, fulfilled m. New-York criteria, with BASDAI ≥4.0 and NSAIDs non-responders were involved in the study. Mean age of AS patients at baseline was 38.35±9.19 years (M ± SD), the duration of AS was 11.4±9.6 years, 22 (73.3%) of patients – male. 20 healthy volunteers were involved as controls (mean age 40.1±7.7 years, male - 12 (60%). All AS patients were treated during the year with Remicade (infliximab, MSD®)) - 5 mg/kg at the recommended scheme. BASDAI, $ASDAS_{CRP}$ indices were calculated, C-RP, TNFα and IL-17A levels were measured before the treatment with anti-TNFα (baseline) and 52±2 weeks after the baseline. Number of patients achieved ASAS 20, ASAS 40 responses, and ASAS partial remission was evaluated. The statistics was performed with SPSS17.
Results: Baseline concentrations of TNFα and IL-17A in AS patients were higher than in healthy subjects (28.4±14.4 and 2.4±2.1, respectively, p<0.000). Significant reduction of AS activity, but not of IL-17A serum concentration was marked at week 52, Table 1.
24 (80%) achieved ASAS 20, 18 (60%) – ASAS 40, 12 (40%) of patients with

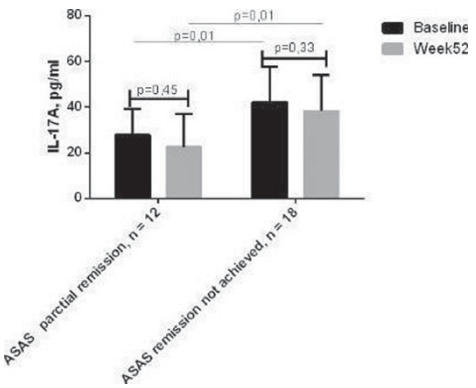

Table 1. Clinical and laboratory characteristics of AS activity at baseline and week 52, n=30

	Baseline	Week 52	p
Pain, Me [Q25;Q75]	6.0 [7.0; 9.0]	3.4 [1.0; 5.0]	<0.000
BASDAI, Me [Q25;Q75]	6.6 [4.4; 8.85]	3.2 [2.1; 7.6]	<0.000
ASDAS, Me [Q25;Q75]	3.8 [3.5; 4.4]	2.1 [1.26; 4.26]	<0.000
C-RP, mg/l, M±SD	12.3±3.9	4.3±1.7	<0.000
TNF α, pg/ml, M±SD	17.8±7.6	7.3±3.2	<0.000
IL-17A, pg/ml, M±SD	28.4±14.4	32.1±12.2	0.29

AS achieved ASAS partial remission. IL-17A was lower in patients who achieved remission compared to patients who did not achieve remission (figure).
Conclusions: Serum concentration of IL-17A remains stable in patients treated with anti-TNFα during the year. The baseline and final concentrations of serum IL-17A are higher in patients with AS who do not achieved ASAS partial remission compared to those who achieved the remission.
Disclosure of Interest: None declared
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THU0371 THERAPY MODIFICATIONS IN PATIENTS WITH ANKYLOSING SPONDYLITIS TREATED WITH A BIOLOGIC IN THE UNITED STATES – DESCRIPTIVE ANALYSES FROM AN ADMINISTRATIVE CLAIMS DATABASE

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Background: For patients with active ankylosing spondylitis (AS), biologic therapy has been shown to be an effective treatment option. Physicians treating patients with biologic therapy may modify the treatment by adding non-biologic medications and/or escalating the dose of the biologic; however, limited data exist on how these therapy modifications are used in patients with AS receiving biologic treatment in real-world settings.
Objectives: To describe therapy modifications (adding non-biologic medications or dose escalation of the biologic therapy) in patients with active AS who newly initiated treatment with biologic therapy in the United States.
Methods: This study used US administrative pharmacy and medical claims data from the Optum Research Database. Adult patients with AS who newly initiated (no evidence of use in the 12 months prior) a biologic between January 1, 2013 and January 31, 2015, and were continuously enrolled in a commercial or Medicare Advantage health plan 12 months before (baseline period) and 15 months following the index date, defined as the date of first pharmacy fill or medical infusion, were included. To reduce confounding by patients with an early switch/discontinuation, therapy modifications were identified only in those who persisted on the index biologic for >90 days. Therapy modifications identified included initiation of add-on medications (disease-modifying antirheumatic drugs, nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, corticosteroids, antidepressants, anxiolytics, sleeping aids and topical analgesics) after the first 90 days of persistence, and dose escalation of the index biologic. Dose escalation was defined as a patient receiving a dose >10% above the reference dose from the product label for ≥90 days.
Results: Of the 333 patients with AS included who persisted on their index biologic for >90 days, 88.3% initiated a subcutaneous tumor necrosis factor inhibitor (TNFi-SC; adalimumab, certolizumab pegol, etanercept or golimumab) as their index biologic and 11.7% initiated an intravenous TNFi (TNFi-IV; infliximab). During the 12-month baseline period, patients had a mean (standard deviation) number of claims of 3.9 (6.6) for opioids, followed by 2.5 (3.1) for NSAIDs, 1.9 (2.8) for corticosteroids and 1.8 (3.7) for antidepressants. Overall, 44.7% of patients received ≥1 additional medication during the period from 90 days after the index date to the end of persistence with the index biologic or 12-month post-index period. The most commonly added medications were corticosteroids (16.8%), opioids (12.9%), NSAIDs (10.2%) and antidepressants (7.2%) (Table 1). Overall, 7.2% of patients had a dose escalation of the index biologic (38.5% for TNFi-IV and 2.7% for TNFi-SC) in the immediate 12-month post-index period.

Table 1. Add-on medications initiated from 90 days after the index date to the end of persistence or 12 months among patients with AS

Additional Medication, n (%)	Total (N = 333)	TNFi-SC (n = 294)	TNFi-IV (n = 39)
Any medication	149 (44.7)	129 (43.9)	20 (51.3)
Corticosteroid	56 (16.8)	46 (15.6)	10 (25.6)
Opioid	43 (12.9)	39 (15.5)	4 (10.3)
NSAID	34 (10.2)	30 (10.2)	4 (10.3)
Antidepressant	24 (7.2)	22 (7.5)	2 (5.1)
Anxiolytic	23 (6.9)	18 (6.1)	5 (12.8)
csDMARD	15 (4.5)	13 (4.4)	2 (5.1)
Topical analgesic	13 (3.9)	9 (3.1)	4 (10.3)
Sleeping aid	9 (2.7)	8 (2.7)	1 (2.6)
tsDMARD	0 (0.0)	0 (0.0)	0 (0.0)

AS, ankylosing spondylitis; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IV, intravenous; SC, subcutaneous; TNFi, tumor necrosis factor inhibitor; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.
* TNFi-SC includes adalimumab, certolizumab, etanercept and golimumab.
† TNFi-IV includes infliximab.

Conclusions: In this descriptive, administrative claims-based study from the US, approximately 45% of patients with AS initiated an add-on medication while receiving biologic therapy. Further research is needed to better understand optimal therapy strategies for patients with AS.
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THU0372 EFFECT OF TNFI VERSUS NSAID ON SPINAL RADIOGRAPHIC PROGRESSION OVER 4 YEARS IN EARLY ANKYLOSING SPONDYLITIS: RESULTS FROM TWO OBSERVATIONAL COHORTS IN SOUTH KOREA

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Background: It is uncertain whether early suppression of inflammation by tumor necrosis factor inhibitor (TNFi) leads to a decreased radiographic progression in axial spondyloarthritis (axSpA).
Objectives: To compare the radiographic progression over 4 years in patients with early ankylosing spondylitis (AS) using TNFi versus nonsteroidal antiinflammatory drug (NSAID)
Methods: A total of 215 patients with early AS (symptom duration<10 years) were included based on the availability of radiographs at baseline and 2- and/or 4-years of follow up. Among them, 135 patients with TNFi were from SNUH-biologics cohort (TNFi group) and other 80 patients with NSAID were from control cohort in Seoul National University Bundang Hospital (NSAID group). Radiographic progression was assessed by two blinded readers using modified Stokes AS Spinal Score (mSASSS). Linear mixed model was applied to compare the radiographic progression between the two groups after adjustment for clinical factors. We also performed a sensitivity analysis after the propensity score matching in which age, smoking status, baseline CRP and baseline mSASSS were included as covariates.
Results: Patients in the TNFi group showed higher baseline BASDAI (6.7 vs. 3.1) and CRP (2.2 vs. 1.1mg/dL) as compared with those in the NSAID group. There were no differences between the two groups regarding age, gender, HLA-B27, smoking status and baseline radiographic damage. Overall, radiographic progression rate (95% CI) during the observation was 0.72 (0.57–0.87) unit/year. TNFi group showed significantly slower progression than NSAID group (β=-0.33 unit/year, p=0.042). This result was consistent after adjusting for age, smoking status, baseline CRP and presence of baseline syndesmophytes (β=-0.50 unit/year, p=0.001) (Table). In the subgroup analysis of patients without baseline syndesmophytes, TNFi group showed no radiographic progression over time whereas NSAID group did not (0.03 [-0.22–0.27] vs. 0.45 [0.20–0.71] unit/year). These results were not changed when the same analysis was performed in the post-matched population (78 TNFi group vs. 78 NSAID group).

Table 1. Radiographic progression over time in early AS patients using NSAID vs. TNFi

	Univariable analysis		Multivariable analysis[b]	
	Regression coefficient (95% CI)[a]	*p* value	Regression coefficient (95% CI)	*p* value
Age>40	0.82 (0.48–1.16)	<0.001	0.27 (-0.07–0.61)	0.124
Ever-smoker	0.31 (-0.01–0.62)	0.056	0.08 (-0.20–0.37)	0.568
Baseline CRP (mg/dL)	0.12 (0.05–0.18)	0.001	0.10 (0.04–0.16)	0.002
Baseline syndesmophytes	1.30 (1.00–1.62)	<0.001	1.14 (0.80–1.48)	<0.001
Group	-0.33 (-0.65–0.01)	0.042	-0.50 (-0.79–0.22)	0.001
NSAID group	0.93 (0.68–1.18)	<0.001	0.45 (0.18–0.71)	0.001
TNFi group	0.60 (0.40–0.79)	<0.001	-0.06 (-0.31–0.19)	0.648

[a]Regression coefficient indicates the progression of mSASSS over one year. [b] Gender, HLA-B27, baseline BASDAI and time-averaged NSAID index were not included because they did not show a significant ($p<0.1$) interaction with time in the univariable analysis.

Conclusions: In patients with early AS, TNFi led to a decreased radiographic progression as compared with NSAID treatment. This result suggests that early and durable suppression of inflammation using TNFi can have beneficial effect on the radiographic outcome of AS.
Disclosure of Interest: None declared
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