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FRI0379

LONG-TERM EVALUATION OF SECUKINUMAB 150 MG IN ANKYLOSING SPONDYLITIS: 5-YEAR END-OF-STUDY EFFICACY AND SAFETY RESULTS FROM A PHASE 3 TRIAL

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Background: Evaluation of long-term efficacy and safety for treatments for ankylosing spondylitis (AS) is important. Secukinumab, a fully human monoclonal antibody that directly inhibits interleukin-17A, has shown significant and sustained improvement in the signs and symptoms of AS through 3 years in the MEASURE 2 study (NCT01649375).¹

Objectives: We report the 5-year end-of-study results of subcutaneous (s.c.) secukinumab 150 mg in the MEASURE 2 study.

Methods: AS patients (pts; N = 219) were randomised to receive s.c. secukinumab 150 mg, 75 mg or placebo at baseline, Weeks (Wks) 1, 2 and 3 and every 4 wks from Wk 4. At Wk 16, placebo-treated pts were re-randomised to receive secukinumab 150/75 mg. Efficacy results are reported for pts initially randomised to secukinumab 150 mg and those who switched from placebo to secukinumab 150 mg at Wk 16 (N = 106). An optional dose escalation from secukinumab 75 mg to 150 mg was initiated beginning Wk 140. Outcome measures at Wk 260 included ASAS20/40, BASDAI50, BASMI, BASFI, SF-36 PCS and ASAS partial remission. Analyses stratified by anti-TNF status (anti-TNF-naïve and anti-TNF inadequate response [IR]) were performed. Safety analysis included all pts who received ≥1 dose of secukinumab. Results are reported as observed.

Results: The retention rate to Wk 260 was 77% (82/106) for secukinumab 150 mg. Sustained efficacy was observed with secukinumab 150 mg across all endpoints through 5 years (Table). Improvements were maintained regardless of prior exposure to anti-TNF therapy with greater responses in anti-TNF-naïve pts. A total of 49 pts on secukinumab 75 mg (46.7%) escalated dose to 150 mg after Wk 140; efficacy responses improved in pts whose dose was escalated. Over the entire study period, the mean exposure (±SD) to secukinumab was 1459.1 ± 597.8 days. Exposure-adjusted incidence rates (per 100 pt-years) with any secukinumab dose for selected adverse events were: *Candida* infections (1.0), Crohn's disease (0.5), major adverse cardiovascular events (0.7), uveitis (0.5), and malignant/unspecified tumours (0.5).

Conclusion: Secukinumab 150 mg provided sustained improvement in the signs, symptoms, and physical function in pts with AS through 5 years of treatment. The safety profile of secukinumab remained consistent with previous reports.¹⁻³

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Table. Efficacy Endpoints with Secukinumab 150 mg at Week 260 (5 year)

Variable	Secukinumab 150 mg ¹		
	Total N = 106	Anti-TNF-naïve N = 66	Anti-TNF-IR N = 40
ASAS20 ²	69.9 (83)	73.7 (57)	61.5 (26)
ASAS40 ²	54.2 (83)	63.2 (57)	34.6 (26)
ASAS-Partial Remission ²	25.3 (83)	28.1 (57)	19.2 (26)
BASDAI50 ²	53.0 (83)	56.1 (57)	46.2 (26)
BASMI ³	-0.7±1.2 (80)	-	-
BASFI ³	-2.8±2.6 (83)	-	-
SF-36 PCS ³	8.0±8.5 (79)	8.5±8.9 (56)	6.8±7.4 (23)

Data are reported as observed; ¹Includes placebo switchers; ²% responders (n); ³mean change from baseline ± SD (n); IR, inadequate response; N, total number of randomised patients; n, number of evaluable patients; TNF, tumour necrosis factor

FRI0380

SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENT OF ENTHESITIS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: POOLED ANALYSIS OF FOUR PIVOTAL PHASE 3 STUDIES

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Background: Enthesitis can be a debilitating extra-articular spondyloarthritis (SpA) manifestation and cause of considerable pain and reduced quality of life/physical function.^{1,2}

Objectives: To evaluate the effect of secukinumab (SEC) on axial and peripheral enthesitis in ankylosing spondylitis (AS) patients (pts) with baseline enthesitis (BLE) across all Maastricht AS Enthesitis (MASES) sites (N=13), axial MASES sites [N=11; 13 MASES minus Achilles tendons (AT); Axs], peripheral sites (N=6; AT + lateral condyles of humerus/femur; PS) and the AT (N=2; AT) at Weeks (W) 16 and 52.

Methods: This post hoc analysis pooled data across 4 SEC studies in AS (MEASURE 1-4) from pts originally randomised to SEC 150mg (approved dose in AS), 300mg (MEASURE 3 only), or placebo (PBO) with BLE (MASES >0). Study designs have been reported previously. Evaluations include mean change from BL in MASES score, complete resolution (CR; MASES=0) and improvement from BL in MASES score of ≥5 counts. Mixed-effect model repeat measurement (MMRM) analysis was done on change from BL in MASES score and non-responder imputation for resolution of enthesitis at W16; data are reported as observed at W52.

Results: A total of 355 (70.4%), 58 (76.3%), and 280 (72%) pts had BLE in 150mg, 300mg and PBO groups, respectively. BL characteristics were generally comparable across groups. At W16, mean change from BL for overall MASES and at Axs was greater for SEC 150mg (-2.4 and -2.3) and 300mg (-2.9 and -2.9) vs PBO (-1.9 and -1.8; P<0.05 and <0.01). At W16, pts treated with SEC 150mg (40.8% and 42.7%) and 300mg (36.2% and 42.1%) vs PBO (28.9% and 30.1%) achieved CR of enthesitis based on overall MASES and at Axs. SEC150mg and 300mg were also consistently associated with higher mean change in MASES and CR of enthesitis at PS and individually at AT vs PBO. A higher proportion of pts treated with SEC 150/300mg vs PBO achieved a higher threshold of improvement (≥5 counts) in overall MASES at W16. Further improvements were observed for all endpoints at W52 (Table).

Conclusion: Secukinumab was associated with higher mean change in MASES and complete resolution of enthesitis compared to placebo at Week 16, which further improved through Week 52.

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Table. Summary of results

	SEC 150 mg N=355		SEC 300mg N=58		PBO N=280
	W16	W52 ^a	W16	W52 ^a	W16
LS mean change from BL in MASES score ^a					
Overall MASES ^a	-2.4 [‡]	-3.5	-2.9 [§]	-3.9	-1.9
AxS ^b	-2.3 [‡]	-3.2	-2.9 [§]	-3.6	-1.8
PS ^c	-1.3	-1.9	-1.6	-2.1	-1.2
AT ^d	-1.0	-1.2	-1.0	-1.3	-0.8
Complete resolution of enthesitis (MASES=0) ^a , %					
Overall MASES ^a	40.8 [§]	56.4	36.2	52.9	28.9
AxS ^b	42.7 [§]	58.6	42.1	60.0	30.1
PS ^c	46.3	65.5	52.5	69.7	38.3
AT ^d	57.0	78.4	55.0	77.8	48.0
Improvement from BL in MASES score (≥5 counts) ^a , %					
Overall MASES ^a	23.7	34.1	27.6	43.1	16.1
AxS ^b	20.1	28.0	22.8	32.0	15.4

[§]P<0.01; [‡]P<0.05 vs PBO. [‡]P-values from repeated MMRM until Week 16. [§]P-values from logistic regression model. SEC 150mg (n=355, ^a344, ^c229, ^d128); 300mg (n=58, ^b57, ^c40, ^d20) and PBO (n=280, ^a272, ^c188, ^d98). ^aObserved data. LS, least squares; N, number of patients analysed; n, number of patients with measurement.

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FRI0381

TROUGH SERUM DRUG LEVELS AND DISEASE ACTIVITY IN AXIAL SPONDYLOARTHRITIS PATIENTS ON LONG-TERM TREATMENT WITH TNF- α INHIBITORS

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Background: In approximately 50% of patients with axial spondyloarthritis (ax-SpA) treated with TNF- α inhibitors, treatment loses efficacy after a period of time.¹ Previous research has shown that high disease activity is associated with low serum drug levels after 6 months of treatment with TNF- α inhibitors.² There is limited literature regarding this subject in axial SpA patients on long-term treatment with TNF- α inhibitors.

Objectives: To investigate the association between trough serum drug level of TNF- α inhibitors and disease activity in axial SpA patients.

Methods: All consecutive ax-SpA patients of the Groningen Leeuwarden Axial SpA (GLAS) cohort, fulfilling the ASAS classification criteria, treated with TNF- α inhibitors and visiting the out-patient clinic in Groningen

between the 1st of June 2015 until the 31st of May 2016 were approached to have a trough serum drug level measurement within two months from the out-patient visit. Serum trough levels were stratified in a 'therapeutic' and 'below-therapeutic' range according to the reference values of Sanquin³. Disease activity was assessed with the ASDAS, BASDAI and CRP.

Results: 67 (60%) of the 112 approached patients were eligible for analyses. Thirty-one (46%) were male, mean age was 45 $\pm$ 12 years, 48 patients (72%) were HLA-B27 positive, mean symptom duration was 20 $\pm$ 12 years and median duration of TNF- α inhibitor treatment was 49 months (IQR 14-64). 34 patients were on adalimumab (51%), followed by 21 on etanercept (31%) and the remaining 12 patients (18%) were on infliximab, certolizumab or golimumab. 32 of the 67 patients (48%) had a 'therapeutic' serum trough drug level and 35 (52%) were 'below-therapeutic', with no significant difference in patient characteristics between these 2 groups, including disease activity (ASDAS 2.2 $\pm$ 1.0 vs. 2.3 $\pm$ 0.8; BASDAI 3.9 $\pm$ 2.4 vs. 4.1 $\pm$ 2.1; CRP 4.5, IQR 2.0-6.6 vs. 3.0, IQR 2.0-6.0). No significant correlations for ASDAS, BASDAI and CRP with adalimumab or etanercept drug level were found (adalimumab r=-0.164, p=0.36; r=-0.191, p=0.29; r=-0.041, p=0.83 resp.; etanercept r=-0.185, p=0.42; r=-0.113, p=0.63; r=-0.216, p=0.36 resp.).

Stratified by gender, only women on adalimumab showed a weak significant negative correlation between serum level and ASDAS and BASDAI (r=-0.444, p<0.05; r=-0.497, p<0.05 resp.) but not for CRP (r=0.038, p=0.87). Compared to men, women had a significantly higher ASDAS and CRP. BASDAI was not significantly different (data not shown). Patient characteristics between patients with and without serum trough level measurements did not differ significantly.

Conclusion: In daily clinical practice random serum trough levels in ax-SpA patients are relatively low according to reference values of Sanquin. Furthermore, only for women on adalimumab a weak correlation was found between trough serum drug level and ASDAS and BASDAI but not for CRP.

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FRI0382

TEN-YEAR RETENTION RATES OF FIRST-LINE BIOLOGICAL AGENT IN AXIAL SPONDYLOARTHRITIS IN DAILY PRACTICE: A ROMANIAN MULTICENTRE EXPERIENCE

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Background: Although the efficacy and long-term persistence of TNF inhibitors (TNF-i) are widely recognized in axial spondyloarthritis (axSpA), up to about one third of patients experience failure (loss of therapeutic response or toxicity) with the first biological agent requiring switching to another drug.