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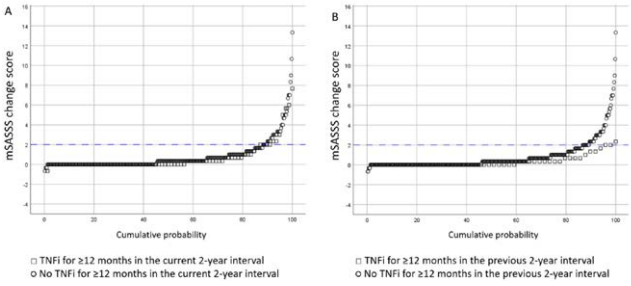
Figure 1. Cumulative probability plots depicting mSASSS change scores over 2 years in patients with axial spondyloarthritis treated vs. not treated with TNFi in the current (A) or previous (B) 2-year interval.



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OP0140

BIOLOGIC REFRACTORY DISEASE IN AXIAL SPONDYLOARTHRITIS - DEFINITION, PREVALENCE AND PATIENT CHARACTERISTICS. A COLLABORATION BETWEEN FIVE NORDIC BIOLOGIC REGISTRIES

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Background: In clinical practice, some patients with axial spondyloarthritis (axSpA) fail several consecutive biological treatments (bDMARDs). How this group of "refractory" patients should best be defined, how common they are, and what their characteristics are, is poorly understood.

Objectives: To explore the point prevalence of bDMARD refractory disease in axSpA over time, according to different definitions, and to describe the characteristics of refractory vs. not-refractory patients upon start of their first bDMARD.

Methods: Observational prospective cohort study. Patients with axSpA (ankylosing spondylitis/non-radiographic axial SpA) starting a first bDMARD 2009-2018 were identified in biologic registries in Denmark, Sweden, Finland, Norway and Iceland. Clinical characteristics and treatments were retrieved, and data were pooled for analysis.

Refractory disease was defined based on the number of different bDMARD treatments started in individual patients: mild (≥3 bDMARDs), moderate (≥4), and strict (5 or more). Restart of same bDMARD with another bDMARD in between counted as separate courses whereas switch from originator to corresponding biosimilar was ignored.

Proportions of patients fulfilling each definition of refractory disease at 2 and 5 years after the start of 1st bDMARD were calculated.

Point-prevalence per calendar-year was calculated as the number of patients with refractory disease at the end of each year, divided by the total number of patients ever having starting a first bDMARD before that time-point, and who were still alive and resident in the country.

Results: The point prevalence of refractory axSpA increased with calendar-time (Figure). Among 12,037 included axSpA patients (64% male), the point-prevalence of bDMARD refractory disease in 2018 was 16%/7%/3% according to mild/moderate/strict definitions (Table).

Table 1. Biologic refractory axSpA according to three definitions

		Refractory definition		
	Overall cohort	MILD	MODERATE	STRICT
A. Baseline characteristics upon start 1st bDMARD				
N	12037	1969	832	351
Age, years	42 (13)	41 (12)	41 (12)	41 (12)
Male, %	64%	57%	54%	56%
Disease duration, years	7 (10)	6 (9)	6 (8)	5 (8)
BASDAI, 0-100	53 (28)	60 (29)	63 (27)	66 (35)
ASDAS	3.3 (1.1)	3.5 (1.2)	3.6 (1.0)	3.7 (1.1)
CRP, mg/L	16 (23)	18 (26)	21 (28)	23 (32)
Patient global, VAS, 0-100	59 (25)	65 (22)	66 (22)	67 (23)
Patient Pain, VAS, 0-100	57 (24)	62 (22)	63 (22)	63 (22)
Fatigue, VAS, 0-100	59 (27)	66 (26)	66 (26)	68 (25)
B. Proportions of patients having refractory disease 2 and 5 years after start of their first bDMARD				
2 years, %		5%	1%	0%
5 years, %		13%	4%	1%

Numbers are means (SD) unless otherwise stated

Upon start of their 1st bDMARD, patients later fulfilling the definitions for refractory axSpA were more frequently women, had shorter disease duration, higher C-reactive protein and higher patient reported outcomes.

Overall, 5%/1%/0% had mild/moderate/strict refractory disease 2 years after start of first bDMARD, after 5 years it was 13%/4%/1% (Table).

Conclusion: In this large Nordic observational cohort of axSpA patients treated in routine care, we could demonstrate that a substantial proportion of all patients had used multiple bDMARDs. In 2018, one in six patients had received ≥3 bDMARDs, indicating a bDMARD refractory disease. Multiple switching was more frequent during later years, probably due to more bDMARDs becoming available. The characteristics of refractory axSpA, including sex and disease activity, will have to be further explored, as will the impact of refractory disease on long-term outcomes.

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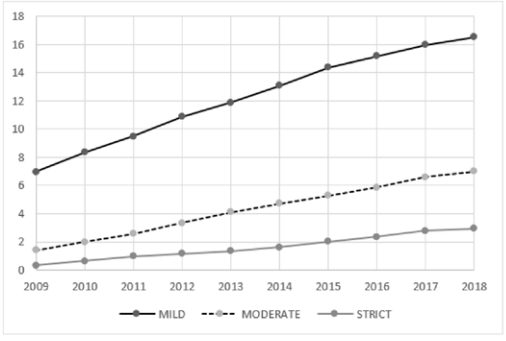
Figure. Point prevalence of bDMARD refractory disease in AxSpA per calendar year according to three different definitions (mild ≥3 bDMARDs, moderate ≥4, strict ≥5)

X-axis: year, Y-axis: percentage



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OP0141

EFFECTS OF FILGOTINIB ON SPINAL LESIONS IN ANKYLOSING SPONDYLITIS: MAGNETIC RESONANCE IMAGING DATA FROM THE TORTUGA TRIAL

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Background: The oral Janus kinase 1 preferential inhibitor filgotinib (FIL) significantly improved Spondyloarthritis Research Consortium of Canada (SPARCC) magnetic resonance imaging (MRI) inflammation scores (bone marrow oedema) in the spine and sacroiliac joints vs placebo (PBO) in the Phase 2 TORTUGA trial (NCT03117270) in patients with active ankylosing spondylitis (AS).[1]

Objectives: This post-hoc analysis evaluated the effects of FIL on Canada-Denmark (CANDEN) MRI measures of spinal inflammation and structural lesions in patients from the TORTUGA trial.

Methods: TORTUGA was a PBO-controlled, multicentre, double-blind, randomised trial. Patients with active AS (as per modified New York classification criteria, with sacroiliitis confirmed by central reading) were treated with FIL 200 mg (n=58) or PBO (n=58) once daily for 12 weeks. MRI of the total spine was conducted at baseline and at treatment end. Scans were re-evaluated post-hoc by 2 independent experts (blinded to time point and assigned treatment) using the CANDEN method;[2] inter-reader discrepancies were resolved by an independent adjudicator. Observed changes from baseline were evaluated using analysis of covariance, with factors for treatment, baseline value, and randomisation stratification by prior tumour necrosis factor inhibitor use. Least-squares (LS) mean changes from baseline and between-group differences with 95% confidence intervals (CI) were calculated; P values are nominal.

Results: MRI scans from 88 patients (47 FIL, 41 PBO) with an evaluable scan at baseline and Week 12 (or early termination) were re-evaluated. Baseline characteristics were generally similar between patients with/without an MRI scan. Of those with MRI scans, mean total spine inflammation score (which ranges from 0–614) was higher, and mean ankylosis score (which ranges from 0–460) was lower, in the FIL vs PBO group at baseline. Total spine inflammation scores decreased from baseline with FIL but not with PBO (Figure and Table; P=0.0003 for between-group difference). Cumulative probability plots favoured FIL over PBO for change from baseline in subregion inflammation scores, including posterolateral elements (i.e. sum of lesions in ribs, transverse processes, spinous processes, soft tissue inflammation, and postero-lateral vertebral body), facet joint, and vertebral body. Total spine fat lesion scores numerically increased from baseline in the FIL but not PBO group (P=0.0878 for between-group difference; Table). There were no significant differences between groups for changes in erosion (P=0.1956) or ankylosis (P=0.3888) scores (Table).

Table 1. Change from baseline at Week 12 in CANDEN total spine inflammation, total spine fat, total spine bone erosion, and ankylosis scores

	Treatment group	n	Sample mean (SE)	LS mean (SE)	95% CI of treatment mean	LS mean of group difference (SE)	95% CI of group difference	Between-group P value
Total spine inflammation score	Filgotinib	47	–4.98 (0.96)	–4.40 (1.13)	–6.65, –2.15	–4.49 (1.21)	–6.85, –2.12	0.0003
	Placebo	41	0.29 (0.78)	0.09 (1.13)	–2.17, 2.34			
Total spine fat score	Filgotinib	47	1.01 (0.62)	1.09 (0.66)	–0.22, 2.40	1.18 (0.69)	–0.18, 2.55	0.0878
	Placebo	41	–0.25 (0.19)	–0.09 (0.66)	–1.40, 1.21			
Total spine bone erosion score	Filgotinib	47	0.01 (0.02)	0.07 (0.03)	0.00, 0.14	0.05 (0.04)	–0.02, 0.12	0.1956
	Placebo	41	–0.02 (0.03)	0.02 (0.03)	–0.04, 0.09			
Total ankylosis score	Filgotinib	47	0.30 (0.29)	0.23 (0.31)	–0.40, 0.85	0.28 (0.34)	–0.37, 0.94	0.3888
	Placebo	41	–0.01 (0.08)	–0.06 (0.31)	–0.68, 0.56			

SE, standard error

Conclusion: This is the first PBO-controlled trial to demonstrate a decrease in inflammatory activity with FIL, not only in the spinal vertebrae but also in the postero-lateral elements of the spine and facet joints. As expected in a 12-week study period, no changes in erosion or ankylosis were seen, while fat lesions showed a tendency to increase with FIL. Larger trials are needed to confirm these results.

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[1] van der Heijde D, et al. *Lancet* 2018;392:2378–87.

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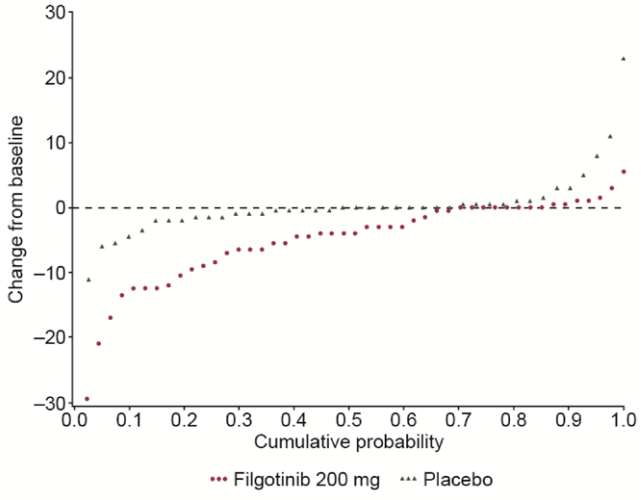
Figure. Change from baseline in total CANDEN spine inflammation score



CANDEN, Canada-Denmark

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