SUPPLEMENTARY MATERIAL

Ixekizumab Improves Signs, Symptoms, and Quality of Life in Patients with Axial Spondyloarthritis Irrespective of Symptom Duration

Victoria Navarro-Compán[1], John D. Reveille[2], Proton Rahman[3], José A. Maldonado-Cocco[4], Marina Magrey[5], Rebecca Bolce[6], Tommaso Panni[6], Andris Kronbergs[6], Martin Rudwaleit[7]

[1]Department of Rheumatology, La Paz University Hospital, IdiPaz, Madrid, Spain; [2]Division of Rheumatology and Clinical Immunogenetics, University of Texas-McGovern Medical School, Houston, Texas, USA; [3]Department of Rheumatology, Memorial University of Newfoundland, St. John's, Newfoundland, Canada; [4]University of Buenos Aires School of Medicine, Buenos Aires, Argentina; [5]Case Western Reserve University School of Medicine/University Hospital, Cleveland, Ohio, USA; [6]Eli Lilly and Company, Indianapolis, Indiana, USA; [7]Department of Internal Medicine and Rheumatology at Klinikum Bielefeld, Bielefeld University, Bielefeld, Germany.

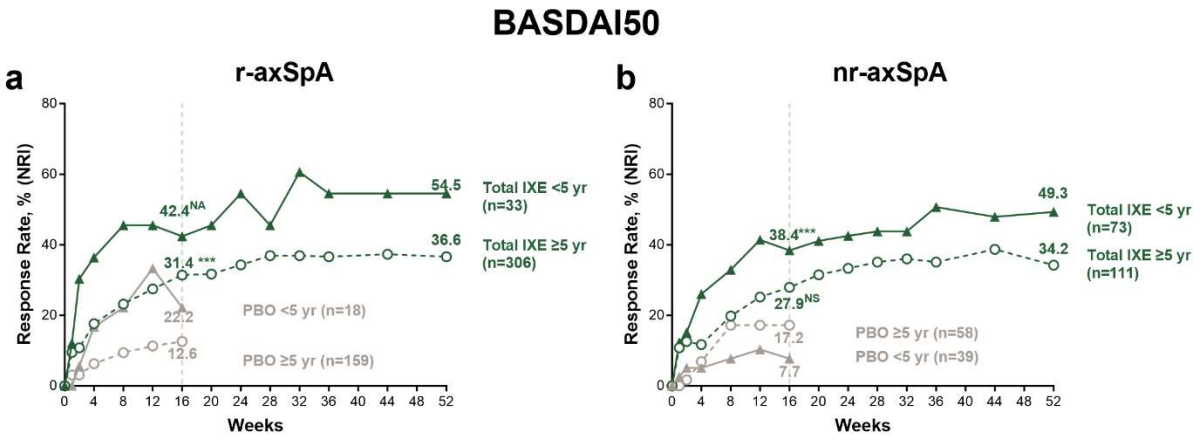
Corresponding author: Victoria Navarro-Compán, MD, PhD

Email: mvictoria.navarroc@gmail.com

Supplemental Table S1. Demographics and baseline disease characteristics for placebo patients

	Placebo-treated patients with r-axSpA		Placebo-treated patients with nr-axSpA	
	<5 years symptom duration (n=18)	≥5 years symptom duration (n=159)	<5 years symptom duration (n=39)	≥5 years symptom duration (n=58)
Age, years	34.3 (9.8)	45.6 (12.0)	32.4 (9.8)	44.2 (11.2)
Male, n (%)	15 (83.3)	137 (86.2)	17 (43.6)	22 (37.9)
Duration of symptoms since axSpA onset, years	3.4 (1.2)	20.0 (11.0)	2.4 (1.3)	14.6 (6.6)
csDMARD use, n (%)	7 (38.9)	53 (33.3)	15 (38.5)	16 (27.6)
Prior use of TNFi, n (%)	9 (50.0)	86 (54.1)	-	-
ASDAS score	3.7 (0.8)	4.1 (0.8)	4.0 (1.0)	3.7 (0.8)
BASDAI score	6.6 (0.9)	7.2 (1.3)	7.2 (1.6)	7.2 (1.5)
SF-36 PCS score	37.3 (7.5)	33.4 (7.5)	33.8 (9.6)	32.2 (7.5)
SF-36 MCS score	48.2 (9.3)	48.7 (11.1)	49.4 (11.4)	47.3 (11.7)
CRP, mg/L	16.7 (20.9)	16.9 (22.4)	19.1 (32.3)	10.3 (17.3)
CRP >5.00 mg/L, n (%)	14 (77.8)	107 (67.3)	27 (69.2)	28 (48.3)

Data are mean (standard deviation) unless otherwise specified. ASDAS: Axial Spondyloarthritis Disease Activity Score; axSpA: axial spondyloarthritis; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; csDMARD: conventional synthetic disease-modifying anti-rheumatic drug; IXE: ixekizumab; MCS: Mental Component Summary; nr-axSpA: non-radiographic axSpA; PCS: Physical Component Summary; r-axSpA: radiographic axSpA; SF-36: 36-Item Short Form Health Survey; TNFi: tumor necrosis factor inhibitor.



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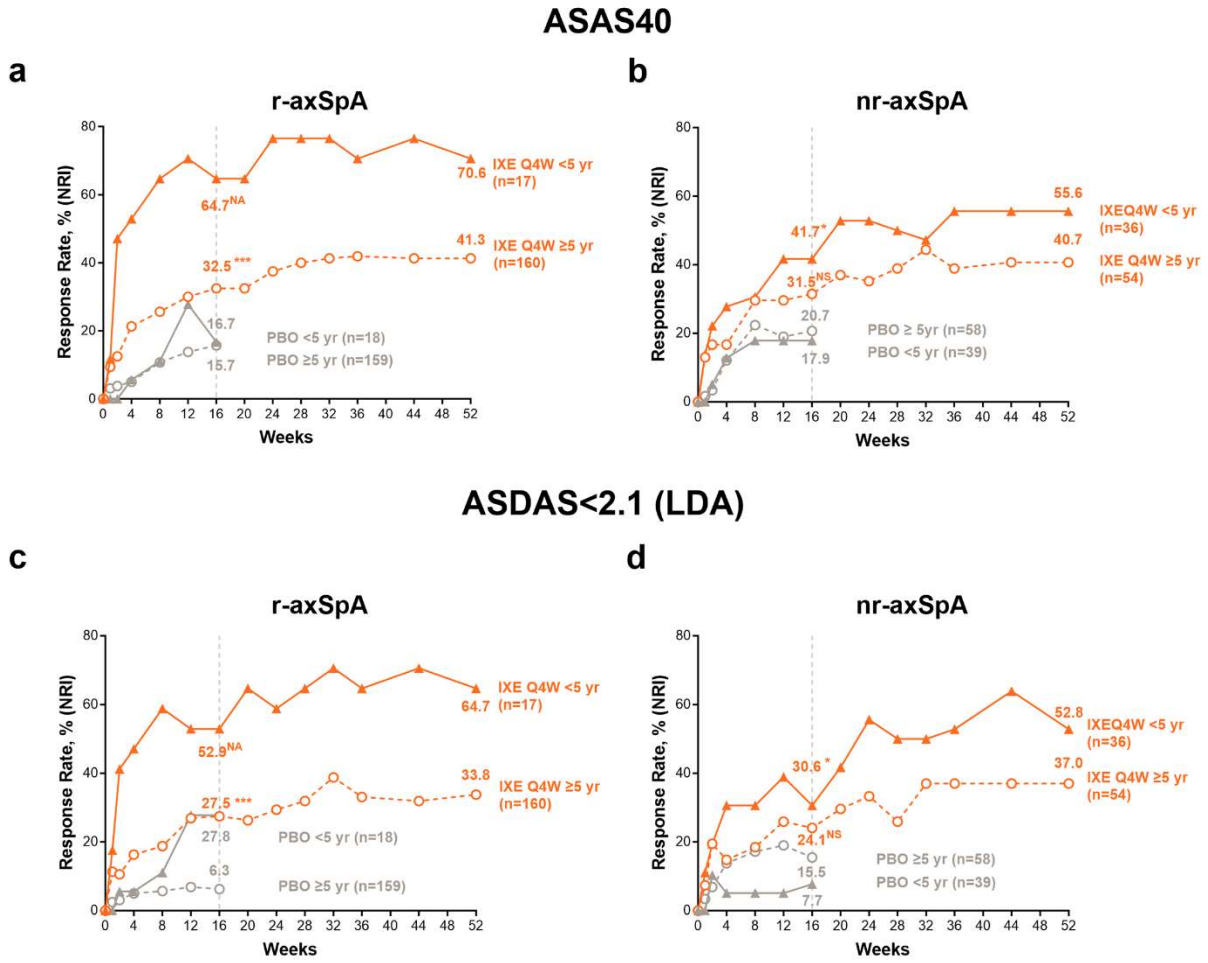
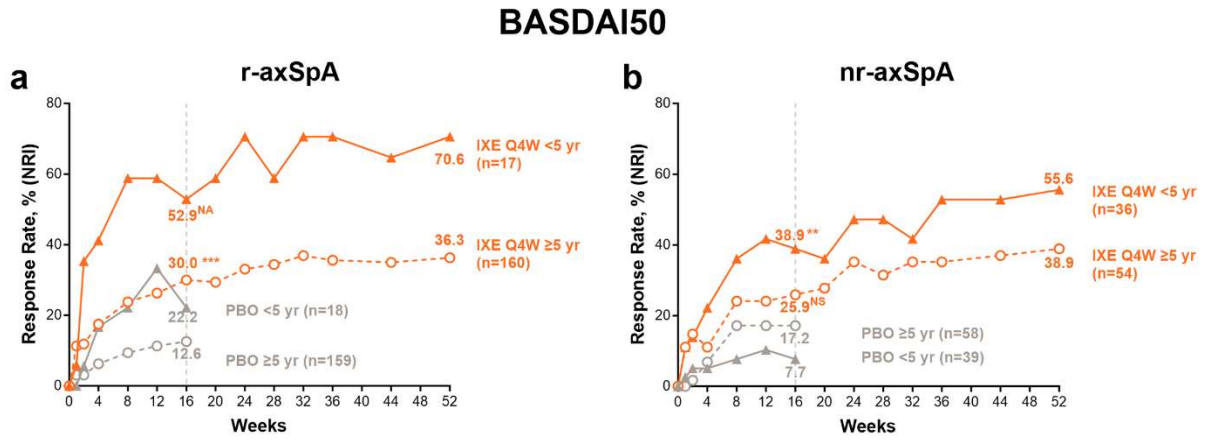
	Patients with r-axSpA		Patients with nr-axSpA	
	<5 years symptom duration (PBO n=18; IXE n=33)	≥5 years symptom duration (PBO n=159; IXE n=306)	<5 years symptom duration (PBO n=39; IXE n=73)	≥5 years symptom duration (PBO n=58; IXE n=111)
BASDAI50 at Week 16				
Relative risk of response, IXE vs PBO	1.91	2.49	4.99	1.62
Relative risk ratio, <5 vs ≥5 years symptom duration	0.77 (0.27, 2.19)		3.08 (0.84, 11.23)	
Number needed to treat with IXE to achieve response	5.0	5.3	3.3	9.4

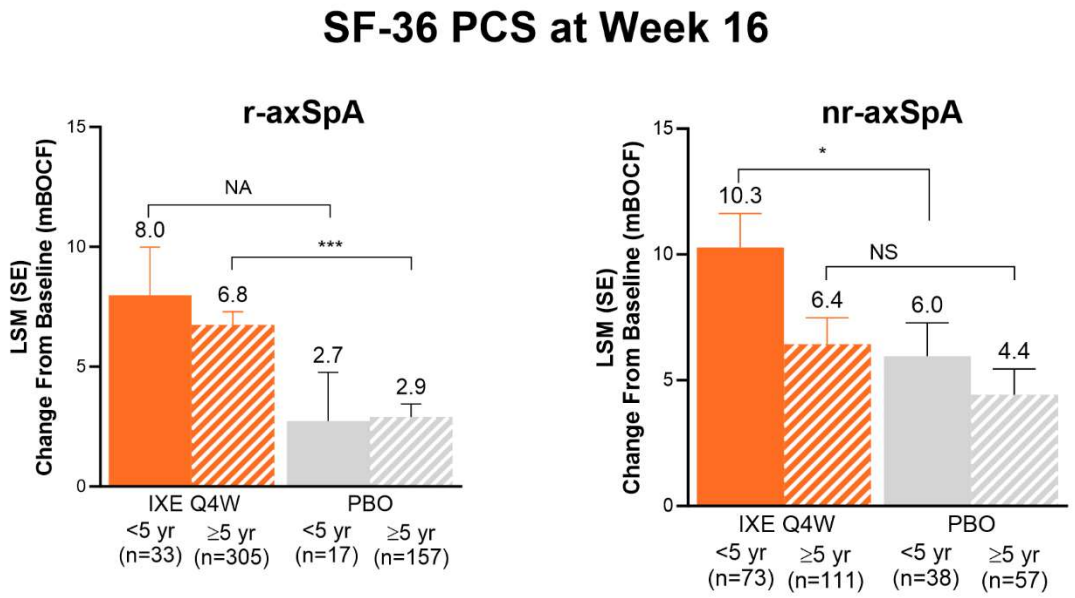
Supplemental Figure S1. Response rates and number needed to treat and relative risk of response for BASDAI50 by shorter versus longer symptom duration (defined as <5 vs. ≥5 years) for patients with r-axSpA and nr-axSpA treated with ixekizumab (combined IXE Q4W and IXE Q2W) or PBO. (a) r-axSpA and (b) nr-axSpA through Week 52 and (c) Number needed to treat and relative risk of response at Week 16. *p<0.05; **p<0.01; ***p<0.001 vs. PBO at Week 16 using Cochran-Mantel-Haenszel test stratified by study (patients with r-axSpA) or the Fisher exact test (patients with nr-axSpA). BASDAI50: Bath Ankylosing Spondylitis Disease Activity Index ≥50% improvement; IXE: ixekizumab; LDA: low disease activity; NA: not applicable as inferential testing was not performed if a subgroup was <10% of the total population; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; NS: not significant; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.



Supplemental Figure S2. IXE Q4W or PBO response rates by early shorter versus longer symptom duration (defined as <5 vs. ≥5 years) for patients with r-axSpA and nr-axSpA. ASAS40 for (a) r-axSpA and (Bb nr-axSpA and ASDAS LDA (ASDAS <2.1) for (c) r-axSpA and (d) nr-axSpA through Week 52. *p<0.05; **p<0.01; ***p<0.001 vs. PBO at Week 16 using Cochran-Mantel-Haenszel test stratified by study (patients with r-axSpA) or the Fisher exact test (patients with nr-axSpA). ASAS40: Assessment of SpondyloArthritis international Society 40% improvement; ASDAS: Axial Spondyloarthritis Disease Activity Score; IXE: ixekizumab; LDA: low disease activity; NA: not applicable as inferential testing was not performed if a subgroup was <10% of the total population; nr-axSpA: non-radiographic axial spondyloarthritis; NS: not significant; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.



Supplemental Figure S3. IXE Q4W or PBO response rates for BASDAI50 by shorter versus longer symptom duration (defined as <5 vs. ≥5 years) for patients with r-axSpA and nr-axSpA treated with IXE Q4W or PBO. (a) r-axSpA and (b) nr-axSpA through Week 52. *p<0.05; **p<0.01; ***p<0.001 vs. PBO at Week 16 using Cochran-Mantel-Haenszel test stratified by study (patients with r-axSpA) or the Fisher exact test (patients with nr-axSpA). BASDAI50: Bath Ankylosing Spondylitis Disease Activity Index 50% improvement; IXE: ixekizumab; NA: not applicable as inferential testing was not performed if a subgroup was <10% of the total population; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; NS: not significant; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.



Supplemental Figure S4. IXE Q4W or PBO SF-36 Physical Component Summary at Week 16 by shorter versus longer symptom duration (defined as <5 vs. ≥5 years symptom duration) for patients with r-axSpA and nr-axSpA. *p<0.05; ***p<0.001 vs. PBO using an ANCOVA model including baseline SF-36 score, study (patients with r-axSpA), treatment, subgroup, and treatment-by-subgroup interaction. ANCOVA: analysis of covariance; IXE: ixekizumab; LSM: least squares mean; mBOCF: modified baseline observation carried forward; NA: not applicable as inferential testing was not performed if a subgroup was <10% of the total population; nr-axSpA: non-radiographic axial spondyloarthritis; NS: not significant; PBO: placebo; PCS: Physical Component Summary; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; SE: standard error; SF-36: 36-Item Short Form Health Survey.