Impact of sonelokimab, a novel IL-17A/F-inhibiting Nanobody, on clinical and imaging outcomes in axial spondyloarthritis: First results of a Phase 2 study supported by ^{18}F-NaF PET imaging and MRI

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Disclosures

BL reports no conflicts of interest.

UK has been paid as a speaker for AbbVie, Eli Lilly, Fresenius, Novartis, and UCB; has worked as a paid consultant for AbbVie, Amgen, Biogen, Chugai, Eli Lilly, Fresenius, Gilead, Grünenthal, GSK, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB; and has received financial grants from AbbVie, Amgen, Biogen, Chugai, Eli Lilly, Fresenius, Gilead, Grünenthal, GSK, Hexal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB.

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RAH is an employee of MoonLake Immunotherapeutics AG; has stock/stock options with MoonLake Immunotherapeutics AG; and was a management consultant for various pharmaceutical companies during his tenure at McKinsey & Company, Inc.

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Sonelokimab is not currently approved for any indication.
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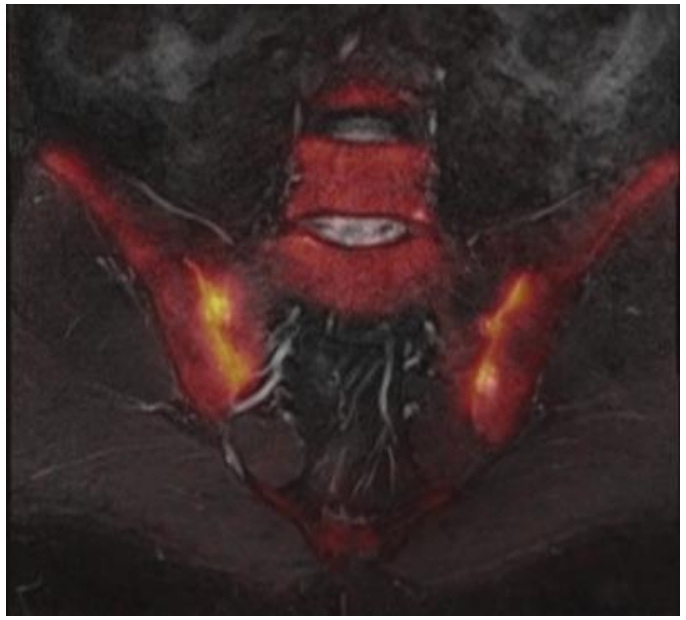
Axial spondyloarthritis (axSpA): Inflammation and new bone formation

- **Dual blockade of IL-17A and IL-17F**—two key inflammatory mediators—has been shown to be **effective in axSpA**[1]

- **Control of inflammation is critical** in axSpA due to potential **new bone formation** leading to **structural damage** and impaired physical function[2,3]

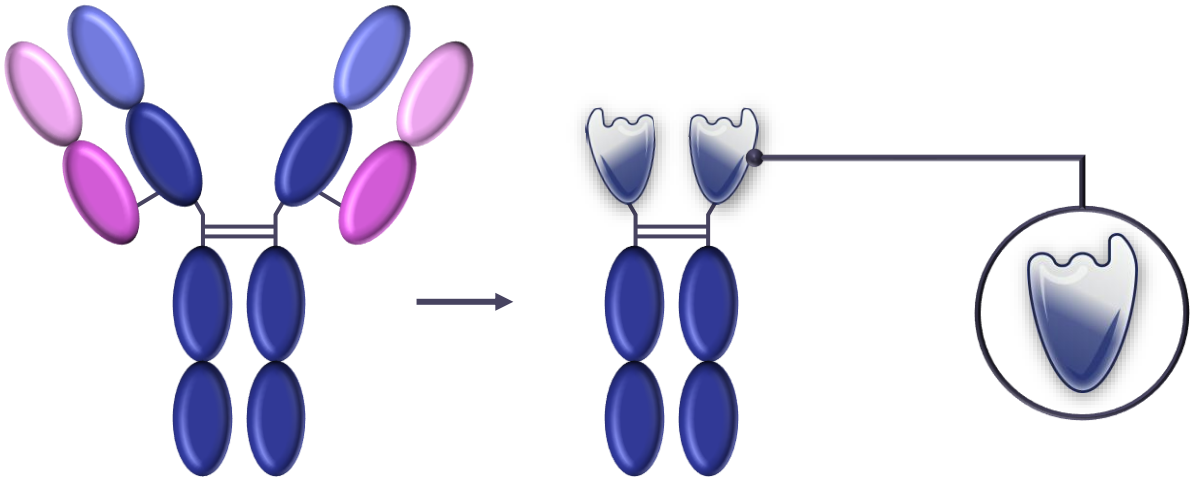


Sacroiliac joint (SIJ) spine fluorine-18 sodium fluoride (^{18}F-NaF) PET/MRI fusion image

^{18}F-NaF PET scans can detect sites of osteoblastic activity and accelerated bone turnover by tracking fluoride uptake into bone[4]

1. Van der Heijde D, *et al*. *Ann Rheum Dis.* 2023;82:515–526. 2. Van der Heijde D, *et al*. *Ann Rheum Dis*. 2017;76:978–991. 3. Baraliakos X, *et al. Ann Rheum Dis.* 2014;73:1819–1825.
4. Bruckmann NM, *et al*. *Arthritis Rheumatol.* 2022;74:1497–1505.

Sonelokimab is a novel IL-17A- and IL-17F-inhibiting Nanobody[1–3]

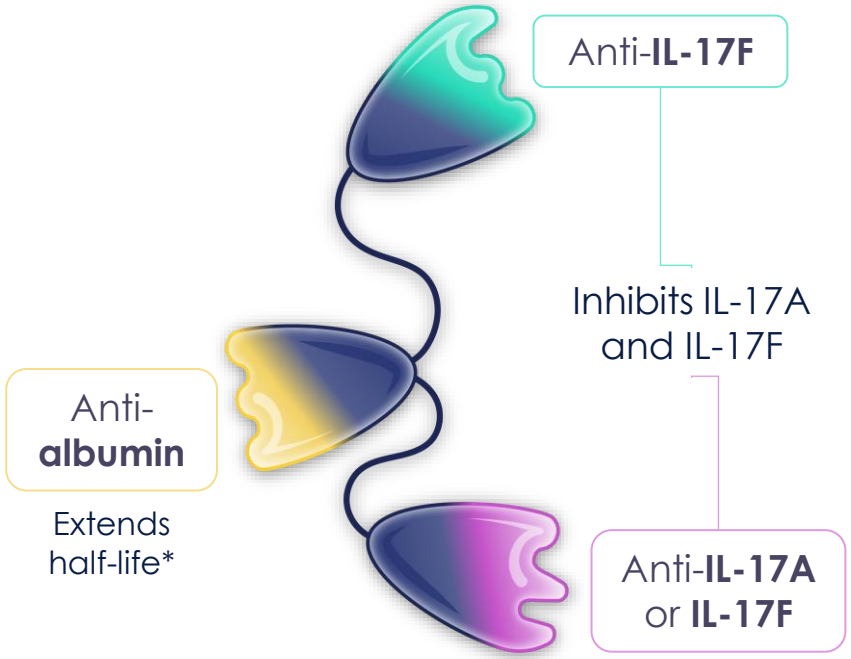


Conventional mAb (typical biologic)

Heavy-chain-only antibody (camelids)

Nanobody building block

- Small
- No Fc domain
- Humanized



A positive placebo-controlled Phase 2 trial has been completed in **psoriatic arthritis**, providing initial evidence of robust multidomain efficacy[2]

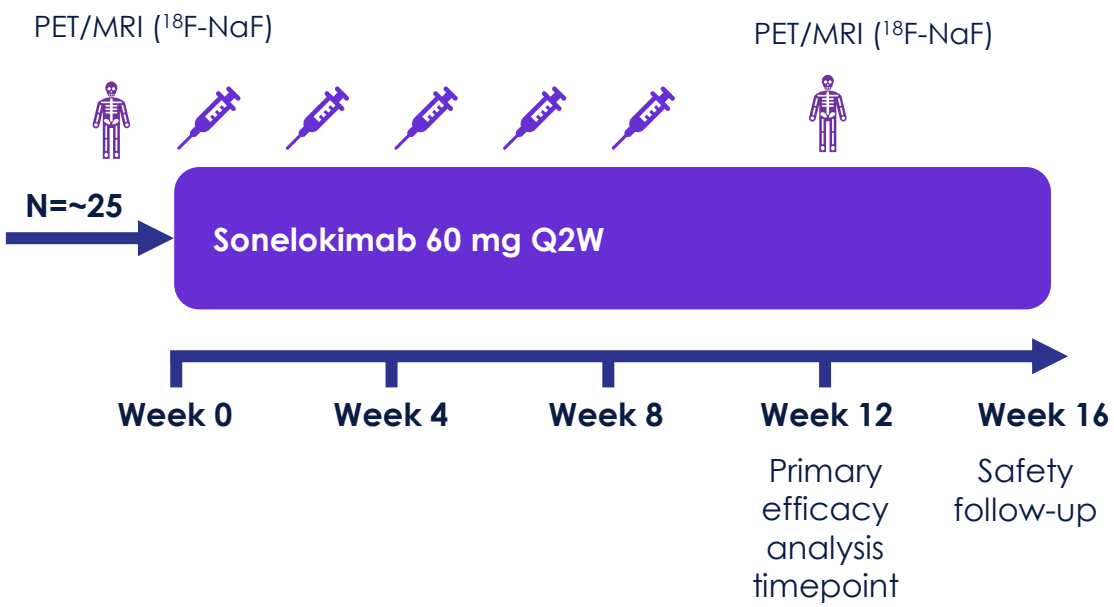
*Albumin binding extends the half-life to the range of larger mAb biologic therapies. Figure adapted from Ref. 2 under the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).

1. Papp KA, *et al*. *Lancet*. 2021;397:1564. 2. McInnes IB, *et al*. *Nat Med*. 2025;31:4160. 3. Jovčevska I, Muyldermans S. *BioDrugs*. 2020;34:11.

S-OLARIS: An innovative phase 2 open label study in active axSpA

Key eligibility criteria

- **≥18** years of age
- Diagnosis of axSpA and fulfilling the 2009 ASAS classification criteria
- BASDAI ≥4, despite treatment with NSAIDs
- Evidence of active disease on **MRI and ^{18}F-NaF PET**



Clinical endpoints included:

- ASAS20 and ASAS40
- ASDAS improvement
- BASDAI, BASFI, and BASMI
- Safety and tolerability

Imaging endpoints included:

- MRI of SIJ and spine (SPARCC)
- ^{18}F-NaF SUV_{max} (primary)

ASAS, Assessment of SpondyloArthritis International Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; SPARCC, Spondyloarthritis Research Consortium of Canada; SUV_{max}, maximum standardized uptake value.

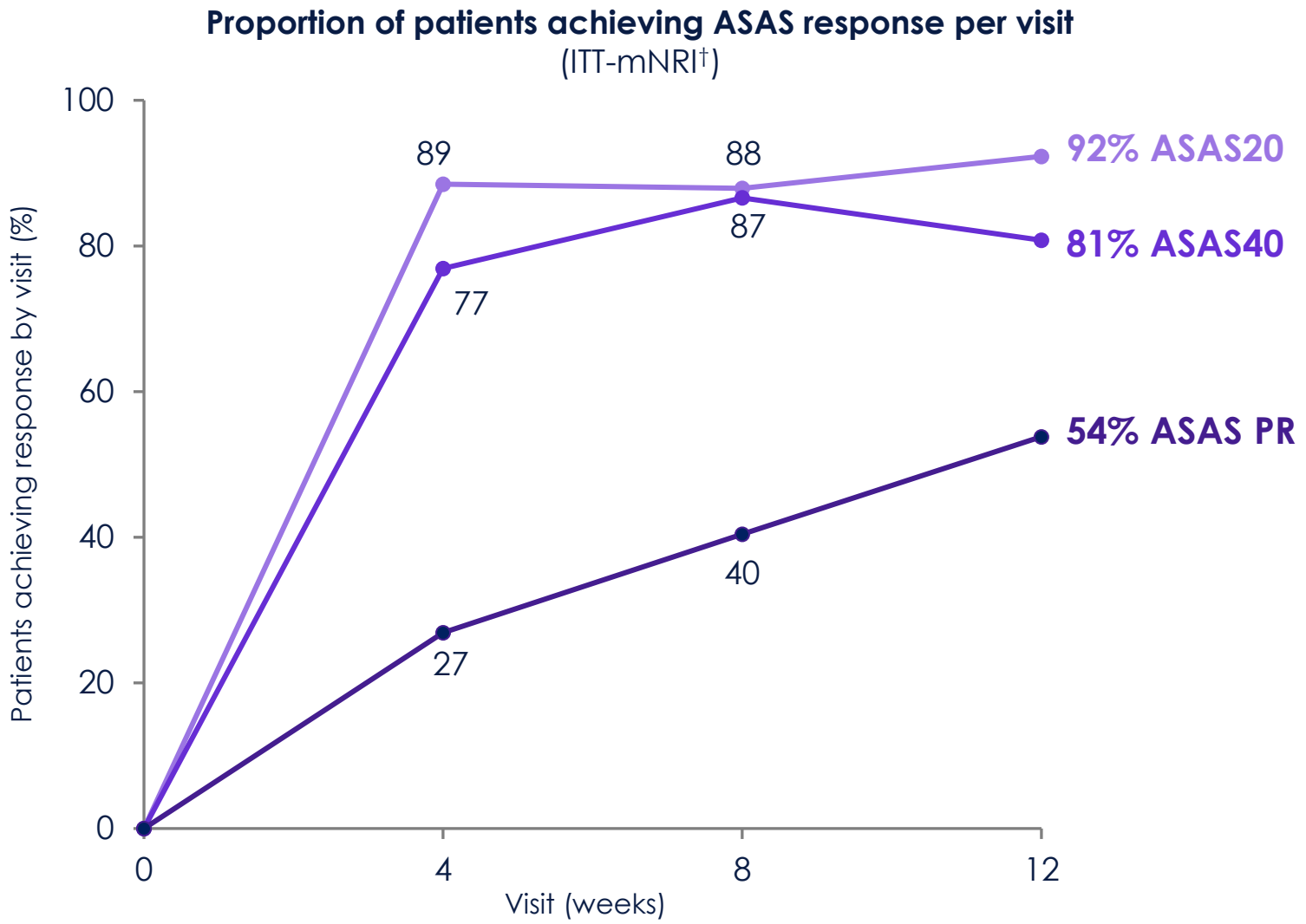
Baseline characteristics

Patient characteristics	Sonelokimab 60 mg (N=26)
Age, years	30.7 (9.5)
Male, n (%)	22 (85)
BMI, kg/m^2	27.0 (4.6)
r-axSpA, n (%)/nr-axSpA, n (%)	17 (65)/9 (35)
HLA-B27 positive, n (%)	19 (73)
Time since axSpA symptom onset, years	8.1 (8.0)
Prior bDMARD use, n (%)	2 (7.7)
Concomitant medications, n (%) NSAIDs/COX-2 inhibitors csDMARDs MTX	 18 (69) 1 (4) 1 (4)
BASDAI	6.4 (0.51)
ASDAS	3.5 (0.41)
hs-CRP, mg/L	6.0 (7.72)
BASFI	4.7 (1.96)
BASMI	1.2 (0.90)

- Clinical outcomes analyzed for n=26 patients; imaging for n=25 (MRI) and n=24 (PET)

Data are mean (SD) unless otherwise specified.

Sonelokimab treatment resulted in early ASAS responses



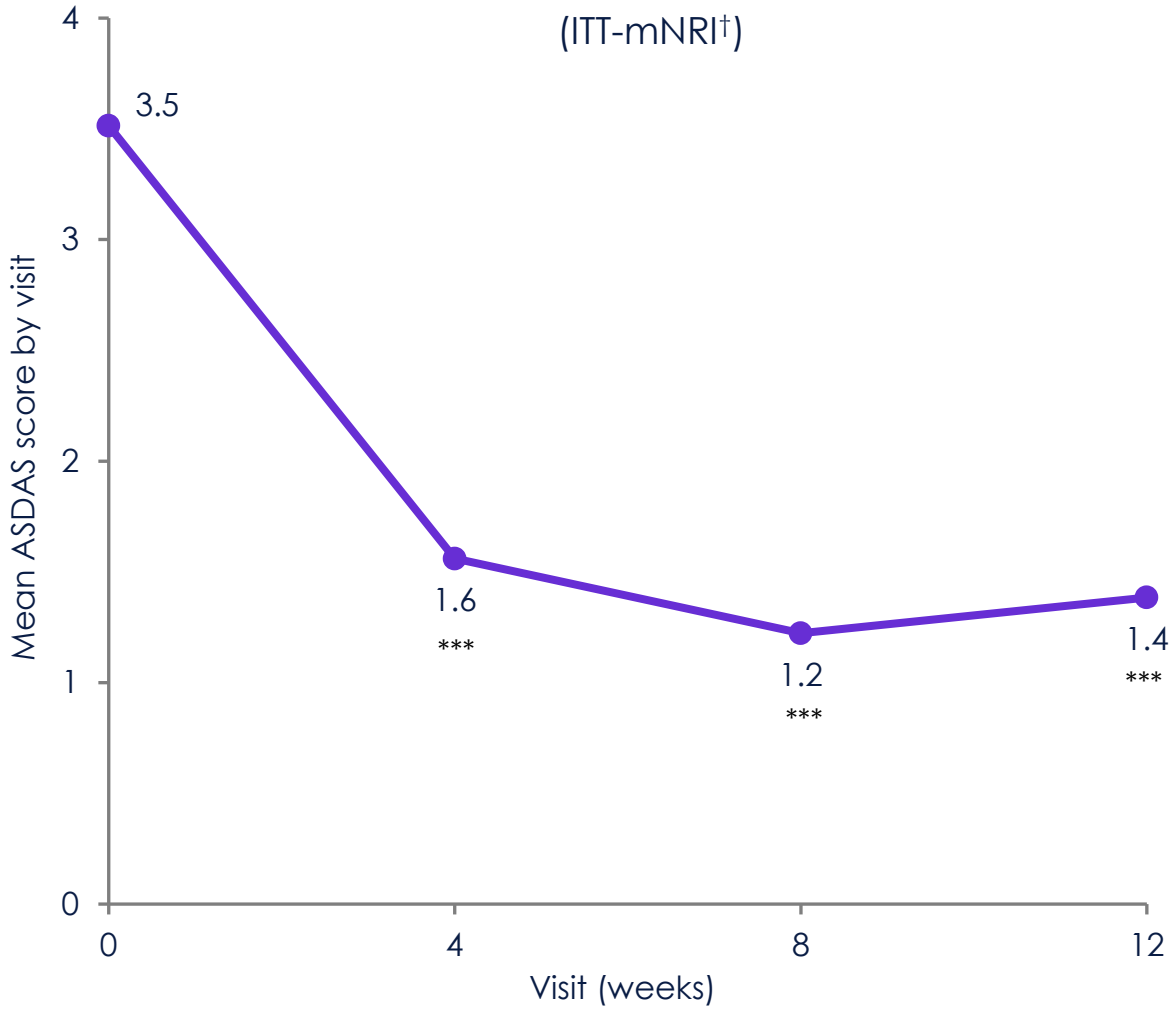
- **>80% of patients achieved ASAS40 and ASAS20** in this open-label study

- **More than half of patients** (n=14/26) **achieved ASAS partial remission** by Week 12

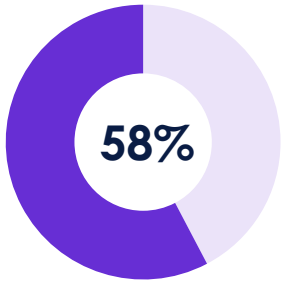
†Modified non-responder imputation (mNRI) analysis whereby patients discontinuing early or using certain prohibited medications were considered non-responders; other missing data were imputed using multiple imputation.

Treatment with sonelokimab resulted in rapid ASDAS improvements

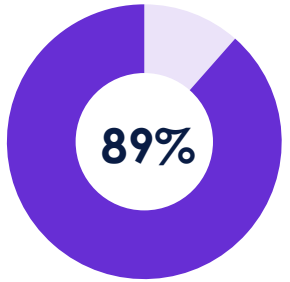
ASDAS score over time
(ITT-mNRI†)



Percentage of patients with ASDAS improvement at Week 12
(ITT-mNRI†)



Major improvement

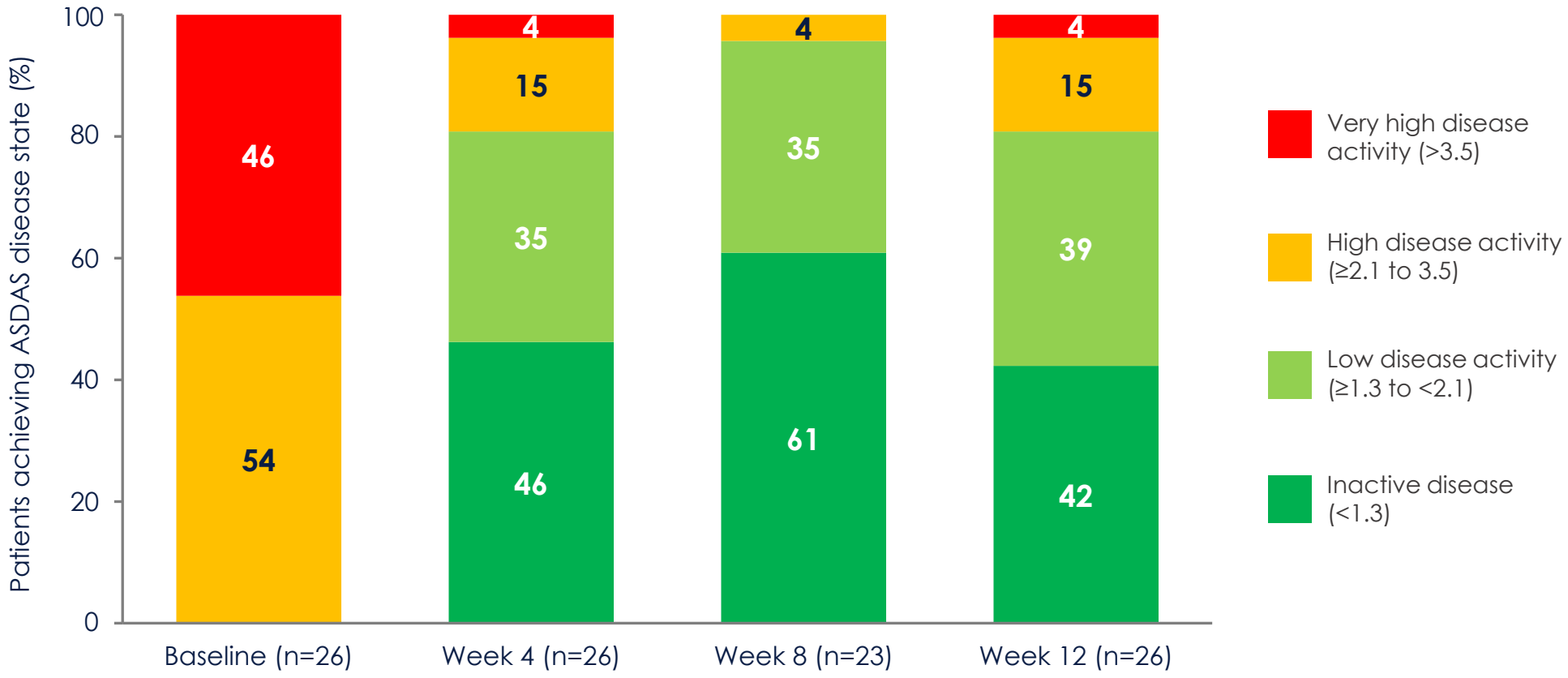


Clinically important improvement

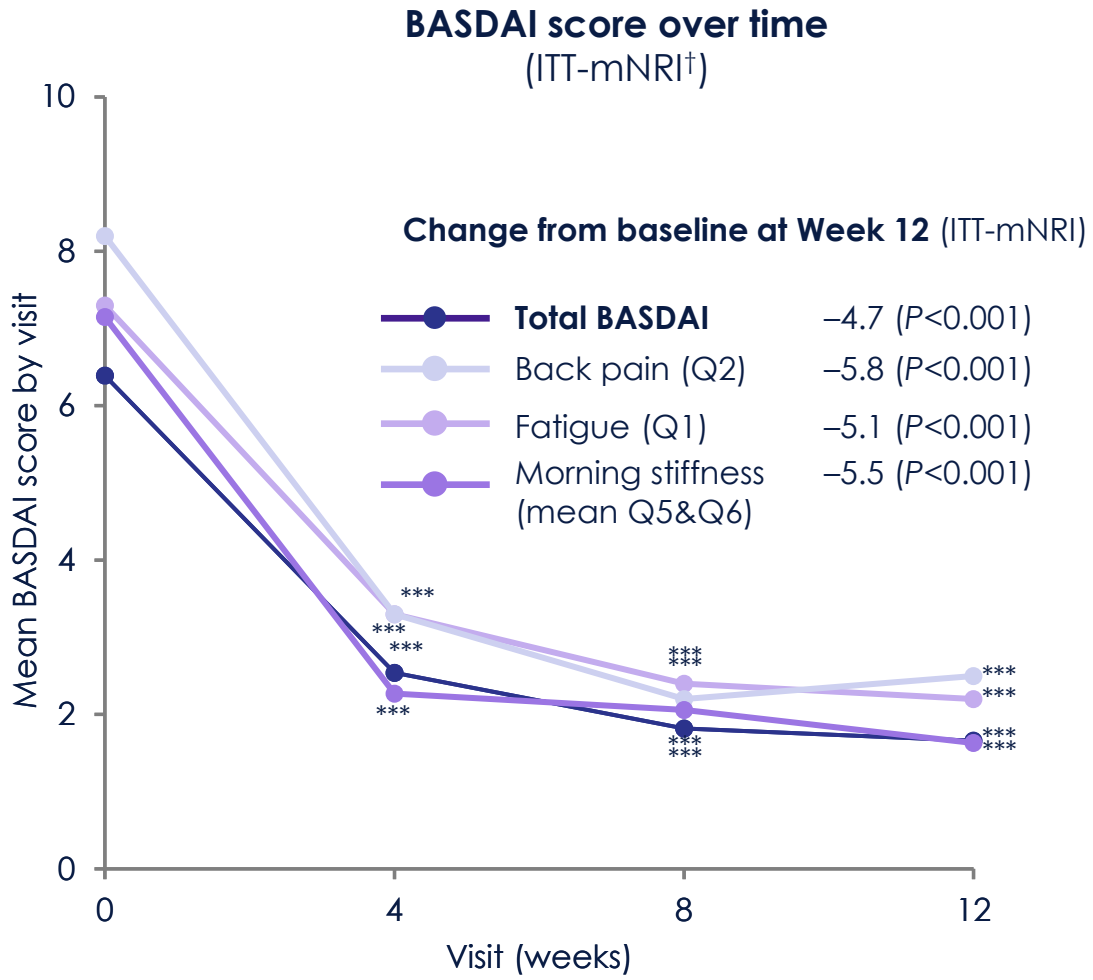
†mNRI analysis whereby patients discontinuing early or using certain prohibited medications were considered non-responders (baseline score carried forward); other missing data were imputed using multiple imputation.
Major improvements and clinically important improvement were defined as reduction of ≥2.0 units and ≥1.1 units, respectively.
***P<0.001 (all statistical analyses were exploratory and were not corrected for multiple testing).

Most patients achieved inactive/low disease activity as early as Week 4

Percentage of patients in each ASDAS disease activity state over time (as observed)



Patient-reported symptoms and function significantly improved



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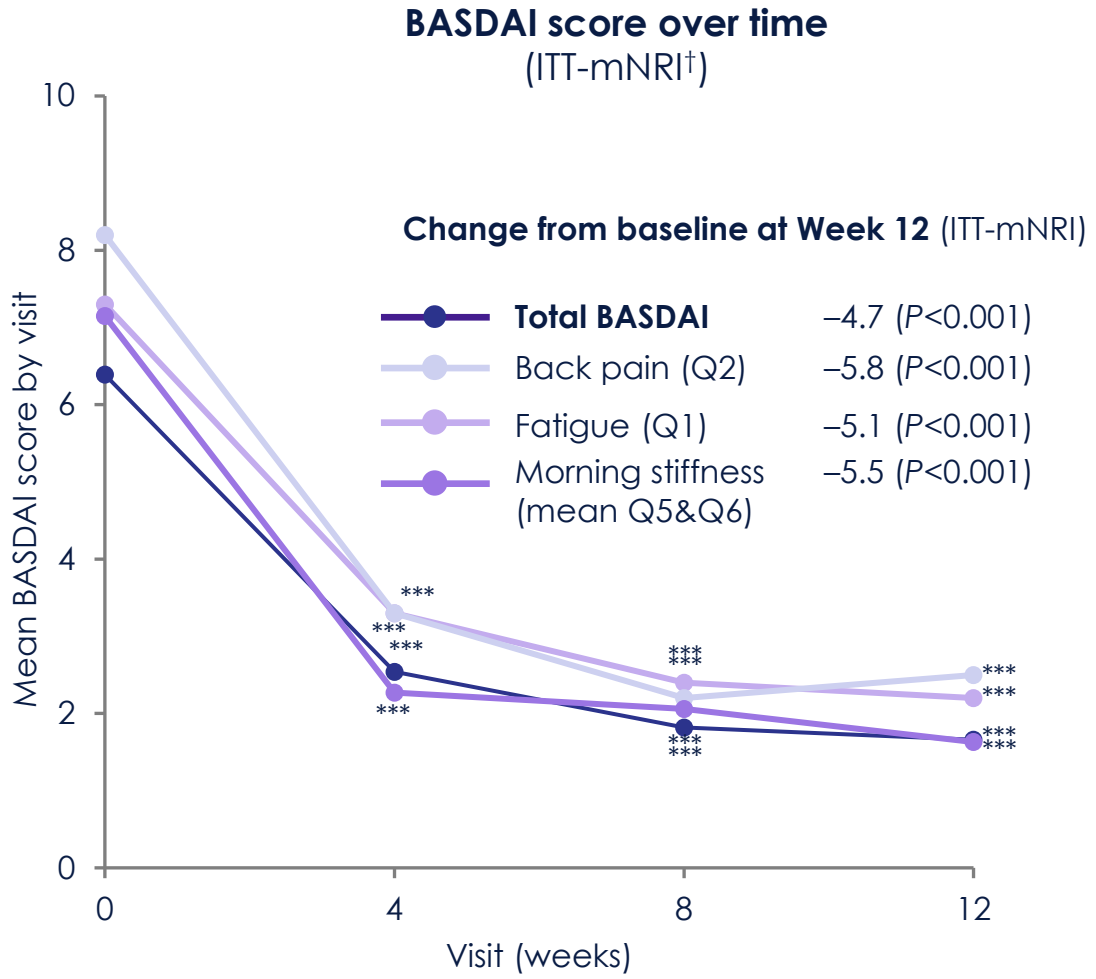
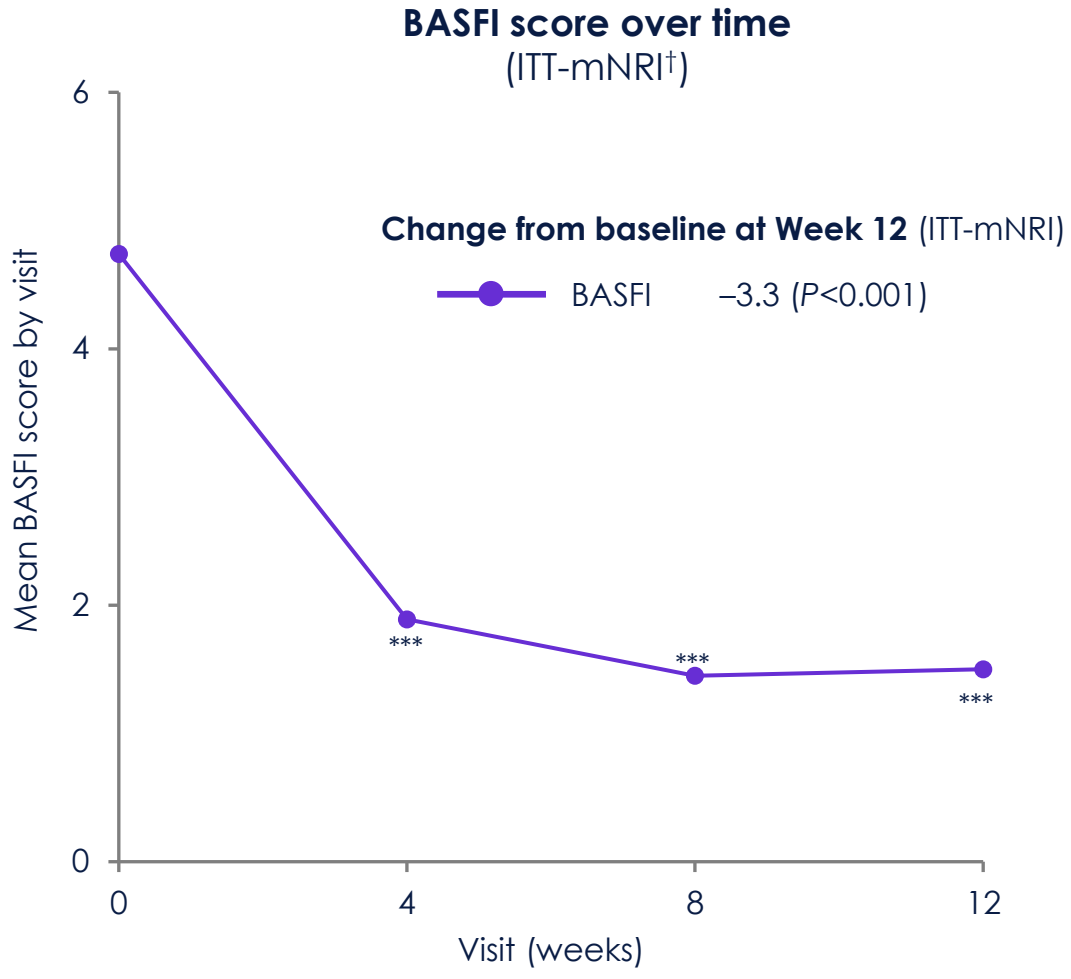


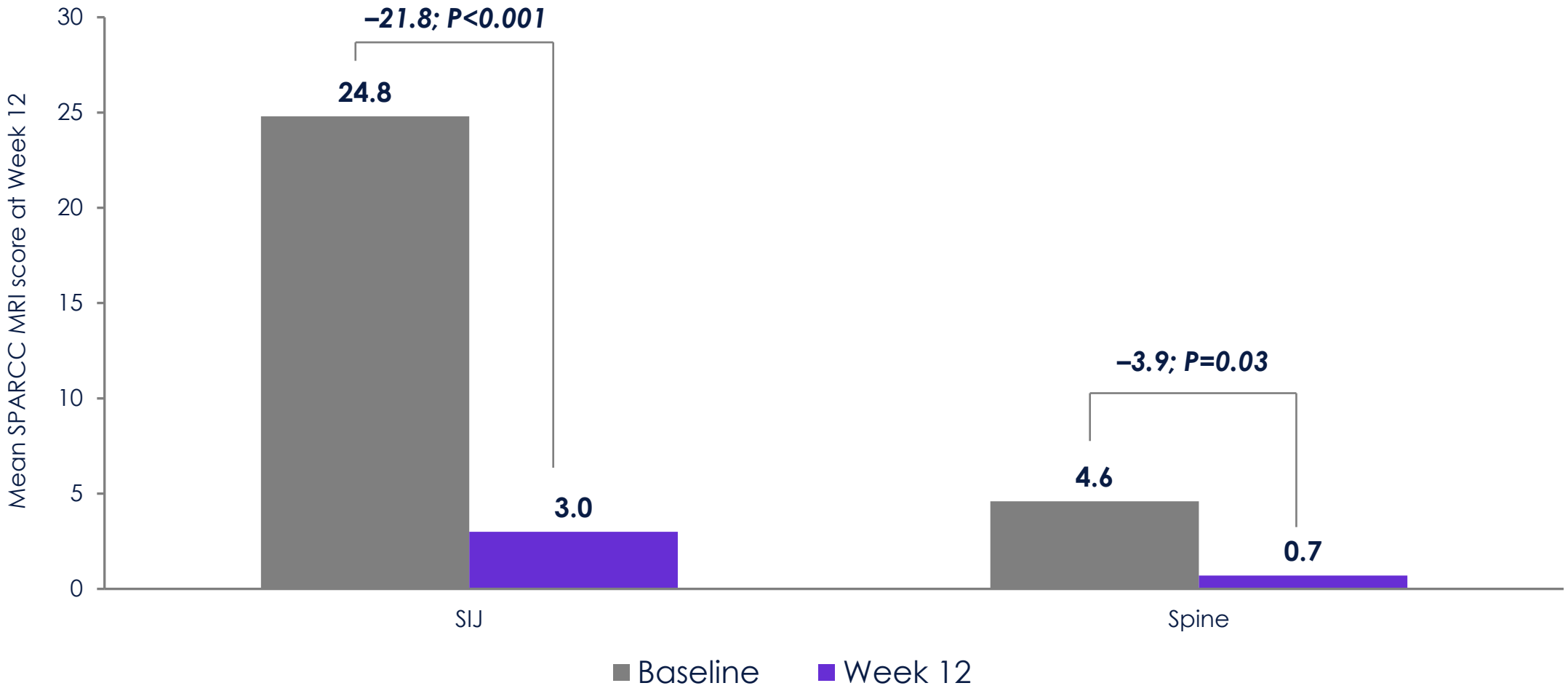


- Spinal mobility was relatively unimpaired at baseline (mean BASMI: 1.2) and remained stable at Week 12

†mNRI analysis whereby patients discontinuing early or using certain prohibited medications were considered non-responders (baseline score carried forward); other missing data were imputed using multiple imputation. ***$P<0.001$ (statistical analyses were exploratory and were not corrected for multiple testing).

By Week 12, sonelokimab significantly reduced inflammatory lesion burden

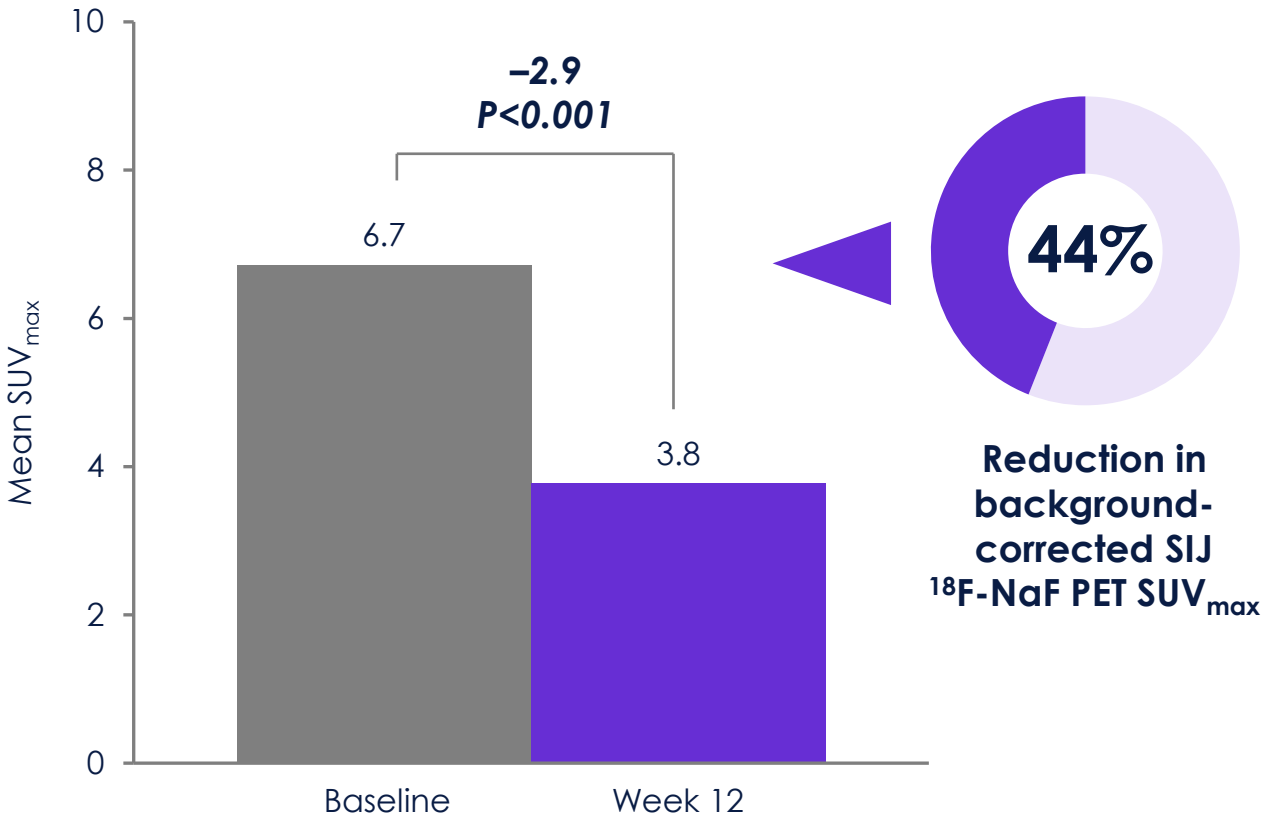
SPARCC MRI score in the SIJ and spine (n=25; as observed†)



†Data analyzed for all 25 patients with baseline and post-baseline MRI scans available. Statistical analyses were exploratory and were not corrected for multiple testing.

Sonelokimab significantly reduced ^{18}F-NaF uptake in the SIJ over 12 weeks

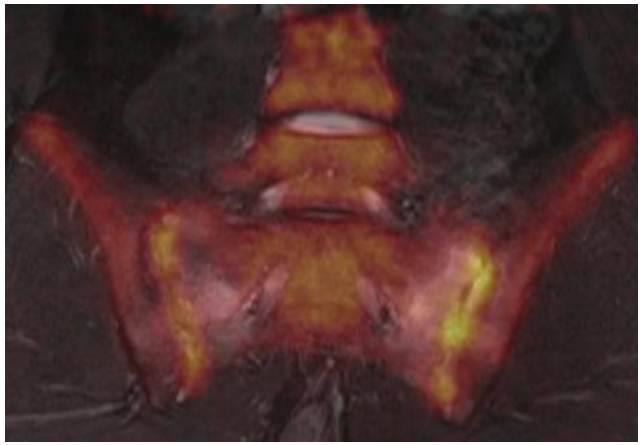
Participant-level adjusted mean ^{18}F-NaF SUV_{max}
(n=24; as observed†)



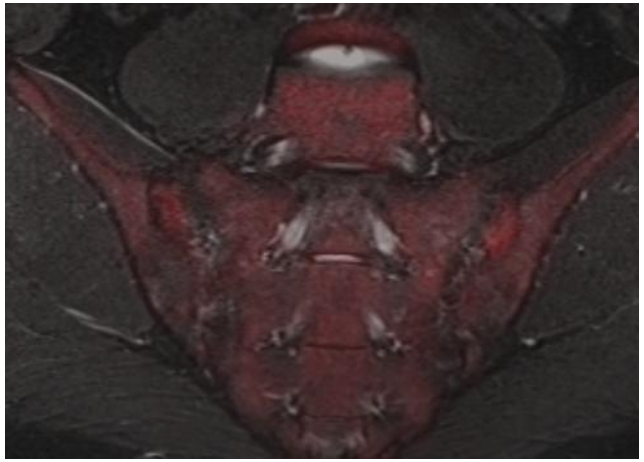
Reduction in background-corrected SIJ ^{18}F-NaF PET SUV_{max}

Example ^{18}F-NaF PET/MRI scan images

Baseline

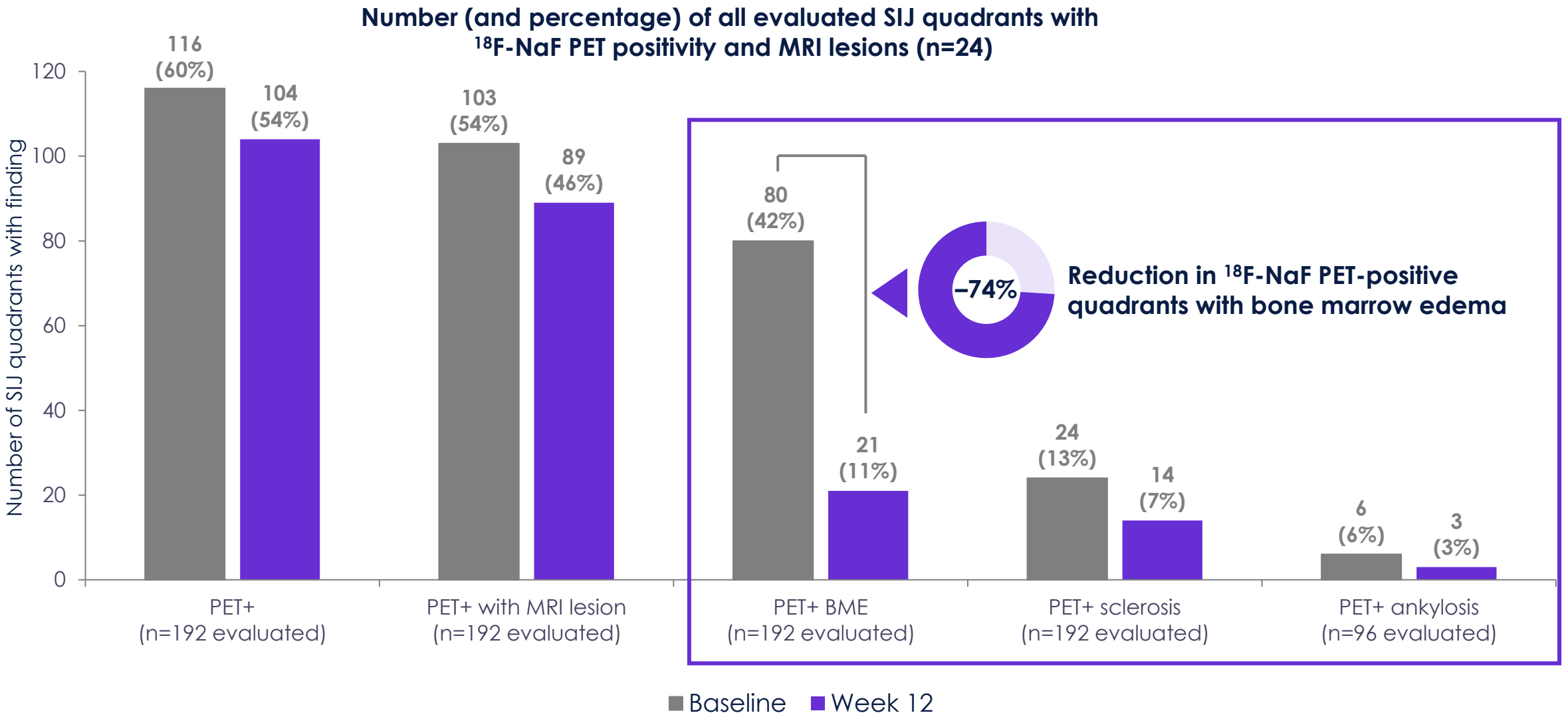


Week 12



Overall mean SUV_{max} was calculated from the mean SUV_{max} across all active SIJ quadrants within each participant, with adjustment to correct for background non-pathological uptake in reference tissue (*os ilium*).
†Data analyzed for all 24 patients with baseline and post-baseline MRI scans available. Statistical analyses were exploratory and were not corrected for multiple testing.

^{18}F-NaF PET+ and MRI lesion burden was reduced across SIJ quadrants



Denominator for percentages is the total number of SIJ quadrants evaluated across n=24 patients (eight quadrants evaluated per patient for BME, sclerosis, and erosions; four quadrants evaluated per patient for ankylosis). BME, bone marrow edema.

Sonelokimab was well tolerated, with no new safety signals

Patients with events, n (%)	**Sonelokimab 60 mg** N=26
Any TEAE	14 (53.8)
Any treatment-related TEAE	4 (15.4)
Any serious TEAE	1 (3.8)
Any TEAE leading to treatment discontinuation	1 (3.8)
Most frequent TEAEs	
Influenza	3 (11.5)
Fatigue	2 (7.7)
Blood creatine phosphokinase increased	2 (7.7)
Other TEAEs of interest	
Oral candidiasis	1 (3.8)
Dermatitis and eczema	0
Serious infections	0
Hepatic events	0
Diarrhea (non-infectious)	0
IBD	0
MACE	0
SIB	0

- **All adverse events were mild or moderate, and few were treatment related**
- **No adverse events of IBD, MACE, SIB, liver injury, or uveitis** were reported

IBD, inflammatory bowel disease; MACE, major adverse cardiovascular event; SIB, suicidal ideation and behavior; TEAE, treatment-emergent adverse event.

Conclusions

- Sonelokimab treatment resulted in **rapid achievement of clinical responses** in this Phase 2 open-label study in axSpA
- **Substantial reductions** in objective imaging-based assessments of **inflammation and pathological osteoblastic activity were observed in the SIJ after only 12 weeks**
    - The inhibition of bone remodeling activity observed suggests **rapid disease-modifying effects within joints** are possible with the Nanobody sonelokimab
- **Sonelokimab was well tolerated**, with no new signals
- Overall, these data provide an **encouraging proof of concept for the potential of sonelokimab in axSpA**

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