Axial Spondyloarthritis: Disease State

Module 1 | **Defining and diagnosing axSpA**

Module 2 | **Pathogenesis, clinical presentation, and disease burden**

Module 3 | **axSpA Disease Assessments**

Module 4 | **axSpA Disease Management**

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- Prescribing information for all products mentioned, can be found at the end of the presentation.

HCP=Healthcare Professional.

Module 4

Management of axSpA

axSpA=Axial Spondyloarthritis.

Learning Objectives

- Describe treatment goals in axSpA.
- Describe advanced treatments available for AS/axSpA and nr-axSpA.
- Explain expert recommendations for managing axSpA.
- Describe consequences of delayed diagnosis in axSpA.
- Describe evidence on the benefits of early treatment in axSpA.

AS=Ankylosing Spondylitis; axSpA=Axial Spondyloarthritis; nr-axSpA=Nonradiographic Axial Spondyloarthritis.

Case Study: Introducing Charlene

Patient Case Study: Charlene

CHARLENE

AGE
46

SEX
Female

OCCUPATION
Consultant

9th provider she has seen regarding symptoms

- Pediatrician
- Physical therapist (x3)
- Chiropractor (x2)
- Internist
- Orthopedist

“It’s been 30 years, and I’m tired of the shooting pain in my buttocks.”

MEDICAL HISTORY

- Has experienced periodic flares of pain in her spine and buttocks that has been worsening since she was a teenager.
- Father had the same symptoms with no official diagnosis.
- Many misdiagnoses including a herniated disk, bone spurs, dysfunctional sacroiliac joints, and spinal misalignment.

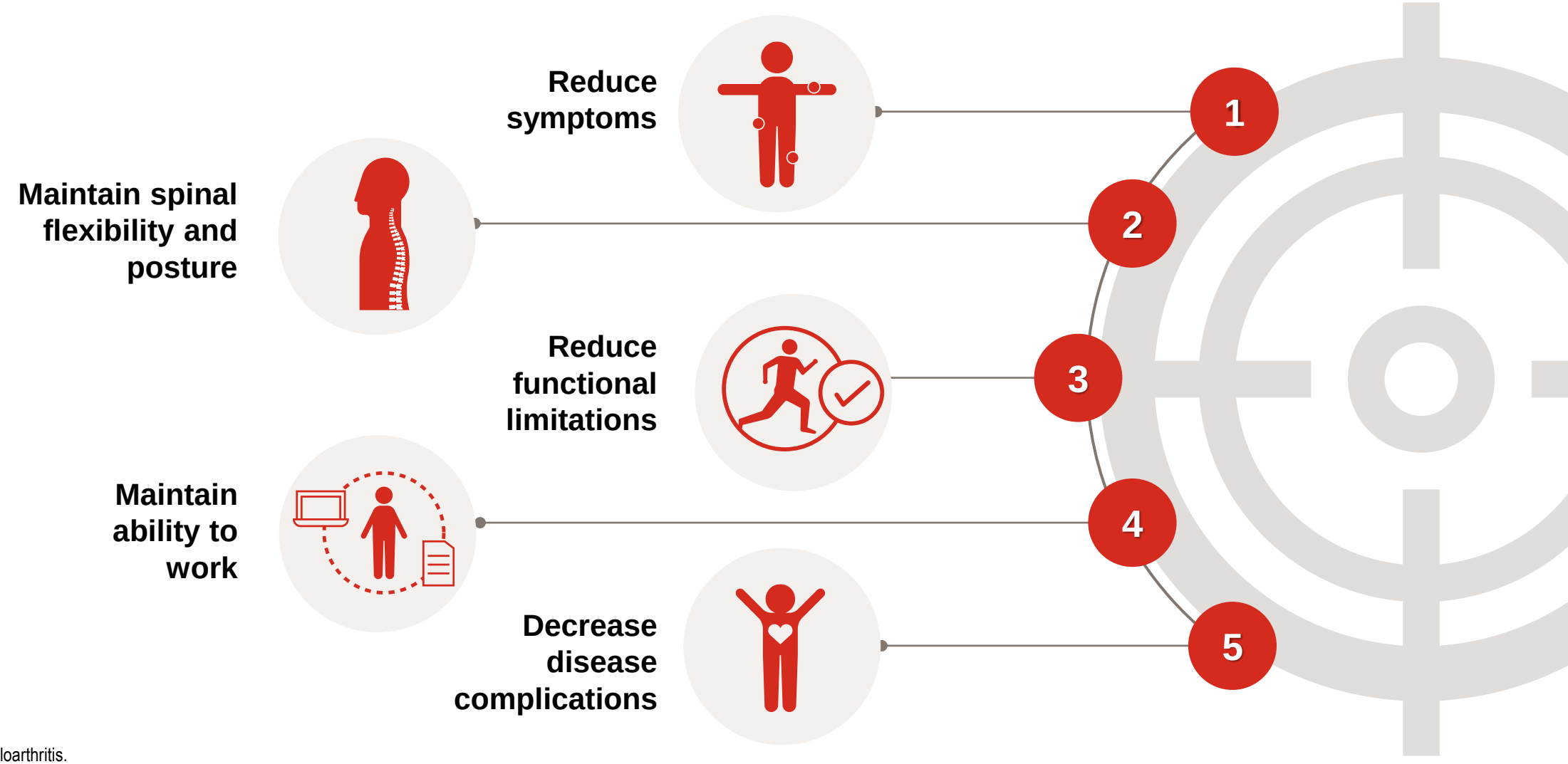
SYMPTOMS AND CLINICAL PRESENTATION

- Severe back pain with insidious onset that is worse in the mornings, improves on movement and is OTC NSAID refractory.

Serology: HLA-B27 negative.

Note: This case is based on a real patient, some elements have been fictionalized or exaggerated for teaching purposes.
HLA-B27=Human Leukocyte Antigen B27; NSAID=Nonsteroidal Anti-inflammatory Drug; OTC=Over The Counter.
www.washingtonpost.com/health/medical-mysteries/back-pain-sacroiliac-medical-mystery/2021/11/12/d864a2b0-239f-11ec-8200-5e3fd4c49f5e_story.html (Accessed April 11, 2023).

Treatment Goals in axSpA



axSpA=Axial Spondyloarthritis.

Ward MM, et al. *Arthritis Rheumatol*. 2016;68:282-298.

Current FDA-approved Treatment Options in axSpA

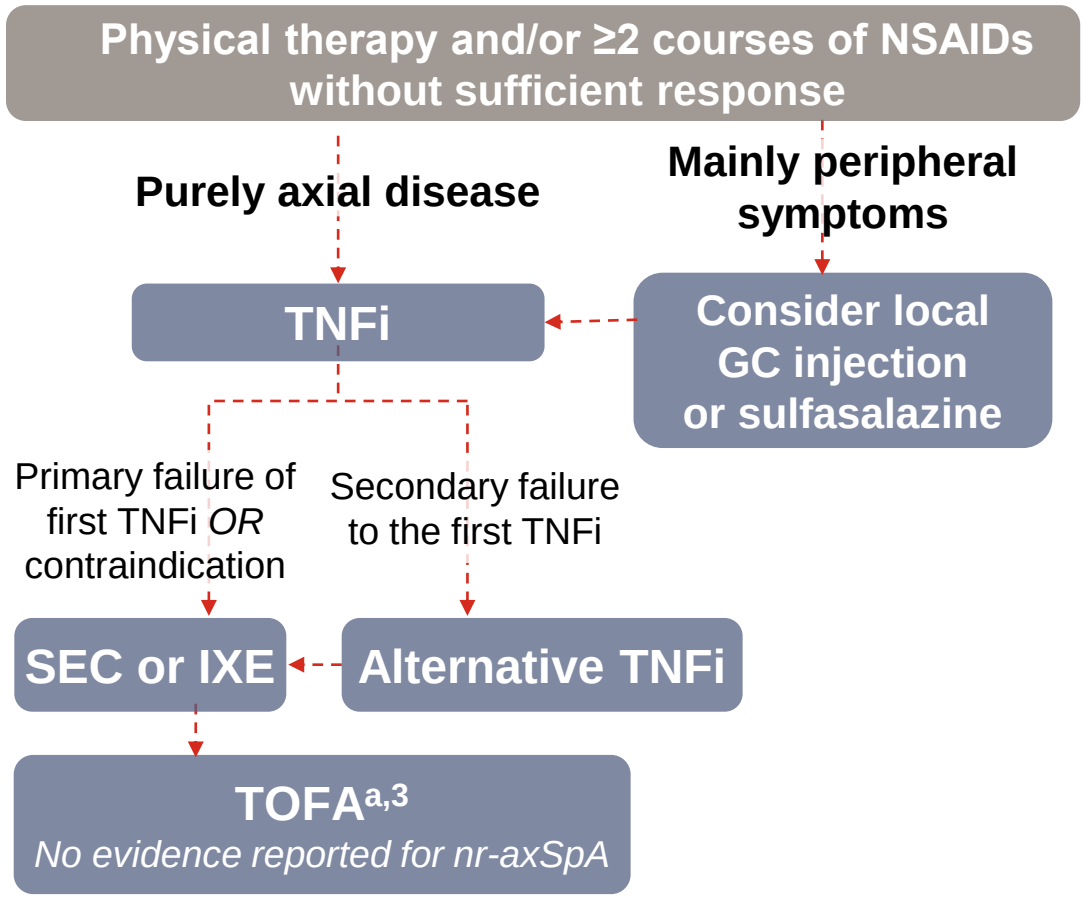
	TNF inhibitors	IL-17A antagonists	JAK inhibitors
AS/r-axSpA	Etanercept[1,2] Infliximab[1,3] Adalimumab[1,4] Certolizumab pegol[1,5] Golimumab SC[1,6] Golimumab IV[7]	Secukinumab SC, IV[8] Ixekizumab[9]	Upadacitinib[10] Tofacitinib[11]
nr-axSpA	Certolizumab pegol[1,5]	Secukinumab SC, IV[8] Ixekizumab[9]	Upadacitinib[10]

AS=Ankylosing Spondylitis; FDA=Food and Drug Administration; IL=Interleukin; JAK=Janus Kinase; nr-axSpA=Nonradiographic Axial Spondyloarthritis; r-axSpA=Radiographic Axial Spondyloarthritis; TNF=Tumor Necrosis Factor.

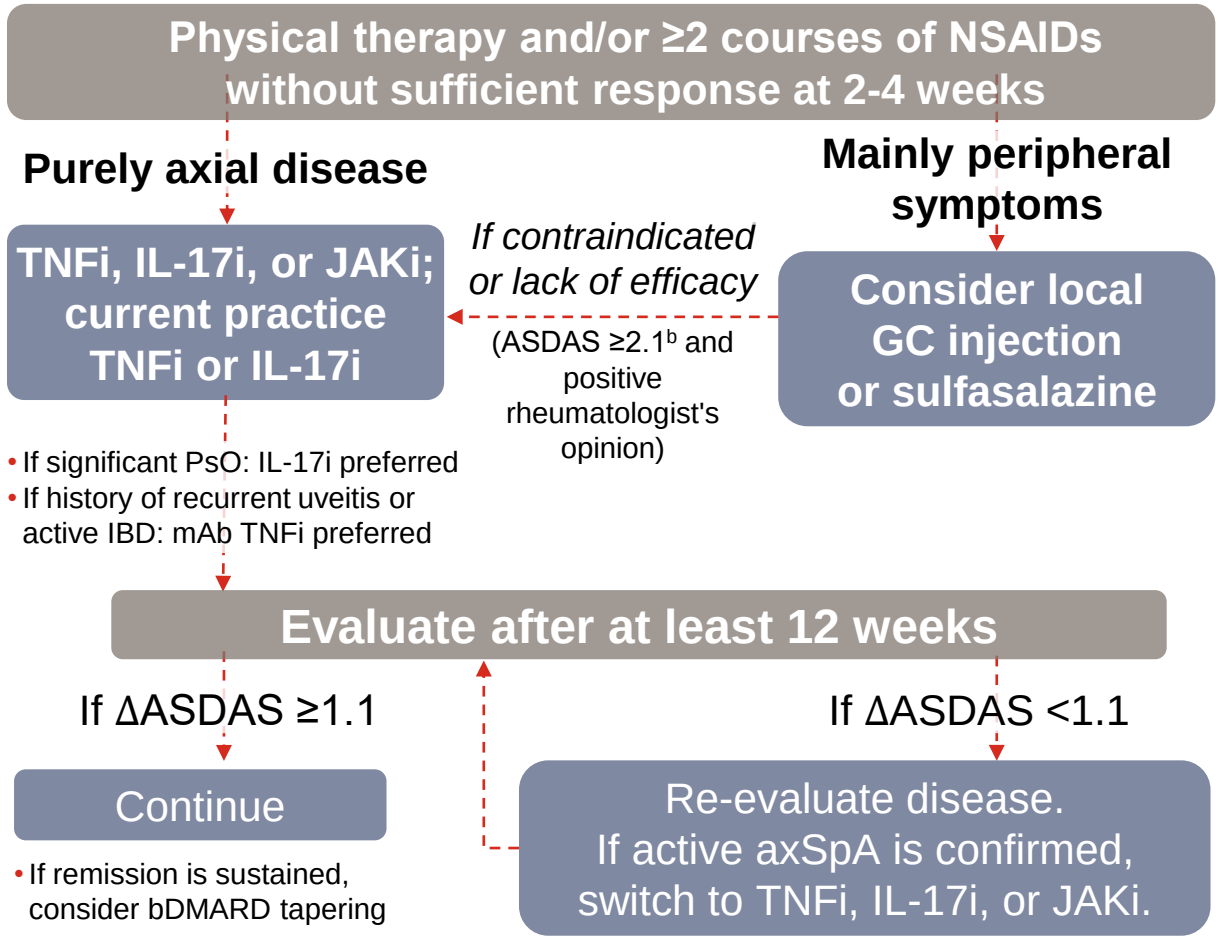
Note: For references, please see the Speaker Notes.

Management of axSpA: Current Recommendations

ACR/SAA/SPARTAN 2019[1,2]



ASAS/EULAR 2022[4]

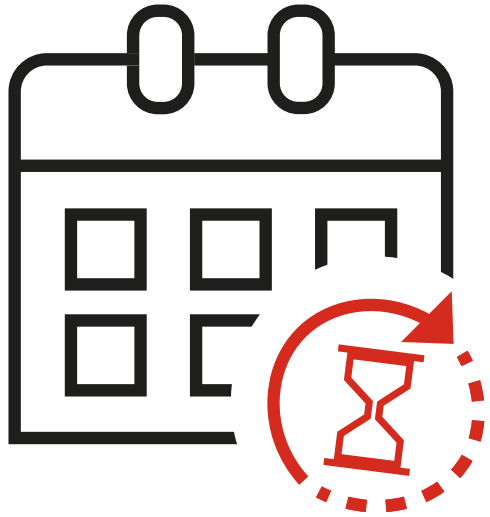


[a]TOFA is not approved for the treatment of nr-axSpA in the USA.[3] [b]High disease activity should be based on the ASDAS ≥2.1 criterion; if it is not possible to follow this recommendation, the BASDAI criterion (≥4) can be used as an alternative.[4]
Note: For abbreviations, please see the speaker notes.

1. Ward MM, et al. *Arthritis Care Res (Hoboken).* 2019;71(10):1285-1299. 2. Ward MM, et al. *Arthritis Rheumatol.* 2019;71(10):1599-1613. 3. https://labeling.pfizer.com/ShowLabeling.aspx?id=959 (Accessed October 2023).
4. Ramiro S, et al. *Ann Rheum Dis.* 2023;82(1):19-34.

Targeting Early vs. Late Disease: Review of Evidence

Delays in Diagnosis Add to the High Disease Burden

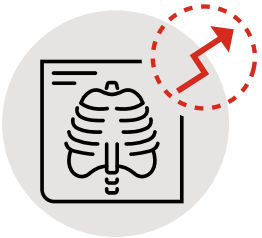


Average time from the onset of symptoms to a diagnosis of axSpA

6.5-10 years[1-3]

A delayed diagnosis of axSpA is associated with:[1,2,4]

Worse physical function



Increased structural damage

Reduced response to treatment

Poorer quality of life

Patients with axSpA have a high prevalence of **osteoporosis** and **fractures.**[5,6]

Estimated prevalence rates after 10 years of axSpA[6]

Osteoporosis	**25%**
Osteopenia	**40%**
Vertebral fractures	**10%**

Osteoporosis **increases the risk of fractures**, meaning diagnosis in the **early stages** of disease is **vital.**[5]

axSpA=Axial Spondyloarthritis.

1. Lapane KL, et al. *BMC Fam Pract*. 2021;22(1):251. 2. Zhao SS, et al. *Rheumatology (Oxford)*. 2021;60(4):1620-1628. 3. Carvalho PD and Machado PM. *Best Pract Res Clin Rheumatol*. 2019;33(4):101427.
4. Yi E, et al. *Rheumatol Ther*. 2020;7(1):65-87. 5. Lim J, Kang KY. *Front Med (Lausanne)*. 2020;7:569449. 6. Winkler AE, Miller M. *Mo Med*. 2022;119(1):79-83.

Effective Treatment Can Improve the Lives of People With axSpA

Several studies showed **improved work attendance**, **productivity**, and **physical function** following effective management of axSpA with bDMARDs.[2,3]

Most important treatment goals reported by patients:[1]

1. **Control of pain**
2. **Reduction of fatigue**
3. **Maintenance of social and physical functions**

Pain reduction often produces notable improvement in QoL.[1]

vs. PBO, TNFi treatment resulted in…

1.0 additional day of paid work and **2.6 fewer days with reduced productivity** /month (PBO: 0.4 and 0.9 days, respectively).[a,3]

An **additional 13.8%** of patients maintaining **full attendance** at work /month (PBO: 4.1%).[a,3]

Significant improvement in spinal mobility:

vs. PBO, improvements in **back pain** and **physical function** were sustained over 5 years of treatment with a TNFi.[4]

axSpA=Axial Spondyloarthritis; bDMARD=Biologic Disease-modifying Anti-rheumatic Drug; PBO=Placebo; QoL=Quality of Life; TNFi=Tumor Necrosis Factor Inhibitor.

[a]In RAPID-axSpA, improvements in workplace productivity in Certolizumab Pegol-treated patients (n=218) were reported from Week 4 and maintained through the 24-week PBO-controlled period.[2] [b]$BASMI_{lin}$ is a composite measure of back pain based on five clinical measurements (cervical rotation, anterior lumbar flexion, lumbar side flexion, intermalleolar distance and tragus-to-wall distance) and scored 0-10, with higher scores indicating worse spinal mobility.[4]

1. Garrido-Cumbrera M, et al. *Rheumatol Ther*. 2017;4(2):219-231. 2. van der Heijde D, et al. *Arthritis Rheum*. 2006;55(4):569-574. 3. van der Heijde D, et al. *RMD Open*. 2018;4(1):e000659.
4. van der Heijde D, et al. *Rheumatology (Oxford)*. 2015;54(7):1210-9.

Golimumab Induces a Higher Response Rate in Patients With Early axSpA

Results From a Post-hoc Analysis of the GO-ALIVE Study (1 of 2)

GO-ALIVE was a Phase 3, double-blind, PBO-controlled trial. This analysis compared the efficacy and safety of GOL in AS patients with early vs. late disease, based on self-reported AS (IBP) symptom duration.

	Early (n=60)	Late (n=52)
Median symptom duration (years)	2-3	21-24
Median time to diagnosis (years)	0.8-1.3	6.8-13

Efficacy at Week 52	Early	Late
ASDAS major improvement (≥2)	51%	vs. 30%
ASDAS inactive disease (<1.3)	37%	vs. 4%

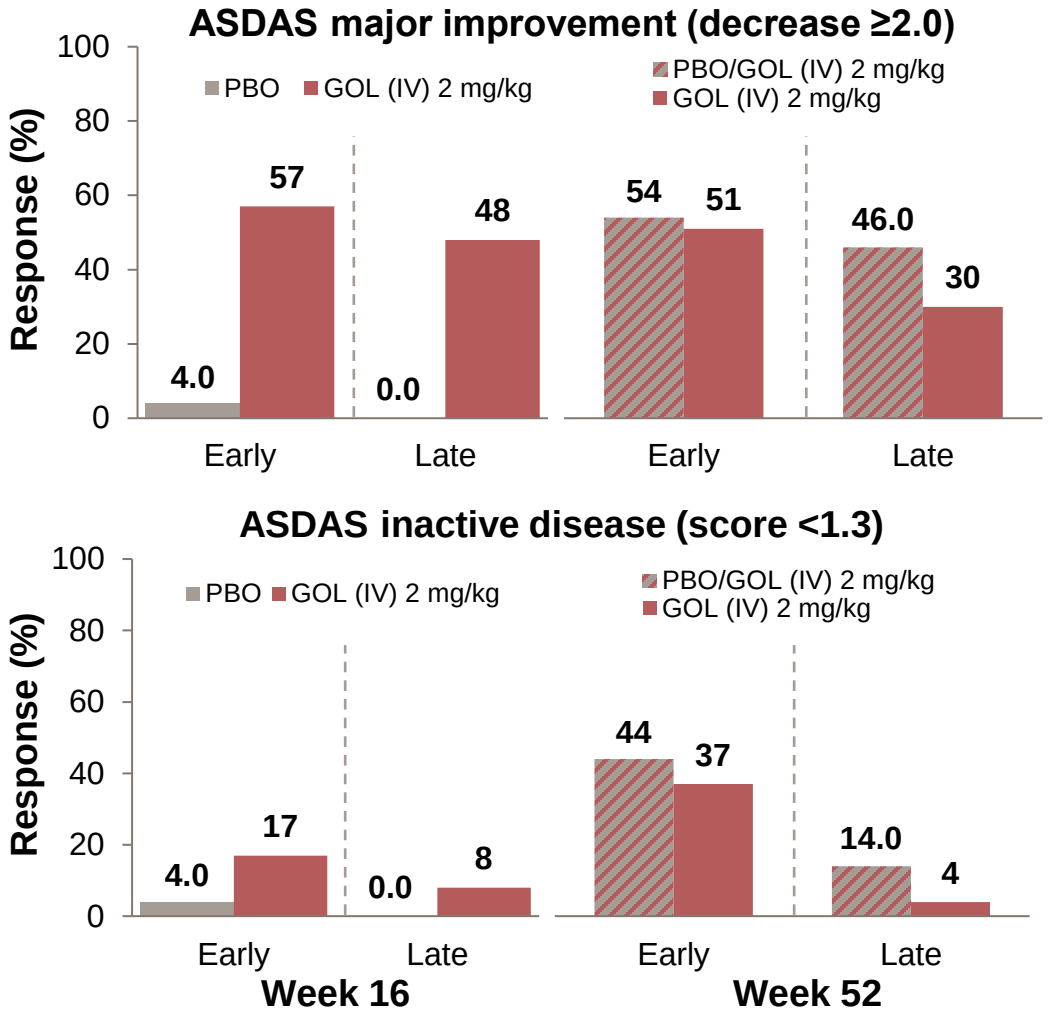
- Through Week 16, a higher proportion of both PBO- and GOL-treated patients reported ≥1 AE in those with late disease vs. early.
- Common AEs (reported in ≥3 patients) were headache, nasopharyngitis, and URT infections.
- Few patients experienced a SAE or discontinued due to an AE.
- The study concluded that GOL had a favorable safety profile, consistent with recent findings.

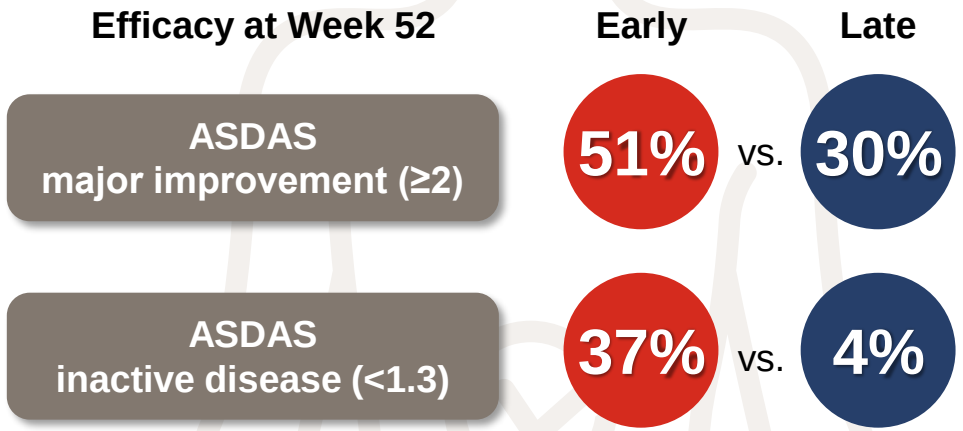
AE=Adverse Event; AS=Ankylosing Spondylitis; axSpA=Axial Spondyloarthritis; ASDAS=Ankylosing Spondylitis Disease Severity Index; GOL=Golimumab; IBP=Inflammatory Back Pain; IV=Intravenous; PBO=Placebo; SAE=Serious Adverse Event; URT=Upper Respiratory Tract.

Deodhar AA, et al. *J Clin Rheumatol.* 2022;28(5):270-277.

Golimumab Induces a Higher Response Rate in Patients With Early axSpA

Results From a Post-hoc Analysis of the GO-ALIVE Study (2 of 2)





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Deodhar AA, et al. *J Clin Rheumatol.* 2022;28(5):270-277.

Treatment With Secukinumab SC is More Effective in Patients With Shorter Disease Durations

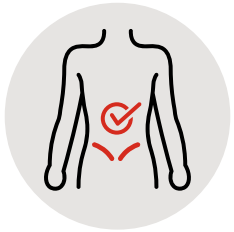
Results From the MEASURE 1-4 Trials in AS (1 of 2)

Post-hoc analysis assessing the impact of age and time since diagnosis[a] on response to SEC (N=852) at 16 weeks

A higher proportion of patients with **shorter disease duration (<3.47 years)** achieved ASAS40.

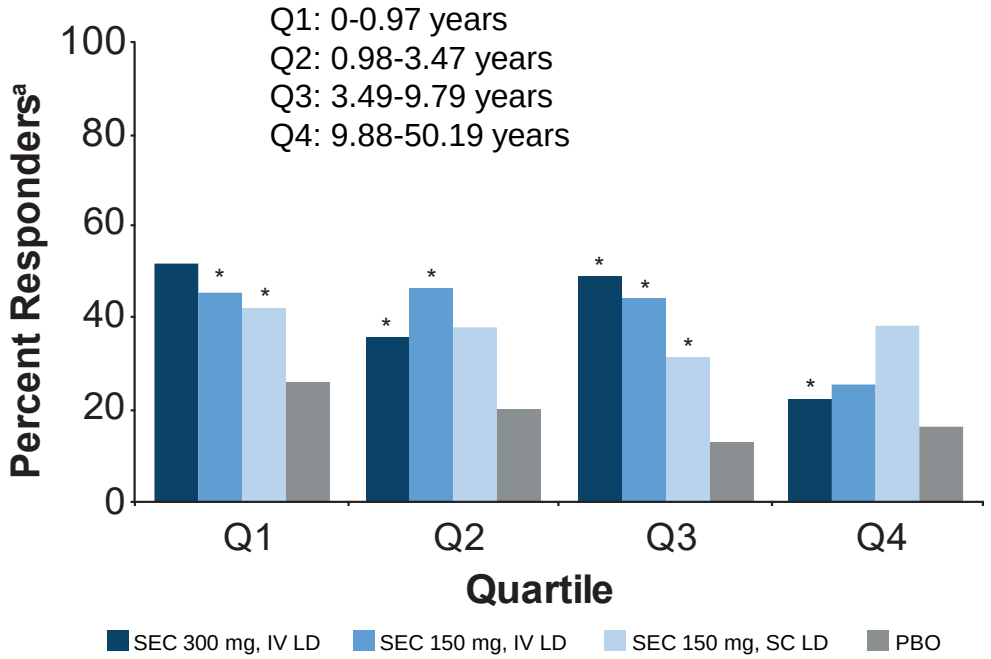
There was also **a trend toward higher responses on BASDAI and PtGA assessments** in those with shorter disease duration.[1]

Reductions in hsCRP were greatest in patients with the shortest disease duration.



A **greater treatment response** was also shown in **younger patients (aged 18-33** vs. 34-42 years).

ASAS40 Response Through Week 16 by Symptom Duration Quartiles, NRI



vs. PBO: *p<.05.

[a]Time since diagnosis was used as a surrogate marker of disease duration as symptom duration was not collected.

AS=Ankylosing Spondylitis; ASAS40=Assessment of Spondyloarthritis International Society 40% Improvement; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; hsCRP=High-Sensitivity C-reactive Protein; IV=Intravenous; LD=Loading Dose; NRI=Nonresponder Imputation; PBO=Placebo; PtGA=Patients Global Assessment of Disease Activity; Q=Quartile; SEC=Secukinumab; SC=Subcutaneous.

Deodhar A, et al. *Arthritis Rheumatol*. 2019;71(Suppl 10).

Treatment With Secukinumab SC is More Effective in Patients With Shorter Disease Durations

Results From the MEASURE 1-4 Trials in AS (2 of 2)

Post-hoc analysis assessing the impact of age and time since diagnosis[a] on response to SEC (N=852) at 16 weeks

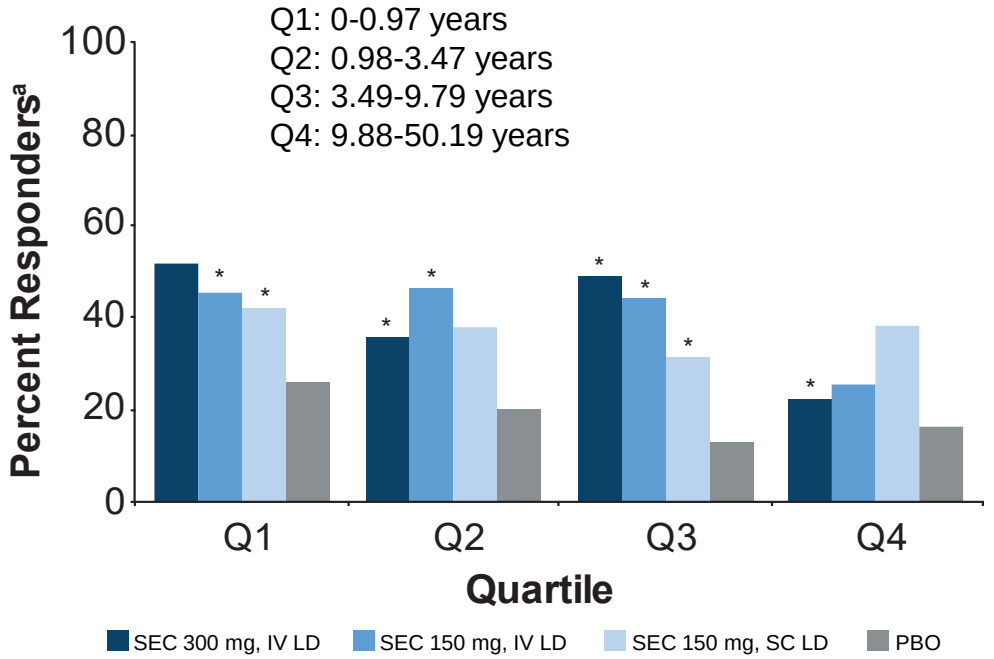
A higher proportion of patients with **shorter disease duration (<3.47 years)** achieved ASAS40.[1]

There was also **a trend toward higher responses on BASDAI and PtGA assessments** in those with shorter disease duration.[1]

Reductions in hsCRP were greatest in patients with the shortest disease duration.[1]

- Infections were more common with SEC than with PBO in MEASURE 1 and 2 through Week 16, with two *Candida* infections reported.[2]
- Common AEs with SEC were nasopharyngitis (MEASURE 1-4), dyslipidemia (MEASURE 1), headache (MEASURE 1-3), diarrhea, cough (MEASURE 3), and URTI (MEASURE 4). One case of Crohn's disease was reported through Week 16 in each of MEASURE 1, 2, and 4.[2-4]
- Frequency of SAEs was low and comparable across treatment groups.[2-4]

ASAS40 Response Through Week 16 by Symptom Duration Quartiles, NRI[1]



vs. PBO: *p<.05.

[a]Time since diagnosis was used as a surrogate marker of disease duration as symptom duration was not collected. AS=Ankylosing Spondylitis; ASAS40=Assessment of Spondyloarthritis International Society 40% Improvement; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; hsCRP=High-Sensitivity C-reactive Protein; IV=Intravenous; LD=Loading Dose; NRI=Nonresponder Imputation; PBO=Placebo; PtGA=Patients Global Assessment of Disease Activity; Q=Quartile; SEC=Secukinumab; SC=Subcutaneous.

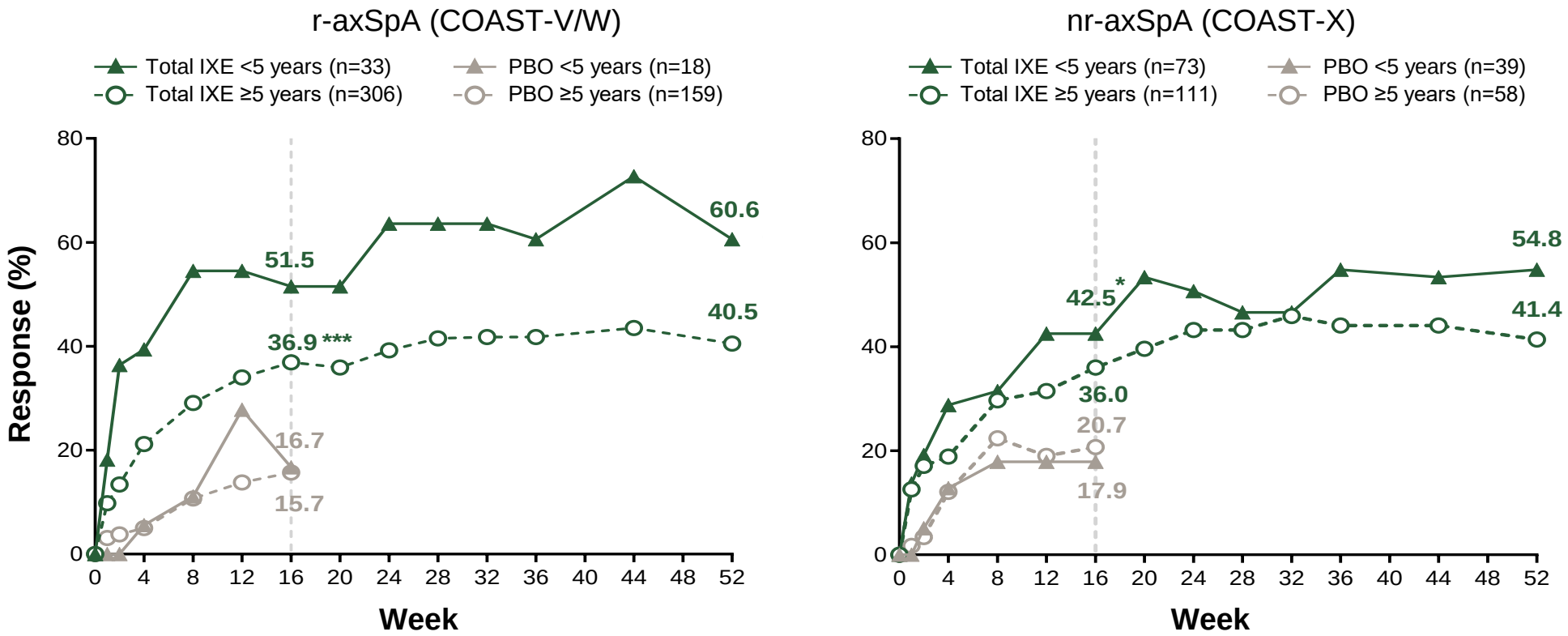
1. Deodhar A, et al. *Arthritis Rheumatol*. 2019;71(Suppl 10). 2. Baeten D, et al. *N Engl J Med*. 2015;373(26):2534-2548. 3. Pavelka K, et al. *Arthritis Res Ther*. 2017;19(1):285. 4. Kivitz AJ, et al. *Rheumatol Ther*. 2018;5(2):447-462.

Treatment With Ixekizumab is Effective in Patients in Both Symptom Duration Groups

Results From the COAST-V, COAST-W and COAST-X Trials (1 of 2)

This post-hoc analysis aimed to assess treatment response to IXE categorized by symptom duration (<5 years, ≥5 years), in patients with r-axSpA and nr-axSpA for up to 52 weeks (N=523).

ASAS40 Response Rate Through Week 52 by Symptom Duration (<5 and ≥5 Years), NRI

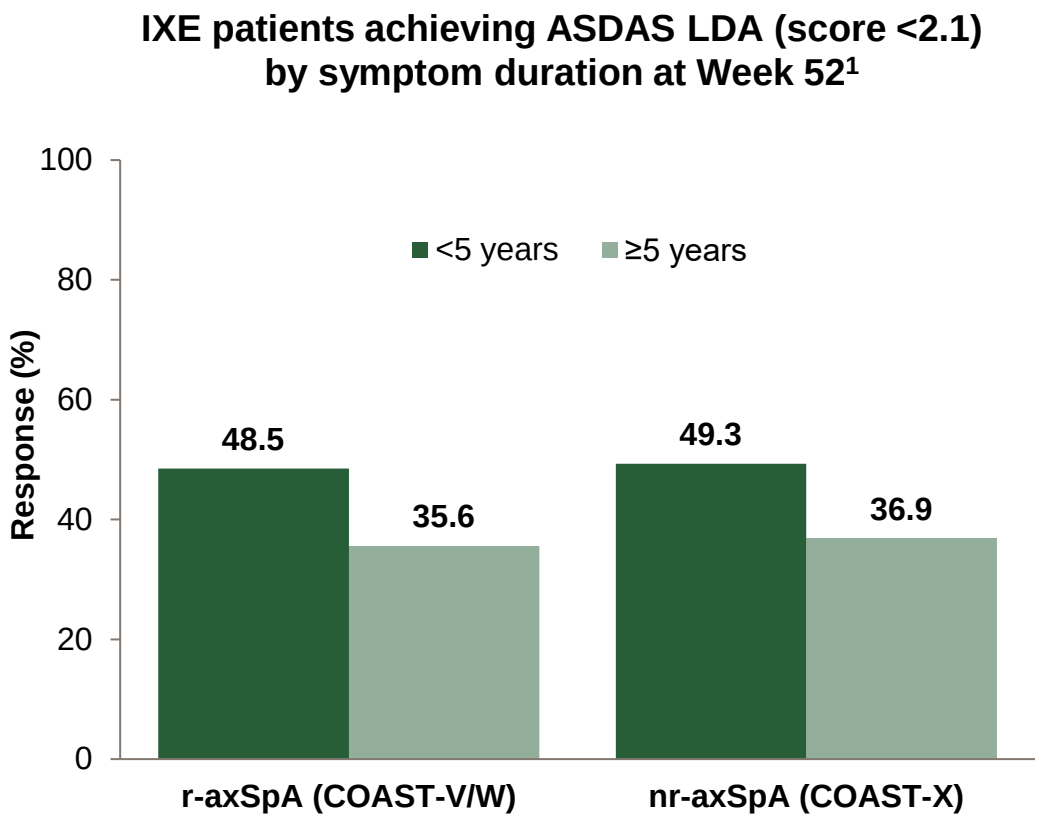


vs. PBO: *p<.05; ***p<.001. ASAS40=Assessment of Spondyloarthritis International Society 40% Improvement; axSpA=Axial Spondyloarthritis; IXE=Ixekizumab; nr-axSpA=Nonradiographic Axial Spondyloarthritis; NRI=Nonresponder Imputation; PBO=Placebo; r-axSpA=Radiographic Axial Spondyloarthritis.

Navarro-Compán V, et al. *Ann Rheum Dis.* 2022;81:24-25.

Treatment With Ixekizumab is Effective in Patients in Both Symptom Duration Groups

Results From the COAST-V, COAST-W and COAST-X Trials (2 of 2)



- In COAST-V/W, 71.6% of Q4W IXE-treated patients reported TEAEs from Weeks 0-52. TEAEs were predominantly mild-to-moderate; nasopharyngitis (11.3%), injection-site reactions (4.0%) and URTIs (8.9%) were the most frequently reported. 5.2% of patients from the Q4W IXE group discontinued the study due to Aes.[2]
- In COAST-X, 66% of Q4W IXE-treated patients reported TEAEs from Weeks 0-52. TEAEs were predominantly mild-to-moderate; nasopharyngitis (19%), injection site reactions (11%), headache (7%), URTIs (4%), and hypertension (6%) were the most frequently reported.[3] One patient from the Q4W IXE group discontinued the study due to Aes.[3]

✓ IXE was efficacious in r- and nr-axSpA patients of both symptom durations (<5 years, ≥5 years).

✓ Stronger responses were observed in patients with <5 years symptom duration.

✓ Earlier treatment of patients may drive better efficacy.

AE=Adverse Event; ASDAS=Ankylosing Spondylitis Disease Severity Index; axSpA=Axial Spondyloarthritis; IXE=Ixekizumab; LDA=Low Disease Activity; nr-axSpA=Nonradiographic Axial Spondyloarthritis; Q4W=Every 4 Weeks; r-axSpA=Radiographic Axial Spondyloarthritis; TEAE=Treatment-emergent Adverse Event; URTI=Upper Respiratory Tract Infection.

1. Navarro-Compán V, et al. *Ann Rheum Dis.* 2022;81:24-25. 2. Dougados M, et al. *Ann Rheum Dis.* 2020;79(2):176-185. 3. Deodhar, et al. *Lancet.* 2020;395:53-64 .

Case Study

Results

Patient Case Study: Charlene

CHARLENE

AGE
46

SEX
Female

OCCUPATION
Consultant

9th provider she has seen regarding symptoms

- Pediatrician
- Physical therapist (x3)
- Chiropractor (x2)
- Internist
- Orthopedist

"It's been 30 years, and I'm tired of the shooting pain in my buttocks."

MEDICAL HISTORY

- Has experienced periodic flares of pain in her spine and buttocks that has been worsening since she was a teenager.
- Father had the same symptoms with no official diagnosis.
- Many misdiagnoses including a herniated disk, bone spurs, dysfunctional sacroiliac joints, and spinal misalignment.

SYMPTOMS AND CLINICAL PRESENTATION

- Severe back pain with insidious onset that is worse in the mornings, improves on movement and is OTC NSAID refractory.

Serology: HLA-B27 negative.

CASE OUTCOME

Note: This case is based on a real patient, some elements have been fictionalized or exaggerated for teaching purposes.

HLA-B27=Human Leukocyte Antigen B27; NSAID=Nonsteroidal Anti-inflammatory Drug; OTC=Over The Counter; r-axSpA=Radiographic Axial Spondyloarthritis; TNF=Tumor Necrosis Factor.

www.washingtonpost.com/health/medical-mysteries/back-pain-sacroiliac-medical-mystery/2021/11/12/d864a2b0-239f-11ec-8200-5e3fd4c49f5e_story.html (Accessed April 11, 2023).

Patient Case Study: Charlene

CHARLENE

AGE
46

SEX
Female

OCCUPATION
Consultant

9th provider she has seen regarding symptoms

- Pediatrician
- Physical therapist (x3)
- Chiropractor
- Internist
- Orthopedist

"It's been 30 years, and I'm tired of the shooting pain in my buttocks."

CASE OUTCOME

Following an assessment with her rheumatologist, Charlene was given a preliminary diagnosis of **r-axSpA**

- Initial treatment with a potent anti-inflammatory drug improved her symptoms, which confirmed her diagnosis, yet treatment caused her to become dizzy and confused.
- She was switched to biweekly injections of a TNF inhibitor and her condition has remained stable ever since.
- Today, Charlene moves without difficulty, walking 5 miles per day and working out 3 times per week with no pain.

DISCUSSION QUESTION:

- Why do you think it took so long for Charlene to be diagnosed?

Note: This case is based on a real patient, some elements have been fictionalized or exaggerated for teaching purposes.

HLA-B27=Human Leukocyte Antigen B27; NSAID=Nonsteroidal Anti-inflammatory Drug; OTC=Over The Counter; r-axSpA=Radiographic Axial Spondyloarthritis; TNF=Tumor Necrosis Factor.

www.washingtonpost.com/health/medical-mysteries/back-pain-sacroiliac-medical-mystery/2021/11/12/d864a2b0-239f-11ec-8200-5e3fd4c49f5e_story.html (Accessed April 11, 2023).

Summary

- Treatment goals are to maintain function, spinal flexibility, ability to work and reduce symptoms and disease complications.[1]
- **Treatment decisions should be tailored** to individual patient needs and consider disease activity, domain involvement, patient symptoms, and safety.[2-5]
- There are several advanced treatment options for patients with axSpA.[6,7]
- Several expert consortiums have developed **evidence-based recommendations** to support clinicians in navigating **individualized treatment** in axSpA.[2-5]
- Delays in diagnosis and effective treatment adds to the high disease burden experienced by patients. Studies have demonstrated that **earlier treatment leads to better responses and improved outcomes.**[8-10]

axSpA=Axial Spondyloarthritis.

1. Ward MM, et al. *Arthritis Rheumatol.* 2016;68:282-298. 2. Ward MM, et al. *Arthritis Care Res (Hoboken).* 2019;71(10):1285-1299. 3. Ward MM, et al. *Arthritis Rheumatol.* 2019;71(10):1599-1613.
4. https://labeling.pfizer.com/ShowLabeling.aspx?id=959 (Accessed October 2023). 5. Ramiro S, et al. *Ann Rheum Dis.* 2023;82(1):19-34. 6. van der Heijde D, et al. *Arthritis Rheum.* 2006;55(4):569-574.
7. van der Heijde D, et al. *RMD Open.* 2018;4(1):e000659. 8. Lapane KL, et al. *BMC Fam Pract.* 2021;22(1):251. 9. Zhao SS, et al. *Rheumatology (Oxford).* 2021;60(4):1620-1628. 10. Yi E, et al. *Rheumatol Ther.* 2020;7(1):65-87.

US Medical Education

For additional resources on axSpA, scan the code

SCAN HERE

Prescribing Information

Please scan the QR code to access the relevant prescribing information

Certolizumab pegol USPI

Secukinumab USPI

Etanercept USPI

Adalimumab USPI

Abatacept USPI

Infliximab USPI

Upadacitinib USPI

Golimumab USPI

Golimumab USPI

Ustekinumab USPI

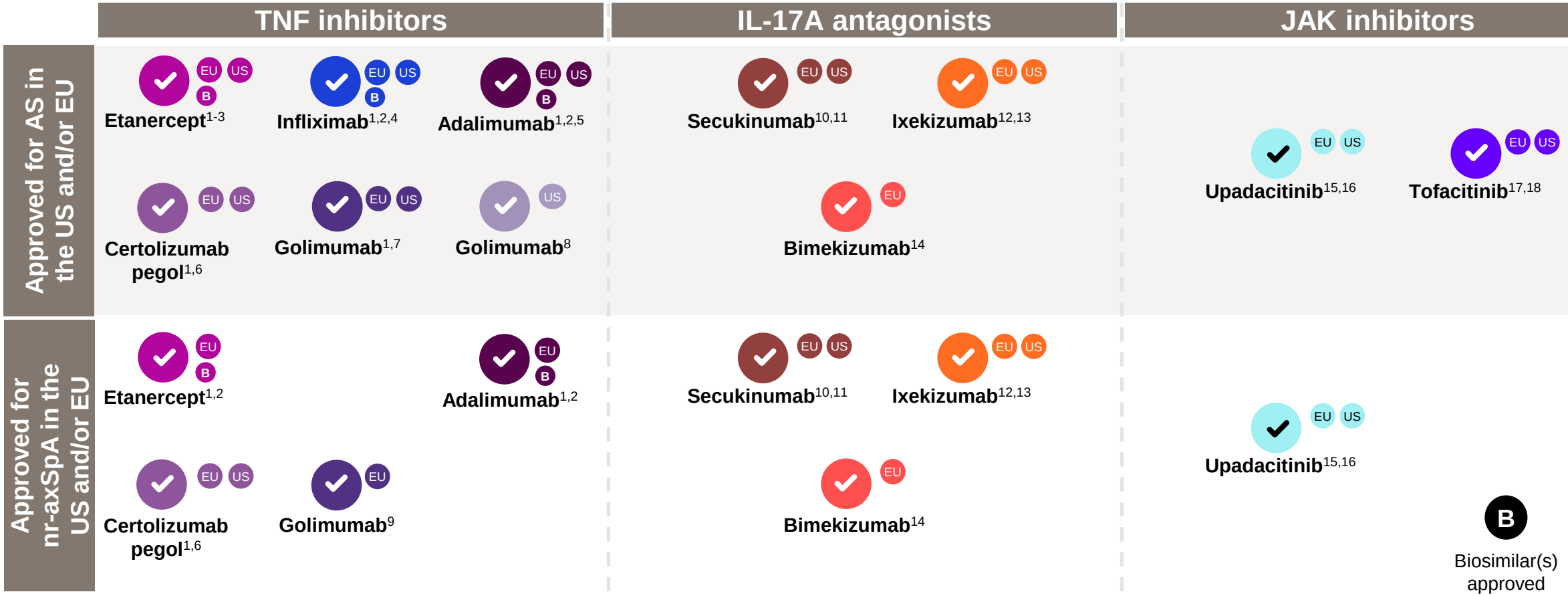
Ixekizumab USPI

Guselkumab USPI

Tofacitinib USPI

Current Advanced Treatment Options in axSpA

Ten drugs are approved, three of which have biosimilars



Secukinumab IV: For US only.

AS=Ankylosing Spondylitis; CHMP=Committee for Medicinal Products for Human Use; EU=European Union; IL=Interleukin; JAK=Janus Kinase; nr-axSpA=Nonradiographic Axial Spondyloarthritis; TNF=Tumor Necrosis Factor; US=United States. For source information, please see the Speaker Notes.