EULAR 2022 Highlights

ASAS-EULAR recommendations for the management of axSpA: 2022 update

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DISCLOSURES

- Speaker honoraria & participation in advisory boards for Celltrion, Pfizer, Sanofi, Gilead, Galapagos, AbbVie, Lilly, Fresenius.
- Recipient of research grants from Pfizer and Lilly.
- Assessment of SpondyloArthritis international Society (ASAS) member.
- Senior methodologist on the task force for the ASAS-EULAR recommendations 2022 update for the management of axSpA.

Existing recommendations

Recommendation

2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis

Désirée van der Heijde,[1] Sofia Ramiro,[1] Robert Landewé,[2,3] Xenofon Baraliakos,[4] Filip Van den Bosch,[5] Alexandre Sepriano,[1,6] Andrea Regel,[4] Adrian Ciurea,[7] Hanne Dagfinrud,[8] Maxime Dougados,[9,10] Floris van Gaalen,[1] Pál Géher,[11] Irene van der Horst-Bruinsma,[12] Robert D Inman,[13] Merryn Jongkees,[14] Uta Kiltz,[4] Tore K Kvien,[15] Pedro M Machado,[16] Helena Marzo-Ortega,[17,18] Anna Molto,[9,10] Victoria Navarro-Compàn,[19] Salih Ozgocmen,[20] Fernando M Pimentel-Santos,[21] John Reveille,[22] Martin Rudwaleit,[23,24,25] Jochen Sieper,[26] Percival Sampaio-Barros,[27] Dieter Wiek,[28] Jürgen Braun[4]

van der Heijde D, *et al*. *Ann Rheum Dis* 2017;**76**:978–991.

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Steering Committee

- Désirée van der Heijde (co-convenor)
- Sofia Ramiro (co-convenor)
- Elena Nikiphorou (methodologist)
- Alexandre Sepriano (co-methodologist)
- Robert Landewé
- Xenofon Baraliakos
- **Augusta Ortolan (fellow)**
- **Casper Webers (fellow)**

- 2 Systematic Literature Reviews (SLRs):
  - Efficacy and safety of non-pharmacological and non-biological interventions (Augusta Ortolan)
  - Efficacy and safety of biological DMARDs (Casper Webers)

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Taskforce members

- Filip van den Bosch
- Adrian Ciurea
- Floris van Gaalen
- Pal Géher
- Uta Kiltz
- Pedro Machado
- Helena Marzo-Ortega
- Anna Molto
- Victoria Navarro-Compán
- Denis Poddubnyy
- Lianne Gensler
- Philippe Carron
- Nelly Ziade
- Martin Rudwaleit
- Michael Nissen
- Josef Hermann
- Marketa Husakova
- Fernando Pimentel-Santos
- Steven Zhao (EMEUNET)
- Manouk de Hooge (EMEUNET)
- Mark Telkman (PARE)
- Boryana Boteva (PARE)
- Ann Bremander (HP)
- Fabian Proft (Y-ASAS)
- Clementina Lopéz-Medina (Y-ASAS)

- 33 task force members, 16 countries
- Rheumatologists, epidemiologists, HP, PARE, EMEUNET, Y-ASAS, members proposed by national societies
- 52% new members vs 2016 recommendations

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Overarching principles

		LoA (0-10)	% score ≥8
A	Axial Spondyloarthritis (axSpA) is a potentially severe disease with diverse manifestations, usually requiring multidisciplinary management coordinated by the rheumatologist.	9.8 (0.4)	100%

All unchanged

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		LoA (0-10)	% score ≥8
A	Axial Spondyloarthritis (axSpA) is a potentially severe disease with diverse manifestations, usually requiring multidisciplinary management coordinated by the rheumatologist.	9.8 (0.4)	100%
B	The primary goal of treating the patient with axSpA is to maximize health related quality of life through control of symptoms and inflammation, prevention of progressive structural damage, preservation/normalisation of function and social participation.	9.8 (0.5)	100%

All unchanged

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C	The optimal management of patients with axSpA requires a combination of non-pharmacological and pharmacological treatment modalities.	9.8 (0.5)	100%

All unchanged

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C	The optimal management of patients with axSpA requires a combination of non-pharmacological and pharmacological treatment modalities.	9.8 (0.5)	100%
D	Treatment of axSpA should aim at the best care and must be based on a shared decision between the patient and the rheumatologist.	9.5 (1.8)	97%

All unchanged

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C	The optimal management of patients with axSpA requires a combination of non-pharmacological and pharmacological treatment modalities.	9.8 (0.5)	100%
D	Treatment of axSpA should aim at the best care and must be based on a shared decision between the patient and the rheumatologist.	9.5 (1.8)	97%
E	axSpA incurs high individual, medical and societal costs, all of which should be considered in its management by the treating rheumatologist.	9.5 (0.9)	94%

All unchanged

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Recommendations

- 15 recommendations:
  - 8 unchanged from the previous recommendations (#2,3,6,7,8,13,14,15)
  - 3 minor edits, mostly on nomenclature (#1,4,5)
  - 2 significantly updated (#9,12)
  - 2 newly formulated (#10,11)

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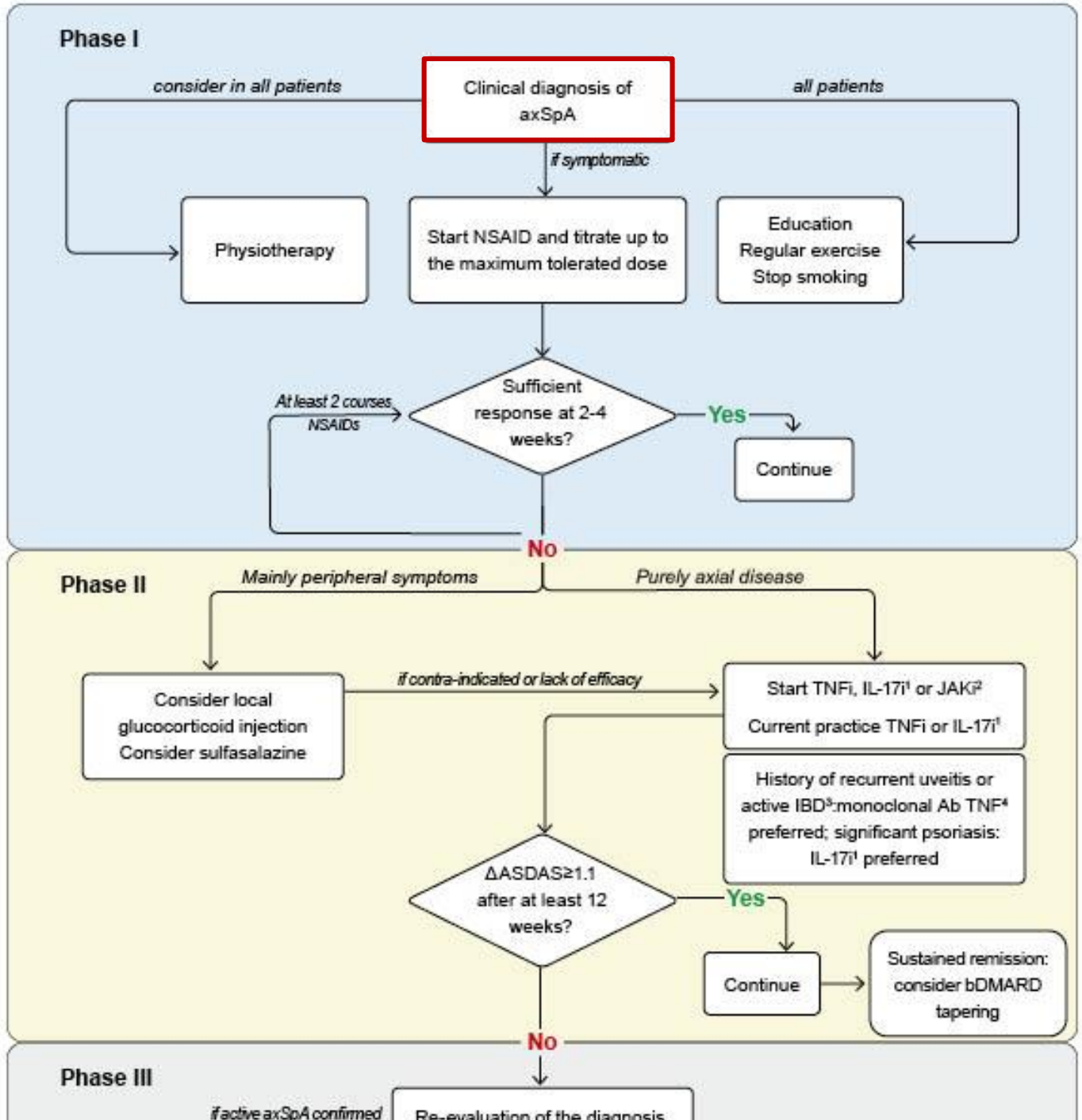
Phase I
consider in all patients
Clinical diagnosis of axSpA
all patients
if symptomatic
Physiotherapy
Start NSAID and titrate up to the maximum tolerated dose
Education
Regular exercise
Stop smoking
At least 2 courses NSAIDs
Sufficient response at 2-4 weeks?
Yes
Continue
No
Phase II
Mainly peripheral symptoms
Purely axial disease
Consider local glucocorticoid injection
Consider sulfasalazine
if contra-indicated or lack of efficacy
Start TNFi, IL-17i[1] or JAKi[2]
Current practice TNFi or IL-17i[1]
History of recurrent uveitis or active IBD[3]:monoclonal Ab TNF[4] preferred; significant psoriasis: IL-17i[1] preferred
ΔASDAS≥1.1 after at least 12 weeks?
Yes
Continue
Sustained remission: consider bDMARD tapering
No
Phase III
if active axSpA confirmed
Re-evaluation of the diagnosis

Recommendations 1-3

		LoE / GoR	LoA (0-10) % score ≥8	
1§	The treatment of patients with axSpA should be individualised according to the current signs and symptoms of the disease (axial, peripheral, extra-musculoskeletal manifestations) and the patient characteristics including comorbidities and psychosocial factors.	5 / D	9.6 (0.8)	97%

§ minor edit on nomenclature (EMM); others unchanged

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Recommendations 1-3

		LoE / GoR	LoA (0-10) % score ≥8	
1§	The treatment of patients with axSpA should be individualised according to the current signs and symptoms of the disease (axial, peripheral, extra-musculoskeletal manifestations) and the patient characteristics including comorbidities and psychosocial factors.	5 / D	9.6 (0.8)	97%
2	Disease monitoring of patients with axSpA should include patient reported outcomes, clinical findings, laboratory tests and imaging, all with the appropriate instruments and relevant to the clinical presentation. The frequency of monitoring should be decided on an individual basis depending on symptoms, severity, and treatment.	5 / D	9.5 (1.1)	97%

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3	Treatment should be guided according to a predefined treatment target.	5 / D	9.0 (1.2)	85%

§ minor edit on nomenclature (EMM); others unchanged

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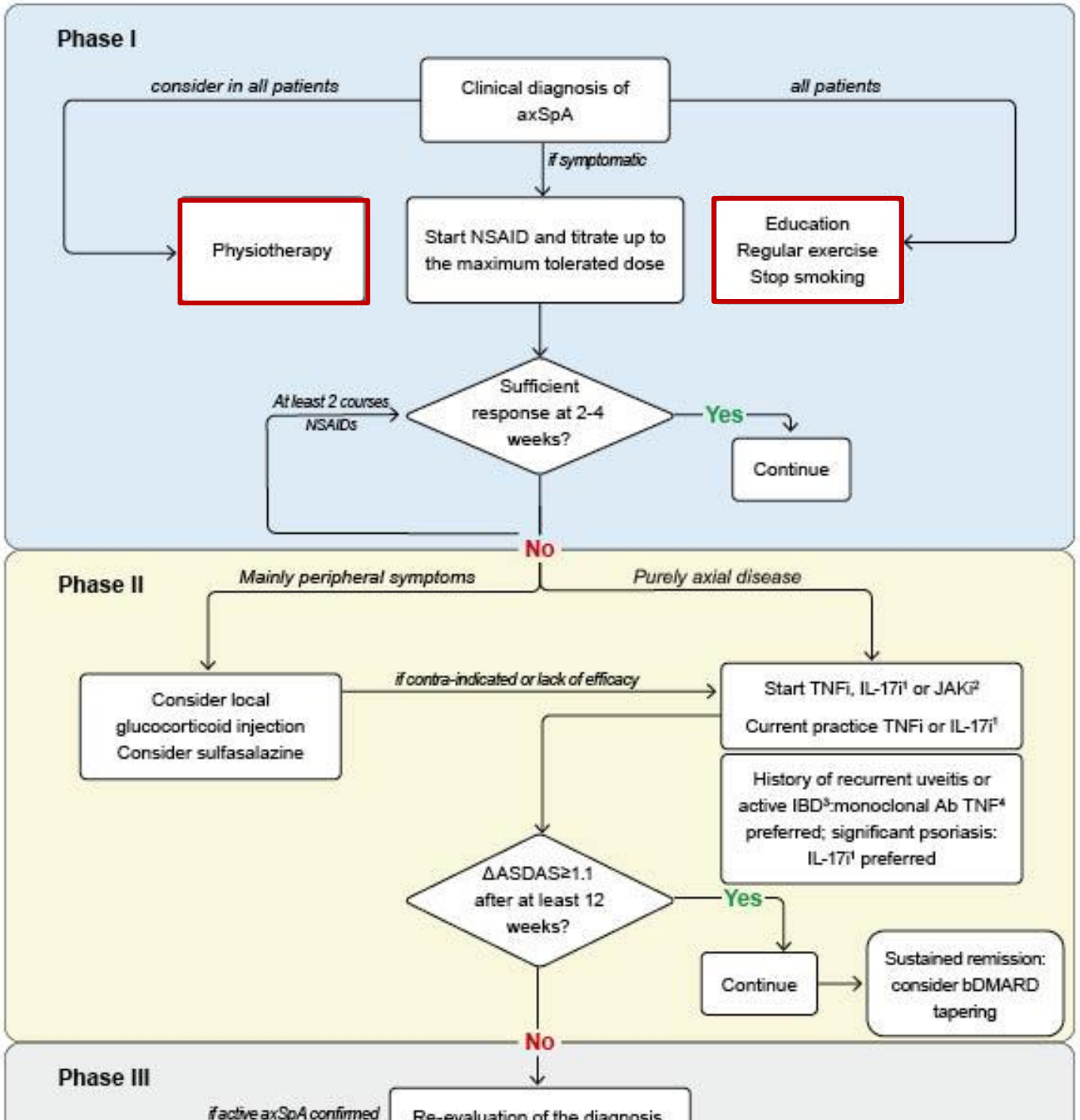
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Phase III
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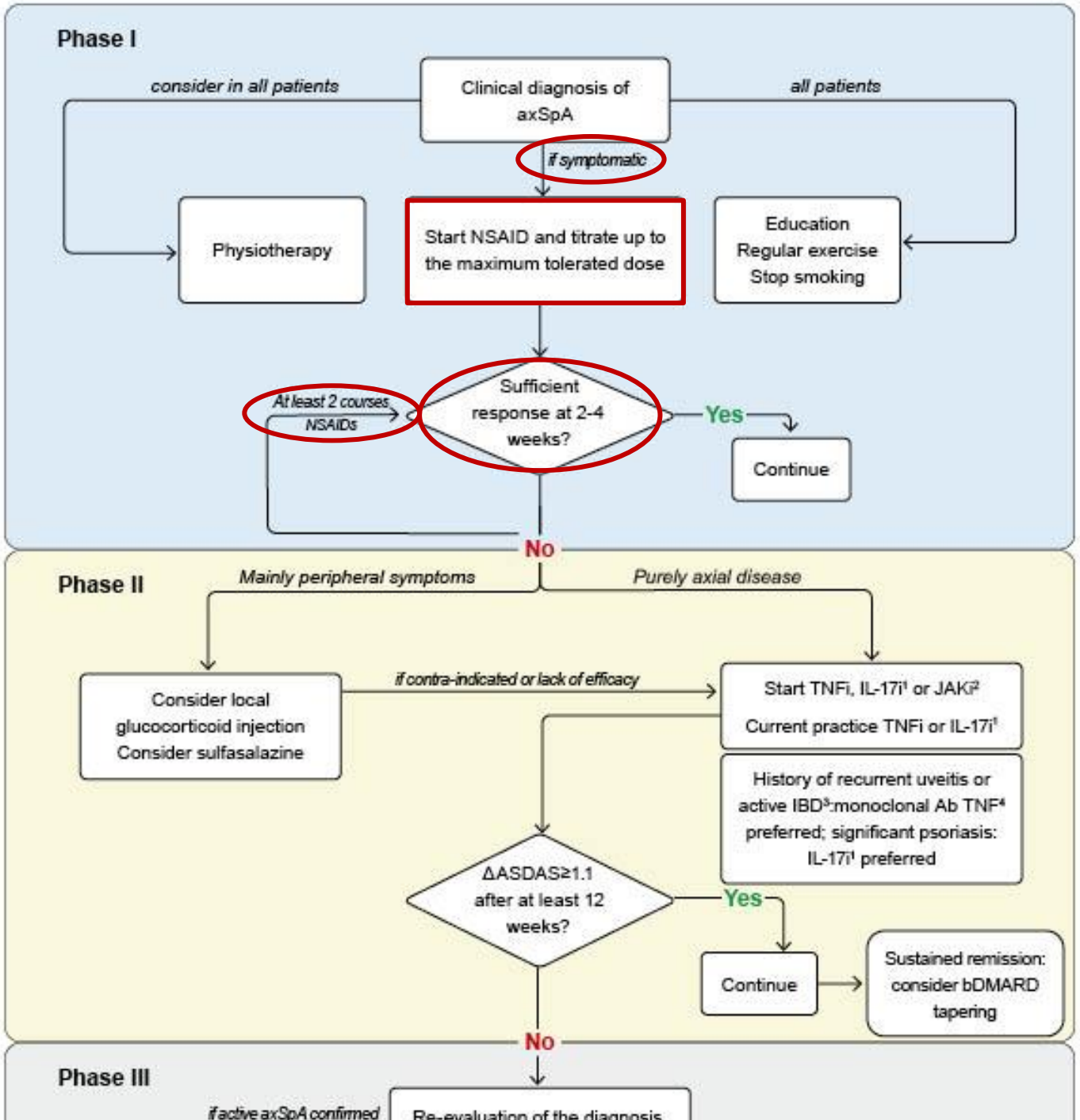
Re-evaluation of the diagnosis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Re-evaluation of the diagnosis

Recommendations 4-5

		LoE / GoR	LoA (0-10)	% score ≥8
4§	Patients should be educated about axSpA and encouraged to exercise on a regular basis and stop smoking; physiotherapy should be considered.	2b / B (education, exercise) 5 / D (stop smoking) 1a / A (physiotherapy)	9.8 (0.5)	100%

§ minor edits
4 nomenclature (physiotherapy)
5 clearer formulation, same content

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Recommendations 4-5

		LoE / GoR	LoA (0-10)	% score ≥8
4§	Patients should be educated about axSpA and encouraged to exercise on a regular basis and stop smoking; physiotherapy should be considered.	2b / B (education, exercise) 5 / D (stop smoking) 1a / A (physiotherapy)	9.8 (0.5)	100%
5§	Patients suffering from pain and stiffness should use an NSAID as first line drug treatment up to the maximum dose, taking risks and benefits into account. For patients who respond well to NSAIDs continuous use is preferred if needed to control symptoms.	1a / A	9.5 (0.8)	97%

§ minor edits
4 nomenclature (physiotherapy)
5 clearer formulation, same content

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Recommendations 6-8

		LoE / GoR	LoA (0-10)	% score ≥8
6	Analgesics, such as paracetamol and opioid-(like) drugs, might be considered for residual pain after previously recommended treatments have failed, are contraindicated, and/or poorly tolerated.	5 / D	8.9 (1.4)	79%

All unchanged

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		LoE / GoR	LoA (0-10)	% score ≥8
6	Analgesics, such as paracetamol and opioid-(like) drugs, might be considered for residual pain after previously recommended treatments have failed, are contraindicated, and/or poorly tolerated.	5 / D	8.9 (1.4)	79%
7	Glucocorticoid injections directed to the local site of musculoskeletal inflammation may be considered. Patients with axial disease should not receive long-term treatment with systemic glucocorticoids.	2 / B (injections) 5 / D (long-term systemic GCs)	9.6 (0.8)	100%

All unchanged

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7	Glucocorticoid injections directed to the local site of musculoskeletal inflammation may be considered. Patients with axial disease should not receive long-term treatment with systemic glucocorticoids.	2 / B (injections) 5 / D (long-term systemic GCs)	9.6 (0.8)	100%
8	Patients with purely axial disease should normally not be treated with csDMARDs; Sulfasalazine may be considered in patients with peripheral arthritis.	1a / A (sulfasalazine, methotrexate) 1b / A (leflunomide) 4 / A (other csDMARDs) 1a /A (sulfasalazine peripheral disease)	9.6 (0.9)	94%

All unchanged

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ASAS-EULAR Recommendations for the treatment of patients with axSpA with b/tsDMARDs

Rheumatologist's diagnosis of axial SpA

and

Elevated CRP or positive MRI-SIJ or Radiographic sacroiliitis*

and

Failure of standard treatment

All patients

At least 2 NSAIDs over 4 weeks (in total)

Patients with predominant peripheral manifestations

One local steroid injection if appropriate

Normally a therapeutic trial of sulfasalazine

and

High disease activity: ASDAS ≥ 2.1

and

Positive rheumatologist's opinion

* Radiographic sacroiliitis is currently mandatory for infliximab and JAKi

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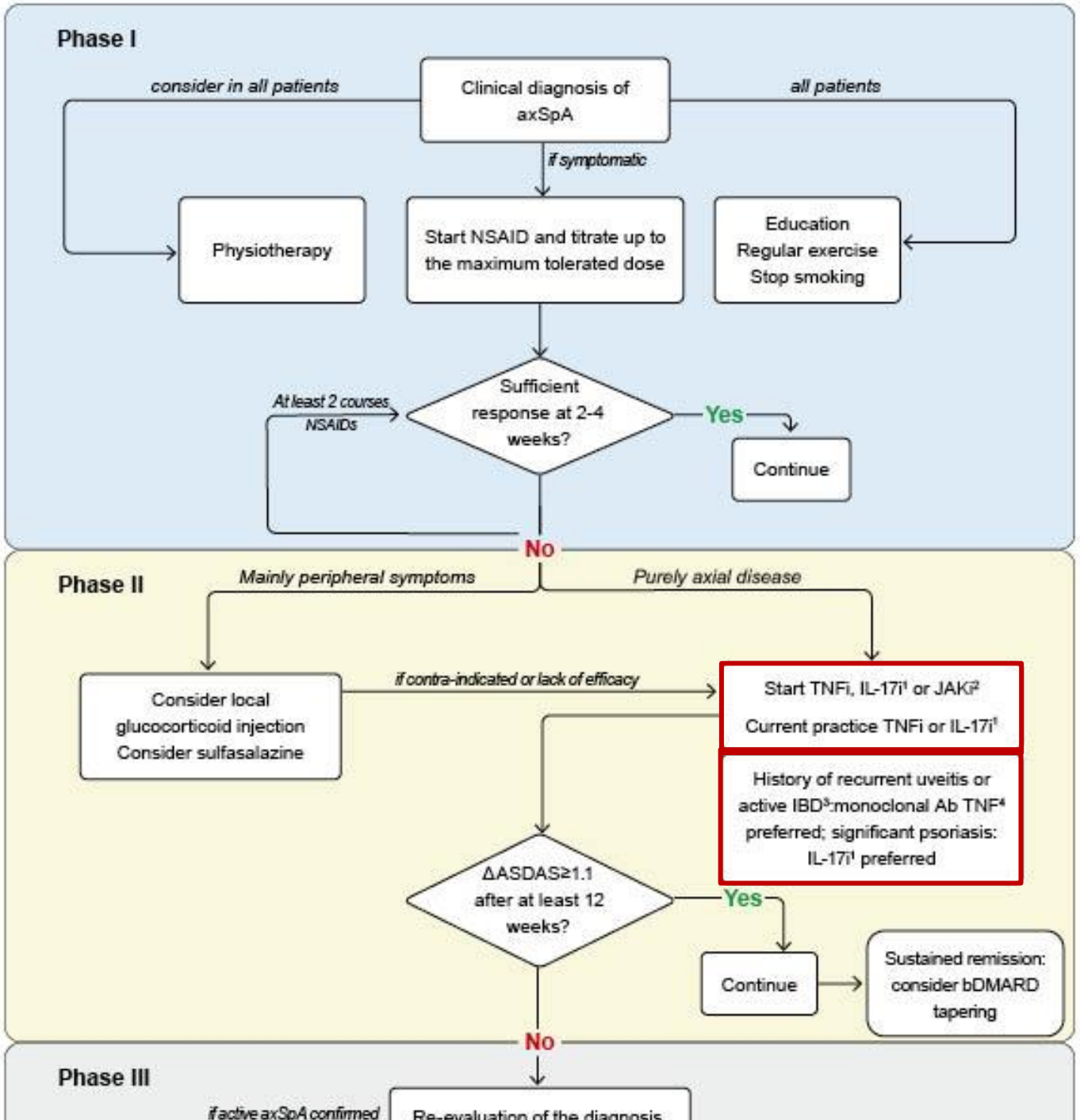
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if active axSpA confirmed
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Recommendations 9-10

		LoE / GoR	LoA (0-10) % score ≥8	
9±	TNFi, IL-17i* or JAKi should be considered in patients with persistently high disease activity despite conventional treatments; current practice is to start a TNFi or IL-17i*.	1a / A	9.2 (1.2)	94%

±significant updates
*IL-17i: refers only to IL-17A-inhibitors

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Efficacy tsDMARDs – what is new

- **Filgotinib** was efficacious in a r-axSpA population including 9% of TNF-experienced patients (n=1 phase II RCT, low RoB)

- **Tofacitinib** was efficacious in a r-axSpA population including 23% of TNF-experienced patients (n=1 phase II RCT and n=1 phase III RCTs, both low RoB)

- **Upadacitinib** is efficacious in naive patients with r-axSpA (n=1 phase III RCT, low RoB)

tsDMARDs– JAKi

	Study	Interventions	N	Timepoint (weeks)	Primary endpoint	ASAS 20 %	NNT	ASAS 40 %	NNT	RoB
r-axSpA	van der Heijde 2018 Lancet **(TORTUGA)***	Filgotinib 200 mg PBO	116	12	**ASDAS change (+)**	**76** 40	2.8	**38** 19	5.3	**L**
	van der Heijde 2017 Ann Rheum Dis	Tofacitinib 2 mg Tofacitinib 5 mg Tofacitinib 10 mg PBO	207	12	**ASAS 20 (+)**	56 **63** **67** 40	6.3 4.4 3.7	**42** **46** **38** 19	4.4 3.8 5.3	**L**
	Deodhar 2020 Ann Rheum Dis**	Tofacitinib 5 mg PBO	269	16	**ASAS 20 (+)**	**56** 29	3.7	**41** 12	3.6	**L**
	van der Heijde 2019 Lancet **(SELECT AXIS 1)**	Upadacitinib 15 mg PBO	187	14	**ASAS 40 (+)**	**65** 40	4.0	**52** 26	3.8	**L**

N/A=not applicable; significant results compared to PBO highlighted in bold

* Stratified by bDMARDs history (9.5% of TNFi experienced)
**Stratified by bDMARDs history (bDMARD-naïve and TNFi-inadequate responder or prior bDMARD use without inadequate response) (23% of TNFi experienced)

Efficacy and Safety of Upadacitinib in Patients With Active Ankylosing Spondylitis Refractory to Biologic Therapy: a Double-Blind, Randomised, Placebo-Controlled Phase 3 Trial

Objective: Assess the efficacy and safety of UPA in patients who are bDMARD-IR with active AS

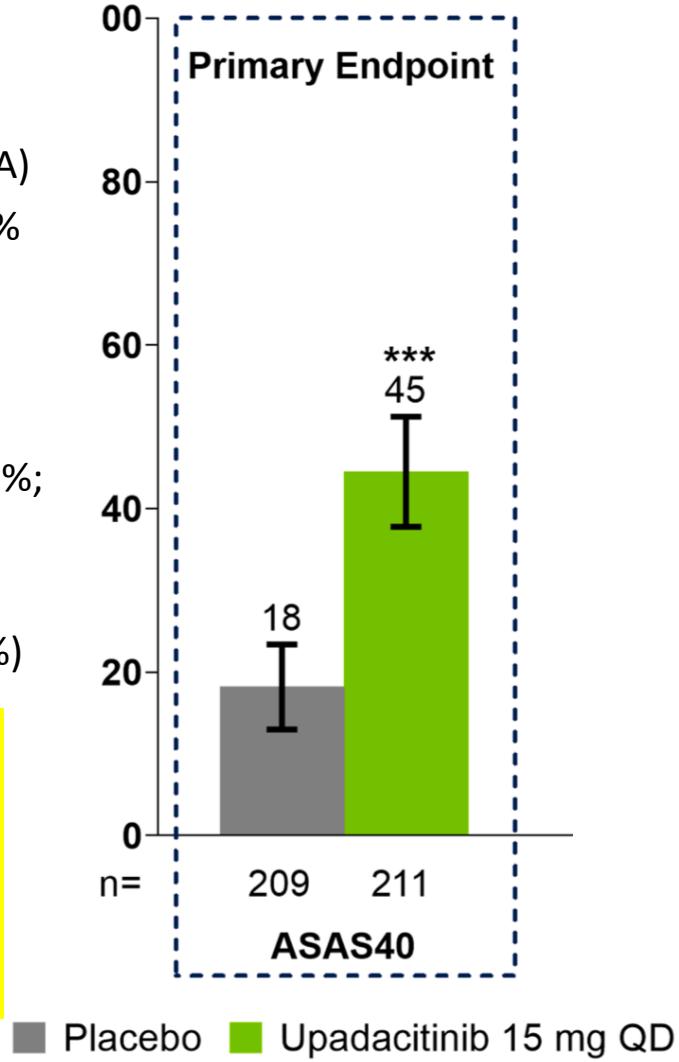
- SELECT-AXIS 2 includes two separate studies (one for AS bDMARD-IR and one for nr-axSpA)
- Patients with active AS received assigned treatment (UPA 15 mg, n=211; PBO, n=209); 97% received study drug through Week 14

Primary endpoint: ASAS40 at Week 14

Results:

- Significantly more patients achieved ASAS40 response at Week 14 with UPA vs PBO (45% vs 18%; P<0.0001)
- UPA showed onset of effect in ASAS40 as early as Week 4 (nominal P≤0.05)
- Rates of TEAEs were similar between treatment groups through Week 14 (UPA, 41%; PBO, 37%)

UPA 15 mg QD significantly more effective than PBO over 14 weeks of treatment in patients with active AS and IR to bDMARDs. No new safety risks identified with UPA



bDMARD-IR

van der Heijde D, et al. Ann Rheum Dis 2022;81(Suppl 1):Poster#POS0306.

Bimekizumab in Patients with Active Ankylosing Spondylitis: 24-Week Efficacy & Safety from BE MOBILE 2, a Phase 3, Multicentre, Randomised, Placebo-Controlled Study

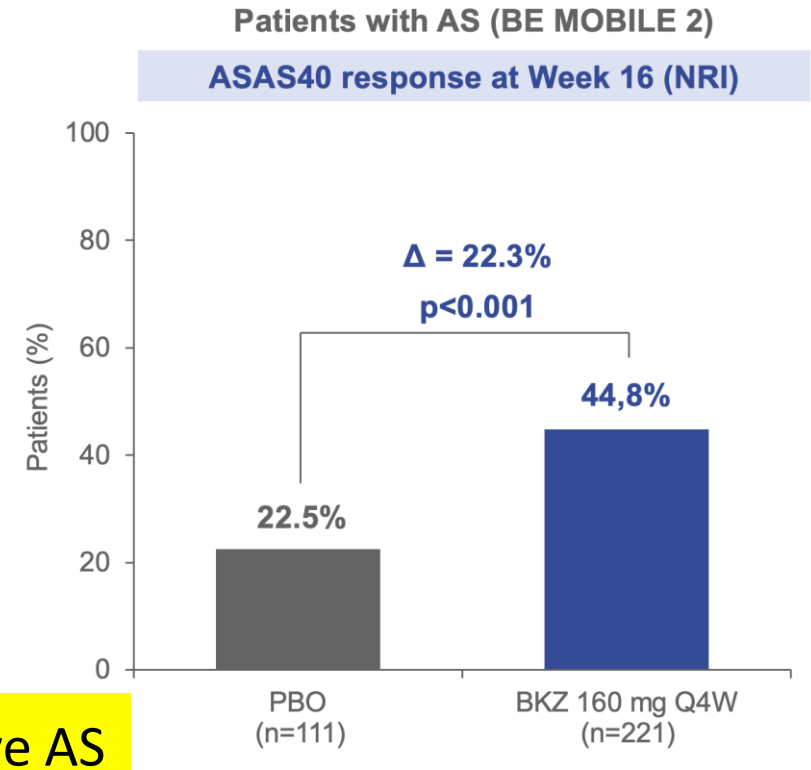
16-week double-blind, PBO-controlled period and 36-week maintenance period (BE MOBILE 2)

- **Objective:** Assess efficacy and safety of BKZ vs PBO in patients with active AS up to Week 24
  - Patients randomised 2:1 to BKZ 160 mg Q4W or PBO
  - From Week 16, all patients received BKZ 160 mg Q4W
- **Primary outcome:** ASAS40 at Week 16

Results:

Primary and all ranked secondary endpoints were met

- ASAS40: 44.8% BKZ vs 22.5% PBO; p<0.001
- At Week 24, ≥50% patients had achieved ASDAS <2.1
- Responses with BKZ were rapid, including PBO patients who switched to BKZ at Week 16, and increased to Week 24
- Substantial reductions of hs-CRP by Week 2 and MRI SIJ and spine inflammation by Week 16 were achieved



mixed population

Dual inhibition of IL-17A and IL-17F with BKZ in patients with active AS resulted in rapid, clinically relevant improvements in efficacy outcomes vs PBO. No new safety signals observed.

van der Heijde D, et al. Ann Rheum Dis 2022;81(Suppl 1):Abstract #OP0019.

Bimekizumab in Patients with Active Non-Radiographic Axial Spondyloarthritis: 24-Week Efficacy & Safety from BE MOBILE 1, a Phase 3, Multicentre, Randomised, Placebo-Controlled Study

- **Objective:** Assess efficacy and safety of BKZ vs PBO in patients with active nr-axSpA up to Week 24 in the ongoing pivotal Phase 3 study, BE MOBILE 1*
  - Patients were randomised 1:1 to BKZ 160 mg Q4W or PBO
  - From Week 16, all patients received BKZ 160 mg Q4W
- Primary (ASAS40) and secondary efficacy endpoints were assessed at Week 16

Results:

Primary and all ranked secondary endpoints were met

- ASAS40: 47.7% BKZ vs 21.4% PBO; $p<0.001$
- At Week 24, ≥50% patients had achieved ASDAS <2.1

- Responses with BKZ were rapid – including PBO patients who switched to BKZ at Week 16 – and increased to Week 24
- Substantial reductions were achieved in hs-CRP by Week 2 and MRI SIJ and spine inflammation by Week 16

Dual inhibition of IL-17A and IL-17F with BKZ in patients with active nr-axSpA resulted in rapid, clinically relevant improvements in efficacy outcomes vs PBO. No new safety signals observed.

*BE MOBILE 1 (NCT03928704) comprises a 16-wk double-blind, PBO-controlled period and 36-wk maintenance period.

Deodhar A, et al. Ann Rheum Dis 2022;81(Suppl 1):Poster#POS0939.

Why preference on TNFi or IL-17i over JAKi?

DRIVEN BY SAFETY!

Most data are from short-term RCTs.

Safety data mainly based on long-term extensions (LTEs) of RCTs.

LTE studies do not include ‘at risk’ patients.

Observational data enable the study of comparative safety of various interventions & include more ‘real-life’ patients.

Safety – What is new (IL17i)

- Open-label/long-term extensions of SEC/BKZ show low rates of:
  - Serious infections for SEC (n=5, up to 5 years) and BKZ (n=1, 1 year follow-up)
  - Malignancies for SEC (n=3, up to 5 years) and BKZ (n=1, 1 year follow-up)
  - Cardiovascular for SEC (n=5, up to 5 years) and BKZ (n=1, 1 year follow-up)
- No data on extension studies for IXE
- No observational studies on IL17i safety

Safety – What is new (JAKi)

- Only short-term RCTs
- No data on extension studies for JAKi
- No observational studies on JAKi safety

Safety of JAKi - RA

- Increased risks of MACE, malignancies in patients with RA treated with Tofacitinib compared to TNFi in **ORAL SURVEILLANCE.**

- No trials with safety as primary endpoint conducted in axSpA.

➢Do these safety issues also apply to patients with axSpA?

➢Do these safety signals represent a JAKi-class concern?

Recommendations 9-10

		LoE / GoR	LoA (0-10)	% score ≥8
9±	TNFi, IL-17i* or JAKi should be considered in patients with persistently high disease activity despite conventional treatments; current practice is to start a TNFi or IL-17i*.	1a / A	9.2 (1.2)	94%
10#	If there is a history of recurrent uveitis or active IBD, preference should be given to a monoclonal antibody against TNFα**. In patients with significant psoriasis, an IL-17i* may be preferred.	2b / B (uveitis, IBD) 1a / B (psoriasis)	9.1 (1.8)	97%

±significant updates
NEW
*IL-17i: refers only to IL-17A-inhibitors; **This includes a pegylated Fab' fragment

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Uveitis – Observational studies [IL17i]

New evidence: limited number of observational studies. One study observed an increased risk in secukinumab when compared to adalimumab and infliximab (n=1, **low RoB**).

Study	Registry	Intervention	Control	Outcome	Measure	Effect	RoB
González-Mazón 2020 EULAR **Abstract**	Hospital (single)	IL17i	TNFi	Uveitis episodes	cIR	2.72/100PY 2.53/100PY	No info
Lindström 2021 Ann Rheum Dis	SRQ	ADA CZP ETN GLM IFX SEC	N/A	Anterior uveitis episodes‡	cIR	4.0/100PY§ 4.5/100PY 7.5/100PY 6.8/100PY 2.9/100PY§ 6.8/100PY§	L
		SEC	ADA	First anterior uveitis diagnosis	aHR[1]	2.32 (1.16-4.63)	

Analyses adjusted for: [1]Sex, age, previous history of AU (>1y before start), patient global.
‡Excluded if recent uveitis (<1 year before biologic start). §Significantly higher for SEC compared to ADA and IFX

New evidence on EMMs

TNFi

- Uveitis: increased risk of first-ever episode with ETN compared to ADA/IFX in observational studies (n=2, **low RoB**)
- IBD and psoriasis: limited number of observational studies and all at **high RoB** (n=3 for IBD, n=1 for psoriasis) or **unknown RoB** (n=1 for IBD and psoriasis), precluding robust conclusions

IL17i

- Uveitis: rates in open-label and long-term extensions (n=7, up to 5 years) similar to those observed in TNFi. Increased risk for SEC compared to ADA/IFX in observational study (n=1, **low RoB**)
- IBD: rates in open-label and long-term extensions (n=8, of up to 5 years) are in line with previous findings (0.7/100PY)
- Psoriasis: rates reported in a limited number of long-term extensions (n=2, up to 3 years), similar to those observed in TNFi
- No new comparative analyses or observational studies on IL17i available for IBD or psoriasis

ASAS-EULAR Recommendations for the continuation of b/tsDMARDs

Consider to continue b/tsDMARDs if after at least 12 weeks of treatment

ASDAS improvement ≥ 1.1

and

Positive rheumatologist's opinion to continue

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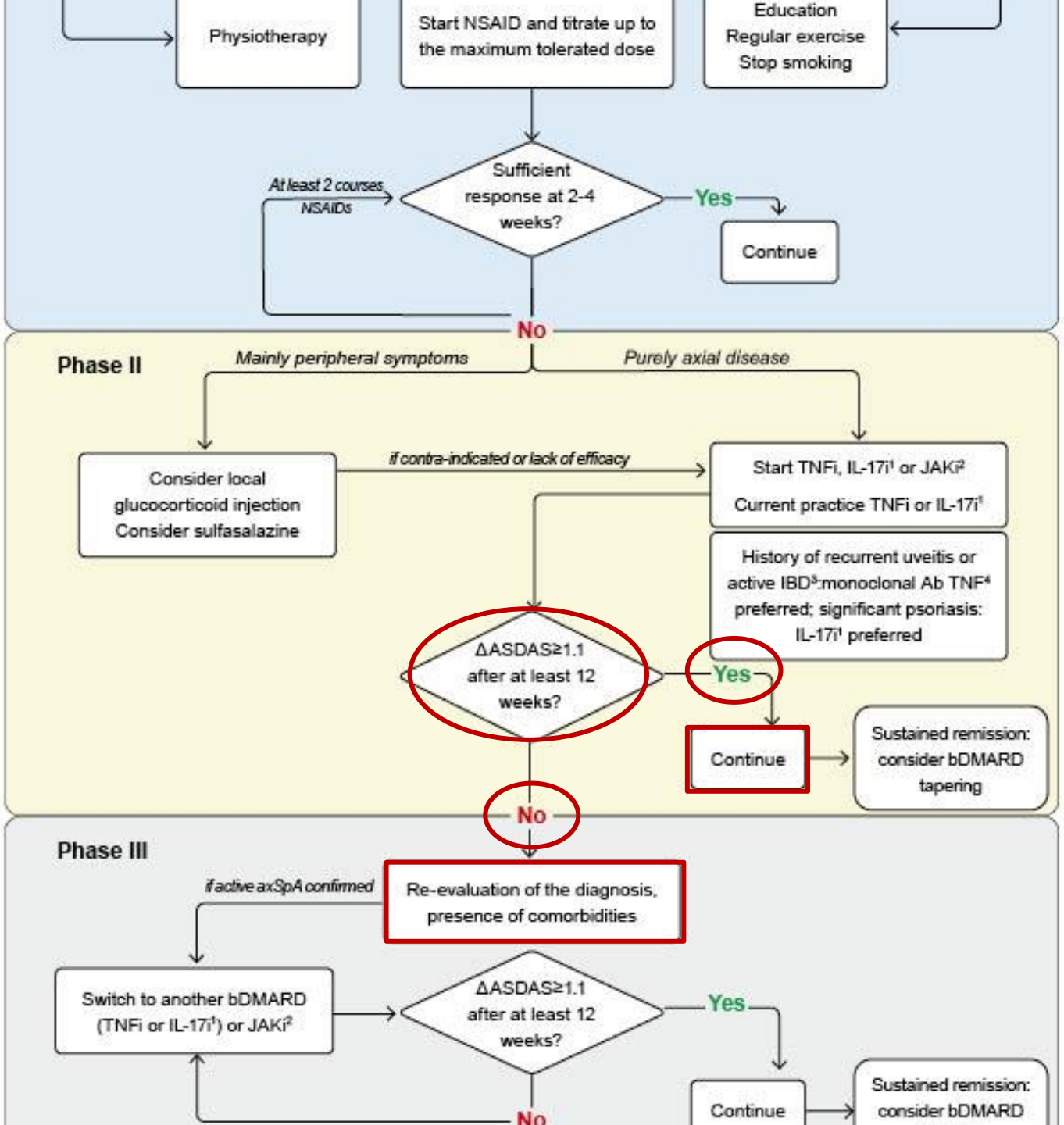

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Recommendation 11

		LoE / GoR	LoA (0-10)	% score ≥8
11#	Absence of response to treatment should trigger re-evaluation of the diagnosis and consideration of the presence of comorbidities	5 / D	9.5 (0.8)	97%

NEW

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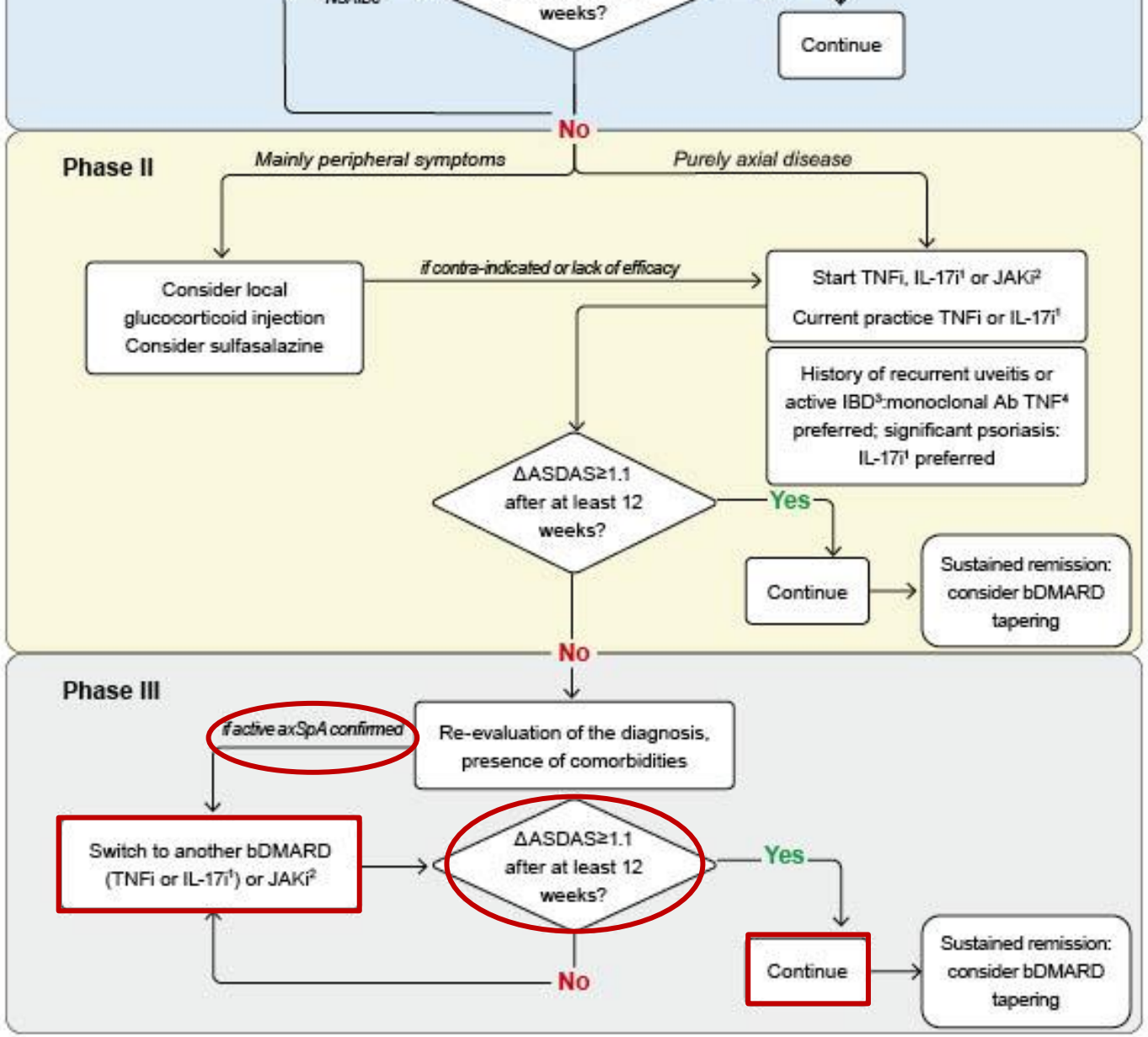

1. *IL-17i refers only to IL-17A-inhibitors*
2. *The following risk factors for cardiovascular events and malignancies must be considered when intending to prescribe a JAK-inhibitor: age over 65 years, history of current or past smoking, other cardiovascular risk factors, other risk factors for malignancy, risk factors for thromboembolic events.*
3. *In patients with active IBD, IL-17i are contraindicated*
4. *Monoclonal antibodies TNF include a pegylated Fab' fragment*

axSpA, axial spondyloarthritis; NSAIDs, non-steroidal anti-inflammatory drugs; ASDAS, ankylosing spondylitis disease activity score; TNFi, tumor necrosis factor inhibitor; IL17-i, interleukin-17 inhibitor, refers only to IL-17A-inhibitors; JAKi, Janus kinase inhibitor; IBD, inflammatory bowel disease; Ab, antibody; bDMARD, biological disease-modifying antirheumatic drug

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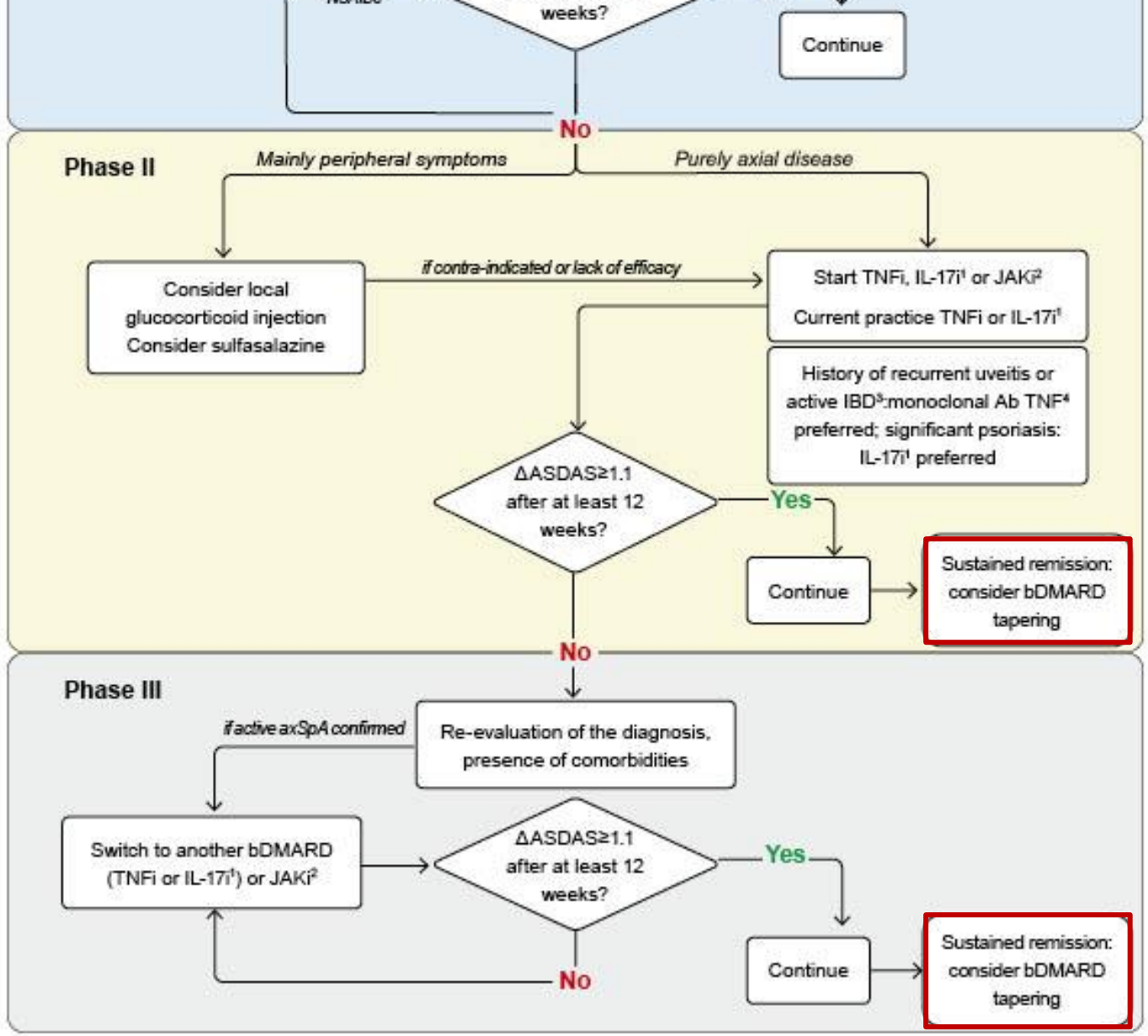

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Recommendations 12-13

		LoE / GoR	LoA (0-10)	% score ≥8
12±	Following a first b/tsDMARD failure, switching to another bDMARD (TNFi or IL-17i*) or a JAKi should be considered	2b / B (TNFi after TNFi failure) 1b / A (IL-17i after TNFi failure) 5 / D (all other switches)	9.3 (1.1)	88%

±significant updates; 13 unchanged
*IL-17i: refers only to IL-17A-inhibitors

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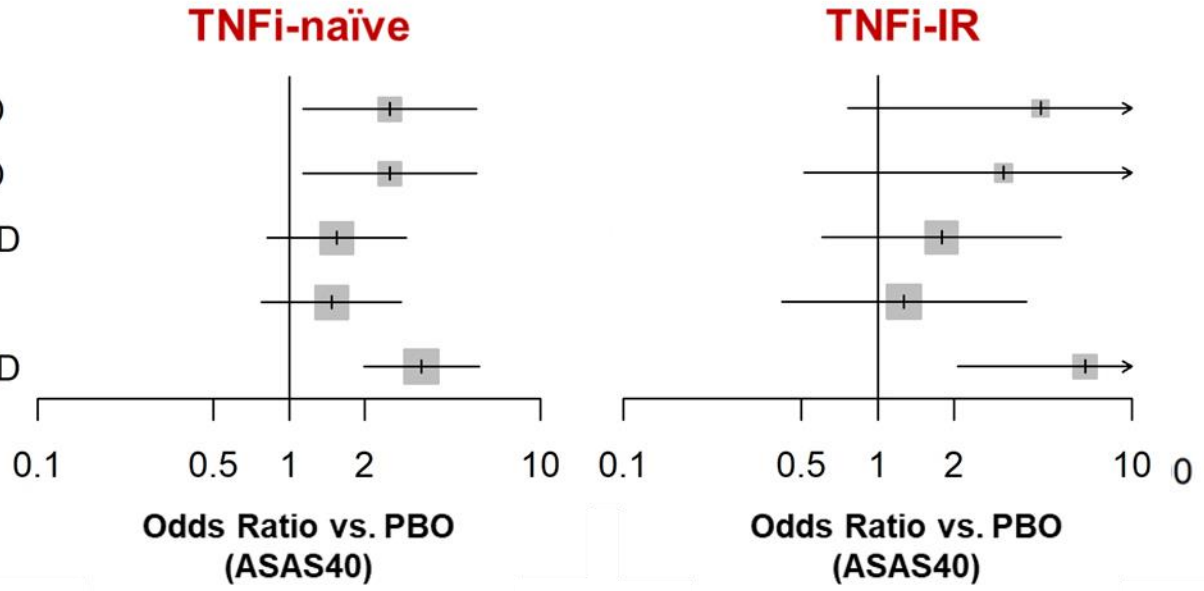
Secukinumab vs placebo – prior TNFi experience

New evidence: higher response rates compared to placebo in both TNFi-naïve and TNFi-IR in r-axSpA (non-significant in TNFi-IR) in 3 phase III trials (**low RoB** or **unclear RoB**).

Study	Intervention
Pavelka, 2017 (MEASURE 3)	Secukinumab 300mg Q4W with IV LD
Pavelka, 2017 (MEASURE 3)	Secukinumab 150mg Q4W with IV LD
Kivitz, 2018 (MEASURE 4)	Secukinumab 150mg Q4W with SC LD
Kivitz, 2018 (MEASURE 4)	Secukinumab 150mg Q4W NL
Huang, 2020 (MEASURE 5)	Secukinumab 150mg Q4W with SC LD



*Subgroup analyses by prior TNFi status (naïve or inadequate responder [IR]) were prespecified for all three studies.
Sample sizes of TNFi-naïve/TNFi-IR were:
MEASURE-3: 57/19 (SEC 300), 57/14 (SEC 150), 59/17 (Placebo)
MEASURE-4: 85/31 (SEC 150 LD), 85/32 (SEC 150 NL), 83/34 (Placebo)
MEASURE-5: 240/65 (SEC 150), 122/31 (Placebo)
†Randomisation was stratified according to previous TNFi therapy (naïve vs inadequate responder/intolerance [IR])

Secukinumab vs placebo – prior TNFi experience

New evidence: higher response rates compared to placebo in both TNFi-naïve and TNFi-IR in r-axSpA (non-significant in TNFi-IR) in 3 phase III trials (**low RoB** or **unclear RoB**).

	Study*	Interventions	Timepoint (weeks)	TNFi-naïve		TNFi-IR		RoB
				ASAS 20 %	ASAS 40 %	ASAS 20 %	ASAS 40 %	
r-axSpA	Pavelka 2017† Arthritis Res Ther [**MEASURE-3**]	SEC 300 Q4W IV LD	16	**64.9**	**43.9**	47.4	36.8	U
		SEC 150 Q4W IV LD		**63.2**	**43.9**	41.2	29.4	
		Placebo		39.0	23.7	29.4	11.8	
	Kivitz 2018† Rheumatol Ther [**MEASURE-4**]	SEC 150 Q4W LD	16	60.0	40.0	58.1	35.5	L
		SEC 150 Q4W NL		62.4	38.8	59.4	28.1	
		Placebo		49.4	30.1	41.2	23.5	
	Huang 2020 Chin Med J [**MEASURE-5**]	SEC 150 Q4W LD	16	**58.3**	**42.5**	**58.5**	**49.2**	L
		Placebo		36.9	18.0	35.5	12.9	

*Subgroup analyses by prior TNFi status (naïve or inadequate responder [IR]) were prespecified for all three studies.
Sample sizes of TNFi-naïve/TNFi-IR were:
MEASURE-3: 57/19 (SEC 300), 57/14 (SEC 150), 59/17 (Placebo)
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MEASURE-5: 240/65 (SEC 150), 122/31 (Placebo)
†Randomisation was stratified according to previous TNFi therapy (naïve vs inadequate responder/intolerance [IR])

Ixekizumab vs placebo – response

Previous SLR: no evidence on ixekizumab in axSpA
New evidence: efficacy demonstrated in r-axSpA (TNFi-naïve and TNFi-experienced) and nr-axSpA (TNFi-naïve) when compared to placebo in 3 phase III trials (n=3, **low RoB**)

	Study	Interventions	N	Timepoint (weeks)	Primary endpoint	ASAS 20 %	NNT	ASAS 40 %	NNT	RoB
r-axSpA	Van der Heijde 2018 Lancet [**COAST-V**] **TNFi-naïve**	IXE 80 Q2W IXE 80 Q4W ADA 40 Q2W Placebo	83 81 90 87	16	ASAS40 (+)	**69** **64** **59** 40	3.4 4.2 5.3	**52** **48** **36** 18	2.9 3.3 5.6	L
	Deodhar 2019 Arthritis Rheum [**COAST-W**] **TNFi-experienced**	IXE 80 Q2W IXE 80 Q4W Placebo	98 114 104	16	ASAS40 (+)	**46.9** **48.2** 29.8	5.8 5.4	**30.6** **25.4** 12.5	5.5 7.8	L
nr-axSpA	Deodhar 2020 Lancet [**COAST-X**] **TNFi-naïve**	IXE 80 Q2W IXE 80 Q4W Placebo	96 102 105	16	ASAS40 (+)	NR	NR	**40.2** **35.4** 19.0	4.7 6.1	L
				52	ASAS40 (+)	NR	NR	**31.4** **30.2** 13.3	5.5 5.9	

Switching after failure of one or more bDMARDs

Evidence of efficacy of a given drug (class) after failure of a previous one is very limited.

IL-17i have shown to be efficacious in TNFi-IR patients, also with a lower efficacy than in TNFi-naïve patients. No data of TNFi in JAKi-IR.

Data on JAKi in bDMARD-IR were not available at the time of the formulation of the recommendations. At EULAR 2022: similar efficacy of upadacitinib in bDMARD-IR.

Observational data suggest that a second TNFi can still be efficacious in TNFi-IR patients, although the level of efficacy may be lower than with the first TNFi.

Recommendations 12-13

		LoE / GoR	LoA (0-10)	% score ≥8
12±	Following a first b/tsDMARD failure, switching to another bDMARD (TNFi or IL-17i*) or a JAKi should be considered	2b / B (TNFi after TNFi failure) 1b / A (IL-17i after TNFi failure) 5 / D (all other switches)	9.3 (1.1)	88%
13	If a patient is in sustained remission, tapering of a bDMARD can be considered.	1a / B (TNFi), 5 / D (IL-17i)	9.1 (1.2)	82%

±significant updates; 13 unchanged
*IL-17i: refers only to IL-17A-inhibitors

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Recommendations 14-15

		LoE / GoR	LoA (0-10) % score ≥8	
14	Total hip arthroplasty should be considered in patients with refractory pain or disability and radiographic evidence of structural damage, independent of age; spinal corrective osteotomy in specialised centres may be considered in patients with severe disabling deformity.	4 / C	9.5 (0.8)	97%
15	If a significant change in the course of the disease occurs, causes other than inflammation, such as a spinal fracture, should be considered and appropriate evaluation, including imaging, should be performed.	5 / D	9.6 (0.9)	97%

All unchanged

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Conclusions: ASAS-EULAR axSpA recommendations 2022 Update

- 5 OAPs and 15 recommendations
- Entire spectrum of axSpA, non-pharmacological and pharmacological treatment
- Importance of non-pharmacological treatment
- NSAIDs remain 1st line pharmacological treatment
- Criteria for start of b/tsDMARDs
- ASDAS≥2.1 as the selected high disease activity criterion

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Conclusions: ASAS-EULAR axSpA recommendations 2022 Update

- Indication for b/tsDMARD: TNFi, IL-17i or JAKi; current practice to start with a TNFi or IL-17i
- EMMs guiding therapeutic decision: recurrent uveitis/IBD – TNF monoclonal antibodies preferred; significant psoriasis – IL-17i preferred
- Treatment failure triggering re-evaluation of the diagnosis and consideration of the presence of comorbidities
- If active axSpA confirmed: (any) switch to another b/tsDMARD
- Tapering of bDMARDs if sustained remission (no recommendation on tsDMARDs)

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THANK YOU

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Summary of the recommendations

		LoA (0-10)	% score ≥8
1	The treatment of patients with axSpA should be individualised according to the current signs and symptoms of the disease (axial, peripheral, extra-musculoskeletal manifestations) and the patient characteristics including comorbidities and psychosocial factors.	9.6 (0.8)	97%
2	Disease monitoring of patients with axSpA should include patient reported outcomes, clinical findings, laboratory tests and imaging, all with the appropriate instruments and relevant to the clinical presentation. The frequency of monitoring should be decided on an individual basis depending on symptoms, severity, and treatment.	9.5 (1.1)	97%
3	Treatment should be guided according to a predefined treatment target.	9.0 (1.2)	85%
4	Patients should be educated about axSpA and encouraged to exercise on a regular basis and stop smoking; physiotherapy should be considered.	9.8 (0.5)	100%
5	Patients suffering from pain and stiffness should use an NSAID as first line drug treatment up to the maximum dose, taking risks and benefits into account. For patients who respond well to NSAIDs continuous use is preferred if needed to control symptoms.	9.5 (0.8)	97%
6	Analgesics, such as paracetamol and opioid-(like) drugs, might be considered for residual pain after previously recommended treatments have failed, are contraindicated, and/or poorly tolerated.	8.9 (1.4)	79%
7	Glucocorticoid injections directed to the local site of musculoskeletal inflammation may be considered. Patients with axial disease should not receive long-term treatment with systemic glucocorticoids.	9.6 (0.8)	100%
8	Patients with purely axial disease should normally not be treated with csDMARDs; Sulfasalazine may be considered in patients with peripheral arthritis.	9.6 (0.9)	94%
9	TNFi, IL-17i* or JAKi^ should be considered in patients with persistently high disease activity despite conventional treatments; current practice is to start a TNFi or IL-17i*.	9.2 (1.2)	94%
10	If there is a history of recurrent uveitis or active IBD±, preference should be given to a monoclonal antibody against TNF**. In patients with significant psoriasis, an IL-17i* may be preferred.	9.1 (1.8)	97%
11	Absence of response to treatment should prompt re-evaluation of the diagnosis and consideration of the presence of comorbidities	9.5 (0.8)	97%
12	Following a first b/tsDMARD failure, switching to another bDMARD (TNFi or IL-17i*) or a JAKi^ should be considered	9.3 (1.1)	88%
13	If a patient is in sustained remission, tapering of a bDMARD can be considered.	9.1 (1.2)	82%
14	Total hip arthroplasty should be considered in patients with refractory pain or disability and radiographic evidence of structural damage, independent of age; spinal corrective osteotomy in specialised centres may be considered in patients with severe disabling deformity.	9.5 (0.8)	97%
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