Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

und

Schriftliche Beteiligung der wissenschaftlich-medizinischen Fachgesellschaften und der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2026-B-066-z Deucravacitinib

Stand: Juni 2026

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA	
Deucravacitinib **[Psoriasis-Arthritis bei Erwachsenen]** **Kriterien gemäß 5. Kapitel § 6 VerfO**	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	Siehe Übersicht „*II. Zugelassene Arzneimittel im Anwendungsgebiet*“.
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	nicht angezeigt
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	Beschlüsse über die Nutzenbewertung nach § 35a SGB V: • Apremilast (Beschluss vom 6. August 2015) • Secukinumab (Beschluss vom 2. Juni 2016) • Ixekizumab (Beschluss vom 16. August 2018) • Tofacitinib (Beschluss vom 21. Februar 2019) • Guselkumab (Beschluss vom 20. Mai 2021) • Upadacitinib (Beschluss vom 15. Juli 2021) • Risankizumab (Beschluss vom 19. Mai 2022) • Bimekizumab (Beschluss vom 21.12.2023) Therapiehinweise: • Leflunomid (Beschluss vom 16. August 2007, zuletzt geändert am 3. September 2008)
Die Vergleichstherapie soll nach dem allgemein anerkannten Stand der medizinischen Erkenntnisse zur zweckmäßigen Therapie im Anwendungsgebiet gehören.	*Siehe systematische Literaturrecherche*

II. Zugelassene Arzneimittel im Anwendungsgebiet

Wirkstoff **ATC-Code** **Handelsname**	**Anwendungsgebiet** (Text aus Fachinformation)
Zu bewertendes Arzneimittel:	
Deucravatinib L04AF07 Sotyktu	Monotherapie oder in Kombination mit Methotrexat (MTX) zur Behandlung Erwachsener mit aktiver Psoriasis-Arthritis (PsA), die auf ein oder mehrere krankheits-modifizierende Antirheumatika (DMARD) unzureichend angesprochen oder diese nicht vertragen haben
Klassische synthetische krankheitsmodifizierende Antirheumatika (csDMARD)	
Methotrexat L01BA01 generisch	[…] und der Psoriasis arthropathica. […]
Leflunomid L04AA13 generisch	Leflunomid (medac®) ist ein antirheumatisches Basistherapeutikum („disease modifying antirheumatic drug“ [DMARD]) zur Behandlung von Erwachsenen mit: • aktiver rheumatoider Arthritis. • aktiver Psoriasis-Arthritis (Arthritis psoriatica).
Biologische krankheitsmodifizierende Antirheumatika (bDMARD)	
TNF-alpha-Inhibitoren	
Etanercept L04AB01 Enbrel®	*Psoriasis-Arthritis (Arthritis psoriatica)* Behandlung der aktiven und progressiven Psoriasis-Arthritis bei Erwachsenen, wenn das Ansprechen auf eine vorhergehende Basistherapie unzureichend ist. Enbrel verbessert die körperliche Funktionsfähigkeit bei Patienten mit Psoriasis-Arthritis und reduziert das Fortschreiten der radiologisch nachweisbaren strukturellen Schädigungen der peripheren Gelenke bei Patienten mit polyartikulären symmetrischen Subtypen der Erkrankung.
Infliximab	*Psoriasis-Arthritis*

II. Zugelassene Arzneimittel im Anwendungsgebiet	
L04AB02 Remicade®/ Inflectra®	Remicade® ist indiziert zur Behandlung der aktiven und fortschreitenden Psoriasis-Arthritis bei erwachsenen Patienten, wenn deren Ansprechen auf eine vorhergehende krankheitsmodifizierende, antirheumatische Arzneimitteltherapie (DMARD-Therapie) unzureichend gewesen ist. Inflectra™ sollte verabreicht werden • in Kombination mit Methotrexat • oder als Monotherapie bei Patienten, die eine Unverträglichkeit gegenüber Methotrexat zeigen oder bei denen Methotrexat kontraindiziert ist. Infliximab verbessert die körperliche Funktionsfähigkeit bei Patienten mit Psoriasis-Arthritis und reduziert die Progressionsrate peripherer Gelenkschaden, wie radiologisch bei Patienten mit polyartikularem symmetrischem Subtyp der Krankheit belegt wurde.
Adalimumab L04AB04 Humira®	*Psoriasis-Arthritis* Humira ist indiziert zur Behandlung der aktiven und progressiven Psoriasis-Arthritis (Arthritis psoriatica) bei Erwachsenen, die nur unzureichend auf eine vorherige Basistherapie angesprochen haben. Humira reduziert das Fortschreiten der radiologisch nachweisbaren strukturellen Schädigungen der peripheren Gelenke bei Patienten mit polyartikularen symmetrischen Subtypen der Erkrankung und verbessert die körperliche Funktionsfähigkeit.
Golimumab L04AB06 Simponi®	*Psoriasis-Arthritis (PsA)* Simponi ist zur Anwendung als Monotherapie oder in Kombination mit MTX zur Behandlung der aktiven und fortschreitenden Psoriasis-Arthritis bei Erwachsenen indiziert, wenn das Ansprechen auf eine vorhergehende Therapie mit krankheitsmodifizierenden Antirheumatika (DMARD) unzureichend gewesen ist. Simponi verringert nachweislich die Progressionsrate der peripheren Gelenkschäden, bestimmt anhand von Röntgenaufnahmen bei Patienten mit polyartikulären symmetrischen Subtypen der Erkrankung und verbessert die körperliche Funktionsfähigkeit.
Certolizumab Pegol L04AB05 Cimzia®	*Psoriasis-Arthritis* Cimzia ist in Kombination mit Methotrexat (MTX) für die Behandlung der aktiven Psoriasis-Arthritis bei Erwachsenen angezeigt, wenn das vorherige Ansprechen auf eine Therapie mit DMARDS ungenügend war. In Fällen von Unverträglichkeit gegenüber Methotrexat oder wenn die Fortsetzung der Behandlung mit Methotrexat ungeeignet ist, kann Cimzia als Monotherapie verabreicht werden.
Interleukin-Inhibitoren	
Bimekizumab L04AC21 Bimzelx®	*Psoriasis-Arthritis* Bimzelx wird allein oder in Kombination mit Methotrexat zur Behandlung erwachsener Patienten mit aktiver Psoriasis-Arthritis angewendet, die auf ein oder mehrere krankheitsmodifizierende Antirheumatika (disease-modifying antirheumatic drugs, DMARDs) unzureichend angesprochen oder diese nichtvertragen haben.
Ustekinumab L04AC05 Stelara®	*Psoriatische Arthritis (PsA)* STELARA ist allein oder in Kombination mit MTX für die Behandlung der aktiven psoriatischen Arthritis bei erwachsenen Patienten indiziert, wenn das Ansprechen auf eine vorherige nicht-biologische krankheitsmodifizierende antirheumatische (DMARD) Therapie unzureichend gewesen ist.

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Ixekizumab L04AC13 Taltz®	Ixekizumab, allein oder in Kombination mit Methotrexat, ist angezeigt für die Behandlung erwachsener Patienten mit aktiver Psoriasis-Arthritis, die unzureichend auf eine oder mehrere krankheitsmodifizierende Antirheumatika (DMARD) angesprochen oder diese nicht vertragen haben.
Secukinumab L04AC10 Cosentyx®	*Psoriasis-Arthritis (PsA)* Cosentyx, allein oder in Kombination mit Methotrexat (MTX), ist angezeigt für die Behandlung erwachsener Patienten mit aktiver Psoriasis-Arthritis, wenn das Ansprechen auf eine vorhergehende Therapie mit krankheitsmodifizierenden Antirheumatika (DMARD) unzureichend gewesen ist.
Guselkumab L04AC16 Tremfya®	*Psoriasis-Arthritis* Tremfya, als Monotherapie oder in Kombination mit Methotrexat (MTX), ist für die Behandlung der aktiven Psoriasis-Arthritis bei erwachsenen Patienten indiziert, die auf eine vorangegangene krankheitsmodifizierende antirheumatische (disease-modifying antirheumatic drug, DMARD) Therapie unzureichend angesprochen oder diese nicht vertragen haben (siehe Abschnitt 5.1).
Risankizumab L04AC18 Skyrizi®	Skyrizi allein oder in Kombination mit Methotrexat (MTX) wird angewendet zur Behandlung erwachsener Patienten mit aktiver Psoriasis-Arthritis, die auf ein oder mehrere krankheitsmodifizierende Antirheumatika (disease-modifying antirheumatic drugs, DMARDs) unzureichend angesprochen oder diese nicht vertragen haben.
JAK-Inhibitoren	
Tofacitinib L04AA29 XELJANZ®	Tofacitinib ist in Kombination mit MTX indiziert zur Behandlung der aktiven Psoriasis-Arthritis (PsA) bei erwachsenen Patienten, die auf eine vorangegangene krankheitsmodifizierende antirheumatische DMARD-Therapie unzureichend angesprochen oder diese nicht vertragen haben. *<u>Anwendung bei Patienten über 65 Jahre</u>* *Angesichts des erhöhten Risikos für schwere Infektionen, Myokardinfarkt und Malignome im Zusammenhang mit Tofacitinib bei Patienten über 65 Jahre sollte Tofacitinib bei diesen Patienten nur angewendet werden, wenn keine geeigneten Behandlungsalternativen zur Verfügung stehen (siehe weitere Einzelheiten in Abschnitt 4.4 und Abschnitt 5.1).*
Upadacitinib L04AA44 Rinvoq®	*Psoriasis-Arthritis* RINVOQ wird angewendet zur Behandlung der aktiven Psoriasis-Arthritis bei erwachsenen Patienten, die auf ein oder mehrere DMARDs unzureichend angesprochen oder diese nicht vertragen haben. RINVOQ kann als Monotherapie oder in Kombination mit Methotrexat angewendet werden.
Weitere	
Abatacept L04AA24	*Psoriasis-Arthritis* ORENCIA ist allein oder in Kombination mit Methotrexat (MTX) indiziert zur Behandlung der aktiven Psoriasis-Arthritis (PsA) bei erwachsenen Patienten, die

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Orencia®	unzureichend auf vorangegangene DMARDs einschließlich Methotrexat ansprachen und für die eine zusätzliche systemische Therapie für psoriatische Hautläsionen nicht notwendig ist.
Apremilast L04AA32 Otezla®	*Psoriasis-Arthritis* Otezla allein oder in Kombination mit krankheitsmodifizierenden antirheumatischen Arzneimitteln (DMARDs) ist indiziert zur Behandlung der aktiven Psoriasis-Arthritis (PsA) bei erwachsenen Patienten, die auf eine vorangegangene DMARD-Therapie unzureichend angesprochen oder diese nicht vertragen haben.
Steroidale Antirheumatika (Glucokortikoide)	
Prednisolon H02AB06 generisch	• andere entzündlich-rheumatische Arthritiden, sofern die Schwere des Krankheitsbildes es erfordert und nicht-steroidale Antirheumatika (NSARs) nicht angewandt werden können: – Spondarthritiden (Spondylitis ankylosans mit Beteiligung peripherer Gelenke (DS b, c), Arthritis psoriatica (DS c, d), enteropathische Arthropathie mit hoher Entzündungsaktivität (DS a)
Prednison H02AB07 generisch	Andere entzündlich-rheumatische Arthritiden, sofern die Schwere des Krankheitsbildes es erfordert und nicht-steroidale Antirheumatika (NSARs) nicht angewandt werden können: – Spondarthritiden (Spondylitis ankylosans mit Beteiligung peripherer Gelenke (DS b, c), Arthritis psoriatica (DS c, d), enteropathische Arthropathie mit hoher Entzündungsaktivität (DS a)
Triamcinolon H02AB08 Volon®	Andere entzündlich-rheumatische Arthritiden, sofern die Schwere des Krankheitsbildes es erfordert und nicht-steroidale Antirheumatika (NSARs) nicht angewandt werden können: Spondarthritiden (Spondylitis ankylosans mit Beteiligung peripherer Gelenke, Arthritis psoriatica, enteropathische Arthropathie mit hoher Entzündungsaktivität);
Nichtsteroidale Antirheumatika (NSAR oder NSAID)	
z. B. Acemetacin M01AB11 generisch	Acemetacin 60 Heumann zusätzlich bei: – akuten Arthritiden (einschließlich Gichtanfall) – chronischen Arthritiden, insbesondere bei rheumatoider Arthritis (chronische Polyarthritis), (Acemetacin Heumann FI, Stand April 2015)

Quellen: AMIce-Datenbank, Fachinformationen

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie

Vorgang: 2026-B-066-z (Beratung nach § 35a SGB V) Deucravacitinib

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	7. Mai 2026

Inhaltsverzeichnis

Abkürzungsverzeichnis

ACR	American College of Rheumatology
AE	Adverse event
AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
bDMARD	Biological disease-modifying antirheumatic drug
CDAI	Clinical Disease Activity Index
csDMARD	Conventional synthetic disease-modifying antirheumatic drug
CTLA	Cytotoxic T-lymphocyte-associated Protein
CVE	cardiovascular event
DAHTA	Deutsche Agentur für Health Technology Assessment
DAS28	Disease Activity Score 28
DMARD	Disease-modifying antirheumatic drug
DSS	Dactylitis Severity Score
EDF	European Dermatology Forum
EULAR	European League Against Rheumatism
FACIT-F	Functional Assessment of Chronic Illness Therapy–Fatigue
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
GRAPPA	Group for Research and Assessment of Psoriasis and Psoriatic Arthritis
HAQ-DI	Health Assessment Questionnaire Disability Index
HR	Hazard Ratio
IBD	Inflammatory bowel disease
IFPA	Global leader in fighting psoriatic disease
IL	Interleukin
IMIDs	Immune-mediated inflammatory diseases
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
JAK	Januskinase-Inhibitoren
JAKi	JAK inhibitor
KI	Konfidenzintervall
LDI	Leeds Dactylitis Index
LEI	Leeds Enthesitis Index
LoE	Level of Evidence
MASES	Maastricht Ankylosing Spondylitis Enthesitis Score
MCID	Minimal clinically important difference

MDA	Minimal disease activity
MHAQ	Modified Health Assessment Questionnaire
MTX	Methotrexat
NGC	National Guideline Clearinghouse
NHS CRD	National Health Services Center for Reviews and Dissemination
NICE	National Institute for Health and Care Excellence
NMA	Netzwerk Meta-Analyse
NOS	Newcastle-Ottawa scale
NPF	National Psoriasis Foundation
NSAID	Non-steroidal anti-inflammatory drugs
OAP	Overarching principles
OR	Odds Ratio
PARS	Psoriatic Arthritis Ratingen Score
PASI	Psoriasis Area Severity Index
PDE	Phosphodiesterase
PsA	Psoriasis Arthritis
PSAQOL	Psoriatic Arthritis Quality of Life
PsARC	Psoriatic Arthritis Response Criteria
PSORIQOL	Psoriasis Index of Quality of Life
P-Y	Patient years
QD	Once daily
RoB	Risk of bias
RR	Relatives Risiko
SAE	Serious adverse event
SIGN	Scottish Intercollegiate Guidelines Network
sPGA	Physician's Global Assessment Scale
TNF	Tumor necrosis factor
TRIP	Turn Research into Practice Database
tsDMARD	Targeted synthetic disease-modifying antirheumatic drug
VAS	Visual analogue scale
vdH-S	van der Heijde-Sharp score
WAEs	Withdrawals due to adverse events
WHO	World Health Organization

1 Indikation

Erwachsene mit aktiver Psoriasis-Arthritis (PsA), die auf ein oder mehrere krankheitsmodifizierende Antirheumatika (DMARD) unzureichend angesprochen oder diese nicht vertragen haben

Hinweis zur Synopse: „Informationen hinsichtlich nicht zugelassener Therapieoptionen sind über die vollumfängliche Darstellung der Leitlinienempfehlungen dargestellt“.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zur Indikation *Psoriasis-Arthritis (PsA)*, durchgeführt und nach PRISMA-S dokumentiert [A]. Die Recherchestrategie wurde vor der Ausführung anhand der PRESS-Checkliste begutachtet [B]. Es erfolgte eine Datenbankrecherche ohne Sprachrestriktion in: *The Cochrane Library (Cochrane Database of Systematic Reviews), PubMed*. Die Recherche nach grauer Literatur umfasste eine gezielte, iterative Handsuche auf den Internetseiten von Leitlinienorganisationen. Ergänzend wurde eine freie Internetsuche (*https://www.startpage.com*) unter Verwendung des privaten Modus, nach aktuellen deutsch- und englischsprachigen Leitlinien durchgeführt.

Der Suchzeitraum der systematischen Literaturrecherche wurde auf die letzten fünf Jahre eingeschränkt und die Recherchen am 15.04.2026 abgeschlossen. Die detaillierte Darstellung der Recherchestrategie inkl. verwendeter Suchfilter sowie eine Auflistung durchsuchter Leitlinienorganisationen ist am Ende der Synopse aufgeführt. Mit Hilfe von EndNote wurden Dubletten identifiziert und entfernt. Die Recherchen ergaben insgesamt 760 Referenzen.

In einem zweistufigen Screening wurden die Ergebnisse der Literaturrecherche bewertet. Im ersten Screening wurden auf Basis von Titel und Abstract nach Population, Intervention, Komparator und Publikationstyp nicht relevante Publikationen ausgeschlossen. Dabei wurde für systematische Reviews, inkl. Meta-Analysen, ein Publikationszeitraum von 2 Jahren und für Leitlinien von 5 Jahren betrachtet. Zudem wurde eine Sprachrestriktion auf deutsche und englische Referenzen vorgenommen. Alle eingeschlossenen Referenzen wurden im Volltext beschafft. Im zweiten Screening wurden die im ersten Screening eingeschlossenen Publikationen im Volltext gesichtet und auf ihre Relevanz und methodische Qualität geprüft. Dafür wurden dieselben Kriterien wie im ersten Screening sowie Kriterien zur methodischen Qualität der Evidenzquellen verwendet.

Basierend darauf, wurden insgesamt elf Referenzen eingeschlossen. Es erfolgt eine synoptische Darstellung wesentlicher Inhalte der identifizierten Referenzen.

3 Ergebnisse

3.1 Cochrane Reviews

Cagnotto G et al., 2025 [1].

(assessed as up to 28 March 2024)

Tumor necrosis factor (TNF) inhibitors for psoriatic arthritis (Review)

Fragestellung

To assess the benefits and harms of TNFi in adults with psoriatic arthritis.

Methodik

Population:

- adults aged 18 years or older with a diagnosis of psoriatic arthritis made by a rheumatologist, or by fulfilment of validated classification criteria (e.g. 'classification of psoriatic arthritis' (CASPAR) criteria)

Intervention:

- We included trials comparing TNFi alone or in combination with csDMARDs, tsDMARDs, or other bDMARDs
- We allowed co-intervention with NSAIDs or other analgesics, provided they were used in all treatment arms.
- We only considered TNFi dosing regimens that are recommended or approved for the treatment of psoriatic arthritis (D'Angelo 2017).
  - Adalimumab: 40 mg subcutaneously once every other week.
  - Certolizumab: 400 mg subcutaneously at weeks 0, 2, 4. Thereafter, 200 mg subcutaneously once every other week or 400 mg subcutaneously once every 4 weeks.
  - Etanercept: 50 mg subcutaneously once a week or 25 mg subcutaneously twice a week.
  - Golimumab: 50 mg subcutaneously once a month, 100 mg subcutaneously once a month, or 2 mg/kg intravenously at weeks 0, 4, and every 8 weeks thereafter.
  - Infliximab: 5 mg/kg intravenously at weeks 0, 2, 6, and every 8 weeks thereafter.
  - We only considered comparators at a dosage recommended or approved for the treatment of psoriatic arthritis.

Komparator:

- placebo;
- physiotherapy;
- NSAIDs;
- oral or intra-articular corticosteroids;
- csDMARDs (cyclosporine, leflunomide, methotrexate, sulfasalazine)

Endpunkte:

- The chosen outcomes explored all the domains of the psoriatic arthritis Core Domain Set, which has recently been updated by the Outcome Measures in Rheumatology initiative (OMERACT) (Orbai 2017)

- Major outcomes - Time points for outcome assessment: 12, 24, and 52 weeks after study entry.
  - 1. Clinical improvement as measured by the ACR50 response criteria or the EULAR good response criteria.
  - 2. Disease activity as measured by MDA-PsA criteria, DAS28, or DAS.
  - 3. Physical function as measured by the HAQ, the proportion of participants achieving the MCID of the HAQ (defined as 0.35), or the MHAQ.
  - 4. Health-related quality of life as measured by the SF-36 or the PSAQOL.
  - 5. Radiographic progression according to the Sharp/Van der Heijde method modified for psoriatic arthritis, the Sharp scoring method modified for psoriatic arthritis, the Psoriatic Arthritis Ratingen Score, or the modified Steinbroker method.
  - 6. Serious adverse events resulting in hospitalization, disability, or death.
  - 7. Withdrawals due to adverse events.
- Minor outcomes - Time points for outcome assessment: 12, 24, and 52 weeks after study entry.
  - 1. Clinical improvement as measured by ACR20 response criteria, the EULAR moderate response criteria, or the PsARC criteria.
  - 2. Improvement in enthesitis in participants with enthesitis at baseline as measured by the LEI or the MASES.
  - 3. Improvement in dactylitis in participants with dactylitis at baseline as measured by a simple quantitative scoring of dactylitis, the LDI, or the LDI basic.
  - 4. Improvement in pain as measured by VAS or NRS.
  - 5. Improvement in psoriasis in participants with psoriasis at baseline as measured by the PASI75 response.
  - 6. Improvement in fatigue as measured by FACIT-F scale or by the FATIGUE VAS.

Recherche/Suchzeitraum:

- Cochrane Central Register of Controlled Trials (CENTRAL; Wiley Cochrane Library), 28 March 2024;
- MEDLINE (PubMed), from inception to 28 March 2024;
- Embase (Embase.com), from inception to 28 March 2024;
- Cumulative Index to Nursing and Allied Health Literature (CINAHL; CINAHL Complete via EBSCOhost), 28 January 2022.
- For assessments of adverse ePects, we searched the websites of the regulatory agencies US Food and Drug Administration-MedWatch), European Medicines Evaluation Agency , Australian Adverse Drug Reactions Bulletin, and UK Medicines and Healthcare products Regulatory Agency (MHRA) pharmacovigilance and drug safety updates.
- ClinicalTrials.gov (www.ClinicalTrials.gov) and the World Health Organization (WHO) clinical trials portal
- […] searched all databases from their inception, and we imposed no restrictions on language of publication

Qualitätsbewertung der Studien:

- risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*

Ergebnisse

Anzahl eingeschlossener Studien:

- We included 25 RCTs randomizing 7857 participants (Antoni 2005a, Antoni 2005b; Araujo 2019; Atteno 2010; Baranauskaite 2012; Corrado 2017; Genovese 2007; Ikonomidis 2013; Kavanaugh 2009; Kavanaugh 2017; McInnes 2020; McInnes 2021; McInnes 2023; Mease 2000; Mease 2004; Mease 2005; Mease 2014; Mease 2017a; Mease 2017b; Mease 2018; Mease 2019; Mease 2020; Torii 2010; Van Mens 2019; Vieira-Sousa 2020).
- In csDMARD-inadequate responders, 11 studies compared TNFi to placebo; four studies compared TNFi to placebo and ixekizumab, bimekizumab, tofacitinib, or upadacitinib; and three studies compared TNFi to ixekizumab, secukinumab, and ustekinumab. Two studies compared different TNFi.
- We found no studies with b/tsDMARD-inadequate responders (b/tsDMARD-IR). No studies compared TNFi to NSAIDs, corticosteroids, or physiotherapy.

Charakteristika der Population/Studien:

Table 2. Study characteristics (csDMARD-inadequate responders)

Study	N[a]	Classification criteria	Intervention	Comparison of interest	Available outcomes
Genovese 2007	102	PsO or history of PsO and arthritis	ADA 40 mg	PBO	ACR50, HAQ, SF-36, SAEs, withdrawal due to AEs, VAS pain, dactylitis, fatigue FACIT-F
McInnes 2020	853	CASPAR	ADA 40 mg	SEC 300 mg	ACR50, MDA, HAQ, safety, ACR 20, LEI, dactylitis, PASI 75
McInnes 2021	1282	CASPAR	ADA 40 mg	1) PBO 2) UPA 15 mg	ACR50, MDA, HAQ, SF-36, SAEs, Sharp/VdH score, withdrawals due to AEs, ACR20, LEI, dactylitis, VAS pain, PASI75, fatigue FACIT-F
McInnes 2023	852	CASPAR	ADA 40 mg	1) PBO 2) BKZ 160 mg	ACR50, MDA, HAQ, Sharp/VdH score, SAEs, withdrawal due to AEs, ACR20, LEI, dactylitis, VAS pain, PASI75, fatigue FACIT-F
Mease 2005	313	PsO or history of PsO and arthritis	ADA 40 mg	PBO	ACR50, HAQ, SF-36, modified Sharp score, safety, ACR20, VAS pain, PASI75, fatigue FACIT-F
Mease 2017a	314	CASPAR	ADA 40 mg	1) PBO 2) IXE 80 mg every 4 weeks	ACR50, MDA, HAQ, SF-36, Sharp/VdH score, safety, ACR20, LEI, dactylitis, VAS pain, PASI75
Mease 2017b	318	CASPAR	ADA 40 mg + csDMARD	1) PBO + csDMARD 2) TOF 5 mg + csDMARD	ACR50, MDA, HAQ, SF-36, Sharp/VdH score, safety, ACR20, LEI, dactylitis, VAS pain, PASI75, fatigue FACIT-F
Mease 2018	96	CASPAR	ADA 40 mg + MTX	MTX + PBO	ACR50, MDA, safety, ACR20, PASI75
Mease 2020	566	CASPAR	ADA 40 mg	IXE 80 mg	ACR50, MDA, HAQ, SF-36, safety, ACR20, LEI, dactylitis, VAS pain, PASI75
Mease 2014	409	CASPAR	CTZ 200 mg every 2 or 4 weeks	PBO	ACR50, MDA, HAQ, SF-36, Sharp/VdH score, safety, ACR20, LEI, dactylitis, VAS pain, PASI75

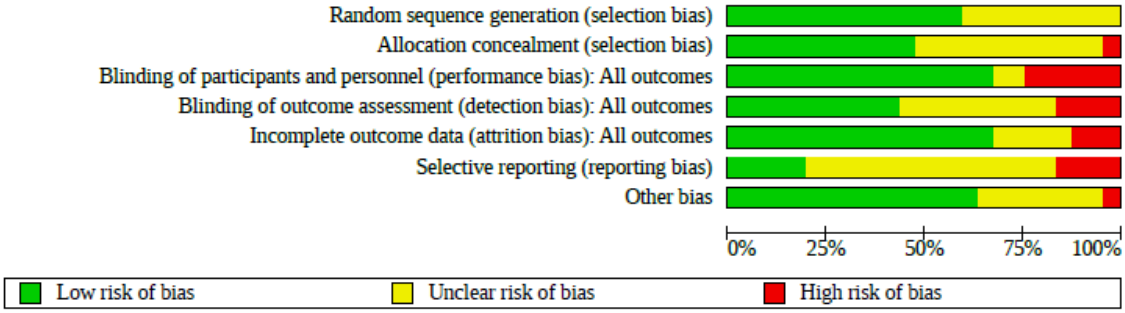
Table 2. Study characteristics (csDMARD-inadequate responders) *(Continued)*

Mease 2000	60	Clinical diagnosis	ETN 25 mg (twice a week)	PBO	ACR50, safety, ACR20, PASI75
Mease 2004	205	Moll and Wright	ETN 25 mg (twice a week)	PBO	ACR50, HAQ, SF-36, modified Sharp score, safety, ACR20, pain on 10-point Lickert scale, PASI75
Kavanaugh 2009	405	Moll and Wright	GOL 50 mg and 100 mg	PBO	ACR50, MDA, HAQ, SF-36, Sharp/VdH score, safety, ACR20, PASI75
Kavanaugh 2017	480	CASPAR	GOL 2 mg/kg iv	PBO	ACR50, MDA, HAQ, SF-36, Sharp/VdH score, safety, ACR20, LEI, dactylitis, PASI75, fatigue FACIT-F
Antoni 2005a	104	Clinical diagnosis	IFX 5 mg/kg	PBO	ACR50, HAQ, safety, ACR20, dactylitis, VAS pain, PASI75
Antoni 2005b	200	Clinical diagnosis	IFX 5 mg/kg	PBO	ACR50, HAQ, SF-36, Sharp/VdH score, safety, ACR20, VAS pain, PASI75
Torii 2010	6	Clinical diagnosis	IFX 5 mg/kg	PBO	ACR20
Atteno 2010	100	CASPAR	TNFi	TNFi	ACR 20
Araujo 2019	47	CASPAR	TNFi	UST 45 or 90 mg	MDA, safety, LEI
Corrado 2017	64	CASPAR	TNFi + MTX + steroids	TNFi + MTX + steroids	None

Qualität der Studien:

- The overall quality of the studies was suboptimal (Figure 3; Figure 4). Performance, detection, and reporting bias are the domains more frequently affected by high risk of bias. Random sequence generation was the only domain where no studies had a high risk of bias.

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies



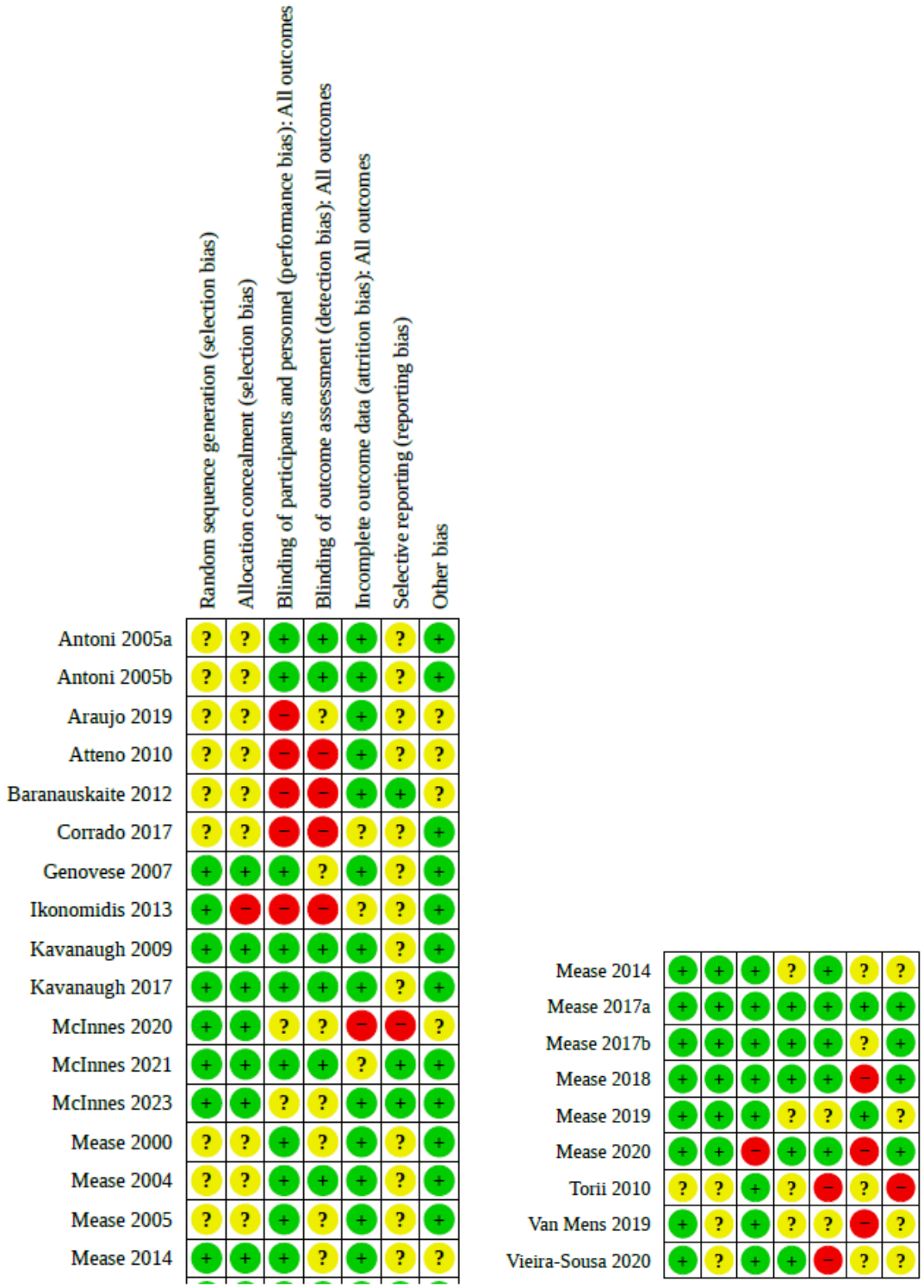


Figure 4. _ Risk of bias summary: review authors' judgements about each risk of bias item for each included study

Studienergebnisse:

Comparison 1. TNFi (monotherapy or combined with csDMARDs) versus placebo

Summary of findings 1. TNFi (monotherapy or combined with csDMARDs) versus placebo

TNFi (monotherapy or combined with csDMARDs) compared with placebo for psoriatic arthritis

Patient or population: participants with psoriatic arthritis

Settings: outpatients

Intervention: TNFi

Comparison: placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk with placebo	Corresponding risk with TNFi				
Clinical improvement by ACR50 response criteria Follow-up: 12 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD inadequate responders					
	77 per 1000	**436 per 1000** (308 to 616)	**RR 5.63** (3.98 to 7.96)	4067 (14 studies)	⊕⊕⊕⊖ **Moderate**[a]	TNFi probably result in a large clinical improvement.
	b/tsDMARD inadequate responders					
	No studies reported this outcome in this population.					
Disease activity as measured by MDA-PsA criteria Follow-up: 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD inadequate responders					
	93 per 1000	**351 per 1000** (223 to 553)	**RR 3.76** (2.39 to 5.92)	2353 (5 studies)	⊕⊕⊕⊖ **Moderate**[a]	TNFi probably result in a higher proportion of participants in minimal disease activity.
	b/tsDMARD inadequate responders					
	No studies reported this outcome in this population.					
Physical function Change from baseline (HAQ: 0 to 3 scale, 0 = no function impairment, MCID = 0.35) Follow-up: 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD inadequate responders					
	Mean change in function **-0.14**[b]	**0.33 lower** (0.41 lower to 0.25 lower)		2949 (8 studies)	⊕⊕⊖⊖ **Low**[c]	TNFi may result in a slight improvement in physical function.
	b/tsDMARD inadequate responders					
	No studies reported this outcome in this population.					
Health-related quality of life Change from baseline (SF-36 MCS: 0 to 100 scale, 100 = best score, MCID = 1.7) Follow-up: 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD inadequate responders					
	Mean change in health-related quality of life **2.4**[b]	**3.29 higher** (2.18 higher to 4.40 higher)		2928 (8 studies)	⊕⊕⊕⊖ **Moderate**[a]	TNFi probably result in a clinically important improvement in health-related quality of life.
	b/tsDMARD inadequate responders					
	No studies reported this outcome in this population.					
Radiographic progression Change from baseline (Sharp/Van der Heijde modified for PsA: 0 to 528 scale, 0 = no radiographic damage) Follow-up: 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD inadequate responders					
	Mean change in radiographic progression **0.25**[b]	**0.37 lower** (0.48 lower to 0.25 lower)		2478 (7 studies)	⊕⊕⊕⊖ **Moderate**[a]	TNFi probably result in a slight reduction of radiographic progression.
	b/tsDMARD inadequate responders					

	No studies reported this outcome in this population.					
Number of participants with serious adverse events at any time Follow-up: up to 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD inadequate responders					
	31 per 1000	**31 per 1000** (21 to 44)	**RR 1.00** (0.70 to 1.42)	3866 (13 studies)	⊕⊕⊖⊖ **Low**[d]	TNFi may result in little to no difference in the number of serious adverse events.
	b/tsDMARD inadequate responders No studies reported this outcome in this population.					
Withdrawals due to adverse events at any time Follow-up: up to 24 weeks	**DMARD-naïve** No studies reported this outcome in this population.					
	csDMARD inadequate responders					
	18 per 1000	**28 per 1000** (18 to 42)	**RR 1.53** (1.01 to 2.33)	4066 (14 studies)	⊕⊖⊖⊖ **Low**[e]	TNFi may result in a slight increase in withdrawals due to adverse events.
	b/tsDMARD inadequate responders					
	No studies reported this outcome in this population.					

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
ACR50: American College of Rheumatology response criteria for 50% improvement; **bDMARD**: biologic DMARD; **CI:** confidence interval; **csDMARD**: conventional synthetic DMARD; **DMARD**: disease modifying anti-rheumatic drug; **HAQ**: Health Assessment Questionnaire; **MCID:** minimal clinically important difference; **MDA-PsA**: Minimal Disease Activity-PsA; **RR:** risk ratio; **SF-36 PCS**: Short Form Health Survey 36-item physical component score; **TNFi:** tumour necrosis factor inhibitors; **tsDMARD**: targeted synthetic DMARD

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[d]Downgraded one level for study limitations: uncertain risk of bias in most of the included studies.
[b]Control group risk was estimated from the mean placebo value at follow-up from McInnes 2021 for function: mean change -0.14 on HAQ (0 to 3 scale, 0 = no function impairment); quality of life: mean change 2.4 (SF-36 MCS: 0 to 100 scale, 100 = best score); for radiographic progression: mean change -0.25 on Sharp/Van der Heijde modified for PsA scale (0 to 528 scale, 0 = no radiographic damage).
[c]Downgraded one level for study limitations: uncertain risk of bias in most of the included studies. Downgraded one level for imprecision: the 95% CI crosses the threshold of clinically important difference.
[d]Downgraded one level for study limitations: uncertain risk of bias in most of the included studies. Downgraded one level for imprecision: wide confidence interval including a potential benefit and a potential harm.
[e]Downgraded one level for study limitations: uncertain risk of bias in most of the included studies. Downgraded one level for imprecision: wide confidence interval including a potential benefit and a potential harm.

Comparison 2. TNFi (monotherapy or combined with csDMARDs) versus csDMARDs

Summary of findings 2. TNF inhibitors (monotherapy or combined with csDMARDs) versus csDMARD

TNFi (monotherapy or combined with csDMARDs) compared with csDMARDs for psoriatic arthritis

Patient or population: participants with psoriatic arthritis

Settings: outpatients

Intervention: TNFi

Comparison: csDMARD (methotrexate)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk with csDMARDs	Corresponding risk with TNFi				
Clinical improvement by ACR50 response criteria Follow-up: 12 weeks	**DMARD-naïve**					
	187 per 1000	**429 per 1000** (343 to 535)	**RR 2.29** (1.83 to 2.86)	1061 (4 studies)	⊕⊕⊕⊖ **Moderate**[a]	TNFi probably result in a large clinical improvement.
	csDMARD-inadequate responders					
	No studies reported this outcome in this population.					
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Disease activity as measured by MDA-PsA criteria Follow-up: 24 weeks	**DMARD-naïve**					
	244 per 1000	**403 per 1000** (320 to 507)	**RR 1.65** (1.31 to 2.08)	946 (3 studies)	⊕⊕⊕⊖ **Moderate**[a]	TNFi probably result in a higher proportion of participants in minimal disease activity.
	csDMARD-inadequate responders					
	No studies reported this outcome in this population.					
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Physical function Change from baseline (HAQ: 0 to 3 scale, 0 = no function impairment, MCID = 0.35) Follow-up: 52 weeks	**DMARD-naïve**					
	Mean change in function **-0.53**[b]	**0.03 lower** (0.11 lower to 0.05 higher)		698 (1 study)	⊕⊕⊕⊖ **Moderate**[c]	TNFi probably result in no difference in physical function.
	csDMARD-inadequate responders					
	No studies reported this outcome in this population.					
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Health-related quality of life Change from baseline (SF-36 MCS 0 to 100 scale, 100 = best health, MCID = 1.7) Follow-up: 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	No studies reported this outcome in this population.					
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Radiographic progression	**DMARD-naïve**					

Change from baseline (Sharp/Van der Heijde modified for PsA: 0 to 528 scale, 0 = no radiographic damage) Follow-up: 52 weeks	Mean change in radiographic progression **0.08**[b]	**0.10 lower** (0.17 to 0.04 lower)		667 (1 study)	⊕⊕⊕⊖ **Moderate**[d]	TNFi probably result in a slight reduction of radiographic progression.
	csDMARD-inadequate responders					
	No studies reported this outcome in this population.					
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Number of participants with serious adverse events at any time Follow-up: up to 52 weeks	**DMARD-naïve**					
	46 per 1000	**51 per 1000** (30 to 88)	**RR 1.10** (0.64 to 1.90)	1061 (4 studies)	⊕⊖⊖⊖ **Very low**[e]	We are uncertain about the effect of TNFi on the number of participants with serious adverse events.
	csDMARD-inadequate responders					
	No studies reported this outcome in this population.					
	b/tsDMARD-inadequate responders No studies reported this outcome in this population.					
Withdrawals due to adverse events at any time Follow-up: up to 52 weeks	**DMARD-naïve**					
	62 per 1000	**66 per 1000** (39 to 111)	**RR 1.07** (0.64 to 1.81)	1061 (4 studies)	⊕⊖⊖⊖ **Very low**[e]	We are uncertain about the effect of TNFi on withdrawals due to adverse events.
	csDMARDs inadequate responders					
	No studies reported this outcome in this population.					
	b/tsDMARD inadequate responders					
	No studies reported this outcome in this population.					

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

ACR50: American College of Rheumatology response criteria for 50% improvement; **bDMARD**: biologic DMARD; **CI:** confidence interval; **csDMARD**: conventional synthetic DMARD; **DMARD**: disease modifying anti-rheumatic drug; **HAQ**: Health Assessment Questionnaire; **MCID:** minimal clinically important difference; **MDA-PsA**: Minimal Disease Activity-PsA; **PSAQOL**: Psoriatic Arthritis Quality of Life; **RR:** risk ratio; **SF-36 PCS**: Short Form Health Survey 36-item physical component score; **TNFi:** tumour necrosis factor inhibitors; **tsDMARD**: targeted synthetic DMARD

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for study limitations: most of the included studies had high or uncertain risk of bias in multiple domains.
[b]Control group risk was estimated from the mean csDMARD value at follow-up from Mease 2019 for function: mean change -0.53 on HAQ (0 to 3 scale, 0 = no function impairment); for radiographic progression: mean change 0.08 on Sharp/Van der Heijde modified for PsA scale (0 to 528 scale, 0 = no radiographic damage).
[c]Downgraded one level for study limitations: the included study had unclear risk of attrition bias and other biases.
[d]Downgraded one level for study limitations: unclear detection bias (blinding of outcome assessors was not clearly reported for radiographic outcome assessors), attrition bias, and other biases.
[e]Downgraded two levels for study limitations: most of the included studies had uncertain or high risk of bias in multiple domains. Downgraded one level for imprecision: very wide confidence interval overlapping no effect.

Comparison 3. TNFi (monotherapy or combined with csDMARDs) versus other bDMARDs

Summary of findings 3. TNF inhibitors (monotherapy or combined with csDMARDs) versus other bDMARDs

TNFi (monotherapy or combined with csDMARDs) compared with other bDMARDs for psoriatic arthritis

Patient or population: participants with psoriatic arthritis

Settings: outpatients

Intervention: TNFi

Comparison: other bDMARDs

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk with other bDMARDs	Corresponding risk with TNFi				
Clinical improvement by ACR50 response criteria **(Adalimumab vs ixekizumab)** Follow-up: 12 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	390 per 1000	**409 per 1000** (347 to 487)	**RR 1.05** (0.89 to 1.25)	774 (2 studies)	⊕⊕⊖⊖ **Low**[a]	TNFi may result in little to no difference in clinical improvement.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Clinical improvement by ACR50 response criteria **(Adalimumab vs secukinumab)** Follow-up: 12 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	319 per 1000	**338 per 1000** (281 to 412)	**RR 1.06** (0.88 to 1.29)	853 (1 study)	⊕⊖⊖⊖ **Very low**[b]	We are uncertain about the effect of TNFi on clinical improvement.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Clinical improvement by ACR50 response criteria **(Adalimumab vs bimekizumab)** Follow-up: 12 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	439 per 1000	**456 per 1000** (373 to 566)	**RR 1.04** (0.85 to 1.29)	571 (1 study)	⊕⊕⊖⊖ **Low**[c]	TNFi may result in little to no difference in clinical improvement.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Disease activity as measured by MDA-PsA criteria **(Adalimumab vs ixekizumab)** Follow-up: 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					

	428 per 1000	**364 per 1000** (257 to 510)	**RR 0.85** (0.60 to 1.19)	774 (2 studies)	⊕⊝⊝⊝ **Very low**[d]	We are uncertain about the effect of TNFi on disease activity.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Disease activity as measured by MDA-PsA criteria **(TNFi vs ustekinumab)** Follow-up: 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	783 per 1000	**462 per 1000** (282 to 743)	**RR 0.59** (0.36 to 0.95)	47 (1 study)	⊕⊝⊝⊝ **Very low**[e]	We are uncertain about the effect of TNFi on disease activity.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Disease activity as measured by MDA-PsA criteria **(adalimumab vs bimekizumab)** Follow-up: 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	485 per 1000	**480 per 1000** (393 to 582)	**RR 0.99** (0.81 to 1.2)	571 (1 study)	⊕⊕⊝⊝ **Low**[c]	TNFi may result in little to no difference in disease activity.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Physical function Change from baseline (HAQ: 0 to 3 scale, 0 = no function impairment, MCID = 0.35) **(Adalimumab vs ixekizumab)** Follow-up: 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	Mean change in function **-0.68**	**0.06 higher** (0.05 to 0.07 higher)		566 (1 study)	⊕⊕⊝⊝ **Low**[f]	TNFi may result in little to no difference in physical function.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Physical function Change from baseline (HAQ: 0 to 3 scale, 0 = no function impairment, MCID = 0.35) **(Adalimumab vs secukinumab)** Follow-up: 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	Mean change in function **-0.58**	**0.02 higher** (0.06 lower to 0.10 higher)		681 (1 study)	⊕⊕⊝⊝ **Low**[g]	TNFi may result in little to no difference in physical function.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Physical function Change from baseline (HAQ: 0 to 3 scale, 0 = no function impairment, MCID = 0.35) **(Adalimumab vs bimekizumab)** Follow-up: 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	Mean change in function **-0.34**	**0.07 lower** (0.18 lower to 0.04 higher		571 (1 study)	⊕⊕⊝⊝ **Low**[h]	TNFi may result in little to no difference in physical function.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Health-related quality of life Change from baseline (SF-36 MCS: 0-100 scale, 100 = best health, MCID = 1.7) **(Adalimumab vs ixekizumab)** Follow-up: 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	Mean change in health related quality of life **5.23**	**0.46 lower** (2.28 lower to to 1.36 higher)		486 (1 study)	⊕⊝⊝⊝ **Very low**[i]	We are uncertain about the effect of TNFi on health-related quality of life.

	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Radiographic progression Change from baseline (Sharp/Van der Heijde modified for PsA: 0-528 scale, 0 = no radiographic damage) **(Adalimumab vs Bimekizumab)** Follow-up: 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	Mean change in radiographic progression **0.1**		**0.22 lower** (0.49 lower to 0.05 higher)	571 (1 study)	⊕⊕⊕⊖ **Moderate**[j]	TNFi probably result in little to no difference in radiographic progression.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Number of participants with serious adverse events at any time **(Adalimumab vs ixekizumab)** Follow-up: up to 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	41 per 1000	**66 per 1000** (25 to 173)	**RR 1.62** (0.62 to 4.22)	774 (2 studies)	⊕⊖⊖⊖ **Very low**[k]	We are uncertain about the effect of TNFi on the number of serious adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Number of participants with serious adverse events at any time **(Adalimumab vs secukinumab)** Follow-up: up to 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	77 per 1000	**66 per 1000** (40 to 107)	**RR 0.85** (0.52 to 1.38)	853 (1 study)	⊕⊖⊖⊖ **Very low**[l]	We are uncertain about the effect of TNFi on the number of serious adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Number of participants with serious adverse events at any time **(TNFi vs ustekinumab)** Follow-up: up to 24 weeks	**DMARD-naïve**					
	0 per 1000	**0 per 1000** (0 to 0)	**RR not estimable**	1 (20)	⊕⊖⊖⊖ **Very low**[m]	We are uncertain about the effect of TNFi on the number of serious adverse events.
	csDMARD-inadequate responders					
	No studies reported this outcome in this population.					
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Number of participants with serious adverse events at any time **(Adalimumab vs bimekizumab)** Follow-up: up to 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	39 per 1000	**36 per 1000** (13 to 95)	**RR 0.91** (0.34 to 2.41)	571 (1 study)	⊕⊖⊖⊖ **Very low**[n]	We are uncertain about the effect of TNFi on the number of serious adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Withdrawals due to adverse events at any time **(Adalimumab vs ixekizumab)** Follow-up: up to 52 weeks	**DMARD-naïve** No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	23 per 1000	**39 per 1000** (17 to 88)	**RR 1.68** (0.74 to 3.81)	774 (2 studies)	⊕⊖⊖⊖ **Very low**[k]	We are uncertain about the effect of TNFi on withdrawals due to adverse events.
	b/tsDMARD-inadequate responders					

	No studies reported this outcome in this population.					
Withdrawals due to adverse events at any time **(Adalimumab vs secukinumab)** Follow-up: up to 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	40 per 1000	**75 per 1000** (42 to 133)	**RR 1.88** (1.06 to 3.33)	853 (1 study)	⊕⊖⊖⊖ **Very low**[o]	We are uncertain about the effect of TNFi on withdrawal due to adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Withdrawals due to adverse events at any time **(TNFi vs ustekinumab)** Follow-up: up to 24 weeks	**DMARD-naïve**					
	0 per 1000	**0 per 1000** (0 to 0)	RR not estimable	20 (1 study)	⊕⊖⊖⊖ **Very low**[m]	We are uncertain about the effect of TNFi on withdrawal due to adverse events.
	csDMARD-inadequate responders					
	43 per 1000	**0 per 1000** (0 to 325)	**RR 0.32** (0.01 to 7.48)	47 (1 study)	⊕⊖⊖⊖ **Very low**[p]	We are uncertain about the effect of TNFi on withdrawal due to adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Withdrawals due to adverse events at any time **(Adalimumab vs bimekizumab)** Follow-up: up to 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	28 per 1000	**50 per 1000** (20 to 124)	**RR 1.80** (0.72 to 4.47)		⊕⊖⊖⊖ **Very low**[q]	We are uncertain about the effect of TNFi on withdrawal due to adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					

*The **assumed risk** is estimated from the outcome values in the control group. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the control group and the **relative effect** of the intervention (and its 95% CI).

ACR50: American College of Rheumatology response criteria for 50% improvement; **bDMARD**: biologic DMARD; **CI:** confidence interval; **csDMARD**: conventional synthetic DMARD; **DMARD**: disease modifying anti-rheumatic drug; **HAQ**: Health Assessment Questionnaire; **MCID:** minimal clinically important difference; **MDA-PsA**: Minimal Disease Activity-PsA; **RR:** risk ratio; **SF-36 PCS**: Short Form Health Survey 36-item physical component score; **TNFi:** tumour necrosis factor inhibitors; **tsDMARD**: targeted synthetic DMARD

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded one level for study limitations: high risk of performance bias in the largest included study. Downgraded one level for imprecision: two small studies, confidence intervals including no effect and both potential moderate benefit and deterioration.
[b]Downgraded two levels for study limitations: high and unclear risk of bias in multiple domains. Downgraded one level for imprecision: one study with few events, wide confidence intervals including no effect and both potential moderate improvement and deterioration.
[c]Downgraded one level for indirectness: about 30% of participants were csDMARD-naïve, thus selecting a potentially easier-to-treat participant population. Downgraded one level for imprecision: one study, with few events, wide confidence interval including no effect and both potential moderate improvement and deterioration.
[d]Downgraded one level for study limitations: high risk of performance bias in the largest included study. Downgraded two levels for imprecision: large confidence interval including large effect and overlapping the no effect line.
[e]Downgraded two levels for study limitations: high and unclear risk of bias in multiple domains. Downgraded one level for imprecision: one small study with few events, including possible large and small effect.
[f]Downgraded two levels for study limitations: high risk of performance bias and selective reporting bias.
[g]Downgraded two levels for study limitations: high and unclear risk of bias in multiple domains.
[h]Downgraded one level for study limitations: uncertain risk of performance and detection bias. Downgraded one level for indirectness: about 30% of participants were csDMARD-naïve, thus selecting a potentially easier-to-treat population.
[i]Downgraded two levels for study limitations: high risk of performance bias and selective reporting bias. Downgraded one level for imprecision: confidence interval overlapping zero and including a potentially clinically important deterioration.
[j]Downgraded one level for indirectness: about 30% of participants were csDMARD-naïve, thus selecting a potentially easier-to-treat population.
[k]Downgraded one level for study limitations: the largest of the two included studies is at high risk of performance bias and selective reporting bias. Downgraded two levels for imprecision: very wide confidence interval including a possible large effect and no effect.
[l]Downgraded two levels for study limitations: high and unclear risk of bias in multiple domains. Downgraded one level for imprecision: wide confidence interval, including a possible large effect and no effect.
[m]Downgraded two levels for study limitations: high and unclear risk of bias in multiple domains. Downgraded one level for imprecision: one study with 20 participants.
[n]Downgraded three levels for imprecision: very wide confidence interval, including no effect, potential large benefit and potential large harm.
[o]Downgraded two levels for study limitations: high and unclear risk of bias in multiple domains. Downgraded one level for imprecision: wide confidence interval including both a non-important effect and a large effect.
[p]Downgraded two levels for study limitations: high and unclear risk of bias in multiple domains. Downgraded one level for imprecision: one small study with few events, large confidence interval including a possible large effect and no effect.

Comparison 4. TNFi (monotherapy or combined with csDMARDs) versus tsDMARDs

Summary of findings 4. TNF inhibitors (monotherapy or combined with csDMARDs) versus tsDMARDs

TNFi (monotherapy or combined with csDMARDs) compared with tsDMARDs for psoriatic arthritis

Patient or population: participants with psoriatic arthritis

Settings: outpatient

Intervention: TNFi

Comparison: tsDMARDs

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk with tsDMARDs	Corresponding risk with TNFi				
Clinical improvement by ACR50 response criteria **(Adalimumab vs tofacitinib)** Follow-up: 12 weeks	**DMARD-naïve** No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	280 per 1000	**331 per 1000** (219 to 496)	**RR 1.18** (0.78 to 1.77)	213 (1 study)	⊕⊕◯◯ **Low**[a]	TNFi may result in little to no difference in clinical improvement.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Clinical improvement by ACR50 response criteria **(Adalimumab vs upadacitinib)** Follow-up: 12 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	375 per 1000	**374 per 1000** (315 to 446)	**RR 1.00** (0.84 to 1.19)	858 (1 study)	⊕⊕⊕◯ **Moderate**[b]	TNFi probably result in little to no difference in clinical improvement.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Disease activity as measured by MDA-PsA criteria **(Adalimumab vs tofacitinib)** Follow-up: 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	262 per 1000	**359 per 1000** (238 to 539)	**RR 1.37** (0.91 to 2.06)	213 (1 study)	⊕⊕◯◯ **Low**[a]	TNFi may result in little to no difference in the proportion of participants in minimal disease activity.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Disease activity as measured by MDA-PsA criteria **(Adalimumab vs upadacitinib)** Follow-up: 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	366 per 1000	**332 per 1000** (277 to 402)	**RR 0.91** (0.76 to 1.09)	858 (1 study)	⊕⊕◯◯ **Low**[a]	TNFi may result in little to no difference in the proportion of participants in minimal disease activity.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Physical function Change from baseline (HAQ: 0 to 3 scale, 0 = no function impairment, MCID = 0.35) **(Adalimumab vs tofacitinib)** Follow-up: 52 weeks	**DMARD-naïve** No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	Mean change in function **-0.54**	**0.09 higher** (0.05 lower to 0.23 higher)		190 (1 study)	⊕⊕⊕◯ **Moderate**[c]	TNFi probably result in little to no difference in physical function.

	b/tsDMARD-inadequate responders				
	No studies reported this outcome in this population.				
Physical function Change from baseline (HAQ: 0 to 3 scale, 0 = no function impairment, MCID = 0.35) **(Adalimumab vs upadacitinib)** Follow-up: 52 weeks	**DMARD-naïve**				
	No studies reported this outcome in this population.				
	csDMARDs-inadequate responders				
	Mean change in function **-0.54**	**0.11 higher** (0.03 higher to 0.19 higher)	731 (1 study)	⊕⊕⊕⊖ **Moderate**[d]	TNFi probably result in little to no difference in physical function.
	b/tsDMARD-inadequate responders				
	No studies reported this outcome in this population.				
Health-related quality of life Change from baseline (SF-36 MCS: 0-100 scale, 100 = best health, MCID = 1.7) **(Adalimumab vs tofacitinib)** Follow-up: 52 weeks	**DMARD-naïve**				
	No studies reported this outcome in this population.				
	csDMARD-inadequate responders				
	Mean change in health-related quality of life **4.82**	**0.01 lower** (2.85 lower to 2.83 higher)	190 (1 study)	⊕⊖⊖⊖ **Very low**[e]	We are uncertain about the effect of TNFi on health-related quality of life.
	b/tsDMARD-inadequate responders				
	No studies reported this outcome in this population.				
Health-related quality of life Change from baseline (SF-36 MCS 0-100 scale, 100 = best health, MCID = 1.7) **(Adalimumab vs upadacitinib)** Follow-up: 52 weeks	**DMARD-naïve**				
	No studies reported this outcome in this population.				
	csDMARD-inadequate responders				
	Mean change in health-related quality of life	**0.90 lower** (2.20 lower to 0.40 higher)	735 (1 study)	⊕⊖⊖⊖ **Very low**[f]	We are uncertain about the effect of TNFi on health-related quality of life.
	5.2				
	b/tsDMARD-inadequate responders				
	No studies reported this outcome in this population.				
Radiographic progression Change from baseline (Sharp/Van der Heijde modified for PsA: 0-528 scale, 0 = no radiographic damage) **(Adalimumab vs tofacitinib)** Follow-up: 52 weeks	**DMARD-naïve**				
	No studies reported this outcome in this population.				
	csDMARD-inadequate responders				
	Mean change in radiographic progression **0.01**	**0.08 lower** (0.27 lower to 0.11 higher)	193 (1 study)	⊕⊕⊕⊖ **Moderate**[c]	TNFi probably result in little to no difference in radiographic progression.
	b/tsDMARD-inadequate responders				
	No studies reported this outcome in this population.				
Radiographic progression Change from baseline (Sharp/Van der Heijde modified for PsA: 0-528 scale, 0 = no radiographic damage) **(Adalimumab vs upadacitinib)** Follow-up: 52 weeks	**DMARD-naïve**				
	No studies reported this outcome in this population.				
	csDMARD-inadequate responders				
	Mean change in radiographic progression **-0.03**	**0.03 lower** (0.22 lower to 0.16 higher)		⊕⊕⊖⊖ **Low**[g]	TNFi may result in little to no difference in radiographic progression.
	b/tsDMARD-inadequate responders				
	No studies reported this outcome in this population.				
Number of participants with serious adverse events at any time **(Adalimumab vs tofacitinib)** Follow-up: up to 52 weeks	**DMARD-naïve**				
	No studies reported this outcome in this population.				
	csDMARD-inadequate responders				

	75 per 1000	85 per 1000 (34 to 212)	RR 1.14 (0.46 to 2.83)	213 (1)	⊕⊖⊖⊖ Very low[h]	We are uncertain about the effect of TNFi on the number of serious adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Number of participants with serious adverse events at any time **(Adalimumab vs upadacitinib)** Follow-up: up to 24 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	33 per 1000	37 per 1000 (18 to 76)	RR 1.14 (0.56 to 2.31)	858 (1 study)	⊕⊖⊖⊖ Very low[h]	We are uncertain about the effect of TNFi on the number of serious adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Withdrawals due to adverse events at any time **(Adalimumab vs tofacitinib)** Follow-up: up to 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	56 per 1000	38 per 1000 (11 to 130)	RR 0.67 (0.20 to 2.32)	213 (1 study)	⊕⊖⊖⊖ Very low[h]	We are uncertain about the effect of TNFi on withdrawals due to adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					
Withdrawals due to adverse events at any time **(Adalimumab vs upadacitinib)** Follow-up: up to 52 weeks	**DMARD-naïve**					
	No studies reported this outcome in this population.					
	csDMARD-inadequate responders					
	49 per 1000	54 per 1000 (30 to 95)	RR 1.10 (0.62 to 1.95)	858 (1 study)	⊕⊖⊖⊖ Very low[h]	We are uncertain about the effect of TNFi on withdrawals due to adverse events.
	b/tsDMARD-inadequate responders					
	No studies reported this outcome in this population.					

*The **assumed risk** is estimated from the outcome values in the control groupThe **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the control group and the **relative effect** of the intervention (and its 95% CI).

ACR50: American College of Rheumatology response criteria for 50% improvement; **bDMARD**: biologic DMARD; **CI:** confidence interval; **csDMARD**: conventional synthetic DMARD; **DMARD**: disease modifying anti-rheumatic drug; **HAQ**: Health Assessment Questionnaire; **MCID:** minimal clinically important difference; **MDA-PsA**: Minimal Disease Activity-PsA; **RR:** risk ratio; **SF-36 PCS**: Short Form Health Survey 36-item physical component score; **TNFi:** tumour necrosis factor inhibitors; **tsDMARD**: targeted synthetic DMARD

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]Downgraded two levels for imprecision: very wide confidence interval overlapping no effect and including possible large effect.
[b]Downgraded one level for imprecision: wide confidence interval overlapping no effect.
[c]Downgraded one level for imprecision: confidence interval overlapping no effect. Optimal information size not met.
[d]Downgraded one level for study limitations: unclear risk of attrition bias.
[e]Downgraded three levels for imprecision: confidence interval overlapping zero and including both potentially clinically significant improvement and deterioration.
[f]Downgraded one level for study limitations: unclear risk of attrition bias. Downgraded two levels for imprecision: confidence interval overlapping zero and including potential clinically significant deterioration.
[g]Downgraded one level for study limitations: unclear risk of attrition bias. Downgraded one level for imprecision: confidence interval overlapping no effect.
[h]Downgraded three levels for imprecision: very wide confidence interval including large improvement, large deterioration, and no effect.

Anmerkung/Fazit der Autoren

In csDMARD-inadequate responders, moderate-certainty evidence showed that TNFi probably result in a large clinical improvement, lower disease activity, small decrease in radiographic progression, and better quality of life compared to placebo. Low-certainty evidence showed that TNFi may lead to a slight improvement in physical function compared to placebo. Low-certainty evidence suggested that TNFi may lead to a slight increase in withdrawals due to adverse events, whereas they may result in little to no difference in

serious adverse events compared to placebo. No trials assessed TNFi compared to placebo in DMARD-naïve participants or in b/tsDMARD-IR.

Our results show a knowledge gap concerning the benefits and harms of TNFi in people with psoriatic arthritis with inadequate response to bDMARDs or tsDMARDs, since no randomized controlled trials (RCTs) were conducted in this population. Furthermore, more data are needed to draw reliable conclusions about the best strategy to use after failure of csDMARDs, given that the evidence on the benefits and harms of TNFi compared to other bDMARDs or tsDMARDs is still unsatisfactory. The certainty of the evidence is overall moderate when it comes to TNFi compared to methotrexate in DMARD-naïve patients. However, a couple of welldesigned randomized trials with appropriate sample sizes would help to confirm the probable superiority of TNFi.

Kommentare zum Review

Die Ergebnisse für die Population DMARD-naiv wurden nicht abgebildet.

3.2 Systematische Reviews

Zeng J et al., 2025 [11].

Clinical benefits and complication profile of IL-23 inhibitors in patients with psoriatic arthritis: a systematic review and meta-analysis

Fragestellung

This meta-analysis aimed to evaluate the clinical efficacy and safety profile of IL-23 inhibitors in the treatment of PsA.

Methodik

Population:

- Adult patients diagnosed with psoriatic arthritis based on established classification criteria (e.g., CASPAR criteria)

Intervention:

- IL-23 inhibitors

Komparator:

- Placebo

Endpunkte:

- clinical efficacy measures and/or safety outcomes

Recherche/Suchzeitraum:

- […] PubMed, Embase, Web of Science, and The Cochrane Library, covering all publications from the date of database inception to June 30, 2025.

Qualitätsbewertung der Studien:

- Cochrane Risk of Bias 2.0 (RoB 2.0) tool

Ergebnisse

Anzahl eingeschlossener Studien:

- 6 studies met the inclusion criteria and were included in the qualitative and quantitative synthesis.
- Deodhar et al., 2018; Mease et al., 2020; Coates et al., 2022; Kristensen et al., 2022; Östör et al., 2022; Mease et al., 2021)

Charakteristika der Population/Studien:

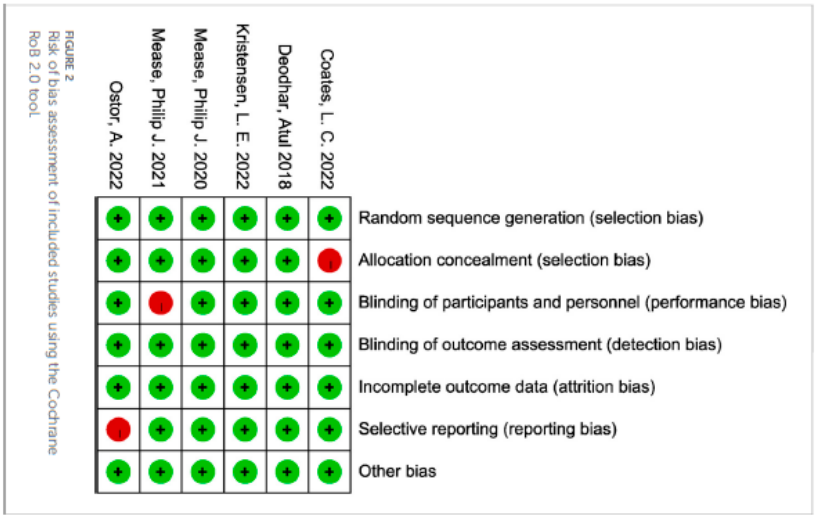
- The studies evaluated three IL-23 inhibitors: guselkumab, risankizumab, and tildrakizumab.
- The mean age of participants ranged from 44 to 53 years across studies. The duration of PsA varied widely, with mean values ranging from 5.5 ± 5.9 to 8.7 ± 7.2 years. The baseline PASI scores ranged from 5.0 ± 6.5 to 13.6 ± 9.0, indicating a moderate to high degree of cutaneous disease severity among enrolled patients.

TABLE 1 Baseline clinical characteristics of patients in included studies.

Author	Year	Treatment group	Mean age (years)	PsA duration (years)	PASI score (0–72)	Swollen joint count (0–66)	Tender joint count (0–68)
Coates, L. C.	2022	Guselkumab 100 mg week 0, week 4, then every 8 weeks	49	8.3 ± 7.8	11.7 ± 11.9	10.0 ± 7.0	21.0 ± 13.0
		Placebo	49	8.7 ± 7.2	9.2 ± 9.4	10.0 ± 7.0	21.0 ± 13.0
Kristensen, L. E.	2022	Risankizumab 150 mg at weeks 0, 4 and 16	52	7.1 ± 7.0	10.9 ± 10.1	9.0 ± 6.0	18.0 ± 11.0
		Placebo	52	7.1 ± 7.7	10.9 ± 10.1	12.1 ± 7.8	20.8 ± 14.1
Ostor, A.	2022	Risankizumab 150 mg at weeks 0, 4 and 16	53	8.2 ± 8.2	7.7 ± 6.7	13.0 ± 8.7	22.8 ± 14.9
		Placebo	52	8.2 ± 8.3	10.0 ± 10.4	12.2 ± 8.0	20.5 ± 12.8
Mease, Philip J.	2021	Tildrakizumab 200 mg every 4 weeks	50	7.5 ± 8.5	8.4 ± 9.9	13.6 ± 9.0	22.3 ± 13.8
		Placebo	48	6.3 ± 6.1	5.0 ± 6.5	11.8 ± 9.8	19.7 ± 14.7
Mease, Philip J.	2020	Guselkumab 100 mg every 4 weeks	46	5.5 ± 5.9	10.8 ± 11.7	12.9 ± 7.8	22.4 ± 13.5
		Placebo	46	5.8 ± 5.6	9.3 ± 9.8	12.3 ± 6.9	21.6 ± 13.1
Deodhar, Atul	2018	Guselkumab 100 mg at week 0, week 4, and every 8 weeks	47	7.0 ± 7.2	12.0 ± 10.5	11.9 ± 7.6	20.7 ± 12.2
		Placebo	44	6.9 ± 7.2	9.9 ± 8.0	10.6 ± 7.5	20.1 ± 12.5

PsA, Psoriatic Arthritis; PASI, Psoriasis Area and Severity Index.

Qualität der Studien:



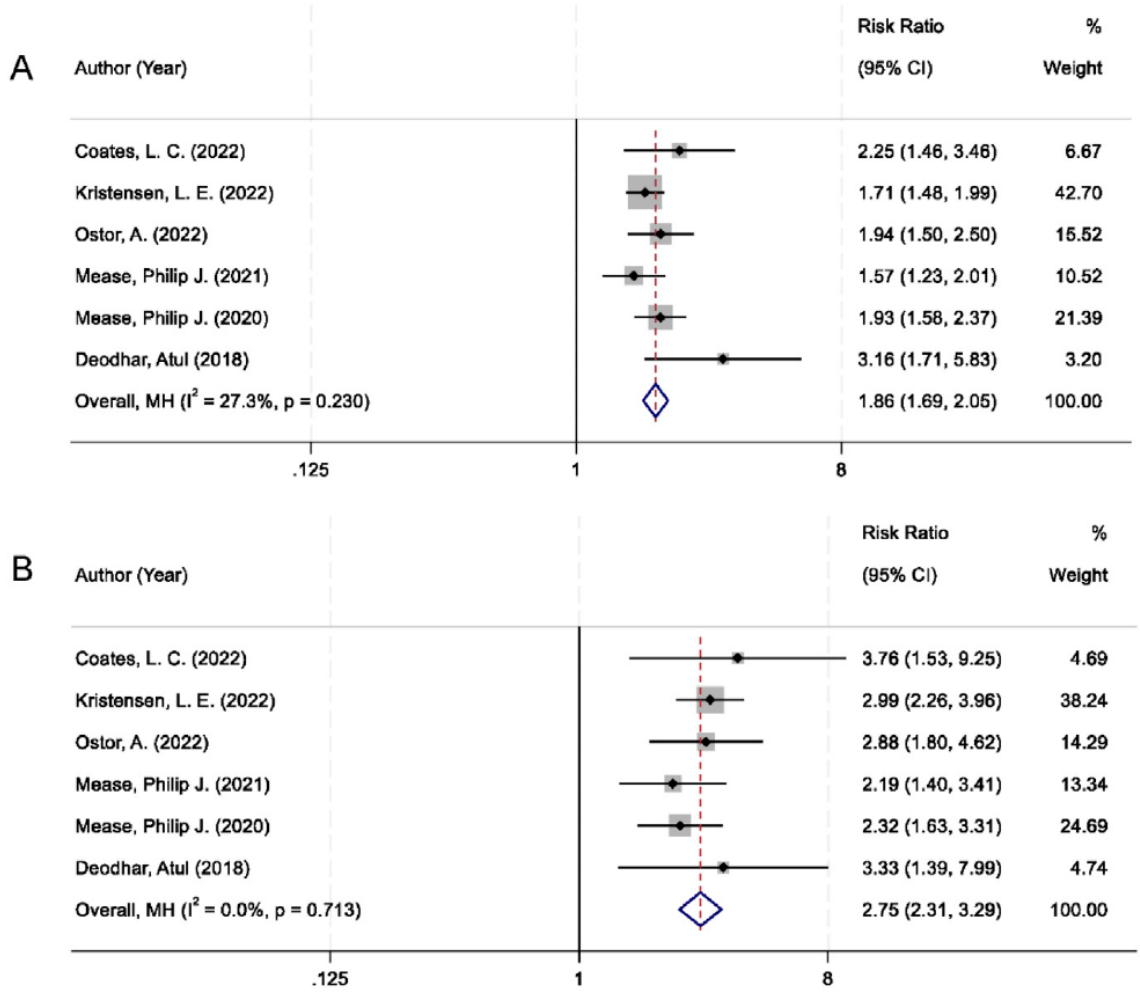
Taken together, the included trials were judged to be of generally high methodological quality, providing a reliable basis for the pooled quantitative analysis.

Studienergebnisse:

3.4 Efficacy outcomes: ACR and PASI responses

- All six randomized controlled trials included in the analysis reported American College of Rheumatology (ACR) response rates at the 20%, 50%, and 70% improvement thresholds (ACR20, ACR50, and ACR70).
- The pooled analysis demonstrated that IL-23 inhibitors were significantly more effective than placebo in achieving ACR20 response. There was no significant between study heterogeneity ($I2 = 27.3\%$, $p = 0.230$), and the combined relative risk (RR) was 1.86 (95% confidence interval [CI]: 1.69–2.05; $p < 0.001$; Figure 3A).

- With respect to secondary outcomes, IL-23 inhibitor therapy also resulted in markedly higher ACR50 and ACR70 response rates compared to placebo. The pooled RR for ACR50 was 2.75 (95% CI: 2.31–3.29; p < 0.001), with no observed heterogeneity among studies (I2 = 0.0%; Figure 3B). Similarly, the ACR70 response was significantly elevated in the IL-23 inhibitor group (RR = 3.06; 95% CI: 2.29–4.10; p < 0.001), with no statistical heterogeneity detected (I2 = 0%; Figure 3C).
- In addition to joint-related outcomes, skin symptom relief was evaluated using the Psoriasis Area and Severity Index 90 (PASI90), which indicates at least 90% improvement from baseline. Patients receiving IL-23 inhibitors were significantly more likely to achieve PASI90 compared to those in the placebo group. The pooled RR was 5.98 (95% CI: 4.68–7.64; p < 0.001), with no heterogeneity observed across studies (I2 = 0%; Figure 3D).



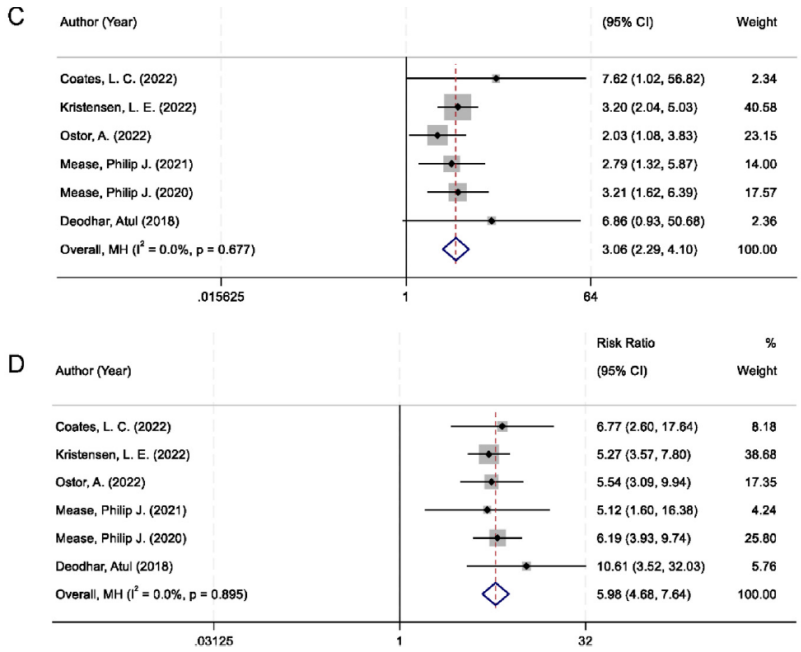


FIGURE 3
Forest plots comparing IL-23 inhibitors vs. placebo in PsA: **(A)** ACR20 response; **(B)** ACR50 response; **(C)** ACR70 response; **(D)** PASI90 response.

3.5 Minimal disease activity and resolution of enthesitis and dactylitis

- All six randomized controlled trials included in the meta-analysis reported MDA as an outcome.
- The pooled analysis demonstrated that patients treated with IL-23 inhibitors had a significantly higher MDA response rate compared to those receiving placebo. The combined RR was 2.85 (95% CI 2.30–3.54; $p < 0.001$), with low heterogeneity among studies (I2 = 25.8%; Figure 4A).
- In addition to global disease activity, the resolution of specific musculoskeletal manifestations, such as enthesitis and dactylitis, was also assessed. These clinical features are not only prevalent in PsA but are also indicative of disease severity and functional impairment. Data from five trials were available for both endpoints. Patients receiving IL-23 inhibitors exhibited a significantly greater resolution of enthesitis compared to placebo (RR = 1.46; 95% CI: 1.29–1.64; $p < 0.001$), with no evidence of heterogeneity (I2 = 0.0%; Figure 4B). Similarly, a significant improvement in dactylitis resolution was observed in the IL-23 inhibitor group (RR = 1.39; 95% CI: 1.20–1.61; $p < 0.001$), with moderate heterogeneity (I2 = 31.1%; Figure 4C).

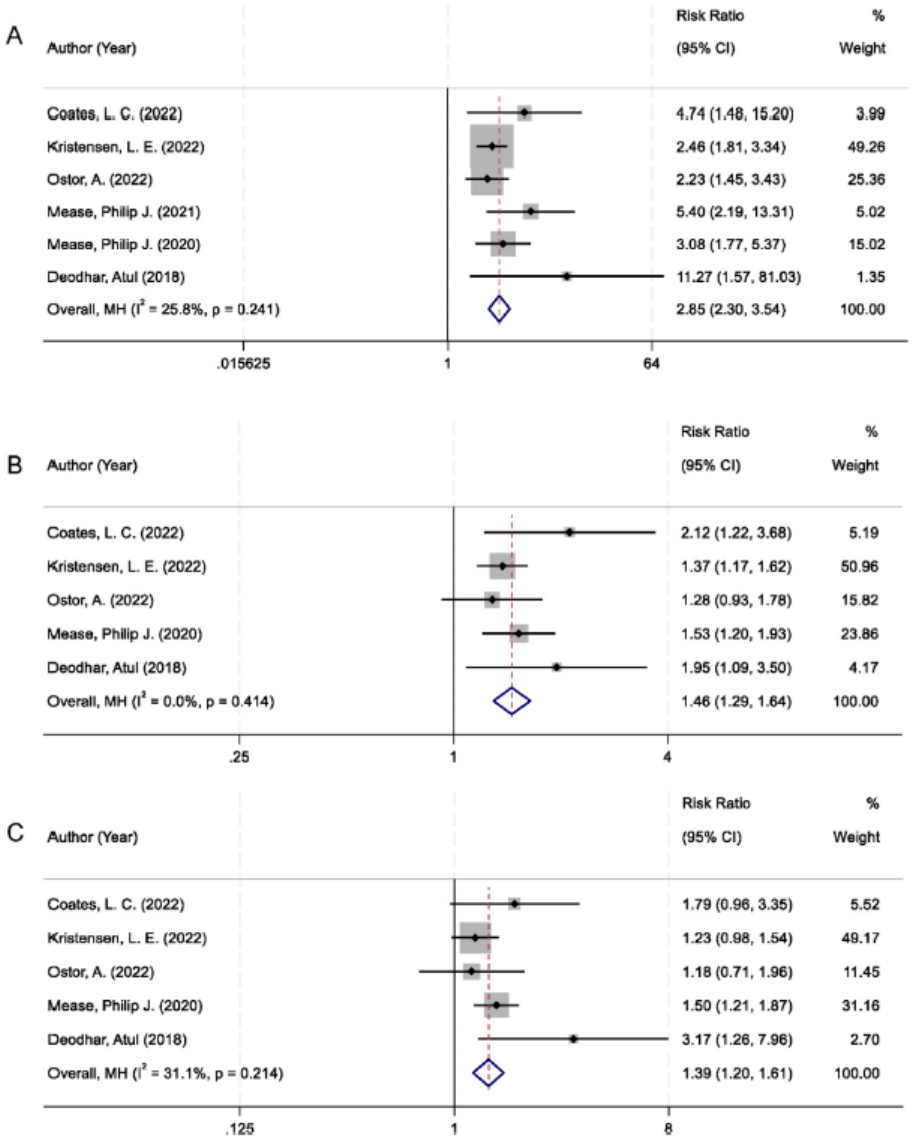


FIGURE 4
Forest plots comparing IL-23 inhibitors and placebo for: **(A)** Minimal Disease Activity; **(B)** Enthesitis resolution; **(C)** Dactylitis resolution.

Anmerkung/Fazit der Autoren

Based on the current meta-analysis, IL-23 inhibitors demonstrate significant efficacy in improving joint and skin symptoms, achieving minimal disease activity, and resolving enthesitis and dactylitis in patients with psoriatic arthritis. These findings support their integration into treatment strategies, particularly for individuals with multidomain involvement or inadequate response to conventional therapies. Further long-term comparative studies are warranted.

Kommentare zum Review

Die Studie von Mease PJ et al. (2022) untersucht die Wirksamkeit eines IL-23-Inhibitors, der für diese Indikation nicht zugelassen ist. Fünf der sechs Studien umfassen jedoch zugelassene Wirkstoffe.

Chai R et al., 2025 [2].

Efficacy and safety of upadacitinib for patients with immune-mediated inflammatory diseases: a systematic review and meta-analysis

Fragestellung

To explore upadacitinib's efficacy and safety in autoimmune disease treatment, we conducted this study.

Methodik

Population:

- Patients were diagnosed with immune-mediated diseases based on pre-established criteria. IMIDs included but were not limited to RA, axSpA including ankylosing spondylitis (AS) and nonradiographic axSpA (nr-axSpA), PsA, CD, and UC.

Intervention:

- Upadacitinib
- monotherapy or in combination with other treatments

Komparator:

- therapy without upadacitinib

Endpunkte:

- clinical remission and endoscopic response for IBD,
- American College of Rheumatology (ACR) response criteria for RA and PsA,
- axial spondyloarthritis disease activity score (ASDAS) and bath ankylosing spondylitis disease activity index (BASDAI) for axSpA, and others.
- Adverse events (AEs) were also recorded and analyzed as key outcome measures

Recherche/Suchzeitraum:

- Three commonly used databases (Pubmed, Web of Science, and Embase) were searched for literature on upadacitinib in the treatment of IMIDs.
- The search period covered from the inception of the databases up to May 31, 2024.

Qualitätsbewertung der Studien:

- Cochrane Risk of Bias Tools

Ergebnisse

Anzahl eingeschlossener Studien:

- 45 records (15–59) were included in the final meta-analysis
- Psoriatic arthritis: Burmeister et al. 2022, McInnes et al. 2023, Mease et al. 2021, Nash et al. 2022, Strand et al. (2021)

Charakteristika der Population/Studien:

Disease	Study	Trial registration number	Country	Age range of the participants	Sample size		Intervention		Primary outcomes	Secondary outcomes	Duration
					Experimental group	Control group	Experimental group	Control group			
	Strand, Schif et al. 2019[52]	NCT02706847	-	adults (18+)	164/165	169	UPA 15/30mg	placebo	-	PtGA, pain VAS, HAQ-DI, SF-36, morning stiffness, etc.	12 weeks
	Zeng et al. 2021[59]	NCT02955212	37 sites in China, Brazil, and South Korea	adults (18+)	169	169	UPA 15mg QD +csDMARDs	placebo+ csDMARDs	ACR20, DAS28(CRP), AEs, etc.	ACR50/70, SF-36, pain VAS, etc.	12 weeks
axSpA	Baral.iakos et al. 2023[15]	NCT02049138	-	adults (18+)	211	209	UPA 15mg QD	placebo→14week UPA 15mg QD	ASAS40, ASDAS ID/LDA, AEs, etc.	BASFI, etc.	52 weeks
	Van Der Heijde, Deodhar et al. 2022[57]	NCT03178487	-	adults (18+)	93	94	UPA 15mg QD	placebo→ UPA 15mg QD	ASAS40, ASDAS ID/LDA, AEs, etc.	back pain, etc.	104 weeks
	Van Der Heijde et al. 2019[58]	NCT03178487	in 20 countries	adults (18+)	93	94	UPA 15mg QD	placebo	ASAS40, ASDAS ID/LDA, AEs, etc.	back pain, etc.	14 weeks
	Van Der Heijde, Baral.iakos et al. 2022[56]	NCT04169373	in 22 countries	adults (18+)	211	209	UPA 15mg QD	placebo	ASAS20/40, BASDAI50, AEs, etc.	SPARCC MRI spine and sacroiliac joint scores, etc.	14 weeks
	Van den Bosch et al. 2024[55]	NCT04169373	-	adults (18+)	156	157	UPA 15mg QD	placebo	ASAS40, AEs, etc.	back pain, BASFI, hs-CRP, etc.	52 weeks
PsA	Burmester et al. 2022[20]	NCT03104400 NCT03104374	-	adults (18+)	907/921	635/429	UPA 15/30mg QD	placebo, ADA 40mg EOW	AEs, etc.	-	3 years(cut-off of June 29, 2020)
	McInnes et al. 2023[36]	NCT03104400	-	adults (18+)	214/210	211	UPA 15/30mg QD	ADA 40mg EOW	ACR20, AEs, etc.	ACR50/70, PASI75/90/100, MDA, mTSS, etc.	104 weeks
	Mease et al. 2021[38]	NCT03104374	-	-	211/219	106/106	UPA 15/30mg QD	placebo→ UPA 15/30mg QD	ACR20, AEs, etc.	ACR50/70, PASI75/90/100, HAQ-DI, etc.	56 weeks
	Nash et al. 2022[40]	NCT03104400 NCT03104374	-	-	189/197 353/341 451/444	188 342 447	UPA 15/30mg QD	placebo	ACR20, AEs, etc.	ACR50/70, PASI75/90/100, HAQ-DI, pain VAS, etc.	24 weeks
	Strand et al. (PsA) 2021[50]	NCT03104400	in 45 countries	adults (18+)	429/423	423/429	UPA 15/30mg QD	placebo/ ADA 40mg EOW	-	PtGA, HAQ-DI, FACIT-F, SF-36, MCID, etc.	56 weeks

Qualität der Studien:

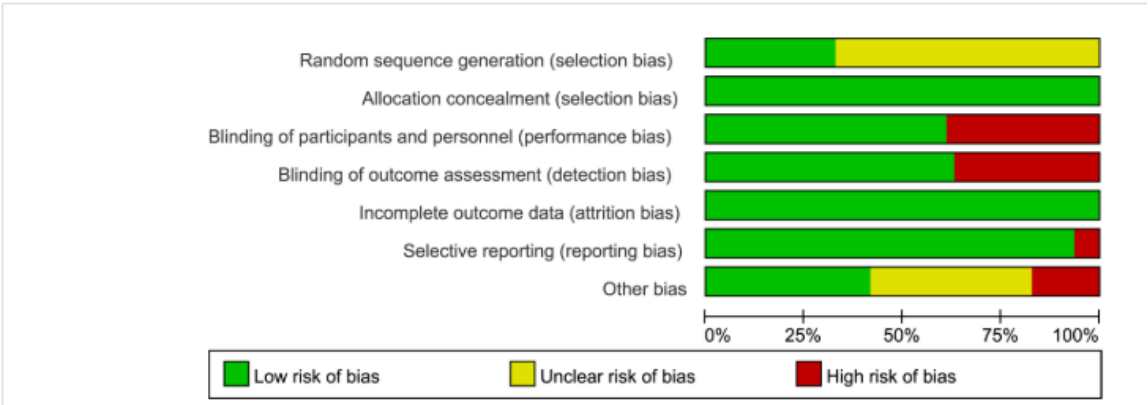


FIGURE 2
Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

- The results noted the variability in the risk of bias across studies. For instance, several studies, particularly those with open-label designs, were assessed at a high risk. Several open-label studies were rated high risk, while some randomized double-blind studies lacked clear reporting of randomization and blinding, resulting in an unclear bias classification. These biases should be considered when interpreting the results, as they may impact the reliability and generalizability of the findings.

Studienergebnisse:

- In PsA, ACR20 was a key endpoint, but high heterogeneity was observed across the included trials (38, 40)($I2 > 50\%$, $P < 0.05$).
- Results showed that upadacitinib 15 mg QD (Figure 5) or 30 mg QD (Supplementary Figure S3) led to a higher proportion of patients achieving ACR responses compared to

placebo (RR = 2.46/2.68, P < 0.001). The ACR70/100 assessments also favored upadacitinib (RR > 1, P < 0.001).

- Regarding psoriasis severity, improvements in PASI scores (PASI75/90/100) demonstrated that upadacitinib was superior to placebo (RR > 1, P < 0.001).
- Regarding complications of PsA, such as dactylitis and enthesitis, upadacitinib showed significant improvement in enthesitis, but did not show significant improvement in dactylitis, based on the Leeds Enthesitis Index (LEI = 0) and Leeds Dactylitis Index (LDI = 0). For the quality of life, as measured by the HAQ-DI in four articles (36, 38, 40, 50), upadacitinib 15 mg or 30 mg QD outperformed both placebo and ADA 40 mg EOW.

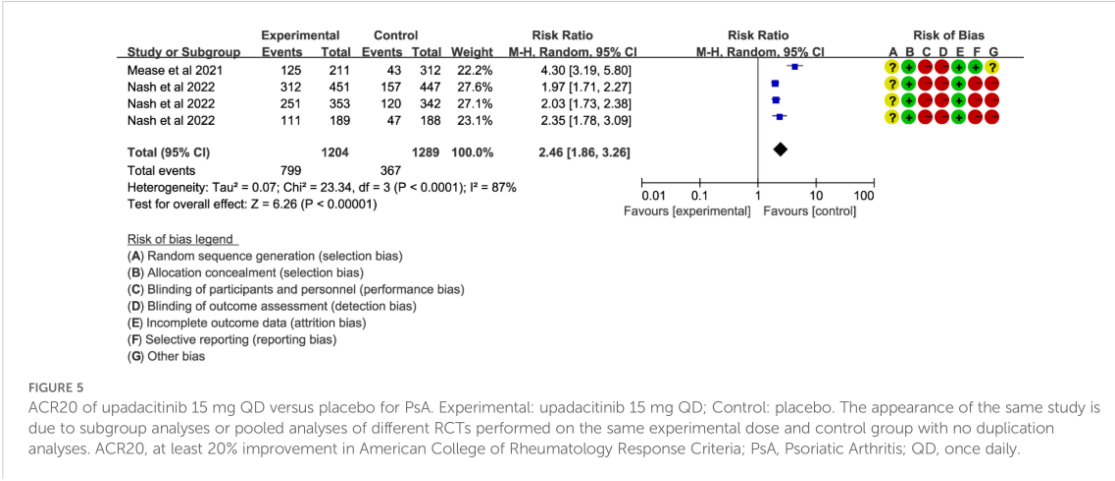


FIGURE 5
ACR20 of upadacitinib 15 mg QD versus placebo for PsA. Experimental: upadacitinib 15 mg QD; Control: placebo. The appearance of the same study is due to subgroup analyses or pooled analyses of different RCTs performed on the same experimental dose and control group with no duplication analyses. ACR20, at least 20% improvement in American College of Rheumatology Response Criteria; PsA, Psoriatic Arthritis; QD, once daily.

Anmerkung/Fazit der Autoren

Overall, the great therapeutic potential of upadacitinib is clear, demonstrating substantial efficacy across a range of IMIDs. It effectively alleviates symptoms, reduces disease activity, and shows notable benefits in improving quality of life. Due to the heterogeneity in our research, the real-world benefits of upadacitinib may vary significantly based on individual patient factors, and further research is needed to clarify its impact on symptoms, quality of life, and overall efficacy. Additionally, the safety profile is generally manageable, but careful monitoring for risks such as infections especially HZ is necessary. A personalized treatment approach (including medicine time, dose, frequency, etc.), considering both efficacy and safety, is crucial to optimizing outcomes for individual patients.

Kommentare zum Review

Es wurden nur die Ergebnisse zu Psoriasis-Arthritis extrahiert. Die eingeschlossenen Studien umfassen Erwachsene mit PsA, die auf ein oder mehrere DMARD unzureichend angesprochen haben.

Dai Q et al., 2024 [6].

Efficacy and safety of tofacitinib for chronic plaque psoriasis and psoriatic arthritis: a systematic review and meta-analysis of randomized controlled trials

Fragestellung

To summarize and analyze the results of published randomized controlled trials of tofacitinib for the treatment of chronic plaque psoriasis and psoriatic arthritis(PsA) and discuss its efficacy and safety.

Methodik

Population:

- adults diagnosed with chronic plaque psoriasis and/or PsA.

Intervention:

- tofacitinib

Komparator:

- placebo

Endpunkte:

- PASI75/PGA response, ACR20/50 response, change in DSS/FACIT-F Score/HAQ-DI Score/LEI Score, AEs, and SAEs

Recherche/Suchzeitraum:

- PubMed, Embase, Cochrane, and Web of Science, a systematic literature searching was conducted in July 2023.
- Keine Angaben zum Suchzeitraum

Qualitätsbewertung der Studien:

- The evaluation of the methodological rigor in the eligible randomized controlled trials (RCTs) was performed in accordance with the guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions

Ergebnisse

Anzahl eingeschlossener Studien:

- A total of six articles, covering 1393 patients (844 treated with tofacitinib and 549 with placebo), were included.

Charakteristika der Population:

- In cases with PsA, there were no significant differences in age (WMD 1.09; 95% CI − 0.30, 2.49; $p = 0.13$), gender (RR 1.05; 95% CI 0.93, 1.19; $p = 0.44$), HAQ-DI scores (WMD 0.04; 95% CI − 0.03, 0.12; $p = 0.29$), PASI scores (WMD − 0.19; 95% CI − 1.21, 0.83; $p = 0.71$), and duration of psoriasis (WMD 0.32; 95% CI − 0.45, 1.09; $p = 0.41$) (see Table S4).

Supplementary Table S3 Baseline characteristics of include studies.

Authors	Study period	Country	Study design	Registration number	Intervention	Participants	Patients (n) Tofacitinib/Placebo	Follow-up
Bachelez 2015a	2010-2012	Multicentre	Phase 3, randomised,multicentre,double-dummy,placebo-controlled,non-inferiority trial	NCT01241591	Tofacitinib 5 mg twice daily at about 12 h intervals	Moderate-tosevere chronic plaque psoriasis	329/107	16 weeks
Bachelez 2015b	2010-2012	Multicentre	Phase 3, randomised,multicentre,double-dummy,placebo-controlled,non-inferiority trial	NCT01241591	Tofacitinib 10 mg twice daily at about 12 h intervals	Moderate-tosevere chronic plaque psoriasis	330/107	16 weeks
Gladman 2017a	2013-2016	Multicentre	Randomized,placebo-controlled, double-blind, phase 3 trial	NCT01882439	5 mg of tofacitinib administered orally twice daily	Psoriatic arthritis with an inadequate response to TNF inhibitors	131/131	6 months
Gladman 2017b	2013-2016	Multicentre	Randomized,placebo-controlled, double-blind, phase 3 trial	NCT01882439	10 mg of tofacitinib twice daily	Psoriatic arthritis with an inadequate response to TNF inhibitors	132/131	6 months
Leng 2023	2018-2021	China	Phase 3, randomised,double- blind, placebo-controlled study	NCT03486457	Tofacitinib 5 mg twice daily	Chinese patients with active psoriatic arthritis	136/68	6 months
Mease 2017a	2014-2015	Multicentre	Double-blind, active-controlled and placebo-controlled, phase 3 trial	NCT01877668	Tofacitinib at a 5-mg dose taken orally twice daily	Patients with active psoriatic arthritis who previously had an inadequate response to conventional synthetic diseasemodifying antirheumatic drugs	107/105	12 months
Mease 2017b	2014-2015	Multicentre	Double-blind, active-controlled and placebo-controlled, phase 3 trial	NCT01877668	Tofacitinib at a 10-mg dose taken orally twice daily	Patients with active psoriatic arthritis who previously had an inadequate response to conventional synthetic diseasemodifying antirheumatic drugs	104/105	12 months
Papp 2012a	2008-2009	USA and Canada	Phase 2b randomized placebo-controlled dose-ranging study	NCT00678210	Oral tofacitinib 2mg twice daily	Moderate-to-severe chronic plaque psoriasis	49/50	12 weeks
Papp 2012b	2008-2009	USA and Canada	Phase 2b randomized placebo-controlled dose-ranging study	NCT00678210	Oral tofacitinib 5 mg twice daily	Moderate-to-severe chronic plaque psoriasis	49/50	12 weeks
Papp 2012c	2008-2009	USA and Canada	Phase 2b randomized placebo-controlled dose-ranging study	NCT00678210	Oral tofacitinib 15 mg twice daily	Moderate-to-severe chronic plaque psoriasis	49/50	12 weeks
Zhang 2017a	2013-2015	China and Korea	Phase 3, randomized, double-blind, placebo-controlled study	NCT01815424	Tofacitinib 5 mg twice daily	Asian patients with moderate to severe chronic plaque psoriasis	88/88	52 weeks
Zhang 2017b	2013-2015	China and Korea	Phase 3, randomized, double-blind, placebo-controlled study	NCT01815424	Tofacitinib 10 mg twice daily	Asian patients with moderate to severe chronic plaque psoriasis	90/88	52 weeks

Qualität der Studien:

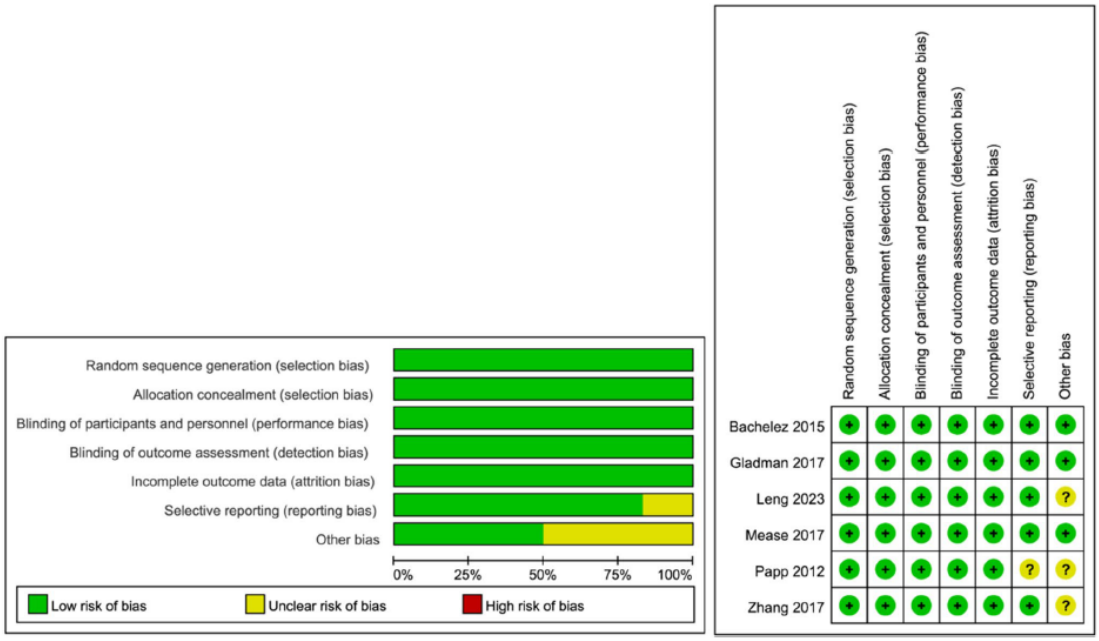


Fig. 2 Risk of bias assessment of the included studies. The quality assessment of eligible RCTs was conducted following the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 based on seven terms: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. Three evaluation outcomes including low risk, high risk, and unclear risk were assigned to every study aspect. Studies with more "low risk" bias evaluations were regarded as superior. Green for low risk, yellow for unclear risk, and red for high risk

Studienergebnisse:

Efficacy (treatment of psoriatic arthritis)

- In the overall analysis, tofacitinib significantly (all p-values < 0.01) improved the metrics of PSAI 75/ACR20/ ACR50 response and DSS/LEI/HAQ-DI/FACIT-F score change.

- In terms of heterogeneity, there was heterogeneity in ACR50 response (I2 = 52, p = 0.08), change in DSS (I2 = 95, p < 0.00001), change in FACIT-F score (I2 = 91, p < 0.00001), change in HAQ-DI score (I2 = 85, p < 0.0001), and change in LEI score (I2 = 98, p < 0.00001) in which there was heterogeneity, and none of the PASI75/ ACR20 response metrics was heterogeneous (all I2 < 50) or biased (Egger's test, p-value > 0.05).

Safety of tofacitinib

- In the overall analysis, tofacitinib significantly (*p* = 0.01) affected the AEs of chronic plaque psoriasis, but not the SAEs of chronic plaque psoriasis, the AEs of psoriatic arthritis, or the SAEs of psoriatic arthritis, a finding supported by the statistical results (no heterogeneity, no bias).

Anmerkung/Fazit der Autoren

The comprehensive analysis revealed that tofacitinib can effectively treat the skin and joint symptoms of chronic plaque psoriasis and PsA, as well as improve patients' quality of life. However, the safety of tofacitinib still requires validation, necessitating ongoing research into its enduring effectiveness in managing chronic plaque psoriasis and PsA. Additionally, an imperative aspect is the examination of the safety profile associated with its prolonged usages. As a result, depending on the patient's condition, dermatologists should rigorously adhere to current national or regional recommendations.

Kommentare zum Review

Es wurden nur die Ergebnisse zu Psoriasis-Arthritis dargestellt.

3.3 Leitlinien

Information zur deutschen S3-Leitlinie:

Die deutsche AWMF S3-LL „Diagnosestellung und medikamentöse Therapie der Psoriasis Arthritis" wurde am 01.03.2021 neu angemeldet. Die Fertigstellung ist für den 28.02.2026 geplant.

Nast A. et al., 2025 [9].

European Dermatology Forum (EDF)

EUROGUIDERM GUIDELINE FOR THE SYSTEMIC TREATMENT OF PSORIASIS VULGARIS; September 2023, partial update February 2025

Zielsetzung/Fragestellung

The overall aim of this guideline is to provide guidance for optimal treatment selection and management in the treatment of adults with moderate to severe plaque type psoriasis. Optimal treatment selection and management are meant to reduce morbidity caused by psoriasis and to improve the health related quality of life of affected individuals.

The target population are patients with plaque type psoriasis of moderate to severe severity, and patients with psoriatic arthritis, who have also been diagnosed with moderate to severe psoriasis vulgaris.

Methodik

Grundlage der Leitlinie

Update der Leitlinien Version von 2021

- Repräsentatives Gremium: **trifft zu**
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt: **trifft zu**
- Systematische Suche, Auswahl und Bewertung der Evidenz: **trifft zu**
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt: **trifft zu**
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt: **trifft teilweise zu**
- Regelmäßige Überprüfung der Aktualität gesichert: **trifft zu**

Recherche/Suchzeitraum:

- May 2022, an update of the Cochrane review has been published 33.
- The EuroGuiDerm Team updated the three systematic reviews supporting the chapters on psoriatic arthritis, heart disease and diabetes.
- Update 3 (November 2022) In November 2022, we performed a further update of the systematic review and meta-analysis conducted for the psoriasis arthritis chapter of the Living EuroGuiDerm Guideline for the systemic treatment of psoriasis vulgaris.
- We searched CENTRAL: CENTRAL is comprised of randomized controlled trial (RCT) and quasi-RCT records systematically and continuously retrieved from PubMed/MEDLINE, Embase, CINAHL, ClinicalTrials.gov, WHO's ICTRP, KoreaMed, all Cochrane Review Groups' Specialized Registers, and records identified by handsearching various biomedical. The search was conducted on 16 November 2022.
- In March 2023, deucravacitinib has been licensed for the treatment of psoriasis vulgaris, consequently all authors reviewed their chapters. The following sections changed and were voted on: […], Psoriatic arthritis […]

LoE

- Cochrane Risk of Bias Tool
- GRADE

GoR

- GRADE

Wording of recommendations [29-32]

Strength	Wording	Symbols	Implications
Strong recommendation **for** the use of an intervention	'We recommend ...'	↑↑	We believe that all or almost all informed people would make that choice. Clinicians will have to spend less time on the process of decision-making, and may devote that time to overcome barriers to implementation and adherence. In most clinical situations, the recommendation may be adopted as a policy.
Weak recommendation **for** the use of an intervention	'We suggest ...'	↑	We believe that most informed people would make that choice, but a substantial number would not. Clinicians and health care providers will need to devote more time on the process of shared decision-making. Policy makers will have to involve many stakeholders and policy making requires substantial debate.
No recommendation with respect to an intervention	'We cannot make a recommendation with respect to ...'	0	At the moment, a recommendation in favour or against an intervention cannot be made due to certain reasons (e.g. no reliable evidence data available, conflicting outcomes, etc.)
Weak recommendation **against** the use of an intervention	'We suggest against...'	↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
Strong recommendation **against** the use of an intervention	'We recommend against . . .'	↓↓	We believe that all or almost all informed people would make a choice against that intervention. This recommendation can be adopted as a policy in most clinical situations.

3. Guidance for specific clinical and comorbid situations

3.1. Psoriatic arthritis: How should psoriasis patients with concomitant psoriatic arthritis be managed?

This chapter is based on the corresponding chapter in the previous versions of the guideline 17,18. An existing systematic review and meta-analysis was updated, details of which can be found in the individual chapter, see website**.**

The aim of this updated review is to continuously inform the guideline development group about new evidence on the treatment of patients with plaque type psoriasis who also have psoriatic arthritis (PsA). Therefore, only treatments approved for plaque-type psoriasis and psoriatic arthritis are discussed. Please note that there are an increasing number of treatments available that are only approved for psoriatic arthritis and that clinical trials are increasingly distinguishing between different manifestations of PsA, namely peripheral arthritis, axial disease, enthesitis and dactylitis. Please consult the relevant guidelines and treatment recommendations, which focus primarily on PsA 133,134.

Results/Answer 135-138:

We **recommend** interdisciplinary cooperation with a rheumatologist for the confirmation of the diagnosis of psoriatic arthritis and the selection of a suitable treatment whenever needed.	↑↑	STRONG CONSENSUS[1] 100 % Agreement EXPERT CONSENSUS

[1] due to personal-financial conflict of interest 4 abstentions

- Treatments are usually categorized as NSAIDs (e. g. diclofenac), conventional synthetic disease modifying anti rheumatic drugs (csDMARDs) e. g. MTX, targeted synthetic (ts)DMARDS (e.g. apremilast) and biological (b)DMARDs (e. g. TNFi).
- Head to head trials allowing direct comparison between the different groups or between the individual drugs are extremely rare. Indirect comparisons, e.g. network meta-analyses, are limited by the low number of trials for psoriatic arthritis. See Table 47 for an overview of RCT data on psoriatic arthritis.

Table 47: Summary of the results for drugs approved for psoriasis of the skin and psoriatic arthritis (Dressler et al. [139] updated, see methods section, blue – new data/studies in March 2023

	Patients achieving ARC20 after 12-24 weeks			Patients with at least one adverse event		
	RR	95% CI	Certainty Evidence (GRADE)	RR	95% CI	Certainty Evidence (GRADE)
Head-to-head comparisons:						
ADA 40 mg Q2W+ MTX 15 mg p.o./s.c. QW vs. MTX up to 20-25 mg p.o./s.c. or highest tolerable dose QW	2.06	1.55 to 2.73	LOW	1.08	0.88 to 1.32	VERY LOW
ADA 40mg EOW (1) vs. SEC 300mg LD then Q4W	0.92	0.82 to 1.02	MODERATE	1.02	0.95 to 1.10	MODERATE
APR vs. MTX (no dosage given)	0.83	0.42 to 1.66	VERY LOW	0.53	0.16 to 1.76	VERY LOW
ETA 50mg QW + MTX up to 20mg QW vs. MTX up to 20mg QW	1.28	1.11 to 1.48	LOW	1.01	0.92 to 1.11	MODERATE
INF 5mg/kg w0, 2, 6, 14 + MTX 15mg QW vs. MTX 15mg/ QW	1.40	1.07 to 1.84	VERY LOW	1.65	1.08 to 2.52	VERY LOW
IXE 80mg Q2W (LD 160mg w0) vs. ADA 40mg EOW (1)	1.08	0.86 to 1.36	LOW	1.02*	0.83 to 1.25	MODERATE

Placebo comparisons:						
ADA 40mg EOW (2)	2.08	1.52 to 2.86	MODERATE	1.07	0.83 to 1.39	MODERATE
APR 30mg BID	2.01	1.69 to 2.40	MODERATE	1.24	1.12 to 1.36	LOW
CZP 400mg LD then 200mg Q2W	2.71	1.95 to 3.76	MODERATE	1.01*	0.86 to 1.19	MODERATE
CZP 400mg LD then 400mg Q4W (3)	2.36	1.68 to 3.31	MODERATE	1.05*	0.90 to 1.23	MODERATE
ETA 25mg BIW	5.47	3.27 to 9.16	LOW	no data		
GUS 100mg LD then Q8W (4)	2.13	1.82 to 2.50	HIGH	0.99	0.87 to 1.13	HIGH
INF 5mg/kg w0, 2, 6, 14	4.38	2.24 to 8.56	MODERATE	1.13	0.87 to 1.47	LOW
IXE 80mg Q2W (LD160mg w0)	2.21	1.71 to 2.86	MODERATE	1.39*	1.09 to 1.78	LOW
MTX 7.5mg to 10mg to 15mg	1.82	0.97 to 3.40	LOW	no data		
RZB 150mg w0, 4, 16	1.76	1.56 to 2.00	HIGH	1.03*	0.92 to 1.15	HIGH
SEC 300mg + LD vs. PBO (ACR20 w16-24)	2.55	2.09 to 3.10	MODERATE	1.01	0.91 to 1.11	MODERATE
SEC 300mg + LD vs. PBO (ACR20 w12)	2.74	1.93 to 3.89	MODERATE	0.83	0.65 to 1.06	LOW
UST 45mg	1.95	1.52 to 2.50	HIGH	no data		
UST 90mg (5)	2.26	1.80 to 2.82	MODERATE	0.96	0.75 to 1.24	VERY LOW

1 - 80mg LD only for pts. with moderate-to-severe PsO
2 - No LD of 80mg (this would be the case for PsO)
3 - For psoriasis vulgaris, 400mg Q2W can also be considered
4 - For patients at high risk of joint damage according to clinical judgement, a dose of 100 mg every 4 weeks may be considered (SMPc)
5- For Pso patient with >=100kg (dosis not licensed for PsA); one study reported induction dose of QW (weeks 0-3).
*treatment emergent adverse events
Abbreviations: ACR20 = 20% improvement in American College of Rheumatology response criteria; RR = risk ratio; 95% CI = 95% confidence interval; ETA = etanercept; MTX = methotrexate; mg = milligrams; QW= once a week; INF = infliximab; kg = kilograms;

Non-steroidal anti-inflammatory drugs (NSAIDs)

The role of NSAIDs is usually in the relief of symptoms of psoriatic arthritis for patients with mild and non-erosive articular as well as para-articular involvement. Treatment of NSAIDs should be limited to the lowest required dosage for the shortest period as needed 140.

Treatment initiation

We **recommend** starting treatment early to prevent progression of disease and erosive destruction of joints.	↑↑	STRONG CONSENSUS [1]  EXPERT CONSENSUS

[1] due to personal-financial conflict of interest 4 abstentions

Peripheral active joint involvement (PsA) despite the use of NSAIDs or glucocorticoid site injections (if applicable) and/or polyarthritis increased inflammatory markers and erosive changes, and extra-articular musculoskeletal manifestations are indicators that systemic therapy is needed.

Conventional synthetic DMARDs (e.g. MTX)

We **suggest** monotherapy with a synthetic DMARD (e.g. MTX) as first-line treatment for most patients with moderate to severe psoriasis of the skin and active joint involvement (PsA).	↑	STRONG CONSENSUS [1] 100 % Agreement EVIDENCE AND EXPERT CONSENSUS TABLE 47

[1] due to personal-financial conflict of interest 4 abstentions

This recommendation takes account of the label/price/reimbursement situation in most European countries, the efficacy on skin and peripheral joints, the safety profile and the long-term experience.

Biological DMARDs

For patients with an inadequate response after at least one synthetic DMARD, we **recommend** using a biological DMARD as monotherapy or in combination with a synthetic DMARD. In cases of severe active joint involvement (PsA) where a sufficient response cannot be expected with the use of a conventional treatment, we recommend using a biologic as first-line therapy.	↑↑	STRONG CONSENSUS [1] 100 % Agreement EVIDENCE AND EXPERT CONSENSUS TABLE 47
When choosing a bDMARD for patients with moderate to severe psoriasis of the skin and active joint involvement (PsA), we **recommend** taking into account aspects of efficacy with regard to skin and the joints, comorbidity, practicability and safety.	↑↑	STRONG CONSENSUS [1] 100 % Agreement EXPERT CONSENSUS

[1] due to personal-financial conflict of interest 4 abstentions

The following drugs have been approved for the treatment of psoriatic arthritis by the European Medicines Agency: the TNFi adalimumab, certolizumab – pegol, etanercept, and infliximab; the IL-17 antagonists ixekizumab and secukinumab; the IL-23 antagonists guselkumab and risankizumab and the IL12/23p40 antagonist ustekinumab.

For the available evidence see Table 47.

Previous guidelines have given preference to TNFi over other bDMARDs. The available evidence does not support this approach any longer and shows that other drugs approved by the European Medicines Agency for PsA might be equally effective. Biological DMARDs can be used as monotherapy or in combination with a conventional synthetic DMARD.

Small molecules

Apremilast is the only small molecule currently approved for both plaque type psoriasis and psoriatic arthritis. There are no head-to-head trials comparing apremilast with biological DMARDs. A head–to-head trial with MTX showed comparable efficacy 141.

We **suggest** using apremilast for patients with moderate to severe psoriasis of the skin and active joint involvement (PsA) if an oral treatment is desired or if other systemic agents have led to an inadequate response or if they are contraindicated or not tolerated.	↑	STRONG CONSENSUS[1] 100 % Agreement EVIDENCE AND EXPERT CONSENSUS TABLE 47

[1] due to personal-financial conflict of interest 4 abstentions

In line with the inclusion criteria of this guideline, for this chapter we included only drugs licensed for both, plaque type psoriasis and PsA. Be aware that updacitinib and tofacitinib are licensed and approved for use in psoriatic arthritis, and can show benefit in psoriasis, although they have not been systematically assessed in the scope of this guideline.

Other treatment options

Local injection of glucocorticoids can be recommended in patients with active mono- or oligoarthritis, dactylitis and in entheseal areas (enthesitis).

Systemic use of glucocorticoids should not be standard for the treatment of psoriatic arthritis, but if needed, e. g. during flares, “systemic steroids at the lowest effective dose may be used with caution” 142. Tapering of glucocorticoids should be done slowly and in a step-wise manner when feasible.

Axial spondyloarthritis

We **suggest** using TNFi or IL-17 antagonists for patients with moderate to severe psoriasis of the skin and concomitant PsA manifestation in the form of axial involvement or enthesitis.	↑	STRONG CONSENSUS [1] 100 % Agreement EXPERT CONSENSUS

[1] due to personal-financial conflict of interest 4 abstentions

Referenzen aus Leitlinien:
17. Nast A, Gisondi P, Ormerod AD, et al. European S3-Guidelines on the systemic treatment of psoriasis vulgaris--Update 2015--Short version--EDF in cooperation with EADV and IPC. Journal of the European Academy of Dermatology and Venereology : JEADV. Dec 2015;29(12):2277-94. doi:10.1111/jdv.13354
18. Nast A, Spuls PI, van der Kraaij G, et al. European S3-Guideline on the systemic treatment of psoriasis vulgaris - Update Apremilast and Secukinumab - EDF in cooperation with EADV and IPC. Journal of the European Academy of Dermatology and Venereology: JEADV. 2017/12 2017;31(12):1951-1963. doi:10.1111/jdv.14454
133. Gossec L, Baraliakos X, Kerschbaumer A, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Annals of the rheumatic diseases. Jun 2020;79(6):700-712. doi:10.1136/annrheumdis-2020-217159
134. Coates LC, Soriano ER, Corp N, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. Nat Rev Rheumatol. Aug 2022;18(8):465-479. doi:10.1038/s41584-022-00798-0
135. Elmamoun M, Chandran V. Role of Methotrexate in the Management of Psoriatic Arthritis. Drugs. Apr 2018;78(6):611-619. doi:10.1007/s40265-018-0898-2
136. McInnes IB, Nash P, Ritchlin C, et al. Secukinumab for psoriatic arthritis: comparative effectiveness versus licensed biologics/apremilast: a network meta-analysis. Journal of comparative effectiveness research. Nov 2018;7(11):1107-1123. doi:10.2217/cer-2018-0075
137. Mease PJ, Smolen JS, Behrens F, et al. A head-to-head comparison of the efficacy and safety of ixekizumab and adalimumab in biological-naive patients with active psoriatic arthritis: 24-week results of a randomised, open-label, blinded-assessor trial. Annals of the rheumatic diseases. Jan 2020;79(1):123-131. doi:10.1136/annrheumdis-2019-215386

138. Nash P, McInnes IB, Mease PJ, et al. Secukinumab Versus Adalimumab for Psoriatic Arthritis: Comparative Effectiveness up to 48 Weeks Using a Matching-Adjusted Indirect Comparison. Rheumatology and therapy. Jun 2018;5(1):99-122. doi:10.1007/s40744-018-0106-6
139. Dressler C, Eisert L, Pham PA, Nast A. Efficacy and safety of systemic treatments in psoriatic arthritis: a systematic review, meta-analysis and GRADE evaluation. Journal of the European Academy of Dermatology and Venereology : JEADV. Jul 2019;33(7):1249-1260. doi:10.1111/jdv.15482

Gossec L et al., 2024 [7].

EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update

Zielsetzung/Fragestellung

New modes of action and more data on the efficacy and safety of existing drugs in psoriatic arthritis (PsA) required an update of the EULAR 2019 recommendations for the pharmacological treatment of PsA.

Methodik

Grundlage der Leitlinie

Update der EULAR 2019 Empfehlungen

- Repräsentatives Gremium: **trifft zu**
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt: **trifft zu**
- Systematische Suche, Auswahl und Bewertung der Evidenz: **trifft zu** (separat veröffentlicht: systematic literature review (SLR), performed […] between November 2022 and April 2023)
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt: **trifft zu**
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt: **trifft teilweise zu**
- Regelmäßige Überprüfung der Aktualität gesichert: **trifft teilweise zu**

Recherche/Suchzeitraum:

- Questions were then defined and addressed through a systematic literature review (SLR), performed by the fellow (AK) between November 2022 and April 2023, for the literature pertaining to pharmacological treatments of PsA and published since the previous SLR (ie, since the end of 2018). [8]
- SLR Kerschbaumer et al. (2024):
  - To update the evidence from the previous SLR with the data cut on 21 December 2018,24 articles published in English language between 1 January 2018 and 28 December 2022 were searched by an experienced librarian (JWS) using Medline (PubMed), Embase (OVID version), the Cochrane CENTRAL Register of Controlled Trials (Central) and the abstract archives of the EULAR and American College of Rheumatology (ACR) annual meetings
  - To prevent missing important publications, we included the year 2018 in the literature search, as manuscripts which carry the date of a specific year might be published with some delay. Like in previous SLRs, conference abstracts from the last 3 years (from 2020 to 2022) were eligible for inclusion. In the case of articles being published after the data cut of the literature search but before the EULAR task force meeting (17 April 2023), fully published manuscripts were eligible to be included only if they had been covered as a conference abstract in the initial systematic search.

LoE/GoR

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

Sonstige methodische Hinweise

- The updated recommendations include 7 OAPs (vs 6 in 2019) and 11 recommendations (vs 12 in 2019, due to merges). Of the 11 recommendations, only 4 are unchanged compared with 2019 […]

Empfehlungen

Table 2 2023 updated EULAR recommendations for the pharmacological management of psoriatic arthritis

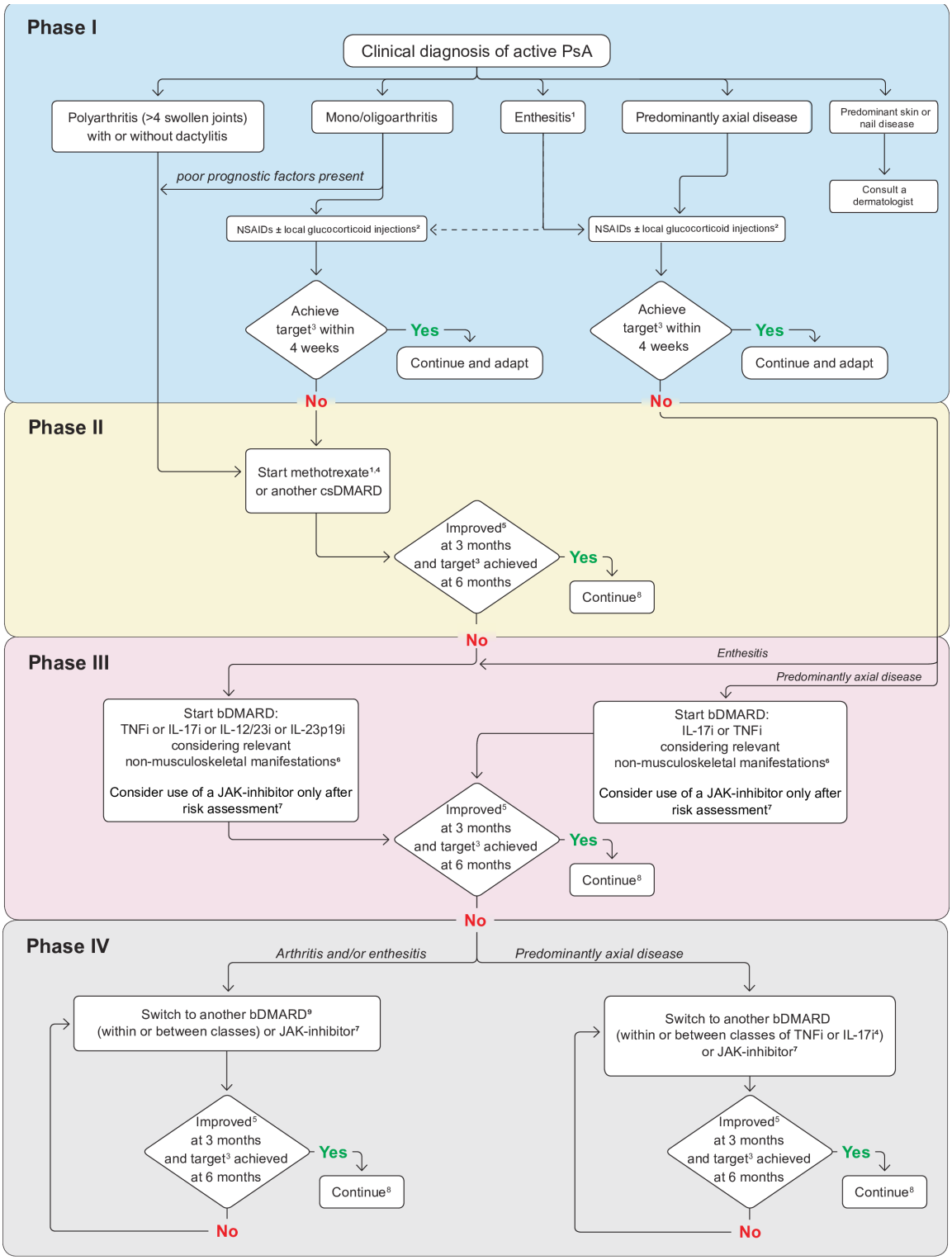
	Overarching principles			Level of agreement, mean (SD)
A	Psoriatic arthritis is a heterogeneous and potentially severe disease, which may require multidisciplinary treatment.			10.0 (0.1)
B	Treatment of psoriatic arthritis patients should aim at the best care and must be based on a shared decision between the patient and the rheumatologist, considering efficacy, safety, patient preferences and costs.			9.7 (0.6)
C	Rheumatologists are the specialists who should primarily care for the musculoskeletal manifestations of patients with psoriatic arthritis; in the presence of clinically relevant skin involvement, a rheumatologist and a dermatologist should collaborate in diagnosis and management.			9.7 (0.5)
D	The primary goal of treating patients with psoriatic arthritis is to maximise health-related quality of life, through control of symptoms, prevention of structural damage, normalisation of function and social participation; abrogation of inflammation is an important component to achieve these goals.			9.9 (0.3)
E	In managing patients with psoriatic arthritis, consideration should be given to each musculoskeletal manifestation and treatment decisions made accordingly.			9.8 (0.4)
F	When managing patients with psoriatic arthritis, non-musculoskeletal manifestations (particularly skin, eye and gastrointestinal tract) should be taken into account; comorbidities such as obesity, metabolic syndrome, cardiovascular disease or depression should also be considered.			9.7 (0.7)
G	The choice of treatment should take account of safety considerations regarding individual modes of action to optimise the benefit–risk profile.			9.9 (0.4)
	Recommendations	**Level of evidence**	**Grade of recommendation**	**Level of agreement, mean (SD)**
1	Treatment should be aimed at reaching the target of remission or, alternatively, low disease activity, by regular disease activity assessment and appropriate adjustment of therapy.	1b	A	9.5 (1.0)
2	Non-steroidal anti-inflammatory drugs may be used to relieve musculoskeletal signs and symptoms[a]; local injections of glucocorticoids may be considered as adjunctive therapy[b].	1b[a], 3b[b]	A[a], C[b]	9.5 (0.7)
3	In patients with polyarthritis, or those with monoarthritis/oligoarthritis and poor prognostic factors[a] (eg, structural damage, elevated acute phase reactants, dactylitis or nail involvement), a csDMARD should be initiated rapidly, with methotrexate preferred in those with clinically relevant skin involvement.	1b, 4[a]	B, C[a]	9.3 (0.8)

4	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD should be commenced.	1a	A	9.5 (1.3)
5	In patients with peripheral arthritis and an inadequate response to at least one bDMARD, or when a bDMARD is not appropriate[a], a JAKi may be considered, taking safety considerations* into account.	1b, 4[a]	B, D[a]	9.1 (1.5)
6	In patients with mild disease and an inadequate response to at least one csDMARD, in whom neither a bDMARD nor a JAKi* is appropriate, a PDE4 inhibitor may be considered.	1b	B	8.7 (1.1)
7	In patients with unequivocal enthesitis and an insufficient response to NSAIDs or local glucocorticoid injections, therapy with a bDMARD should be considered.	1b	B	9.5 (0.9)
8	In patients with clinically relevant axial disease with an insufficient response to NSAIDs, therapy with an IL-17A inhibitor, a TNF inhibitor, an IL-17 A/F inhibitor or a JAKi* should be considered.	1b	B	9.4 (1.3)
9	The choice of the mode of action should reflect non-musculoskeletal manifestations related to psoriatic arthritis; with clinically relevant skin involvement, preference should be given to an IL-17A or IL-17A/F or IL-23 or IL-12/23 inhibitor; with uveitis to an anti-TNF monoclonal antibody; and with IBD to an anti-TNF monoclonal antibody or an IL-23 inhibitor or IL-12/23 inhibitor or a JAKi*.	1b	B	9.6 (0.7)
10	In patients with an inadequate response or intolerance to a bDMARD or a JAKi, switching to another bDMARD or JAKi* should be considered[a], including one switch within a class[b].	1b[a], 4[b]	C	9.5 (0.7)
11	In patients in sustained remission, tapering of DMARDs may be considered.	2b	B	9.4 (1.2)

'Mild disease' is defined as oligoarticular or entheseal disease without poor prognostic factors and limited skin involvement.
csDMARDs (conventional synthetic DMARDs) include methotrexate, sulfasalazine or leflunomide. bDMARDs (biologic DMARDs) here include TNF inhibitors (both original and biosimilars), drugs targeting the IL-17 and IL-12–23/IL-23-p19 pathways, and in the context of recommendation 10 also CTLA4 (cytotoxic T-lymphocyte–associated antigen 4) inhibition. JAKis (Januse kinase inhibitors) include tofacitinib and upadacitinib.
The superscript letters 'a' and 'b' are used to link a part of the recommendation to a level of evidence.
The table shows the level of evidence, grade of recommendation and level of agreement among taskforce members (0–10 scale).
*For JAKis, caution is needed for patients aged 65 years or above, those who are current or past long-time smokers, with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors or with other malignancy risk factors, and with known risk factors for venous thromboembolism.
bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; CTLA4, cytotoxic T-lymphocyte–associated antigen 4; DMARDs, disease-modifying antirheumatic drugs; IBD, inflammatory bowel disease; IL, interleukin; JAKi, Janus kinase inhibitor; NSAIDs, non-steroidal anti-inflammatory drugs; PDE4, phosphodiesterase 4; TNF, tumour necrosis factor.

Recommendations

Of note, these recommendations are centred on non-topical pharmacological treatments; topical and non-pharmacological treatments are also important in PsA but are outside our scope. Figure 1 shows a summarised algorithm of the treatment proposals. Some safety issues will be briefly addressed, but for a full picture of the adverse event profile of different drugs the package inserts should be consulted.



1. *Some studies suggest that enthesitis may respond to methotrexate, but the level of evidence is low.*
2. *No glucocorticoids for axial disease.*
3. *The target is remission or low disease activity (especially with long standing disease) in accordance with the treat-to-target recommendations.*
4. *Preferred in the presence of relevant skin involvement, however in case of concomitant inflammatory bowel disease or uveitis, a TNF monoclonal antibody or (for IBD) IL-23i or 12/23i or JAKi is recommended.*
5. *Improvement means at least 50% reduction in disease activity.*
6. *Arthritis/enthesitis: TNFi or IL-17i or IL-12/23i or IL-23p19i; Skin: IL-17i or IL-12/23i or IL-23p19i; Uveitis: anti-TNF monoclonal antibody; IBD: anti-TNF monoclonal antibody or IL-12/23i or IL-23p19i or JAKi; Consider using PDE4i in mild disease if bDMARD and JAKi is inappropriate.*
7. *For JAK-inhibitors, caution is needed for patients aged 65 years or above, current or past long-time smokers, with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors or with other malignancy risk factors; with known risk factors for venous thromboembolism.*
8. *Consider tapering in sustained remission.*
9. *Including abatacept.*

Figure 1 2023 EULAR recommendations algorithm for the management of PsA. bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IBD, inflammatory bowel disease; L, interleukin; JAK, Janus kinase inhibitor; JAKi, Janus kinase inhibitor; NSAID, non-steroidal anti-inflammatory drugs; TNF, tumour necrosis factor; TNFI, tumour necrosis factor inhibitor.

Recommendation 3

In patients with polyarthritis or those with monoarthritis/ oligoarthritis and poor prognostic factors (eg, structural damage, elevated acute phase reactants, dactylitis or nail involvement), a csDMARD should be initiated rapidly, with methotrexate preferred in those with clinically relevant skin involvement.

Hintergrundinformationen:

Among patients with peripheral arthritis,34 35 a distinction is made according to the number of swollen joints and according to prognostic factors.36 In 2019, polyarthritis and monoarthritis/ oligoarthritis with poor prognostic markers were addressed in separate bullet points, which were merged for clarity in this update (table 3). Oligoarticular disease is defined as arthritis (swollen joints) of up to four (included) joints.9 This definition applies to clinical detection (rather than imaging). The prognostic factors have also been previously defined9 17 and are unchanged.

We recommend rapid csDMARD start, concomitant (or close) with the initiation of symptomatic therapy, for both patients with polyarticular disease and patients with oligoarticular disease and poor prognostic factors. Patients with oligoarticular disease and lack of poor prognostic factors should also receive a csDMARD, but there is less urgency for these patients given the more favourable long-term prognosis. The latter may receive csDMARDs after a longer delay, and potentially a period of symptomatic treatment alone (see recommendation 2). Since there is a lack of strong evidence to support this approach of rapid treatment introduction, this recommendation was mainly based on expert opinion.

Of note, there is no specific recommendation for dactylitis. We consider dactylitis as an association of (oligo)synovitis, tenosynovitis and enthesitis. Patients with isolated dactylitis should be treated similarly to patients with oligoarthritis; this includes the use of joint glucocorticoid injections and csDMARDs, which have shown efficacy in relieving dactylitis.37

The first DMARD should be a csDMARD (meaning MTX, leflunomide or sulfasalazine). The decision concerning the first-line DMARD is important and led to much taskforce discussion, and has been put as an element for further research in the research agenda (table 4). The continued prioritisation of csDMARDs reflects consensual expert opinion within the taskforce that favoured the benefit–risk–cost balance of csDMARDs and in particular MTX over targeted drugs. The absence of new data indicating the superiority of a b/tsDMARD as first-line, and in the presence of new data on MTX, was seen as confirming the efficacy of this drug in PsA.5 37–39

Since the EULAR recommendations adhere to a treat-to- target (T2T) approach which implies a reduction of disease activity by at least 50% within 3 months and reaching the treatment target within 6 months, a csDMARD should not be continued if these therapeutic goals are not attained. On csDMARD inefficacy, another DMARD, such as a bDMARD (see recommendation 4), can be rapidly instituted. Generally speaking, we recommend assessing the efficacy of the csDMARD and deciding if it should be pursued as monotherapy or not, after 12 weeks, in line with the T2T recommendations.26 Although MTX use in PsA has typically been founded on evidence from other immune-mediated diseases such as RA and psoriasis,40 there is also evidence for its efficacy in PsA, with recent confirmatory data both from observational data sources and from a randomised trial indicating that a proportion of patients will respond to escalation of doses of MTX.39 41–43 The efficacy–safety balance of MTX should be assessed regularly, given the general metabolic profile of patients with PsA which can put them at a higher risk for adverse events such as hepatotoxicity.42–44 The MTX dose should be sufficient, that is, usually between 20 mg and 25 mg weekly (about 0.3 mg/ kg), and use of folate supplementation is recommended to reduce the adverse effects of MTX.45 Other csDMARDs (ie, leflunomide and sulfasalazine) are potential treatment options and have demonstrated efficacy in PsA peripheral arthritis.15 A recent trial of the combination of MTX with leflunomide indicated a low efficacy to safety ratio; thus, this association is not recommended.38

Recommendation 4

In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD should be commenced.

This recommendation is relevant to patients with peripheral arthritis and therefore is meant to include both those with monoarticular/oligoarticular and those with polyarticular disease. However, where peripheral involvement is limited and without poor prognostic factors, it is not unreasonable to apply a second csDMARD course before initiating a bDMARD/ tsDMARD, when this decision is agreed by the prescriber and the patient.

After failure of at least one csDMARD, the taskforce proposed as next step one of the many available bDMARDs (table 1).5 JAKi is efficacious in PsA, but the taskforce decided that at

present the efficacy–safety balance, costs and long-term experience with many bDMARDs clearly favour their recommendation over JAKi. Relevant comorbidities in many patients with PsA also favour bDMARD selection.

Regarding bDMARDs, no order of preference is given since no bDMARD has demonstrated superiority for joint involvement over other bDMARDs (table 1).46–48 Herein they are listed in numeric order of the targeted cytokine, and not in order of preference. However, in the context of the present recommendation, CTLA4 (cytotoxic T-lymphocyte– associated antigen 4) inhibition is not considered a good option due to its limited efficacy in clinical trials.49 The GoR is high for this bullet point, reflecting robust accrued data.50

Unlike MSK manifestations, non-MSK domains of PsA allow differential order of bDMARD recommendation (se recommendation 9).5 Two head-to- head trials of bDMARDs in PsA, both comparing an IL-17A inhibitor with adalimumab, showed similar efficacy for IL-17A inhibition and TNF inhibition, as regards efficacy on the joints, while skin responses are better with the former.46 47 We also note that there is evidence on the better efficacy of a bDMARD compared with MTX in skin psoriasis (and evidence for differences between bDMARDs, please see recommendation 9).51 52

All bDMARDs and JAKi showed efficacy regarding inhibition of radiographic progression; such data are lacking for apremilast. The safety of the different available categories of bDMARDs appears acceptable in our SLR.5 All bDMARDs increase the risk of infections.5 The risks of TNF inhibitors (TNFis) are well known. Candidiasis (usually mucocutaneous) is more frequent with IL-17A and IL-17A/ F inhibition, particularly the latter.53 54 While IL-23- p19i is a more recent addition to the armament, its safety appears satisfactory, in line with ustekinumab which also interferes with IL-23 (p40 chain) whose adverse event profile is well known and appears satisfactory.5

As a general rule, safety and comorbidities need to be taken into account when a decision to start a new drug is taken. More complete information regarding the safety aspects of bDMARDs is provided in the individual drug's product information. Costs should also be taken into account, but these may vary at the country level; cost savings will occur in many countries due to the availability of biosimilar TNF blockers and potentially other biosimilars in due course. Personalised medicine, to facilitate an optimal choice of the first bDMARD, is currently difficult due to the lack of individualised predictors of response to treatment.55 As previously discussed, it is of key importance to take into account the patient phenotype and potential extra-MSK features (figure 1). Comorbidities are also to be considered.23 56 More research is needed on the predictors of drug response, including the effect of sex.57 58

Combination of a bDMARD with a csDMARD

First-line bDMARDs are often given in combination with csDMARDs, such as MTX.41 59 However, there are conflicting data regarding the added benefit of concomitant MTX with targeted DMARDs in patients with peripheral disease and no evidence of a benefit of MTX in patients with axial symptoms. 33 60 61

MTX combination with bDMARDs has been explored mainly for TNFi; studies have generally found similar efficacy with or without concomitant MTX, although with increased drug survival when using MTX, in some studies.41 59 62 A recent large study reported increased remission rates with TNFi plus MTX combination therapy.59 With other modes of action, there is a lack of data to support comedication. Overall, the taskforce proposed to combine a first bDMARD with the previously prescribed csDMARD, in all cases where such a treatment has already been tolerated by the patient and in particular when the first bDMARD is a TNFi. For other modes of action, given the lack of data, we cannot recommend comedication, although the usual practice would be to continue a csDMARD when initiating a bDMARD (doses of the csDMARD can be diminished if needed).

Recommendation 5

In patients with peripheral arthritis and an inadequate response to at least one bDMARD, or when a bDMARD is not appropriate, a JAKi may be considered, taking safety considerations into account.

This recommendation elicited much debate. On the one hand, since 2019, new data have accrued on JAKis in terms of efficacy, such as the publication of positive trials on upadacitinib in PsA.63 On the other hand, there is currently a worldwide cautionary statement issued by both the Food and Drug Administration and the European Medicine Agency restricting the use of JAKis in all diseases including PsA, based on an increased risk of cardiovascular and malignancy events observed with tofacitinib in older patients with RA with cardiovascular risk factors.6–8 JAKis lead to increased general infection rates of similar magnitude to bDMARDs, but higher for herpes zoster infections.5 Drug safety for the JAKis tofacitinib and upadacitinib in the specific context of PsA was recently reported and appeared reassuring; however, follow-up was short and further data are warranted.64 65 While currently long-term extension data do not show increased cardiovascular/ cancer risk related to JAKi use in PsA, there are no RCTs similar to the ORAL-Surveillance trial available at present in PsA. Therefore, the taskforce felt that the precautions related to RA also have to be taken for PsA, especially since various comorbidities important for the JAKi risk profile may be more prevalent in PsA than in RA (eg, obesity and cardiovascular risk factors). On the other hand, controlling inflammation is important to decrease cardiovascular risk.

Safety of JAKis should be carefully considered66; we propose in table 2 and figure 1 a shortened version of the EMA warning/ limitation to use, which includes age, smoking status and other cardiovascular/venous/cancer risk factors.7 8

After much discussion, we considered that the efficacy–safety balance of JAKis did not justify putting JAKis on the same level as bDMARDs for order of choice (ie, proposing JAKis as usual treatment after insufficient response and/or intolerance to csDMARD treatment).

Therefore, JAKis are proposed usually as second-line targeted therapies (or third-line DMARDs). Of note, we recognise that, for some patients, JAKis may be a relevant option after a csDMARD; this is reflected in the wording of the bullet point ('when a bDMARD is not appropriate'). This 'non-appropriateness' may include contraindications to bDMARDs, practical issues leading to a strong preference for oral administrations (eg, lack of proper conservation at regulated temperatures) and patient preferences, including risk of non-adherence to injections (in accordance with the first OAP concerning shared decision-making). Nevertheless, patients will have to weigh their preferences against potential risks.

The GoR was low for this recommendation, in particular regarding safety considerations, since the data are sparse in PsA and we had to rely on data taken from RA. The taskforce suggests using JAKi after bDMARDs have failed because several new bDMARDs with excellent effects on skin involvement and relatively good safety data are now available (IL-23, IL-17 inhibitors) and more long-term data on JAKi efficacy and safety are needed in PsA. The efficacy to safety ratio of JAKis was also put into the research agenda (table 4).

Currently, drugs from the tyrosine kinase 2 (TYK2) pathway inhibition are being assessed in PsA5; they are not currently licensed for use, and indeed the data are at this point limited in particular for safety (including in psoriasis where such therapy is licensed). Thus, we did not include TYK2 inhibition in the current recommendations.

Recommendation 6

In patients with mild disease and an inadequate response to at least one csDMARD, in whom neither a bDMARD nor a JAKi is appropriate, a PDE4 inhibitor may be considered.

This recommendation is unchanged from 2019, with unchanged LoE. ‘Mild disease’ is defined as oligoarticular or entheseal disease without poor prognostic factors and limited skin involvement.9 67 The FOREMOST trial recently confirmed the efficacy of apremilast compared with placebo in oligoarticular PsA.67 Nevertheless, the reason to place apremilast differently from bDMARDs or other tsDMARDs is not only based on its consistently relatively low efficacy, but also on the lack of structural efficacy data (thus putting the term ‘DMARD’ at risk since there are no data on inhibition of damage progression). This recommendation received the lowest LoA within the taskforce, reflecting that more than a quarter of the taskforce participants were in favour of only discussing apremilast in the text without a specific bullet point. The use of apremilast in combination with TNFi is off-label, and is a more costly drug combination with no supporting data and cannot be recommended.

Recommendation 10

In patients with an inadequate response or intolerance to a bDMARD or a JAKi, switching to another bDMARD or JAKi should be considered, including one switch within a class.

This recommendation is unchanged from 2019, with unchanged LoE.9 After failing one targeted drug, it is logical to switch to another targeted drug; there are currently no strong data to prefer a switch with a change in mode of action to a switch within the same mode of action. Of note, this recommendation does not limit the total number of switches for a given patient. It also does not necessarily mean that more switches within a class could not be done, but the taskforce felt that a switch should not necessarily be done after one drug of a class has failed. Switches can be made, as appropriate, between bDMARDs, or between bDMARDs and JAKis. We include abatacept as a treatment option (table 1),49 but note that it demonstrated modest efficacy and hence this is an option to be used only after failing one or more other targeted drugs. The efficacy of bimekizumab, the dual IL-17 A/F inhibitor, appeared similar in TNF-naïve and TNF-experienced populations; this will warrant confirmation. 53 54 Finally, a combination of bDMARDs is being explored, but cannot be recommended at this time.

Referenzen aus Leitlinien

5 Kerschbaumer A, Smolen JS, Ferreira RJO, et al. Efficacy and safety of pharmacological treatment of psoriatic arthritis: a systematic literature research informing the 2023 update of the EULAR recommendations for the management of psoriatic arthritis. Ann Rheum Dis 2024;83:760–74.
6 Ytterberg SR, Bhatt DL, Mikuls TR, et al. Cardiovascular and cancer risk with tofacitinib in rheumatoid arthritis. N Engl J Med 2022;386:316–26.
7 European Medicine Agency statement. Available: https://www.ema.europa.eu/en/ medicines/human/referrals/janus-kinase-inhibitors-jaki [Accessed 7 Nov 2023].
8 US food and Drug Administration. Available: https://www.fda.gov/safety/ medical-product-safety-information/janus-kinase-jak-inhibitors-drug-safetycommunication-fda-requires-warnings-about-increased-risk [Accessed 7 Nov 2023].
9 Gossec L, Baraliakos X, Kerschbaumer A, et al. EULAR recommendations for the management of Psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis 2020;79:700–12.
15 Gossec L, Smolen JS, Ramiro S, et al. European League against rheumatism (EULAR) recommendations for the management of Psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis 2016;75:499–510.
16 FitzGerald O, Ogdie A, Chandran V, et al. Psoriatic arthritis. Nat Rev Dis Primers 2021;7:59.
17 Kerola AM, Kazemi A, Rollefstad S, et al. All--cause and cause--specific mortality in rheumatoid arthritis, psoriatic arthritis and axial spondyloarthritis: a nationwide registry study. Rheumatology (Oxford) 2022;61:4656–66.
23 Leung YY, Eder L, Orbai A-M, et al. Association between obesity and likelihood of remission or low disease activity status in psoriatic arthritis applying index-based and patient-based definitions of remission: a cross-sectional study. RMD Open 2023;9:e003157.

26 Smolen JS, Schöls M, Braun J, et al. Treating axial spondyloarthritis and peripheral spondyloarthritis, especially psoriatic arthritis, to target: 2017 update of recommendations by an international task force. Ann Rheum Dis 2018;77:3–17.
33 Ramiro S, Nikiphorou E, Sepriano A, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis2023;82:19–34
34 Zabotti A, Fagni F, Gossec L, et al. n.d. Subclinical psoriatic arthritis and new onset psoriatic arthritis in subjects transitioning from psoriasis: an analysis of 2 longitudinal cohorts. In Review, RMD Open
35 de Vlam K, Steinfeld S, Toukap AN, et al. The burden of psoriatic arthritis in the biologics era: data from the Belgian epidemiological psoriatic arthritis study. Rheumatology 2021;60:5677–85.
36 Kishimoto M, Deshpande GA, Fukuoka K, et al. Clinical features of psoriatic arthritis. Best Pract Res Clin Rheumatol 2021;35:101670.
37 Vieira--Sousa E, Alves P, Rodrigues AM, et al. GO--DACT: a phase 3B randomised, double--blind, placebo--controlled trial of golimumab plus methotrexate (MTX) versus placebo plus MTX in improving dactylitis in MTX--naive patients with psoriatic arthritis. Ann Rheum Dis 2020;79:490–8.
38 Mulder MLM, Vriezekolk JE, van Hal TW, et al. Comparing methotrexate monotherapy with methotrexate plus leflunomide combination therapy in psoriatic arthritis (COMPLETE--PSA): a double--blind, placebo--controlled, randomised, trial. Lancet Rheumatol 2022;4:e252–61.
39 Coates LC, Tillett W, D'Agostino M--A, et al. Comparison between adalimumab introduction and methotrexate dose escalation in patients with inadequately controlled psoriatic arthritis (CONTROL): a randomised, open--label, two--part, phase 4 study. Lancet Rheumatol 2022;4:e262–73.
40 Smolen JS, Landewé RBM, Bergstra SA, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease--modifying Antirheumatic drugs: 2022 update. Ann Rheum Dis 2023;82:3–18.
41 Lindström U, di Giuseppe D, Exarchou S, et al. Methotrexate treatment in early Psoriatic arthritis in comparison to rheumatoid arthritis: an observational nationwide study. RMD Open 2023;9:e002883.
42 Wilsdon TD, Whittle SL, Thynne TR, et al. Methotrexate for psoriatic arthritis. Cochrane Database Syst Rev 2019;1:CD012722.
43 Felten R, Lambert De Cursay G, Lespessailles E. Is there still a place for methotrexate in severe psoriatic arthritis. Ther Adv Musculoskelet Dis 2022;14.
44 Curtis JR, Beukelman T, Onofrei A, et al. Elevated liver enzyme tests among patients with rheumatoid arthritis or psoriatic arthritis treated with methotrexate and/or leflunomide. Ann Rheum Dis 2010;69:43–7.
45 Liu L, Liu S, Wang C, et al. Folate supplementation for methotrexate therapy in patients with rheumatoid arthritis: a systematic review. J Clin Rheumatol 2019;25:197–202.
46 Mease PJ, Smolen JS, Behrens F, et al. SPIRIT H2H study group. A head--to--head comparison of the efficacy and safety of Ixekizumab and adalimumab in biological-naïve patients with active psoriatic arthritis: 24--week results of a randomised, open-label, blinded--assessor trial. Ann Rheum Dis 2020;79:123–31.
47 McInnes IB, Behrens F, Mease PJ, et al. Secukinumab versus adalimumab for treatment of active psoriatic arthritis (EXCEED): a double--blind, parallel--group, randomised, active--controlled, phase 3B trial. Lancet 2020;395:1496–505.
48 Gossec L, Siebert S, Bergmans P, et al. Persistence and effectiveness of the IL--12/23 pathway inhibitor ustekinumab or tumour necrosis factor inhibitor treatment in patients with psoriatic arthritis: 1--year results from the real--world Psabio study. Ann Rheum Dis 2022;81:823–30.
49 Mease PJ, Gottlieb AB, van der Heijde D, et al. Efficacy and safety of abatacept, a T--cell modulator, in a randomised, double--blind, placebo--controlled, phase III study in psoriatic arthritis. Ann Rheum Dis 2017;76:1550–8.
50 McInnes IB, Sawyer LM, Markus K, et al. Targeted systemic therapies for psoriatic arthritis: a systematic review and comparative synthesis of short--term articular, dermatological, enthesitis and dactylitis outcomes. RMD Open 2022;8:e002074.
51 Sbidian E, Chaimani A, Garcia--Doval I, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta--analysis. Cochrane Database Syst Rev 2022;5:CD011535.
52 Sbidian E, Chaimani A, Guelimi R, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta--analysis. Cochrane Database Syst Rev 2023;7:CD011535.
53 McInnes IB, Asahina A, Coates LC, et al. Bimekizumab in patients with psoriatic arthritis, naive to biologic treatment: a randomised, double--blind, placebo--controlled, phase 3 trial (BE OPTIMAL). Lancet 2023;401:25–37.
54 Merola JF, Landewé R, McInnes IB, et al. Bimekizumab in patients with active psoriatic arthritis and previous inadequate response or intolerance to tumour necrosis factor-A inhibitors: a randomised. The Lancet 2023;401:38–48.
55 Miyagawa I, Nakayamada S, Nakano K, et al. Precision medicine using different biological Dmards based on characteristic phenotypes of peripheral T helper cells in psoriatic arthritis. Rheumatology (Oxford) 2019;58:336–44.

56 Drosos GC, Vedder D, Houben E, et al. EULAR recommendations for cardiovascular risk management in rheumatic and musculoskeletal diseases, including systemic lupus erythematosus and antiphospholipid syndrome. Ann Rheum Dis 2022;81:768–79.
57 Tarannum S, Leung Y--Y, Johnson SR, et al. Sex- and gender--related differences in Psoriatic arthritis. Nat Rev Rheumatol 2022;18:513–26.
58 Orbai A--M, Perin J, Gorlier C, et al. Determinants of patient--reported psoriatic arthritis impact of disease: an analysis of the association with sex in 458 patients from fourteen countries. Arthritis Care Res (Hoboken) 2020;72:1772–9.
59 Lindström U, Di Giuseppe D, Delcoigne B, et al. Effectiveness and treatment retention of TNF inhibitors when used as monotherapy versus comedication with csDMARDs in 15 332 patients with psoriatic arthritis. Ann Rheum Dis 2021;80:1410–8.
60 Behrens F, Cañete JD, Olivieri I, et al. Tumour necrosis factor inhibitor monotherapy vs combination with MTX in the treatment of PSA: a systematic review of the literature. Rheumatology (Oxford) 2015;54:915–26.
61 Koehm M, Rossmanith T, Foldenauer AC, et al. Methotrexate plus ustekinumab versus ustekinumab monotherapy in patients with active psoriatic arthritis (MUST): a randomised, Multicentre, placebo--controlled, phase 3B, non--inferiority trial. Lancet Rheumatol 2023;5:e14–23.
62 Fagerli KM, Lie E, van der Heijde D, et al. The role of methotrexate co--medication in TNF--inhibitor treatment in patients with psoriatic arthritis: results from 440 patients included in the NOR--DMARD study. Ann Rheum Dis 2014;73:132–7.
63 McInnes IB, Anderson JK, Magrey M, et al. Trial of upadacitinib and adalimumab for psoriatic arthritis. N Engl J Med 2021;384:1227–39.
64 Burmester GR, Cohen SB, Winthrop KL, et al. Safety profile of upadacitinib over 15 000 patient--years across rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and atopic dermatitis. RMD Open 2023;9:e002735.
65 Mease P, Charles--Schoeman C, Cohen S, et al. Incidence of venous and arterial thromboembolic events reported in the tofacitinib rheumatoid arthritis, psoriasis and psoriatic arthritis development programmes and from real--world data. Ann Rheum Dis 2020;79:1400–13.
66 Kristensen LE, Danese S, Yndestad A, et al. Identification of two tofacitinib subpopulations with different relative risk versus TNF inhibitors: an analysis of the open label, randomised controlled study ORAL surveillance. Ann Rheum Dis 2023;82:901–10. 10.1136/ard-2022-223715 Available: http://dx.doi.org/10.1136/ ard-2022-223715
67 Mease P, Gladman D, Coates L, et al. 16--week results from FOREMOST, a placebo-controlled study involving oligoarticular psoriatic arthritis treated with apremilast. Arthritis Rheumatol 2023;75.

Coates LC et al., 2022 [5].

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 treatment recommendations for psoriatic arthritis

Siehe auch:

- Coates LC et al., 2021 [4].
- Coates LC et al., 2021 [3].

Leitlinienorganisation/Fragestellung

To update the 2009 Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) treatment recommendations for the spectrum of manifestations affecting patients with psoriatic arthritis (PsA).

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium; zutreffend
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt; zutreffend

Systematische Suche, Auswahl und Bewertung der Evidenz; searches were initially run in 2019 but were updated in 2020 owing to delays in the recommendation. Additional searches identified evidence published in abstract form at key rheumatology and dermatology conferences (ACR, EULAR and American Academy of Dermatology annual meetings) from 2017 to 2020. Data that had only been published in abstract form at the time the recommendations were created were included so as to provide consideration of the newest data in this fast- evolving discipline, but, as in 2015, it was decided that data derived from abstracts alone should be clearly identified in the recommendations.

- Formale Konsensusprozesse und externes Begutachtungsverfahren unklar; recommendations were critically reviewed and edited via in-person discussion and online survey.
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt; the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach was applied
- Regelmäßige Überprüfung der Aktualität gesichert, zutreffend
- GRAPPA rheumatologists, dermatologists, and PsA patients drafted recommendations

<u>Sonstige methodische Hinweise</u>

- Bewertung der internen Validität der Einzelstudien unklar
- Z.T. keine eindeutige Zuordnung der zugrundeliegenden Evidenz zu den Empfehlungen
- Der Ausblick einer überarbeiteten Version ist veröffentlicht jedoch steht die Veröffentlichung der aktualisierten und vollumfänglichen Leitlinie noch aus.

Empfehlungen

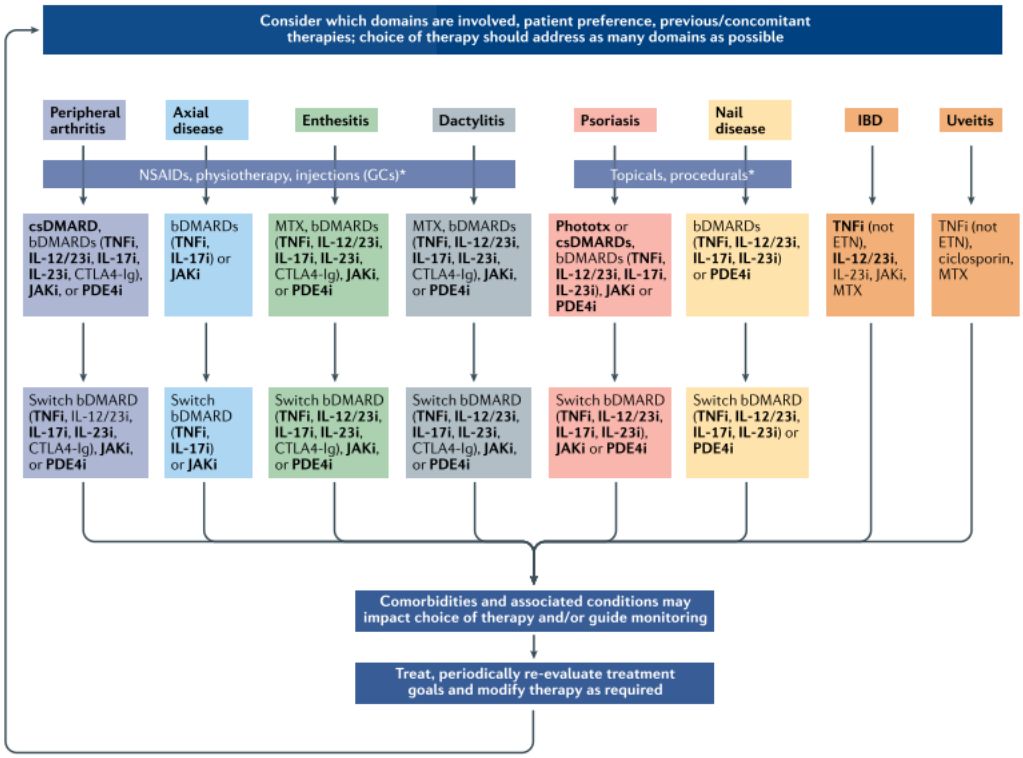


Fig. 2 | **GRAPPA 2021 treatment schema.** The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) 2021 treatment recommendations for psoriatic arthritis (PsA) use a domain-based approach, but, considering that most patients present with disease in multiple domains, this treatment schema combines the recommendations for each domain to guide therapeutic decisions. Disease activity should be assessed in each of the domains and consideration given to comorbidities, previous therapies and patient preference. Standard 'step-up' approaches, as well as expedited treatment routes, are indicated. Treatment efficacy and tolerability should be re-evaluated periodically and treatment adjusted as appropriate. The order of the products in the boxes is sorted by mechanism of action and does not reflect guidance on relative efficacy or suggested usage. Bold text indicates a strong recommendation, standard text a conditional recommendation. The asterisks indicate a conditional recommendation based on data from abstracts only. bDMARD, biologic DMARD; CTLA4-Ig, CTLA4–immunoglobulin fusion protein; csDMARD, conventional synthetic DMARD; ETN, etanercept; GC, glucocorticoid; IBD, inflammatory bowel disease; JAKi, Janus kinase inhibitor; MTX, methotrexate; PDE4i, phosphodiesterase 4 inhibitor; TNFi, TNF inhibitor.

Table 3 | **Summary of recommendations for treatment of PsA**

Indication	Strong recommendation for	Conditional recommendation for	Conditional recommendation against	Strong recommendation against	No recommendation: insufficient or conflicting evidence
Peripheral arthritis, DMARD naive	csDMARDs (except CsA), TNFi, IL-12/23i, IL-17i, IL-23i, JAKi, PDE4i	NSAIDs, oral GC, IA GC	–	–	–
Peripheral arthritis, DMARD inadequate response	TNFi, IL-12/23i, IL-17i, IL-23i, JAKi, PDE4i	csDMARDs, NSAIDs, oral GC, IA GC, CTLA4-Ig	–	–	–
Peripheral arthritis, bDMARD experienced	TNFi, IL-17i, IL-23i, JAKi	NSAIDs, oral GC, IA GC, IL-12/23i, PDE4i, CTLA4-Ig	–	–	–
Axial disease, bDMARD naive	NSAIDs, physiotherapy, simple analgesia, TNFi, IL-17i, JAKi	GC SIJ injections, bisphosphonates	PDE4i	csDMARDs	IL-12/23i, IL-23i
Enthesitis	TNFi, IL-12/23i, IL-17i, IL-23i, JAKi, PDE4i	NSAIDs, physiotherapy, MTX, CTLA4-Ig, GC injections (with extreme caution)	–	–	Other csDMARDs
Dactylitis	TNFi, IL-12/23i, IL-17i, IL-23i, JAKi, PDE4i	NSAIDs, GC injections, MTX, CTLA4-Ig	Other csDMARDs	–	–
Psoriasis (plaque)	Topical therapies, phototherapy, cdDMARDs (MTX, fumarate, fumaric acid esters, CsA), TNFi, IL-12/23i, IL-17i, IL-23i, PDE4i, JAKi	Acitretin	–	–	–
Nail psoriasis	TNFi, IL-12/23i, IL-17i, IL-23i, PDE4i	Topical GC, tacrolimus and calcipotriol combination or individual therapies, pulsed dye laser, csDMARDs (MTX, LEF, CsA), acitretin, JAKi	–	–	Topical CsA, tazarotene, fumarate, fumaric acid esters, UVA and UVB phototherapy, alitretinoin
IBD: Crohn's disease	TNFi (not ETN), IL-12/23i	IL-23i, JAKi, MTX	–	IL-17i	ETN
IBD: UC	TNFi (not ETN), IL-12/23i	IL-23i, JAKi, MTX	–	IL-17i	ETN, PDE4i
Uveitis	–	TNFi (not ETN), CsA, MTX	ETN	–	Other csDMARDs, IL-17i, IL-12/23i

bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD (MTX, SSZ, LEF, CsA; unless otherwise specified); CsA, ciclosporin; ETN, etanercept; GC, glucocorticoids; IA, intra-articular; IBD, inflammatory bowel disease; IL-12–IL-23i, IL-12–IL-23 inhibitor; IL-17i, IL-17 inhibitor; IL-23i, IL-23 inhibitor; JAKi, Janus kinase inhibitor; LEF, leflunomide; MTX, methotrexate; PDE4i, phosphodiesterase 4 inhibitor (apremilast); PsA, psoriatic arthritis; SIJ, sacroiliac joint; SSZ, sulfasalazine; TNFi, TNF inhibitor; UC, ulcerative colitis.

<u>Peripheral Arthritis</u>

- NSAIDs and intra- articular and oral glucocorticoids are conditionally recommended for relieving symptoms of peripheral arthritis as per the 2015 recommendation, as no new relevant data were identified.
- For treatment- naive patients, there remains a low level of evidence to support the use of csDMARDs for the treatment of peripheral arthritis. However, in view of supportive observational data7–10 and universal accessibility, the use of csDMARDs (methotrexate, sulfasalazine or leflunomide) is strongly recommended.
- In many circumstances, csDMARDs can be used as first- line therapy, with regular assessment of clinical response (every 12–24 weeks) and early escalation of therapy (between 12 and 24 weeks) advised as necessary. It is important to acknowledge that new, high- quality data support the superiority of TNF inhibitors over csDMARDs as first-line therapy, particularly in patients with early disease8–10.
- The decision to use TNF inhibition as first- line therapy should be made as part of a shared decision- making process between the clinician and the patient, with consideration of the risks, benefits and the individual's preference. For all RCTs reviewed for phosphodiesterase 4 inhibitors (PDE4i), TNF inhibitors, IL-17 inhibitors, IL-12/23 inhibitors, IL-23 inhibitors and JAK inhibitors, there were no differences in efficacy for these treatment options in subgroups of patients with or without concurrent csDMARDs.

- In a large RCT that was adequately powered to compare methotrexate, etanercept and their combination, there was no difference in efficacy between the etanercept monotherapy arm and the etanercept–methotrexate combination arm8.
- These findings support the conclusion that a combination of csDMARDs with bDMARDs might not be necessary to achieve short- term response. With JAK inhibitors, the evidence is scarce but also points in the same direction However, the potential benefit of concomitant therapy with csDMARDs with all bDMARDs is incompletely defined, with conflicting evidence derived largely from uncontrolled studies; further study is indicated to define potential benefits.
- For patients with an inadequate response to csDMARDs, high- quality evidence supports the use of TNF inhibitors, IL-17 inhibitors, IL-23 inhibitors and JAK inhibitors; and moderate- quality evidence supports IL-12/23 inhibitors or PDE4 inhibitors being superior to placebo. Similar magnitudes of effect sizes for efficacy were observed across RCTs for TNF inhibitors, IL-17 inhibitors, IL-23 inhibitors and JAK inhibitors compared with placebo, whereas effect sizes for PDE4 inhibitors and IL-12/23 inhibitors seemed to be lower (see Supplementary Table 9). These classes of drugs are all strongly recommended on the basis of this evidence. Concerning the choice between different bDMARDs or tsDMARDs, two head- to- head RCTs compared IL-17 inhibition with TNF inhibition11,12, and one compared JAK inhibition with TNF inhibition13.
- These studies were adequately powered to inform a direct comparison between these therapies. On the basis of current evidence, the efficacies of IL-17 inhibitors and TNF inhibitors are comparable for the peripheral arthritis domain in patients with an inadequate response to csDMARDs. Superiority of a JAK inhibitor (given at the higher of two doses) over a TNF inhibitor for some, but not all, peripheral arthritis outcomes was seen in a single RCT13; consistent superiority of JAK inhibitors over other bDMARDs is yet to be shown.
- Based on the evidence, including head- to- head studies, TNF inhibitors, IL-17 inhibitors and JAK inhibitors are equally recommended. There are no current head- to- head studies comparing IL-23 inhibitors with other bDMARDs or JAK inhibitors. Although IL-23 inhibition is still strongly recommended, it might be considered slightly lower in terms of recommendations for use in patients with peripheral arthritis. One small, open- label study comparing IL-12/23 inhibition with TNF inhibition did not show the superiority of IL-12/23 inhibition over TNF inhibition in peripheral joint domains14.
- For patients with previous experience with bDMARDs, TNF inhibitors, IL-17 inhibitors, IL-23 inhibitors and JAK inhibitors are strongly recommended on the basis of moderate- to high- quality evidence. PDE4 inhibition is conditionally recommended. The limitations for these recommendations include the issue that the evidence was derived from patients with PsA who predominantly had polyarthritis, with this evidence then extrapolated to oligoarthritis and other phenotypes. For inadequate responders, there are insufficient data for specific recommendations based on primary versus secondary failure of prior treatment.

<u>Axial disease.</u>

- For patients with axial symptoms who have not responded to treatment with NSAIDs, physiotherapy and/or sacroiliac joint glucocorticoid injections (when appropriate), initiation of a targeted therapy is strongly recommended. TNF inhibition and IL-17 inhibition have demonstrated efficacy in both radiographic and non- radiographic axSpA and were recommended for axial PsA in the previous GRAPPA recommendations2.
- Since the 2015 recommendations2, several phase II, upadacitinib16 and phase II–III RCTs have demonstrated the efficacy of the JAK inhibitors tofacitinib15 and filgotinib17 in

ankylosing spondylitis. Data from a . Extrapolating phase III study of tofacitinib in ankylosing spondylitis published in 2021 confirm this efficacy18 from the evidence in axSpA, we recommend these agents for axial PsA as well.

- Only one study was designed specifically to assess axial PsA19. In this phase IIIb RCT, the IL-17 inhibitor secukinumab demonstrated significant improvement in the signs and symptoms of axial disease compared with placebo in patients with PsA who had an inadequate response to NSAIDs; a reduction in MRI scores was also noted As IL-17 inhibitors have shown efficacy and have been approved for use in the treatment of axSpA, these agents are strongly recommended for axial PsA. Although IL-12/23 inhibitors and IL-23 inhibitors have not demonstrated efficacy in ankylosing spondylitis20, post hoc analyses from the trials of ustekinumab and guselkumab in patients who have had axial symptoms suggest that these agents might be effective in axial PsA19,20.
- However, it is also possible that improvement in the outcome measures used (for example, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)) could reflect disease activity in other PsA domains. Because these studies included primarily patients with active PsA, and these agents did not prove effective in axSpA, the evidence is currently too limited and conflicting such that these medications cannot be recommended for axial PsA at this time.

<u>Enthesitis.</u>

- Classes of advanced therapies found to be effective and thus strongly recommended as treatment options for active enthesitis in patients with PsA include TNF inhibitors, IL-17 inhibitors, IL-12/23 inhibitors, IL-23 inhibitors, JAK inhibitors and PDE4 inhibitors. Despite novel information about the comparative efficacy of different classes of medications emerging from head- to- head studies, including comparisons of IL-17 inhibitors with TNF inhibitors11,12 , methotrexate with TNF inhibitors8,9, and IL-12/23 inhibitors with TNF inhibitors14, none of the evaluated classes of medications was found to have clear and consistent superiority over the other. Therefore, none of the medication classes detailed above was prioritized for the treatment of enthesitis in the recommendations. Methotrexate received a conditional recommendation for the treatment of active enthesitis. This is a change from previous guidelines, in which methotrexate was not recommended owing to a lack of evidence1,2.
- The change was made on the basis of expert opinion and data emerging from the SEAM-PsA trial, which suggested efficacy of methotrexate for enthesitis that was similar to that observed for etanercept8 . It should be noted that the SEAM- PsA trial did not include a placebo arm, so the evidence is limited and therefore the recommendation is conditional.
- The use of NSAIDs, local glucocorticoid injections and physiotherapy was conditionally recommended, despite the lack of high- quality studies that investigated their efficacy for enthesitis in PsA or SpA. These modes of treatment, which are commonly used as first- line therapies for enthesitis, provide a relatively safe and affordable option, especially for localized enthesitis

<u>Dactylitis</u>

- Meaningful advances have been made in the treatment of dactylitis since the last GRAPPA recommendations2.
- In the SEAM- PsA RCT8 , no statistically significant difference was found between methotrexate monotherapy, etanercept monotherapy and methotrexate–etanercept combination therapy, neither in the change from baseline in the Leeds Dactylitis Index

(LDI) nor in the proportion of patients achieving complete resolution of dactylitis. However, no definite conclusion regarding effect size could be drawn owing to the lack of a placebo control group.

- The therapeutic armamentarium for dactyli, ixekizumab24 and brodalumab25 tis has increased considerably. The IL-17 inhibitors secukinumab21–23 demonstrated superior efficacy compared with placebo for improving dactylitis signs and symptoms in RCTs; another IL-17 inhibitor, bimekizumab, is being studied. In RCTs the IL-23 inhibitors guselkumab and risankizumab were found to be effective for dactylitis as assessed by the proportion of patients with total resolution of dactylitis at week 24 (refs26,27); another IL-23 inhibitor, tildrakizumab, decreased mean LDI at week 52 compared with baseline in a phase II trial28 . The T cell modulator abatacept (CTLA4- Ig) numerically improved the proportion of patients achieving resolution of dactylitis at week 24 compared with placebo29.
- Head- to- head trials comparing TNF inhibitors and IL-17 inhibitors11,12 assessed the proportion of patients achieving resolution of dactylitis at week 24 and did not find a statistically significant difference between the two classes of biologic agents.
- Dactylitis- related outcomes were assessed as secondary outcomes in trials of JAK inhibitors, and these drugs were considered statistically superior to placebo in most of these studies13,30,31.
- In a head- to- head trial comparing JAK inhibition with TNF inhibition, the improvements in dactylitis disease activity of upadacitinib and adalimumab at week 24 were similar13.
- Considering the evidence, the group made a conditional recommendation for the use of methotrexate and against the use of other csDMARDs in the treatment of dactylitis. The use of NSAIDs and local glucocorticoid injections was also conditionally recommended for the treatment of dactylitis. A strong recommendation was established for the use of TNF inhibitors, IL-12/23 inhibitors, IL-23 inhibitors, IL-17 inhibitors, JAK inhibitors and PDE4 inhibitors, and a conditional recommendation was established for the use of CTLA4- Ig in the treatment of dactylitis in PsA.

Skin disease

- The evidence reviewed for the update of the recommendations for the treatment of skin psoriasis was limited to that presented in RCTs for PsA and interpreted in the context of the large body of psoriasis literature and previous GRAPPA recommendations. Topical agents are strongly recommended as first- line treatment for patients with limited body surface area involvement.
- For patients with more widespread psoriasis or psoriasis unresponsive to topicals, phototherapy, oral therapies (methotrexate, ciclosporin, PDE4 inhibitors and JAK inhibitors) and bDMARDs (TNF inhibitors, IL-17 inhibitors, IL-12/23 inhibitors and IL-23 inhibitors) are strongly recommended. Phototherapy is efficacious for psoriasis affecting the trunk and extremities. Acitretin, an oral retinoid, is conditionally recommended for psoriasis in patients with PsA owing to its limited efficacy as monotherapy for plaque psoriasis and scarce evidence from the PsA population; however, this agent can be efficacious for pustular psoriasis.
- Strong recommendations were made for TNF inhibitors, IL-17 inhibitors, IL-12/23 inhibitors and IL-23 inhibitors; newer mode of action drugs (inhibitors of IL-17, IL-12/23 and IL-23) show higher efficacy for skin involvement than TNF inhibitors in studies of psoriasis and/or PsA. The selection of one drug over another should be influenced by the results of head- to- head studies in psoriasis populations, the presence of comorbidities, and disease activity in other PsA domains.

- It should be noted that some csDMARDS (leflunomide and sulfasalazine) have limited evidence for efficacy in skin disease and were graded in the context of other available therapies as having limited evidence for cutaneous psoriasis. CTLA4- Ig (abatacept) also has limited evidence for efficacy in skin disease.

Nail disease

- As with psoriatic skin disease, the evidence reviewed for the update of the treatment of nail psoriasis was limited to that presented in RCTs for PsA and interpreted in the context of the large body of psoriasis literature and previous GRAPPA recommendations.
- As in the previous recommendations2 , strong recommendations were made for bDMARDs given the rigorous evidence from RCTs. bDMARDs, including TNF inhibitors, IL-17 inhibitors, IL-12/23 inhibitors and IL-23 inhibitors, are strongly recommended for the treatment of psoriatic nail disease; the selection of one of these agents over another should be informed by head- to- head studies in psoriasis, comorbidities and activity in other PsA domains.
- Conditional recommendations were made for a number of topical and/or local therapies as well as systemic medications. Topical therapies that can be considered include calcipotriol and glucocorticoid preparations, topical tacrolimus, topical ciclosporin, intralesional glucocorticoids and pulsed dye laser.

Systemic medications that should also be considered are ciclosporin, methotrexate, acitretin, JAK inhibitors and PDE4 inhibitors. In many cases, evidence specifically for nail psoriasis remains insufficient. Agents with limited evidence preventing recommendations include topical glucocorticoids, topical tazarotene, dimethyl fumarates/fumaric acid esters, phototherapy and alitretinoin

---

Tucker L et al., 2022 [10].

The 2022 British Society for Rheumatology guideline for the treatment of psoriatic arthritis with biologic and targeted synthetic DMARDs

Zielsetzung/Fragestellung

This guideline offers systematic and evidence-based recommendations to support UK clinicians in the prescription of bDMARD and tsDMARD therapies in adults with PsA. The guideline also includes guidance for managing those patients with extra-articular manifestations [uveitis and inflammatory bowel disease (IBD)], as well as those who smoke or are overweight. The guideline provides a stepwise management plan giving clear advice on treatment, including drug eligibility, sequencing, switching and treatment strategy.

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium: **trifft zu**
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt: **trifft zu**
- Systematische Suche, Auswahl und Bewertung der Evidenz: **trifft zu**
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt: **trifft zu**
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt: **trifft zu**
- Regelmäßige Überprüfung der Aktualität gesichert: **trifft zu** (The planned review date for this guideline will be in five years' time.)

Recherche/Suchzeitraum:

- systematic literature review (SLR), including electronic bibliographic databases (Medline and Embase) and the Cochrane Database of Systematic Reviews up to 10 December 2020.

LoE

- GRADE
- This guideline uses three levels and a letter (A, B, C) to reflect high, moderate or low/very low quality of evidence. High quality is where further research is very unlikely to change the confidence in the estimate of effect. Moderate quality is where further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality is where further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. Very low-quality is where any estimate of effect is very uncertain.

GoR

- Strength of the recommendation A strong recommendation to offer (or not to offer) something, where the benefits clearly outweigh the risks (or vice versa) for nearly all patients, is denoted by the number 1 in the guideline. A conditional recommendation (to consider or not) is made either when the risks and benefits are more closely balanced or are more uncertain and is denoted by the number 2 in this guideline.
- The strength of agreement across the GWG for each recommendation is presented as the mean of the members' individual strength of recommendation, expressed as a percentage (e.g. 100% implies all responses were 10/10.

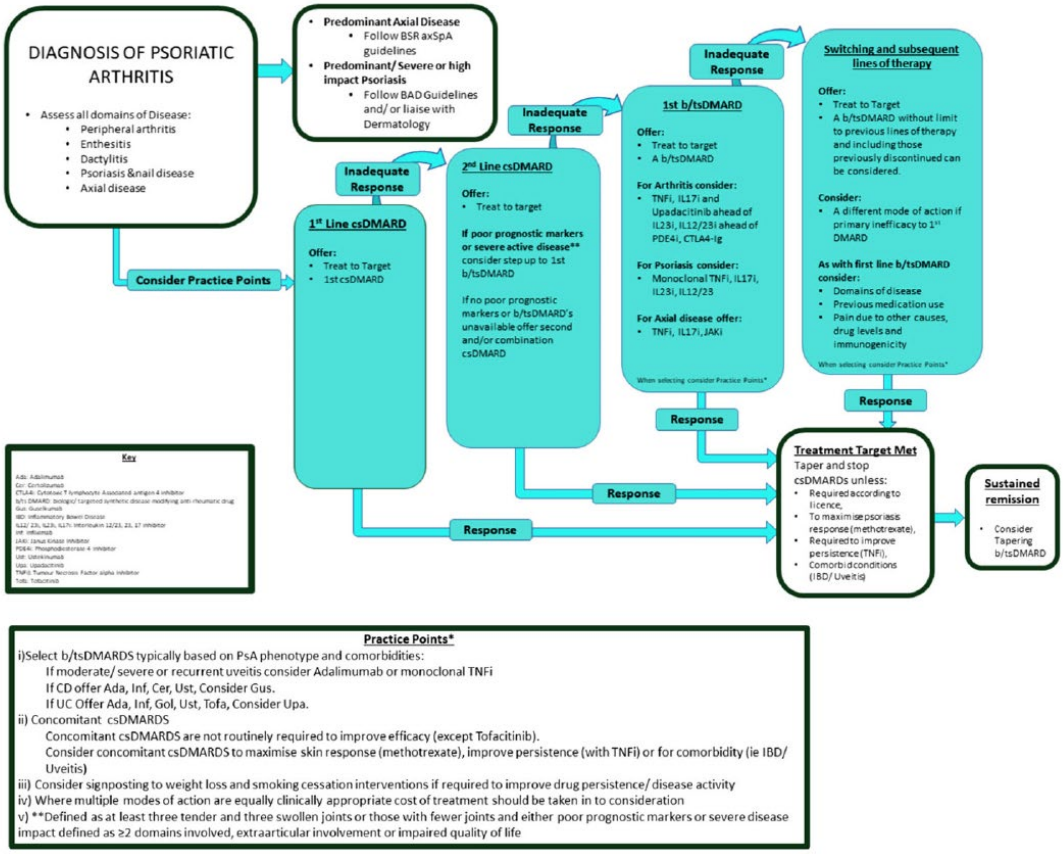
Sonstige methodische Hinweise

This guideline complements existing BSR guidelines and therefore does not include:

- i. detailed assessment of the safety of bDMARDs;
- ii. biologic or tsDMARD therapies for juvenile idiopathic arthritis;
- iii. use of csDMARDs in PsA;
- iv. use of biologics or tsDMARDs in pregnancy; or v. biologic or tsDMARD therapies for adults with psoriatic disease confined to the skin only (in this situation, please refer to BAD guidelines for management of psoriasis at https://www.bad.org.uk/healthcare-profes sionals/psoriasis).

New treatment algorithm

Fig. 1 Summary algorithm for the treatment of an individual with PsA with b/tsDMARDS



Overarching generic recommendations and levels of agreement

- iv. If people with PsA have an inadequate response to a b/tsDMARD, consider potential factors that could be addressed including: confirming correct diagnosis, adherence, pain due to other causes, drug levels and immunogenicity (SoA 95%).

Treatment by domains

Peripheral arthritis (mono-, oligo- and polyarthritis)

- In people with active psoriatic arthritis (defined as at least three tender and three swollen joints or those with fewer joints and either poor prognostic markers or severe disease impact defined as _2 domains involved, extraarticular involvement or impaired quality of life), with inadequate response or intolerance to one csDMARD, consider escalation to b/tsDMARDs (GRADE 2A, SoA 98%).

Hintergrundinfromationen:

This recommendation refers to people with active peripheral PsA (at least three tender and three swollen joints or those with fewer joints but severe disease impact), with an inadequate response or intolerance to a csDMARD (methotrexate, leflunomide, sulfasalazine). In these individuals, escalation to a b/tsDMARD should be considered. This eligibility recommendation was made through group consensus and would bring the UK in line with the majority of European healthcare settings. However, the use of biologics after one csDMARD or for people with less than three tender/swollen joints is not currently permitted by NICE TAGs. A full assessment of evidence for csDMARD effectiveness was beyond the scope of this guideline, which focusses on biologic and tsDMARD treatments. The GWG discussed the appropriateness of initiating a b/tsDMARD first-line, taking into consideration the efficacy, safety and cost effectiveness of conventional synthetic, biologic and tsDMARDS. Based on anecdotal and observational data supporting the efficacy of

csDMARDs, especially methotrexate, in achieving low disease activity/remission in PsA and from a costeffective perspective, the group agreed that a csDMARD should be initiated first-line. There is little evidence to base a judgement on how many csDMARDs should be failed before considering a b/tsDMARD therapy; however, two relevant randomized controlled trials addressing eligibility for b/tsDMARDs were discussed: the SEAM-PsA and the CONTROL studies. The SEAM-PsA trial compared etanercept to etanercept plus methotrexate combination therapy and methotrexate monotherapy. The results demonstrated superiority of etanercept over methotrexate [24]. The CONTROL trial compared dose escalation of methotrexate to the addition of TNFi in people with inadequate disease control PsA after initial methotrexate therapy. A significantly higher proportion of individuals achieved minimal disease activity (MDA) at week 16 after introducing adalimumab compared with dose escalation of methotrexate [25]. The GWG therefore proposed earlier use of a b/tsDMARD therapy after failure of just one csDMARD be considered in those individuals with poor prognostic factors (polyarticular disease, high systemic inflammation levels, presence of radiographic erosions or significantly impaired functional ability) [6, 26–29] or severe active disease.

- ii. In people with active peripheral psoriatic arthritis, with inadequate response or intolerance to csDMARDs, offer a bDMARD (TNFi, IL12/23i, IL-17i, IL-23i, CTLA4- Ig) or tsDMARD (JAKi, or PDE4i) (GRADE 1A, 94%). When selecting therapy, consider using TNFi, IL17i or upadacitinib (UPA) ahead of IL12/23i or IL23i ahead of PDE4i ahead of CTLA4-Ig (GRADE 2B, SoA 88%).

Hintergrundinfromationen:

A summary of the results from RCTs of (b/ts)DMARDs in PsA is shown in Table 1. The data supporting the first recommendation to offer a b/tsDMARD was based on trials of medication vs placebo in the relevant domains of disease. There are no data to support optimal selection of drugs for individuals, but the guideline group developed a consensus recommendation to support biologic choice based on efficacy data, speed of onset and adverse events (Table 1). TNF inhibitors remain the most widely used first line biologic in PsA and none of the other therapies have shown superiority to them for articular disease. Head-to-head studies now exist for IL- 17i and upadacitinib showing non-inferiority to TNFi, hence their inclusion as potential first choices. Despite a lack of head-to-head data, there were concerns that clinical responses to IL12/23i, IL23i, PDE4i and CTLA4-Ig might be slightly lower and slower than TNFi. Physicians should be aware of the MHRA safety warning around the use of tofacitinib [30]. The safety data demonstrating increased rates of venous thromboembolic disease (VTE), major cardiovascular event (MACE) and malignancy with tofacitinib compared with TNFi available at the time of writing prompted the committee to differentiate between upadacitinib and tofacitinib in the recommendation.

PsA with enthesitis

- In people with active psoriatic enthesitis, with inadequate response or intolerance to a csDMARD, offer any bDMARD (TNFi, IL12/23i, IL-17i, IL-23i) or tsDMARD (JAKi, or PDE4i) (GRADE 1A, SoA 91%).

PsA with dactylitis

- iv. In people with active psoriatic dactylitis, with inadequate response or intolerance to a csDMARD, offer any bDMARD (TNFi, IL12/23i, IL-17i, IL-23i) or tsDMARD (JAKi, or PDE4i) (GRADE 1A, SoA 92%).

PsA with axial disease

- v. In people with active psoriatic axial disease, with inadequate response or intolerance to at least two NSAIDs, offer any TNFi or IL-17i or consider a JAKi (GRADE 1A, SoA 92%).

Referenzen aus Leitlinie:

6. McHugh NJ, Balachrishnan C, Jones SM. Progression of peripheral joint disease in psoriatic arthritis: a 5-yr prospective study. Rheumatology 2003;42:778–83.

25 Coates LC, Tillett W, D'Agostino MA, et al. Comparison between adalimumab introduction and methotrexate dose escalation in patients with inadequately controlled psoriatic arthritis (CONTROL): a randomised, open-label, two-part, phase 4 study. Lancet Rheumatol 2022;4:E262– 73.

26 Bond SJ, Farewell VT, Schentag CT et al. Predictors for radiological damage in psoriatic arthritis: results from a single centre. Ann Rheum Dis 2007;66:370–6.
27 Cresswell L, Chandran V, Farewell VT et al. Inflammation in an individual joint predicts damage to that joint in psoriatic arthritis. Ann Rheum Dis 2011;70:305–8.
28 Gladman DD, Mease PJ, Choy EH et al. Risk factors for radiographic progression in psoriatic arthritis: subanalysis of the randomized controlled trial ADEPT. Arthritis Res Ther 2010;12:R113.
29 Simon P, Pfoehler C, Bergner R et al. Swollen joint count in psoriatic arthritis is associated with progressive radiological damage in hands and feet. Clin Exp Rheumatol 2012;30:45–50.
30 Medicines and Healthcare products Regulatory Agency. Tofacitinib (Xeljanz): new measures to minimise risk of major adverse cardiovascular events and malignancies. 2021 6th October 2021. https://www.gov.uk/drug-safetyupdate/ tofacitinib-xeljanzv-new-measures-to-minimiserisk- of-major-adverse-cardiovascular-events-andmalignancies (24 November 2021, date last accessed).

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 04 of 12, April 2026) am 14.04.2026

#	Suchschritt
1	[mh "Arthritis, Psoriatic"]
2	(psoria* NEAR/3 (arthriti* OR arthropath*)):ti,ab,kw
3	#1 OR #2
4	#3 with Cochrane Library publication date from Apr 2021 to present
5	#4 with Cochrane Library publication date from Apr 2024 to present
	#4 NOT #5

Leitlinien und systematische Reviews in PubMed am 14.04.2026

verwendeter Suchfilter für Leitlinien ohne Änderung:
Konsentierter Standardfilter für Leitlinien (LL), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 20.03.2026.

verwendeter Suchfilter für systematische Reviews ohne Änderung:
Konsentierter Standardfilter für Systematische Reviews (SR), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 01.01.2026.

#	Suchschritt
	Leitlinien
1	Arthritis, Psoriatic[mh]
2	psoria*[tiab] AND (arthriti*[tiab] OR arthropath*[tiab])
3	(#1 OR #2) AND (Guideline[pt] OR Practice Guideline[pt] OR Consensus Statement [pt] OR Consensus Development Conference, NIH[pt] OR guideline*[ti] OR recommendation*[ti] OR ((consensus[ti] OR position[ti]) AND (expert[ti] OR delphi[ti] OR statement*[ti] OR paper*[ti] OR document*[ti] OR report*[ti])))
4	((((#3) AND ("2021/04/01"[PDAT] : "3000"[PDAT])) NOT ("The Cochrane database of systematic reviews"[Journal]) NOT ((comment[ptyp]) OR letter[ptyp]))) NOT ("retracted publication"[pt] OR "retraction notice"[pt] OR "preprint"[pt])
	systematische Reviews
5	(#1 OR #2) AND ("systematic review"[pt] OR "meta-analysis"[pt] OR "network meta-analysis"[pt] OR (systematic*[tiab] AND (review*[tiab] OR overview*[tiab])) OR metareview*[tiab] OR umbrella review*[tiab] OR "overview of reviews"[tiab] OR meta-analy*[tiab] OR metaanaly*[tiab] OR metanaly*[tiab] OR meta-synthes*[tiab] OR metasynthes*[tiab] OR meta-study[tiab] OR metastudy[tiab] OR integrative review[tiab] OR integrative literature review[tiab] OR evidence review[tiab] OR (("evidence-based medicine"[mh] OR evidence synthes*[tiab]) AND "review"[pt]) OR ((("evidence based"[tiab:~3]) OR evidence base[tiab]) AND (review*[tiab] OR overview*[tiab])) OR (review[ti] AND (comprehensive[ti] OR studies[ti] OR trials[ti])) OR ((critical appraisal*[tiab] OR critically appraise*[tiab] OR study selection[tiab] OR

#	Suchschritt
	((predetermined[tiab] OR inclusion[tiab] OR selection[tiab] OR eligibility[tiab]) AND criteri*[tiab]) OR exclusion criteri*[tiab] OR screening criteri*[tiab] OR systematic*[tiab] OR data extraction*[tiab] OR data synthes*[tiab] OR prisma*[tiab] OR moose[tiab] OR entreq[tiab] OR mecir[tiab] OR stard[tiab] OR strobe[tiab] OR "risk of bias"[tiab]) AND (survey*[tiab] OR overview*[tiab] OR review*[tiab] OR search*[tiab] OR analysis[ti] OR apprais*[tiab] OR research*[tiab] OR synthes*[tiab]) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR bibliographies[tiab] OR published[tiab] OR citations[tiab] OR database*[tiab] OR references[tiab] OR reference-list*[tiab] OR papers[tiab] OR trials[tiab] OR studies[tiab] OR medline[tiab] OR embase[tiab] OR cochrane[tiab] OR pubmed[tiab] OR "web of science" [tiab] OR cinahl[tiab] OR cinhal[tiab] OR scisearch[tiab] OR ovid[tiab] OR ebsco[tiab] OR scopus[tiab] OR epistemonikos[tiab] OR prospero[tiab] OR proquest[tiab] OR lilacs[tiab] OR biosis[tiab])) OR "technical report"[pt] OR HTA[tiab] OR technology assessment*[tiab] OR technology report*[tiab])
6	((#5) AND ("2021/04/01"[PDAT] : "3000"[PDAT]) NOT "The Cochrane database of systematic reviews"[Journal]) NOT ("retracted publication"[pt] OR "retraction notice"[pt] OR "preprint"[pt])
	systematische Reviews ohne Leitlinien
7	(#6) NOT (#4)
8	(#7) AND ("2024/04/01"[PDAT] : "3000"[PDAT])
9	#7 NOT #8

Iterative Handsuche nach grauer Literatur, abgeschlossen am 15.04.2026

- Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)
- National Institute for Health and Care Excellence (NICE)
- Scottish Intercollegiate Guideline Network (SIGN)
- World Health Organization (WHO)
- ECRI Guidelines Trust (ECRI)
- Dynamed / EBSCO
- Guidelines International Network (GIN)
- Trip Medical Database

Referenzen

1. **Cagnotto G, Bruschettini M, Stróżyk A, Scirè CA, Compagno M.** Tumor necrosis factor (TNF) inhibitors for psoriatic arthritis. Cochrane Database of Systematic Reviews [online]. 2025(2):Cd013614. URL: http://dx.doi.org/10.1002/14651858.CD013614.pub2.

2. **Chai R, Li X, Shen W, Jin Z, Yao G, Tang X, et al.** Efficacy and safety of upadacitinib for patients with immune-mediated inflammatory diseases: a systematic review and meta-analysis. Front Immunol 2025;16:1586792. https://dx.doi.org/10.3389/fimmu.2025.1586792.

3. **Coates LC, Corp N, van der Windt DA, O'Sullivan D, Soriano ER, Kavanaugh A.** GRAPPA treatment recommendations: 2021 update. J Rheumatol 2022;49(6 Suppl 1):52-54. https://dx.doi.org/10.3899/jrheum.211331.

4. **Coates LC, Corp N, van der Windt DA, Soriano ER, Kavanaugh A.** GRAPPA treatment recommendations: an update from the 2020 GRAPPA Annual Meeting. J Rheumatol Suppl 2021;97:65-66. https://dx.doi.org/10.3899/jrheum.201681.

5. **Coates LC, Soriano ER, Corp N, Bertheussen H, Callis Duffin K, Campanholo CB, et al.** Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. Nat Rev Rheumatol 2022;18(8):465-479. https://dx.doi.org/10.1038/s41584-022-00798-0.

6. **Dai Q, Zhang Y, Liu Q, Zhang C.** Efficacy and safety of tofacitinib for chronic plaque psoriasis and psoriatic arthritis: a systematic review and meta-analysis of randomized controlled trials. Clin Rheumatol 2024;43(5):1605-1613. https://dx.doi.org/10.1007/s10067-024-06940-5.

7. **Gossec L, Kerschbaumer A, Ferreira RJO, Aletaha D, Baraliakos X, Bertheussen H, et al.** EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update. Ann Rheum Dis 2024;83(6):706-719. https://dx.doi.org/10.1136/ard-2024-225531.

8. **Kerschbaumer A, Smolen JS, Ferreira RJO, Bertheussen H, Baraliakos X, Aletaha D, et al.** Efficacy and safety of pharmacological treatment of psoriatic arthritis: a systematic literature research informing the 2023 update of the EULAR recommendations for the management of psoriatic arthritis. Ann Rheum Dis 2024;83(6):760-774. https://dx.doi.org/10.1136/ard-2024-225534.

9. **Nast A, Spuls P, Dressler C, Bata-Csörgö Z, Bogdanov I, Boonen H, et al.** Euroguiderm guideline for the systemic treatment of psoriasis vulgaris [online]. 2025. [Zugriff: 15.04.2026]. URL: https://guidelines.edf.one//uploads/attachments/cm9h6g6wp9exorwjr9msyrqbc-0-euroguiderm-pso-gl-feb-2025.pdf.

10. **Tucker L, Allen A, Chandler D, Ciurtin C, Dick A, Foulkes A, et al.** The 2022 British Society for Rheumatology guideline for the treatment of psoriatic arthritis with biologic and targeted synthetic DMARDs. Rheumatology (Oxford) 2022;61(9):e255-e266. https://dx.doi.org/10.1093/rheumatology/keac295.

11. **Zeng J, Lin L, Li W, Gao X, Li Q, Zhou X, et al.** Clinical benefits and complication profile of IL-23 inhibitors in patients with psoriatic arthritis: a systematic review and meta-analysis. Front Pharmacol 2025;16:1669786. https://dx.doi.org/10.3389/fphar.2025.166978.

[A] **Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, et al.** PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev 2021;10(1):39. https://doi.org/10.1186/s13643-020-01542-z

[B] **McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C.** PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin Epidemiol 2016;75:40-46. https://doi.org/10.1016/j.jclinepi.2016.01.021

Beteiligung von Fachgesellschaften und der AkdÄ zu Fragen der Vergleichstherapie nach §35a Abs. 7 SGB V i.V.m. VerfO 5. Kapitel § 7 Abs. 6

Verfahrens-Nr.: 2026-B-066-z

Verfasser	
Name der Institution	Deutsche Gesellschaft für Rheumatologie und klinische Immunologie e.V. (DGRh)
Namen aller beteiligten Sachverständigen	
Datum der Erstellung	5. Mai 2026

(Bei mehreren beteiligten Fachgesellschaften bitte mit entsprechenden Angaben.)

Indikation
Behandlung Erwachsener mit aktiver Psoriasis-Arthritis (PsA), die auf ein oder mehrere krankheits-modifizierende Antirheumatika (DMARD) unzureichend angesprochen oder diese nicht vertragen haben.
Fragen zur Vergleichstherapie
Was ist der Behandlungsstandard in o.g. Indikation unter Berücksichtigung der vorliegenden Evidenz? Wie sieht die Versorgungspraxis in Deutschland aus? *(Bitte begründen Sie Ihre Ausführungen; geben Sie ggf. zitierte Quellen in einer Referenzliste an.)*

Behandlungsstandard in der Indikation

Für erwachsene Patientinnen und Patienten mit aktiver Psoriasis-Arthritis (PsA), die auf eine oder mehrere DMARD-Therapien nicht ausreichend angesprochen haben oder diese nicht vertragen, ist eine Einleitung eines Biologikums (bDMARD) oder eines targeted-synthetic DMARD (tsDMARD) entsprechend des evidenzbasierter Behandlungsstandard indiziert. Dies entspricht internationalen Therapieempfehlungen der GRAPPA sowie den Empfehlungen der European Alliance of Associations Against Rheumatism (EULAR) (1, 2).

Festzuhalten ist hierbei, dass keine hinreichende Evidenz vorliegt, dass die Einleitung einer csDMARD-Therapie nach Versagen einer vorausgegangen csDMARD Therapie sinnvoll sein kann.

Charakteristisch für die PsA und deren heterogene klinische Manifestationen ist dabei, dass eine Therapieentscheidung nicht allein anhand der peripheren Gelenkbeteiligung getroffen werden soll, sondern unter Berücksichtigung aller klinischen Manifestation der unterschiedlichen sog. Domänen zu erfolgen hat. Zu den relevanten Krankheitsdomänen zählen periphere Arthritis, axiale Manifestation, Enthesitis, Daktylitis, Haut- und Nagelbeteiligung. Alle diese Manifestationen machen die Krankheitslast der Indexerkrankung PsA aus. Zusätzlich spielt ein mögliches Vorhandensein sogenannter assoziierte Erkrankungen wie Uveitis und chronisch-entzündliche Darmerkrankungen eine Rolle. Unter assoziierten Erkrankungen verstehen wir solche Erkrankungen, die zum einen bezüglich der Wahrscheinlichkeit des Auftretens einen klaren Zusammenhang mit der Indexerkrankung PsA aufweisen aber darüber hinaus auch einen pathophysiologischen

Zusammenhang aufweisen, der beim Vorliegen einer solchen ass. Erkrankung unmittelbaren Einfluss auf die Auswahl des Wirkprinzips der Indexerkrankung hat.

GRAPPA betont entsprechend einen domänenorientierten, evidenzbasierten Therapieansatz unter Einbezug von Shared Decision Making sowie Sicherheits- und Komorbiditätsaspekten (1). Auch die Therapieziele orientieren sich an den verschiedenen Krankheitsdomänen und gehen über eine isolierte Verbesserung der reinen peripheren Gelenksymptomatik hinaus (3).

Die aktuellen EULAR-Empfehlungen sehen den Einsatz von NSAID allenfalls kurzfristig und bei sehr milder Erkrankung vor. Bei peripherer Arthritis wird initial die rasche Einleitung eines csDMARDs empfohlen, bevorzugt Methotrexat. Bei unzureichendem Ansprechen erfolgt jedoch die direkte Eskalation auf eine bDMARD -Therapie (2).

Als etablierte Therapieoptionen stehen hierbei insbesondere TNF-α-Inhibitoren, IL-17- und IL-17A/F-Inhibitoren, IL-12/23- bzw. IL-23-Inhibitoren sowie JAK-Inhibitoren zur Verfügung. In ausgewählten Situationen können zudem Apremilast (PDE4-Inhibitor) oder in seltenen Fällen Abatacept (CTLA4-Ig) eingesetzt werden.

Versorgungspraxis in Deutschland

Die Versorgungspraxis in Deutschland folgt im Wesentlichen dem evidenzbasierten Therapiealgorithmus von GRAPPA bzw. EULAR. In der Regel erfolgt initial der Einsatz eines csDMARDs, meist Methotrexat, bei peripherer Arthritis. Wenn kein systemtherapiebedürftiger Hausbefall vorliegt, kann ebenfalls Leflunomid eingesetzt werden. Bei anderen Manifestationen wie z.B. Enthesitis, Daktylitis spielen csDMARDs als Erstlinientherapie nur eine untergeordnete Rolle, bei axialer Manifestation der PsA können csDMARDs, auch in Analogie zur axialen Spondylarthritis, als unwirksam angesehen werden.

Bei unzureichendem Ansprechen oder Unverträglichkeit wird in der rheumatologischen Versorgung typischerweise eine Eskalation auf eine zielgerichtete Therapie mittels Biologikum oder targeted-synthetic DMARD vorgenommen. Der Einsatz eines zweiten csDMARDs nach unzureichendem Ansprechen des ersten entbehrt einer relevanten Evidenz und wird daher in der klinischen Praxis in der Regel auch nicht eingesetzt. Bei Unverträglichkeit des ersten kann ein zweites csDMARD eingesetzt werden.

TNF-α-Inhibitoren haben dabei historisch und praktisch eine zentrale Stellung als erste Biologika-Therapie. Gleichzeitig zeigt sich in der Versorgung zunehmend eine differenzierte, domänenspezifische Auswahl anderer Wirkstoffe, insbesondere von IL-17- und IL-23-Inhibitoren sowie JAK-Inhibitoren, abhängig vom individuellen Manifestationsprofil der Erkrankung.

Zur Abbildung der Versorgungssituation in Deutschland liefern Registerdaten wichtige Erkenntnisse. Das RABBIT-SpA-Register, initiiert am Deutschen Rheuma-Forschungszentrum, erhebt prospektiv Daten zu Patientinnen und Patienten mit PsA und axialer Spondyloarthritis, einschließlich Therapieverlauf, Wirksamkeit und Sicherheit. Ein Vergleich zwischen dem rheumatologischen RABBIT-SpA-Register und dem dermatologisch geprägten PsoBest-Register zeigt, dass in beiden Versorgungsrealitäten überwiegend Biologika eingesetzt werden. Während im rheumatologischen Setting TNF-α-Inhibitoren häufiger verwendet werden, kommen im dermatologischen Kontext verstärkt IL-17- und IL-23-Inhibitoren zum Einsatz (4), da bei der kutanen Manifestation eine klinisch

relevante Überlegenheit im Ansprechen dieser Wirkprinzipen gegenüber TNFi oder auch JAKi bewiesen ist

Insgesamt zeigt sich damit, dass die Versorgungspraxis in Deutschland die leitlinienempfohlene Therapieeskalation auf zielgerichtete Therapien nach DMARD-Versagen widerspiegelt, wobei Unterschiede in der Wirkstoffwahl insbesondere durch Fachdisziplin, Krankheitsdomänen und Komorbiditäten geprägt sind.

Gibt es Kriterien für unterschiedliche Behandlungsentscheidungen in der o.g. Indikation, die regelhaft berücksichtigt werden? Wenn ja, welche sind dies und was sind in dem Fall die Therapieoptionen?
(Bitte begründen Sie Ihre Ausführungen; geben Sie ggf. zitierte Quellen in einer Referenzliste an.)

Bei erwachsenen Patientinnen und Patienten mit aktiver PsA nach unzureichendem Ansprechen auf eine oder mehrere DMARD-Therapien oder bei Unverträglichkeit dieser Substanzen erfolgt die Therapieentscheidung regelhaft individualisiert und basiert auf mehreren klinisch relevanten Kriterien.

Entsprechend den Empfehlungen der GRAPPA sowie der European Alliance of Associations Against Rheumatism (EULAR) ist die Auswahl der Therapie nicht uniform, sondern orientiert sich an einem domänenspezifischen und patientenbezogenen Ansatz (1, 2).

Ein zentrales Kriterium stellt die dominierende Krankheitsdomäne dar. Die PsA ist durch ein heterogenes klinisches Bild gekennzeichnet, das periphere Arthritis, axiale Manifestationen, Enthesitis, Daktylitis sowie Haut- und Nagelbeteiligung umfassen kann. Je nach vorherrschender Manifestation ergeben sich unterschiedliche therapeutische Präferenzen.

Als **zweckmäßigen Vergleichstherapien nach Versagen von mind. einer vorausgegangenen DMARD-Therapie** bei unterschiedlichen klinischen Szenarien können folgendes Wirkprinzipien bzw. Substanzen festgelegt werden:

Bei peripherer Arthritis, Daktylitis und Enthesitis…

…und milder Hautbeteiligung: TNFi, Tofacitinib, Upadacitinib, Apremilast, IL-17i (A; A/F), IL-23i, IL12/23i

…und moderat bis schwerer Hautbeteiligung: IL-17i (A; A/F), IL-23i, IL12/23i

Bei axialer Manifestation (Spondylarthritis)…

…und milder Hautbeteiligung: TNFi, Tofacitinib, Upadacitinb, IL-17i (A; A/F)

…und moderat bis schwerer Hautbeteiligung: IL-17i (A; A/F),

Neben der Krankheitsdomäne spielen assoziierte Erkrankungen wie Uveitis und CED sowie Komorbiditäten eine wesentliche Rolle bei der Therapieentscheidung. Auch kardiovaskuläre Risikofaktoren, metabolische Begleiterkrankungen oder ein erhöhtes Infektionsrisiko werden bei der Nutzen-Risiko-Abwägung berücksichtigt.

Ein weiteres zentrales Entscheidungskriterium stellt die individuelle Therapievorgeschichte dar. Nach Versagen eines csDMARDs erfolgt gemäß Leitlinien die Eskalation auf eine zielgerichtete Therapie. Bei unzureichendem Ansprechen auf ein Biologikum wird die Therapie in der Regel durch

einen Wechsel innerhalb der Wirkstoffklasse oder durch einen Klassenwechsel angepasst. Dabei kann auch zwischen primärem und sekundärem Therapieversagen unterschieden werden, was die weitere Strategie beeinflusst.

Darüber hinaus werden Krankheitsaktivität und Schweregrad sowie radiographische Progression in die Therapieentscheidung einbezogen. Bei hoher Krankheitsaktivität oder radiographischer Progression besteht die Indikation zu einer frühzeitigen und effektiven zielgerichteten Therapie, während bei milderen Verläufen zeitweise auch weniger potente Therapieoptionen in Betracht gezogen werden können.

Schließlich sind patientenindividuelle Faktoren von Bedeutung. Hierzu zählen unter anderem Alter, Präferenzen hinsichtlich der Applikationsform, Lebenssituation (z. B. Familienplanung), sowie Aspekte der Adhärenz. Diese Faktoren werden im Sinne eines Shared Decision Making gemeinsam mit den Patientinnen und Patienten in die Therapieentscheidung einbezogen.

Die Auswahl der Therapie bei PsA erfolgt auf Grundlage klar definierter, regelhaft berücksichtigter Kriterien, die zu einer differenzierten und individualisierten Auswahl zwischen etablierten Therapieoptionen führen.

Referenzliste:

1. Coates LC, Soriano ER, Corp N, Bertheussen H, Callis Duffin K, Campanholo CB, et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. Nat Rev Rheumatol. 2022;18(8):465–79.
2. Gossec L, Kerschbaumer A, Ferreira RJO, Aletaha D, Baraliakos X, Bertheussen H, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2023 update. Ann Rheum Dis. 2024;83(6):706–19.
3. Coates LC, Helliwell PS. Validation of minimal disease activity criteria for psoriatic arthritis using interventional trial data. Arthritis Care Res (Hoboken). 2010;62(7):965–9.
4. Augustin M, Lindner L, Kühl L, Weiss A, Rustenbach SJ, Stephan B, et al. [Charakterisierung von Patienten mit Psoriasisarthritis in der dermatologischen und rheumatologischen Versorgung: Analyse von zwei Registern: Characterization of patients with psoriatic arthritis in dermatologic and rheumatologic care: analysis of two registries]. J Dtsch Dermatol Ges. 2023;21(10):1170–8.