USZ Universitäts Spital Zürich

Sarkoidose
Diagnostik und Therapie

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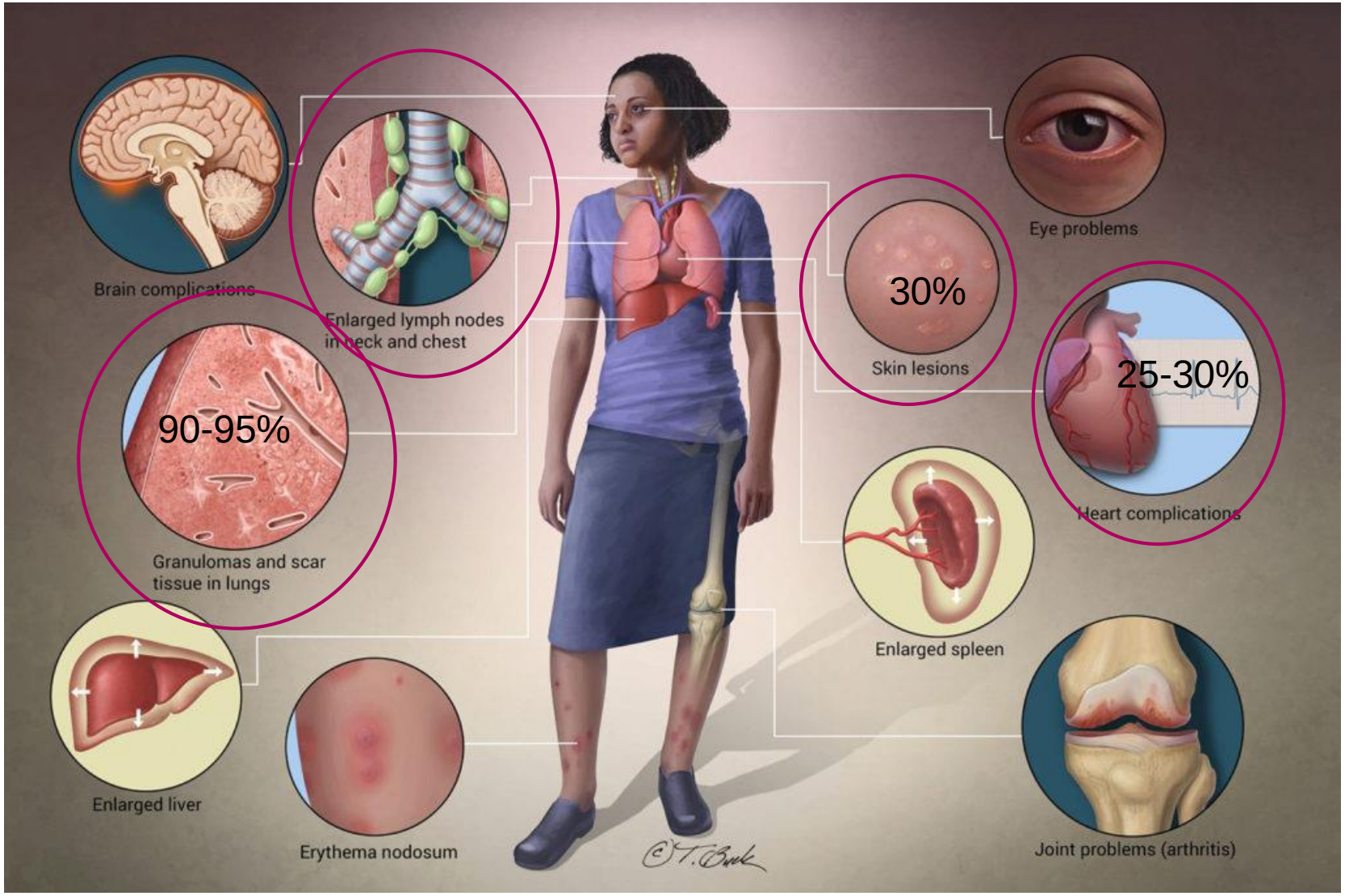
Rheumaworkshop, 14.12.2023

Agenda

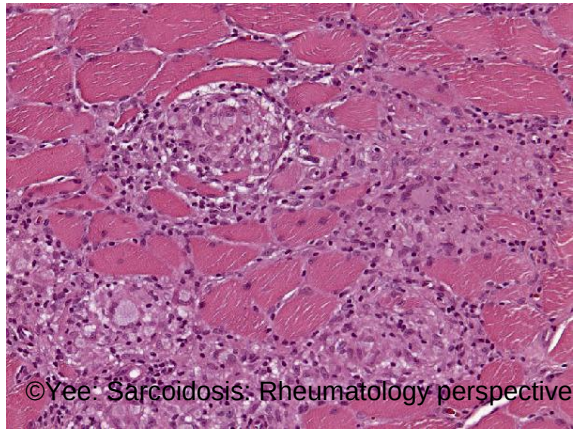
1. Kurzrepetition: Klinik und Pathomechanismus
2. Diagnostik
3. Therapie
   - Pulmonale Sarkoidose
   - Kardiale Sarkoidose
   - Moysitis, Arthritis, Ossäre Sarkoidose
4. Konklusion
5. Anhang

Kurzrepetition: Klinik und Pathomechanismus

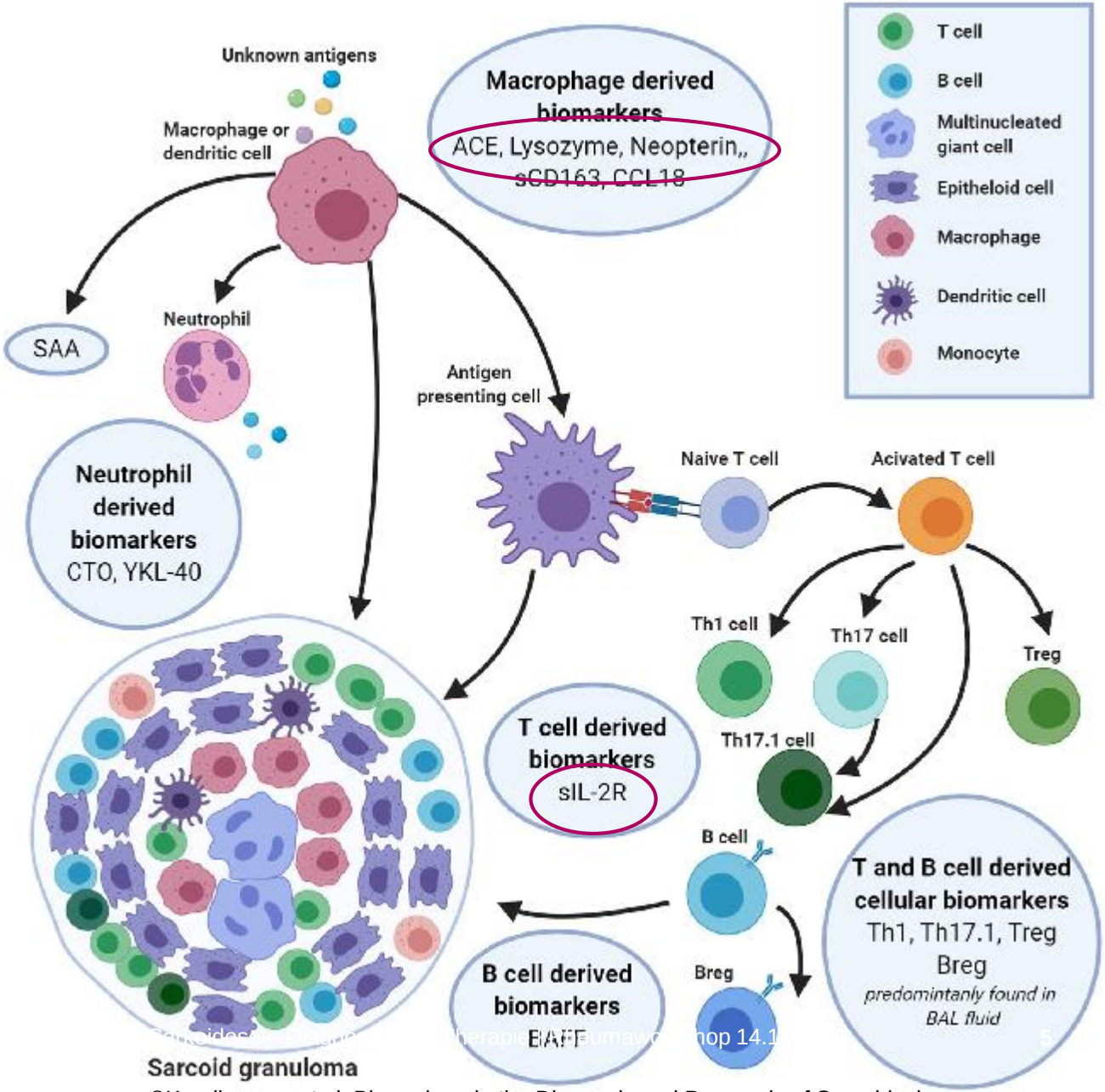
Klinik und Pathomechanismus



Klinik und Pathomechanismus


©Yee: Sarcoidosis: Rheumatology perspective

- Macrophagen, Monozyten, Vielkernige Riesenzellen
- TNF-alpha wichtige Rolle in Granulombildung und –erhalt
- Hypercalcämie durch vermehrte 1,25-OH Bildung in Granulomen



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Diagnostik

Diagnostik

Diagnosestellung

American thoracic society (ATS) Guidelines

Ist nicht standardisiert, aber basiert auf 3 Majorkriterien:

- Passende Klinik
- Histologischer Nachweis von nicht-verkäsenden Granulomen in ≥ 1 Gewebeprobe
- Ausschluss anderer Ursachen granulomatöser Erkrankungen

Die Diagnose einer Sarkoidose ist niemals endgültig sicher.

Diagnostik

Diagnosestellung

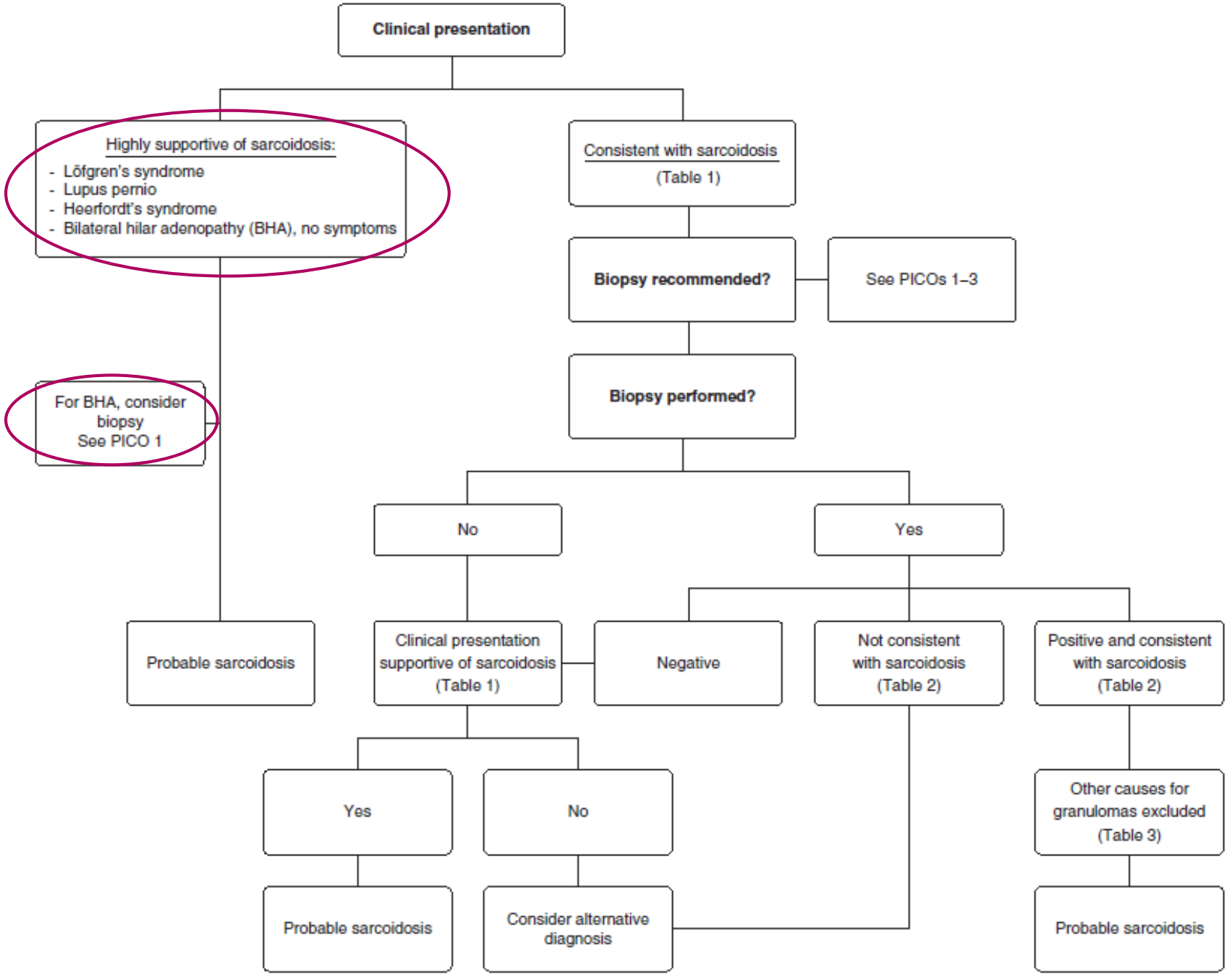

Figure 3. Schematic of recommended diagnostic algorithm. The figure outlines a general approach to the diagnosis of sarcoidosis and refers to tables presented with this article. PICO = problem, intervention, comparison, outcome question format. © ATS Diagnosis and Detection of Sarcoidosis

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Diagnostik

Diagnosestellung

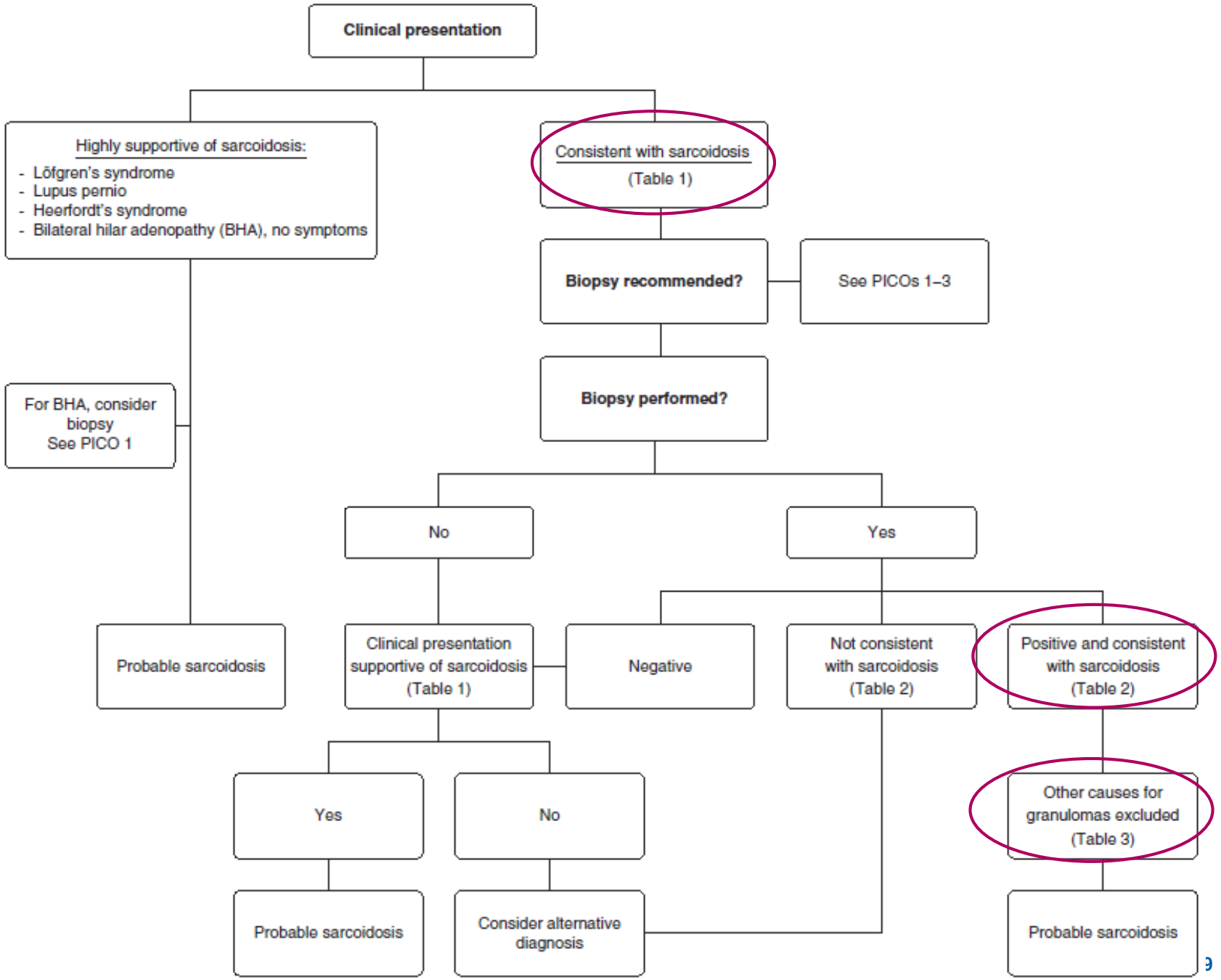


Figure 3. Schematic of recommended diagnostic algorithm. The figure outlines a general approach to the diagnosis of sarcoidosis and refers to tables presented with this article. PICO = problem, intervention, comparison, outcome question format. © ATS Diagnosis and Detection of Sarcoidosis

Table 3. Key Infectious and Noninfectious Differential Diagnoses for Granulomatous Lesions within Commonly Biopsied Sites

	Granulomatous Lesion within These Sites:					
	Lung	Lymph Node	Skin	Liver	Bone Marrow	Testing and Clinical Pearls
Infectious etiologies						
Bacteria						
Tuberculosis*	X	X	X	X	X	Culture is diagnostic gold standard; IFN-γ release assay used for screening, and preferable to tuberculin skin testing due to anergy
Nontuberculous mycobacteria (MAC and *M. kansasii*)*	X	X	X	X	X	Culture is the gold standard
Aspiration pneumonia*	X					Culture
Brucella		X	X	X	X	Serum agglutination and ELISA; livestock exposure history
Tropheryma whippelii		X		X		Periodic acid–Schiff stain; immunohistochemistry testing; diarrhea, weight loss, and joint pains
Mycobacterium leprae			X			Culture is the gold standard, but can be difficult; histology; PCR
Francisella tularensis		X	X			Serologic assay, then repeat in 2 wk; rabbit exposure
Bartonella henselae		X	X			Titers >1:256; cat exposure
Coxiella burnetii				X	X	Serology; PCR; livestock exposure
Fungi						
*Aspergillus**	X		X		X	Culture; *Aspergillus* IgG; histology
*Histoplasma**	X	X	X		X	Culture; urine histoplasma antigen
*Blastomyces**	X		X			Culture; histology; blasto Ag is nonspecific
*Coccidioides**	X				X	Serologic tests using EIA for IgM and IgG; then confirmatory immunodiffusion
Cryptococcus	X		X	X	X	Cryptococcal serum antigen
Pneumocystis	X					Histology; screen with β-D-glucan assay
Viruses						
Herpes zoster	X		X			Granulomas may occasionally be found
Parasitic						
Toxoplasma gondii		X	X	X		Toxoplasma serologic assay IgM and IgG
Schistosomiasis	X		X	X		Serology and microscopic visualization of eggs in stool or urine
Leishmaniasis			X	X		Histology and PCR for *Leishmania*
Echinococcosis			X	X		EIA; ultrasound imaging
Enterobius			X	X		Pinworm paddle test, then microscopy
Dirofilaria	X					Histology; eosinophilia
Noninfectious etiologies						
Malignancy						
Lymphoma*	X	X	X	X	X	Clonal cell population; rarely can have elevated serum ACE
Sarcoid-like reaction to tumor*	X	X	X	X	X	PET useful for selecting biopsy site but not diagnostic; biopsy must be performed to diagnose
Lymphomatoid granulomatosis			X			Atypical clonal EBV-positive B cells; multiple pulmonary nodules with lymphocytic transmural angiitis and granulomas noted sometimes in skin
Germ cell tumor		X				Serum α fetoprotein, human chorionic gonadotropin, lactate dehydrogenase
Autoimmune or immune dysfunction						
ANCA-associated vasculitides (GPA, MPA, and EGPA)	X		X			MPO or PR3 ANCA+, renal disease, necrotizing vasculitis; eosinophilic infiltration if EGPA
GLILD associated with CVID	X	X				Nonnecrotizing granulomas, LIP, and follicular bronchiolitis on lung biopsy; hypogammaglobulinemia and recurrent infections
Rheumatoid nodules			X			Multiple subpleural nodules in patient with anti-CCP antibodies, arthralgias; necrotizing granulomas
Langerhans cell histiocytosis	X	X	X	X	X	Young smoker; multiple bizarre-shaped upper lung zone cysts and/or nodules; Langerhans cell stain CD1a and S100 positive; eosinophilic granulomas most common
IgG4-related disease	X	X	X	X	X	Elevated serum IgG4; elevated tissue IgG4+ plasma cell count and IgG4:IgG ratio; granulomas rare; differential diagnosis with multicentric Castleman disease
Inflammatory bowel disease	X		X	X		GI symptoms; granulomatous bronchiolitis
Primary biliary cholangitis				X		Cholestasis; antimitochondrial antibodies; portal based, poorly formed granulomas with bile duct destruction
Primary sclerosing cholangitis				X		Cholestasis; P-ANCA+; ulcerative colitis associated; biliary strictures present, granulomas rare and not associated with bile duct destruction
Autoimmune hepatitis						Abnormal liver function tests and autoantibodies (e.g., anti–smooth muscle); syncytial multinucleated giant cells are rare in adults but may be observed in children or adolescents
Exposures						
Hypersensitivity pneumonitis*	X	X				Organic exposure, small poorly formed interstitial granulomas in interstitium, prominent lymphocytic infiltrates, chronic inflammatory infiltrates accentuated around bronchioles
Hot tub lung syndrome (MAC exposure with hypersensitivity features)	X	X				Aerosolized water exposure, MAC cultured from sputum, lung or hot tub, large well-formed granulomas in bronchiole lumens
Pneumoconiosis (such as beryllium, titanium, aluminum, zirconium, cobalt, and others)	X	X	X			Inorganic exposure history
Drug-induced granulomatous disease (including but not limited to IFN, checkpoint inhibitor, anti-TNF, and/or biologic therapies)*	X	X	X	X	X	Usually nonnecrotizing granulomas. Drug exposure history essential. *See* www.pneumotox.com for full list
Foreign body granulomatosis (such as talc aspirated or injected, tattoo ink)*	X	X	X			Serum ACE elevated in many patients; particles found on biopsy; perivascular granulomas
Steatosis (lipogranulomas)				X		Central lipid vacuole; ingestion of mineral oil or hepatic steatosis
Idiopathic						
Sarcoidosis	X	X	X	X	X	Multisystemic; well formed, usually nonnecrotic granulomas
Necrotizing sarcoid granulomatosis	X	X				Granulomatous pneumonitis with necrosis and vasculitis; multiple necrotic lung nodules
Histiocytic necrotizing lymphadenitis (Kikuchi's disease)		X				Cervical lymphadenopathy and low-grade fever. Granulomas are not found, although necrotic areas with histiocytes are present
GLUS		X	X	X	X	Lacks progressive lung parenchymal disease, elevated serum calcium, 1,25-dihydroxyvitamin D, and ACE
Bronchocentric granulomatosis	X					Associated with asthma and *Aspergillus* infection in 50%. Necrotizing granulomas exclusively in bronchi and bronchioles

Definition of abbreviations: ACE = angiotensin-converting enzyme; Ag = antigen; EIA = enzyme-linked immunoassays; ANCA = antineutrophil cytoplasmic antibody; CCP = cyclic citrullinated peptide; CVID = common variable immune deficiency; EBV = Epstein-Barr virus; EGPA = eosinophilic GPA; GI = gastrointestinal; GLILD = granulomatous–lymphocytic interstitial lung disease; GLUS = granulomatous lesions of unknown significance syndrome; GPA = granulomatosis with polyangiitis; LIP = lymphocytic interstitial pneumonia; MAC = *Mycobacterium avium* complex; *M. kansasii* = *Mycobacterium kansasii*; MPA = microscopic polyangiitis; MPO = myeloperoxidase; p-ANCA = perinuclear ANCA; PR3 = PR3-ANCA; PET = positron emission tomography; TNF = tumor necrosis factor.

*More commonly found alternative diagnoses for granulomatous disease in U.S. populations. The differential diagnosis should be prioritized on the basis of the individual's clinical history and presentation.

Diagnostik

Baseline-Diagnostik

Auch bei fehlender Klinik:

- ophthalmologische Vorstellung
- Kreatinin, AP, Ca, BB, +/- Transaminasen; 25-OH- *und* 1,25-OH-Vitamin D *wenn* Bedarf nach ViDe Substitution
- EKG, aber kein Routine-TTE
- BTS: ACE Spiegel

Bei vermuteter kardialer Beteiligung:

- Herz-MRI > PET > TTE

Bei vermuteter PAH:

- TTE → Rechtsherzkatheter

Diagnostik

… und dann?

BTS: LuFu regelmässig bei aktiven/therapierten Patienten

Table 5. Best Practice Recommendations for Detection of Delayed Onset of Extrapulmonary Sarcoidosis Manifestations after Negative Baseline Screening

Test Parameter	Routine Testing for New Sarcoidosis Involvement	New Conditions Triggering a Specific Testing for Extrapulmonary Sarcoidosis Involvement
Calcium	Annually	Kidney stones Acute or acute on chronic renal failure
Creatinine	Annually	—
Alkaline phosphatase	Annually	—
Eye exam	None	Change in vision • Floaters • Blurry • Visual field loss Eye pain, photophobia, or redness (sustained)
Cardiac testing (*see* Questions 9)	None	Chest pains Palpitations Near syncope/syncope Sustained bradycardia or tachycardia Dyspnea out of proportion to lung disease New ECG findings
Pulmonary hypertension testing (*see* Question 10)	None	Clinical signs of pulmonary hypertension (*see* main text)

Approximately 23% of patients with sarcoidosis will develop a new disease manifestation within 3 years of baseline evaluation. Annual testing is recommended for calcium, creatinine, and alkaline phosphatase, because these manifestations are often asymptomatic. In contrast, routine testing is not recommended for ocular or heart sarcoidosis, unless the patient presents with related symptoms, as above.

Diagnostik

… und was ist mit:

ACE:

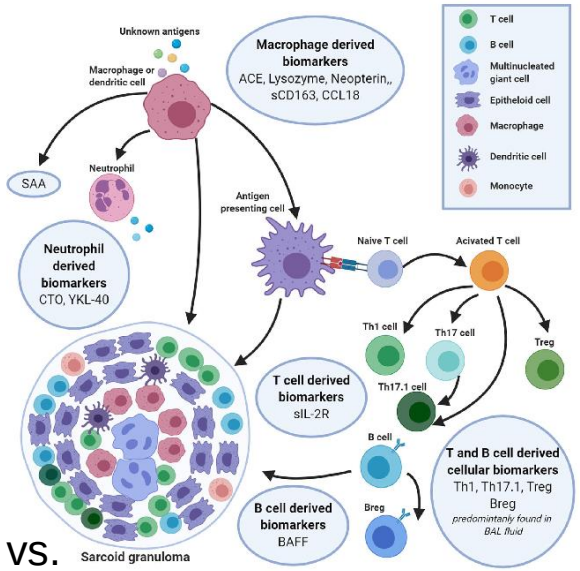
- Sensitivität 22-86%; Spezifität 54-94%
- Spiegelhöhe unabhängiger prognostischer Faktor für Krankheitsausprägung (nur pulmonaler vs. Mehrorgan-Befall) als auch mit Krankheitsaktivität im Verlauf korrelierend

sIL2-Rezeptor:

- Sensitivität 88%; Spezifität 85%; in Zusammenschau mit anderer Diagnostik sinnvoll
- Tendenziell höher bei Mehrorgan-Befall; mit Krankheitsaktivität im Verlauf korrelierend
- Prognostisch für Rezidiv
- CAVE: erhöht bei Niereninsuffizienz

Neopterin:

- Aufgrund schlechter Spezifität wenig Relevanz als diagnostischer Biomarker



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Kraaijvanger et al., Review 2020; Zhou et al 2023

Diagnostik

in Zeiten des 18-FDG-PET

Bei pulmonaler Sarkoidose:

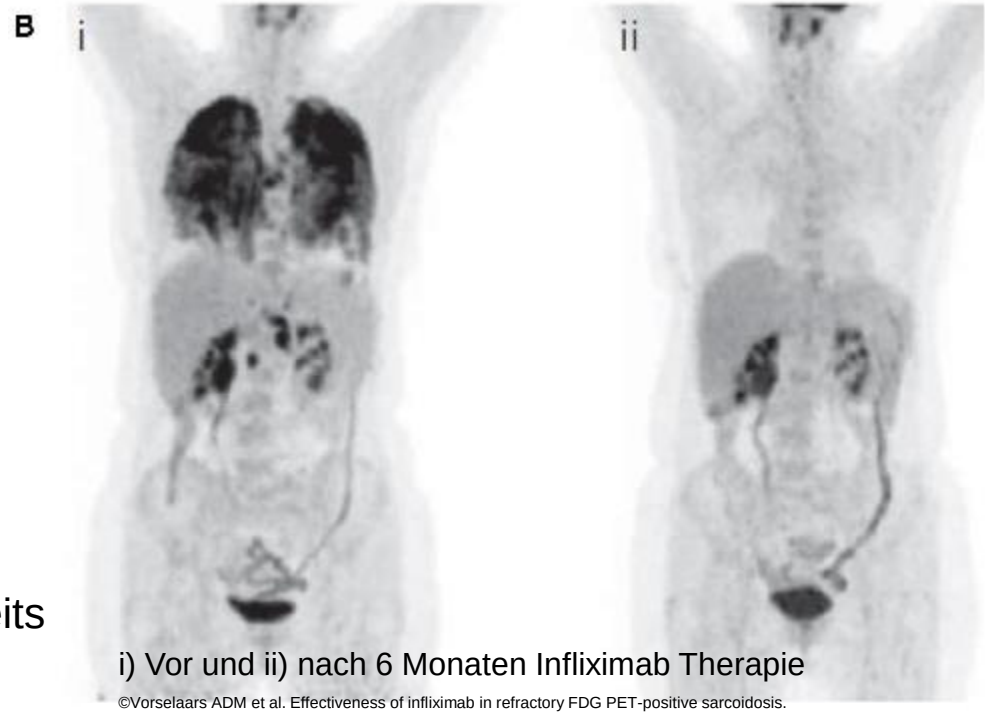
Diagnostisch

- Ausdehnung Erkrankung; teils Aufdeckung okkulter Organbefall bei bereits gestellter Diagnose
- Sensitivität zwischen 75 – 100%

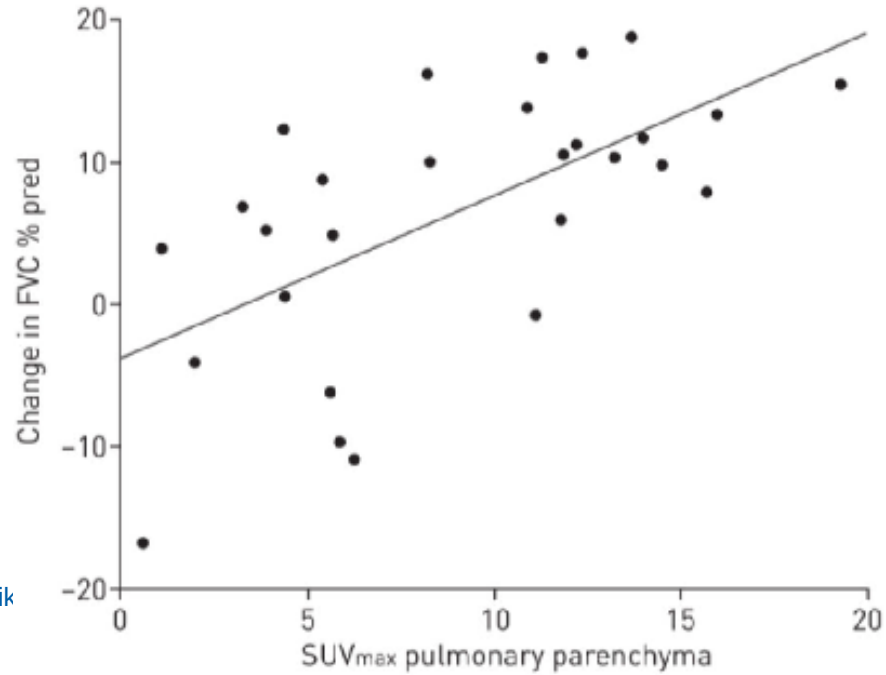
Prognostisch

- Nachweis von hoher parenchymaler Aktivität → Prädiktor für gutes Steroid- oder TNF-Hemmer-Ansprechen mit Besserung der LuFu

Kraaijvanger et al., Review 2020



i) Vor und ii) nach 6 Monaten Infliximab Therapie



Therapie

Therapie

Erst Fragen:

- Welches Organ befallen?
- Therapieindikation vs. watch and wait
- Unterscheidung Krankheitsaktivität vs. Krankheitsschäden

Spezifische Therapie schwierig

- Wenige RCTs
  - Wenn vorhanden: häufig auf sehr spezifische Manifestationen beschränkt, sehr klein
- Wenige konkrete Empfehlungen, daher möchte **European Respiratory Society (ERS)** bzgl. pulmonalem und kardialen Befall aufführen

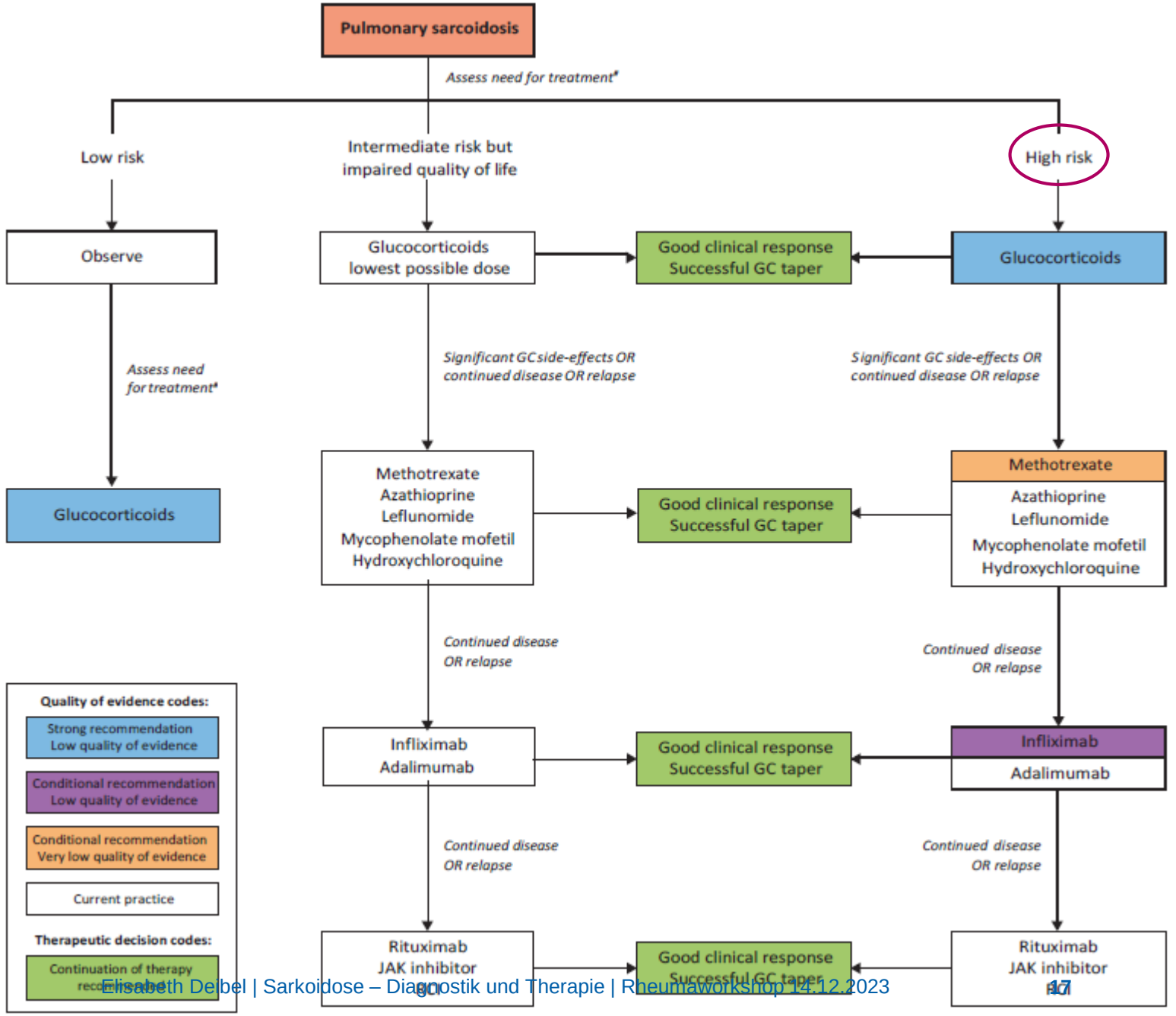
Therapie

Pulmonale Sarkoidose

Wann?

- high risk* =
  - Moderate bis schwere Fibrose; radiologisches Stadium IV
  - Relevant reduzierte FVC und DLCO
  - Signifikante Belastungsintoleranz
  - Präkapilläre pulmonale Hypertonie
- Krankheitsprogredienz

* Def. je nach uptodate/ESR



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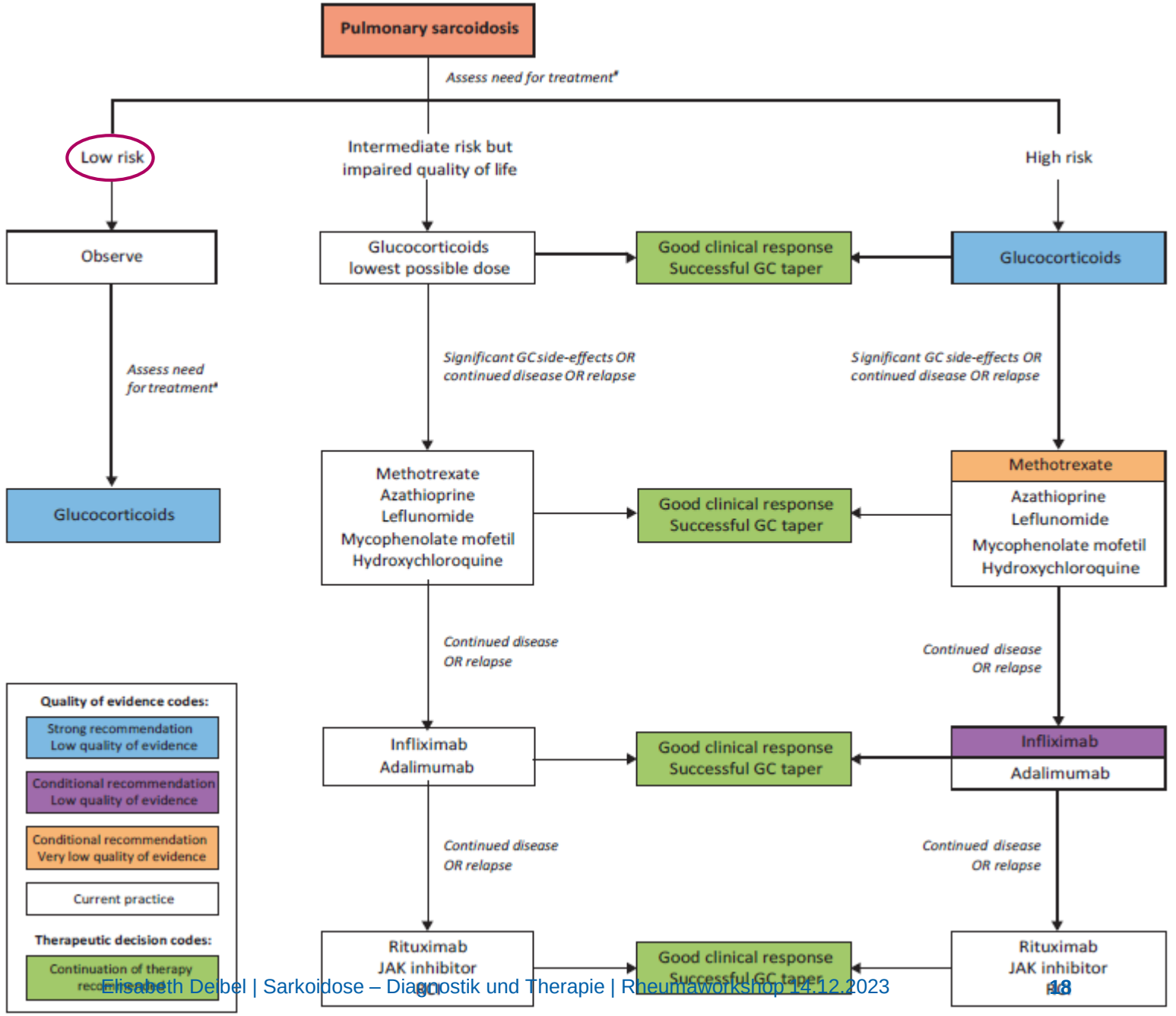
Therapie

Pulmonale Sarkoidose

Wann *nicht*?

- low risk:
  - V.a. Stadium I und II
  - asymptomatisch



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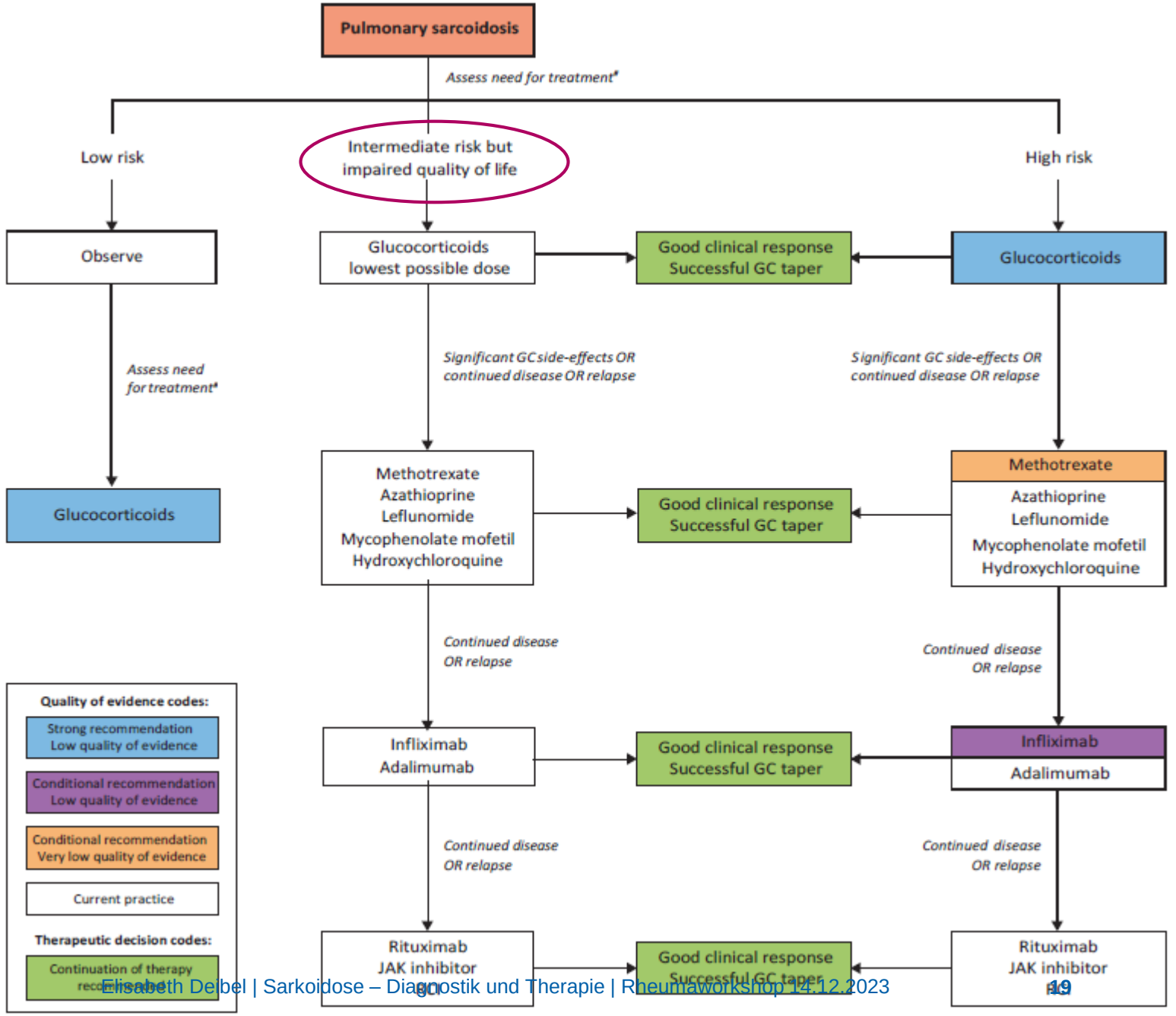
Therapie

Pulmonale Sarkoidose

Wann *vielleicht*?

- high risk nicht erfüllend aber relevante Symptome



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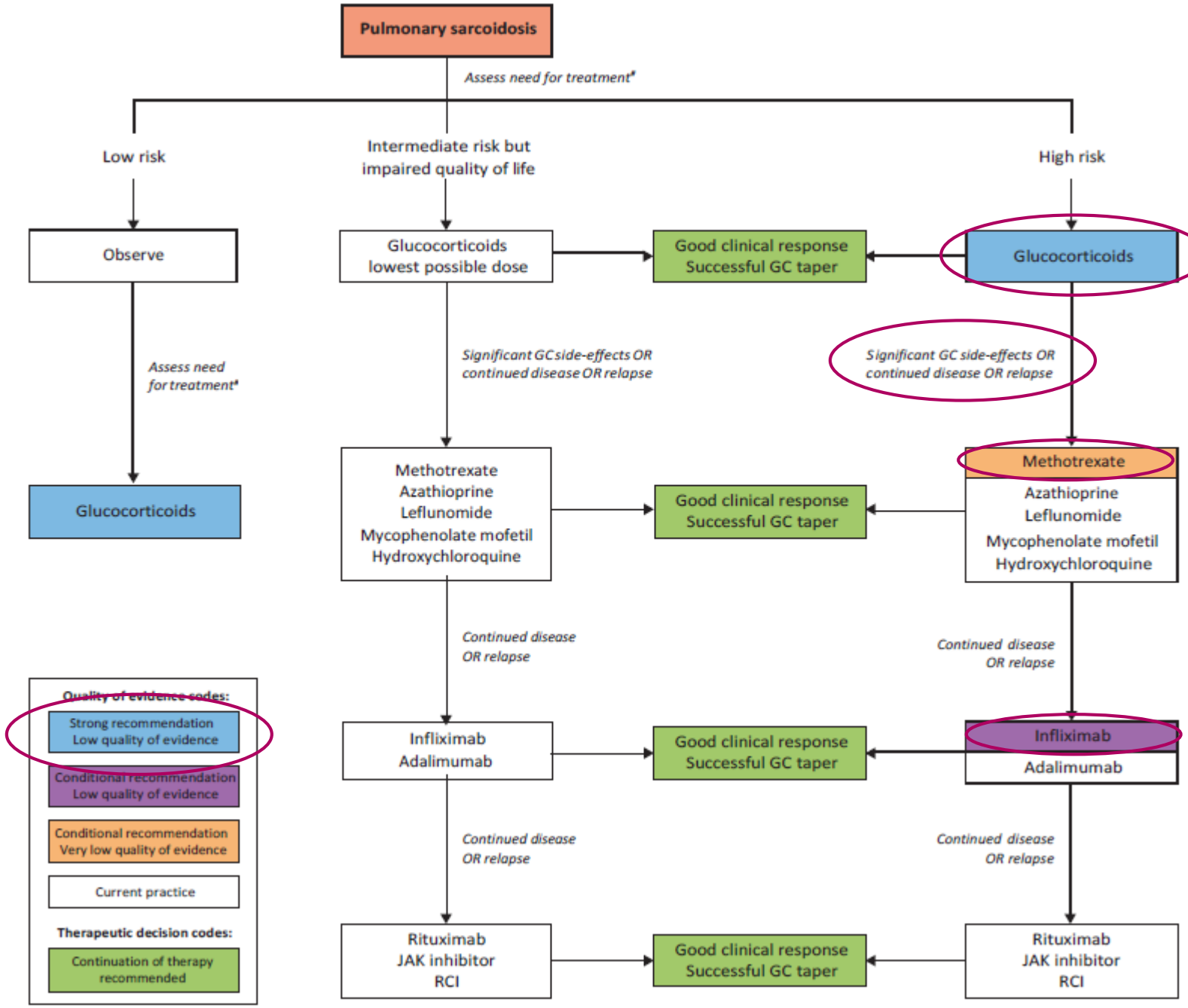
Therapie

Pulmonale Sarkoidose

Wie?

- Oral Prednison 20 mg für 4-6 Wochen*
- Tapering zur niedrigsten nötigen Dosis
- Steroidsparend: add-on von
  - MTX
  - Infliximab

*BTS: 20-40mg 4-6 Wo, - 5mg/2Wo; auf 5-10mg für 6-12 Monaten



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Therapie

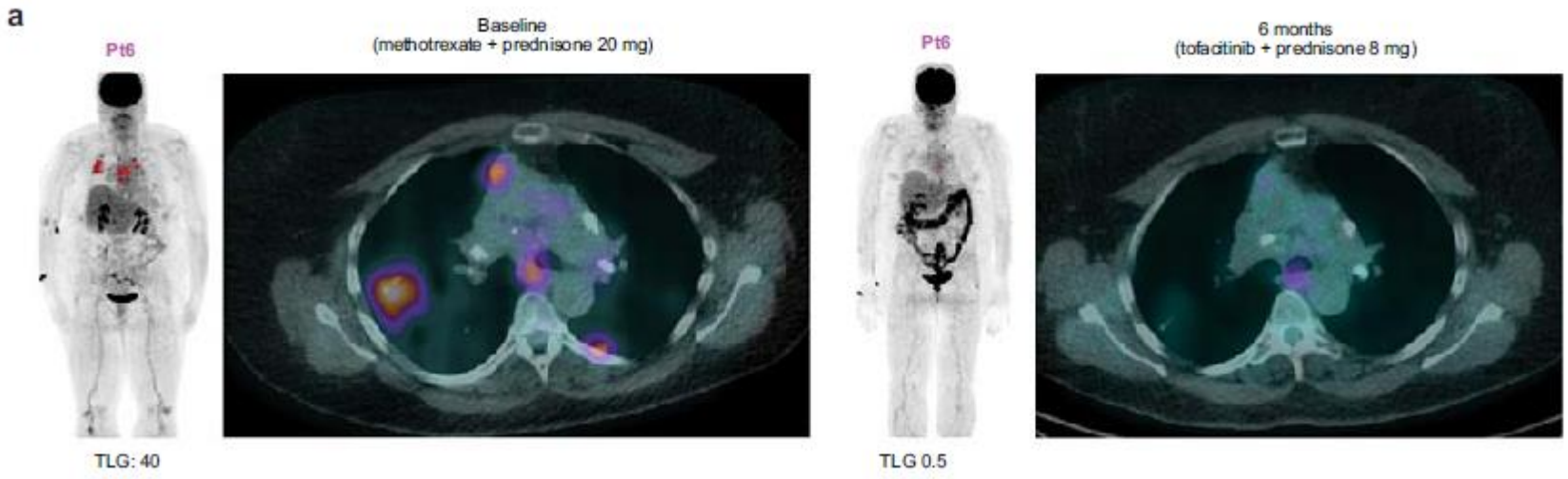
Pulmonale Sarkoidose

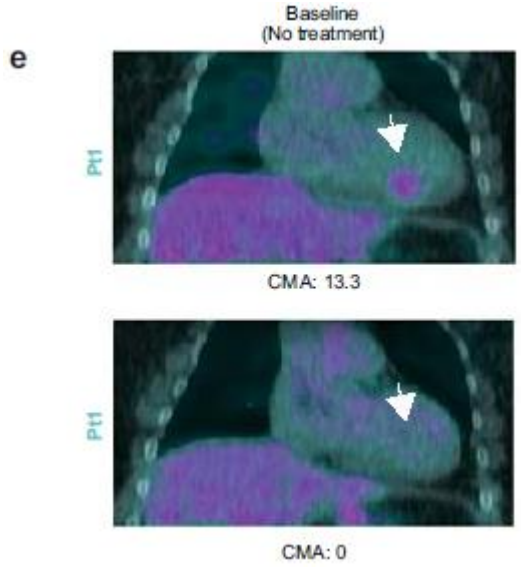
ARTICLE

https://doi.org/10.1038/s41467-022-30615-x OPEN

Inhibition of type 1 immunity with tofacitinib is associated with marked improvement in longstanding sarcoidosis

William Damsky[1,2✉], Alice Wang[1], Daniel J. Kim[1], Bryan D. Young[3], Katelyn Singh[1], Michael J. Murphy[1], Joseph Daccache[1], Abigale Clark[4], Ruveyda Ayasun[5], Changwan Ryu[6], Meaghan K. McGeary[2], Ian D. Odell[1,7], Ramesh Fazzone-Chettiar[3], Darko Pucar[8], Robert Homer[2], Mridu Gulati[6], Edward J. Miller[3], Marcus Bosenberg[1,2,7], Richard A. Flavell[7,9] & Brett King[1✉]

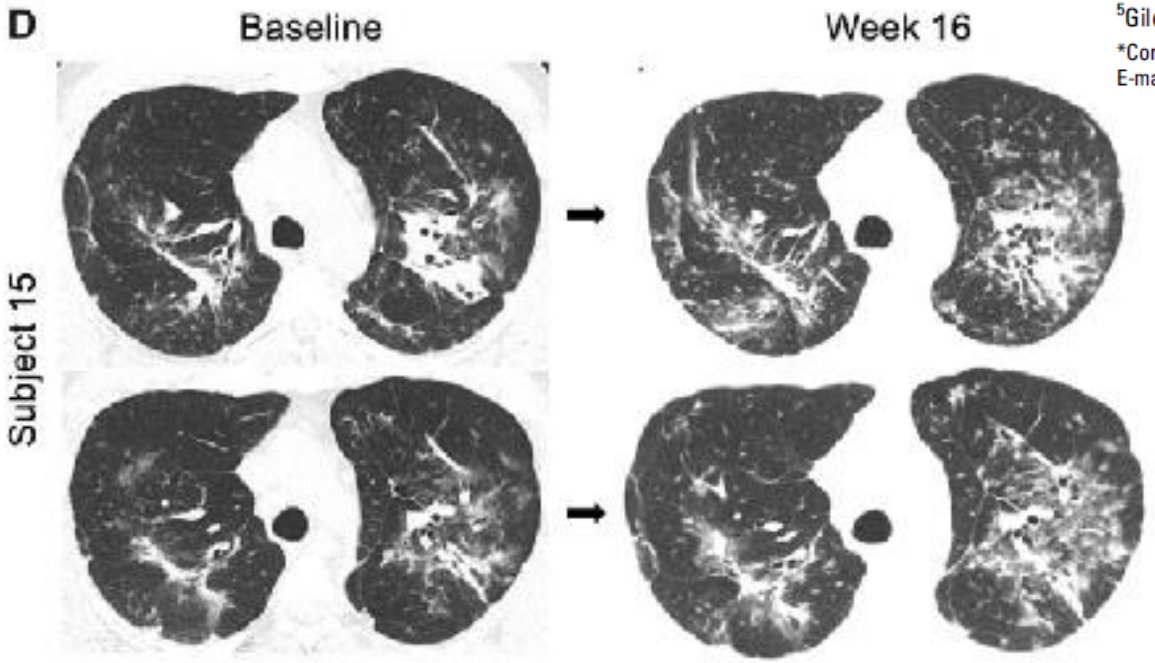




Therapie

Pulmonale Sarkoidose

- Sarilumab scheint keinen Benefit bei Steroid-abhängiger, aktiver pulmonaler Sarkoidose zu haben;
- Zumindest nicht hinsichtlich Steroid-Reduktion
- Potentieller Benefit bei Arthritis (2 Pat.)



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Advance access publication 20 July 2023
Original Article

British Society for Rheumatology RHEUMATOLOGY OXFORD

Clinical science

A double-blind, placebo-controlled, randomized withdrawal trial of sarilumab for the treatment of glucocorticoid-dependent sarcoidosis

Matthew C. Baker [1,*], Audra Horomanski [1], Yiwen Wang[2], Yuhan Liu[2], Shima Parsafar[1], Robert Fairchild[1], Joshua J. Mooney[3], Rishi Raj[3], Ronald Witteles[4], Mark C. Genovese[1,5]

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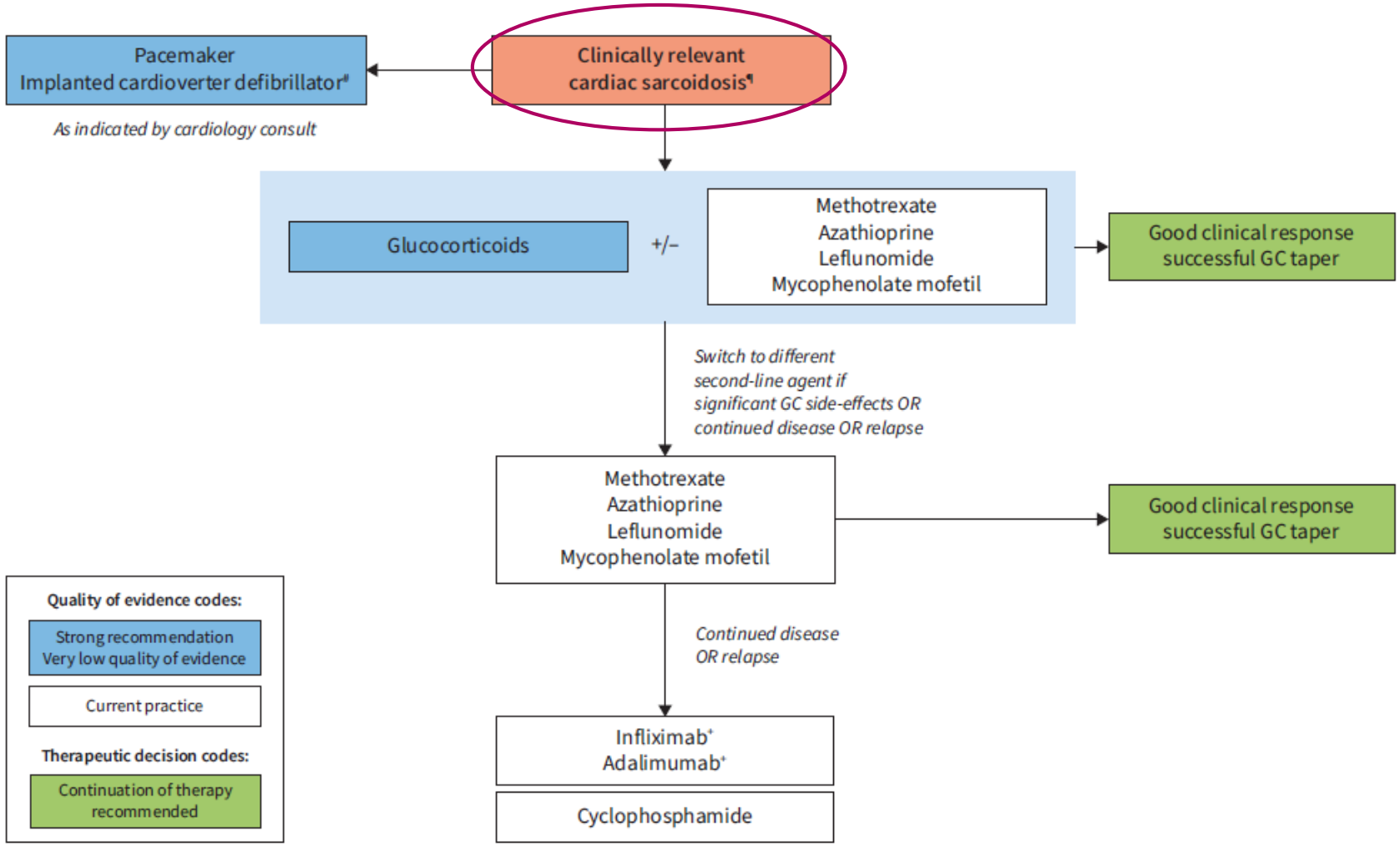
E-mail: mbake13@stanford.edu

Therapie

Cardiale Sarkoidose

Wann?

- Reizleitungsblöcke
- Rhythmusstörungen
- Cardiomyopathie



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Therapie

Cardiale Sarkoidose

Wann vielleicht, bzw. unklar?

- Bislang nicht beantwortete Frage ist die Behandlung asymptomatischer Patienten mit zB. aktiven Entzündungszeichen im PET oder Gadoliniumanreicherung im MRI

TABLE 4 Prognostic variables that may influence treatment decisions for cardiac sarcoidosis
• Age >50 years
• Left ventricular ejection fraction <40%
• New York Heart Association Functional Class III or IV
• Increased left ventricular end-diastolic diameter
• Late gadolinium enhancement on cardiac magnetic resonance imaging
• Ventricular tachycardia
• Cardiac inflammation identified by fluorodeoxyglucose positron emission tomography scan
• Echocardiographic evidence of abnormal global longitudinal strain
• Interventricular septal thinning
• Elevated troponin or brain natriuretic peptide
Features found to be associated with increased risk for morbidity or mortality from cardiac sarcoidosis [150–159].

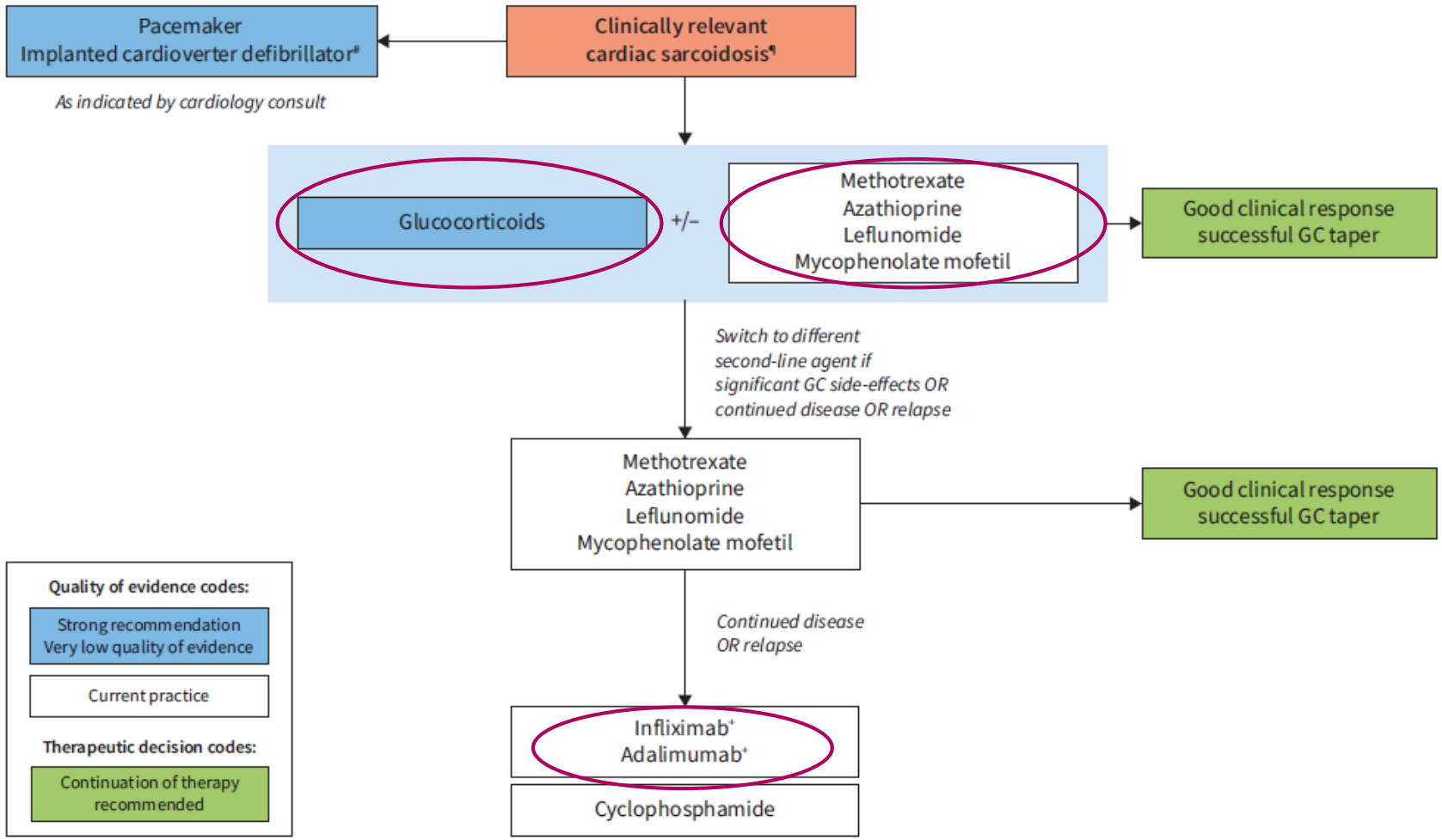
Therapie

Cardiale Sarkoidose

Wie?

- Keine klare Empfehlung zur Dosis, a.e. PDN 0.5mg/kgKG
- Keine Empfehlung über Dauer
- Steroidsparend:

- Evidenz insgesamt unzureichend
- Keine explizite Empfehlung welche, aber insgesamt aufgrund Steroid-NW früher Beginn «to be considered»



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Therapie

Cardiale Sarkoidose

CAVE von TNF-Hemmern bei fortgeschrittener Herzinuffizienz → ATTACH trial 2003

→ Auch gültig bei Sarkoidose?

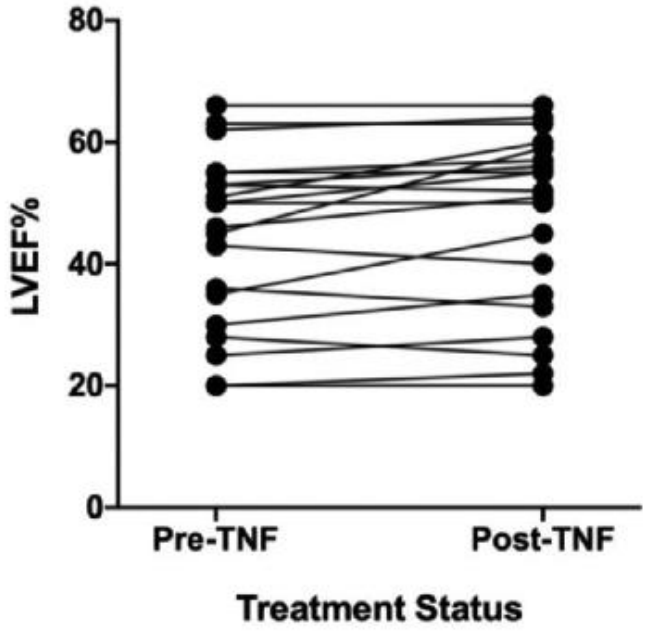

Fig. 5. Change in left ventricular ejection fraction after TNF-α inhibitor treatment in 20 cardiac sarcoidosis patients.

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

TNF-alpha inhibition for the treatment of cardiac sarcoidosis

Matthew C. Baker[a,*], Khushboo Sheth[a], Ronald Witteles[b], Mark C. Genovese[a], Stanford Shoor[a], Julia F. Simard[a,c]

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[c] Department of Health Research and Policy, Division of Epidemiology, Stanford University, United States

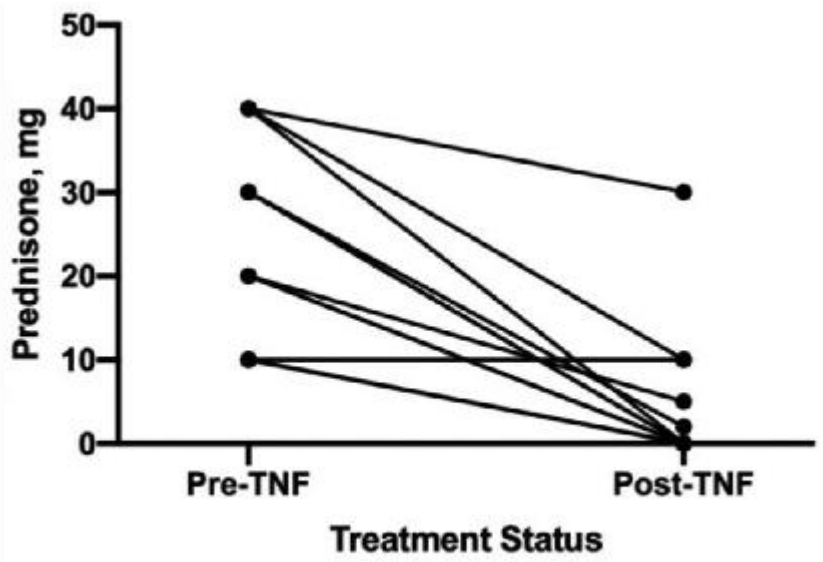


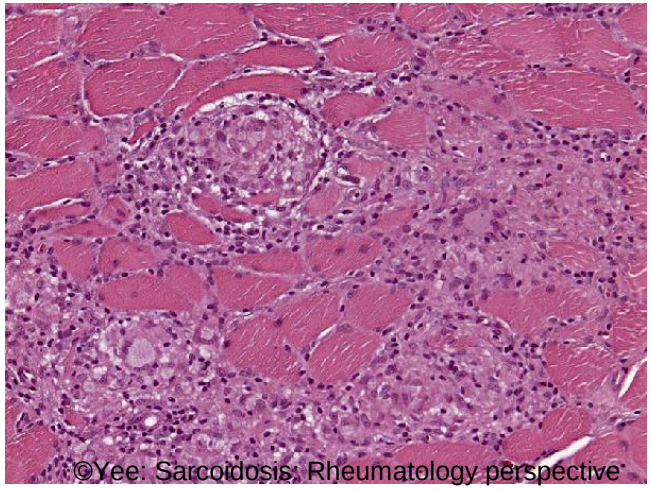
Fig. 4. Change in prednisone dose after TNF-α inhibitor treatment in 13 cardiac sarcoidosis patients.

Therapie

… und für den Rheumatologen?

Myositis

- Keine RCTs, keine direkten Empfehlungen
- Gemäss klinischer Erfahrung:
  - Steroide
  - MTX (20-25mg/Wo), AZA (bis 2mg/kgKG)
  - TNF-Hemmer (Infliximab: 3-5mg/kgKG; Adalimumab 40mg/2Wo)
- Steroiddosis:
  - Akute oder noduläre Myositis:
    - Prednison 0.5-1mg/kgKG, ausschleichend über 3 Monate (4-8 Wochen 7.5mg)
      - Unzureichend oder Rezidiv: MTX oder AZA
  - Chronische Moysitis:
    - Prednison 1mg/kgKG, ausschleichend über 6-12 Monate
      - MTX je nach Komorbiditäten ggfs. als add-on von Beginn



©Yee: Sarcoidosis: Rheumatology perspective

Therapie

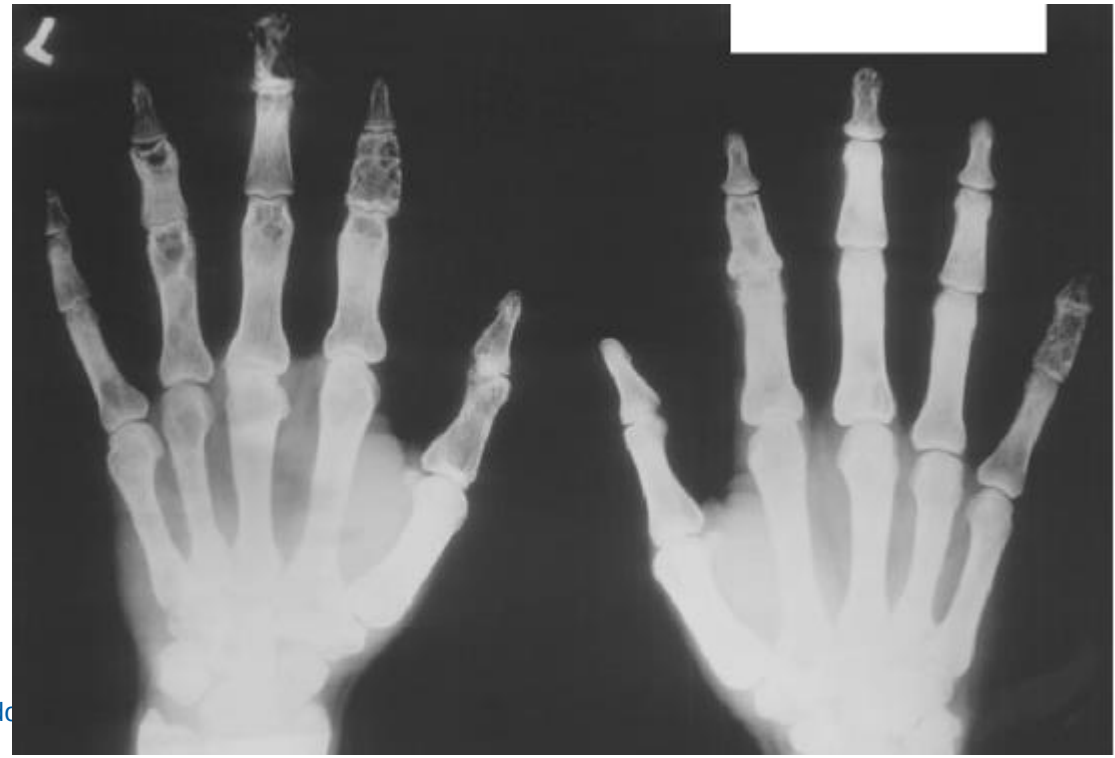
… und für den Rheumatologen?

Arthritis

- Aktue Arthritis i.R. Löfgren-Syndrom: NSAR
- Steroide: akut 10-20mg, chronisch <10mg
- HCQ
- > 3 Monate: MTX oder Leflunomid
- Ggfs. Infliximab add-on

Ossäre Sarkoidose

- Asymptomatisch, keine Therapie
- Ggfs. Steroide für Weichteilschwellung, keine Auswirkung auf Knochenstruktur



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Therapiedauer

Von Steroiden

- Bis zu ¾ der Pat. mit pulmonalem Befall relapsen nach Stopp von Steroiden innh. weniger Monate
- Empfehlung: mind. 6 Monate Therapiedauer mit Remission vor Ausschleichversuch (BTS)
- Re-Therapie bei Rezidiv erfolgreich

Therapiedauer

Von TNF-Hemmern

- Bisher mehrere Studien mit Nachweis von zeitnahen Rezidiven nach Stopp der TNF-Hemmer Therapie

- Yee:
  - Stopp wenn seit 1 Jahr in Remission ohne Steroidbedarf
  - Mind. 1 Jahr Rezidiv-frei

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Original Research

Durable medication-free remission of sarcoidosis following discontinuation of anti-tumor necrosis factor-α therapy

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Therapie

Was ist in Aussicht?

Phase 3 trial in kardialer Sarkoidose:

- Cardiac Sarcoidosis multi-center randomized controlled (CHASM-CS) trial:
  - niedrig dosierte Steroide + MTX vs. Standarddosis Steroide

Phase 2 trial in kardialer Sarkoidose:

- Multimodality assessment of granulomas in cardiac sarcoidosis: Anakinra Randomized (MAGIC-ART) trial:
  - open-label anakinra add-on zu Standard-of-care

ERS Guidelines update bis 2025 erwartet.

Konklusion

Konklusion

- Insgesamt schlechte Evidenz für Therapie seltener Erkrankung mit heterogenem Krankheitsbild
- Wenige Richtlinien, oftmals nicht spezifiziert und in Einzelfällen nicht immer hilfreich
- Therapeutisches Grundprinzip: Prednison – Methotrexat – Infliximab
- Die Diagnose ist nie abschliessend sicher – bei fehlendem Therapieansprechen: DDs!

→ interdisziplinäre Zusammenarbeit

→ Rolle der Rheumatologen bei zunehmender Vielfältigkeit der immunsuppressiven Therapie

Anhang

Anhang

- Therapieguidelines ESR Neurosarkoidose
- Therapieguidelines ESR Kutane Sarkoidose
- Therapieguidelines ESR Fatigue
- Therapieguidelines ESR Small-fiber Neuropathie
- Tabelle Klinische Befunde bei Sarkoidose (aus ATS)
- Diagnostik bei Myopathie, Arthritis, Spondylarthritis, ossäre Sarkoidose
- Literaturempfehlungen
  - Thillai M, et al. BTS Clinical Statement on pulmonary sarcoidosis. Thorax. 2021 Jan;76(1):4-20
  - Baughman RP, et al. ERS clinical practice guidelines on treatment of sarcoidosis. Eur Respir J. 2021
  - Crouser ED, et al. Diagnosis and Detection of Sarcoidosis. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2020 Apr
  - Yee AM. Sarcoidosis: Rheumatology perspective. Best Pract Res Clin Rheumatol. 2016 Apr;30(2):334-356. doi: 10.1016/j.berh.2016.07.001. Epub 2016 Aug 28. PMID: 27886804.

Danke für die Aufmerksamkeit!

Therapie

Neurosarkoidose

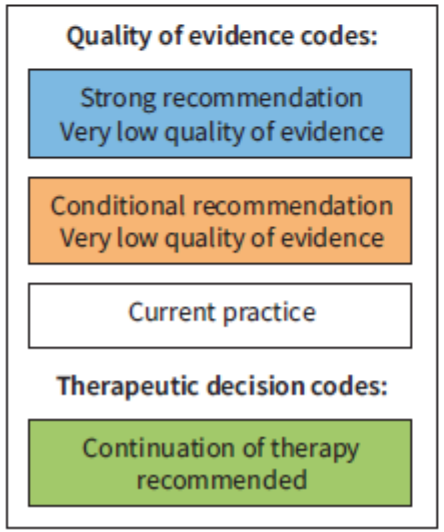
Wann?

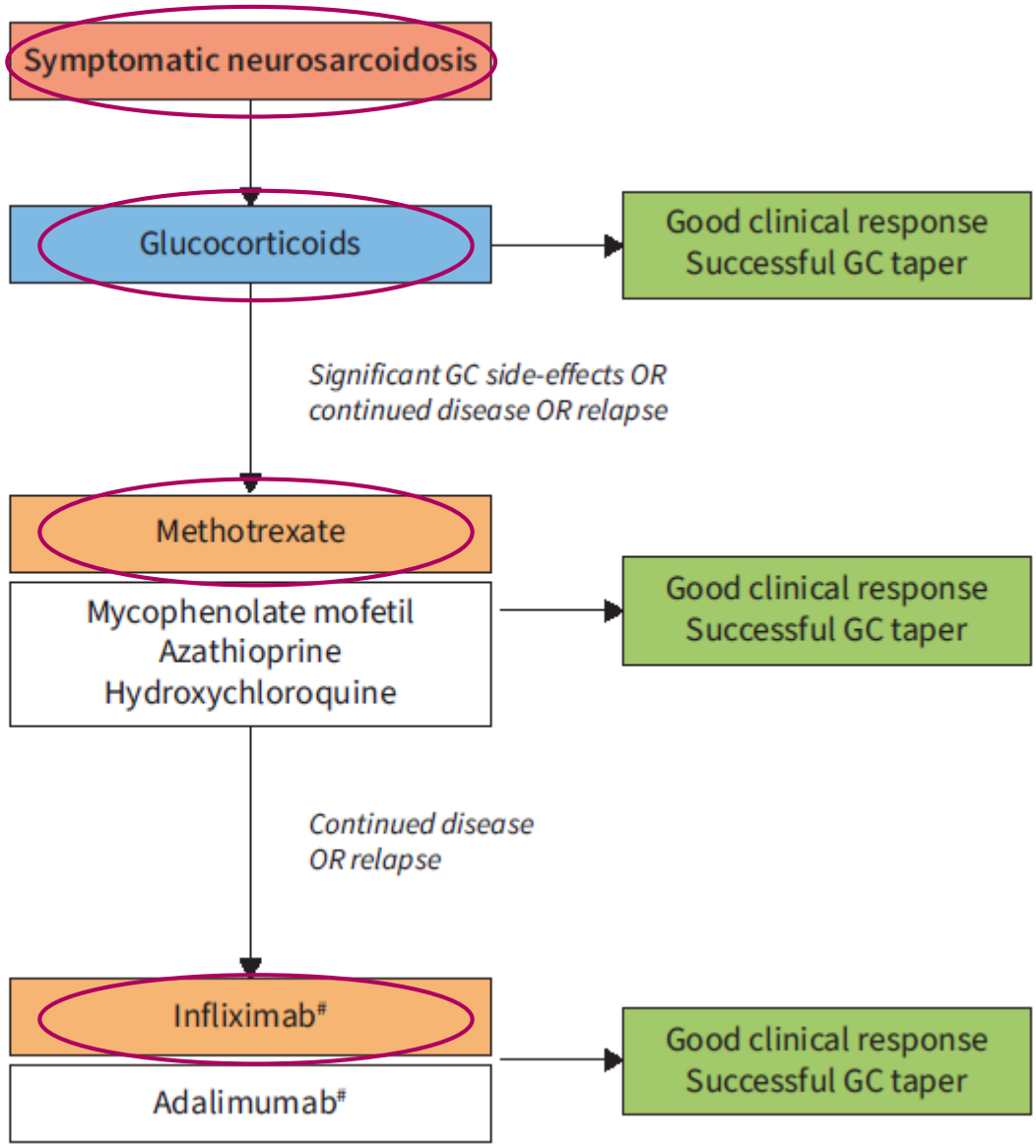
Symptomatisch; klinisch signfikant

Wie?

- Prednison (Dosis?)

- 2nd line: add-on von MTX
- 3rd line: add-on von Infliximab





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Therapie

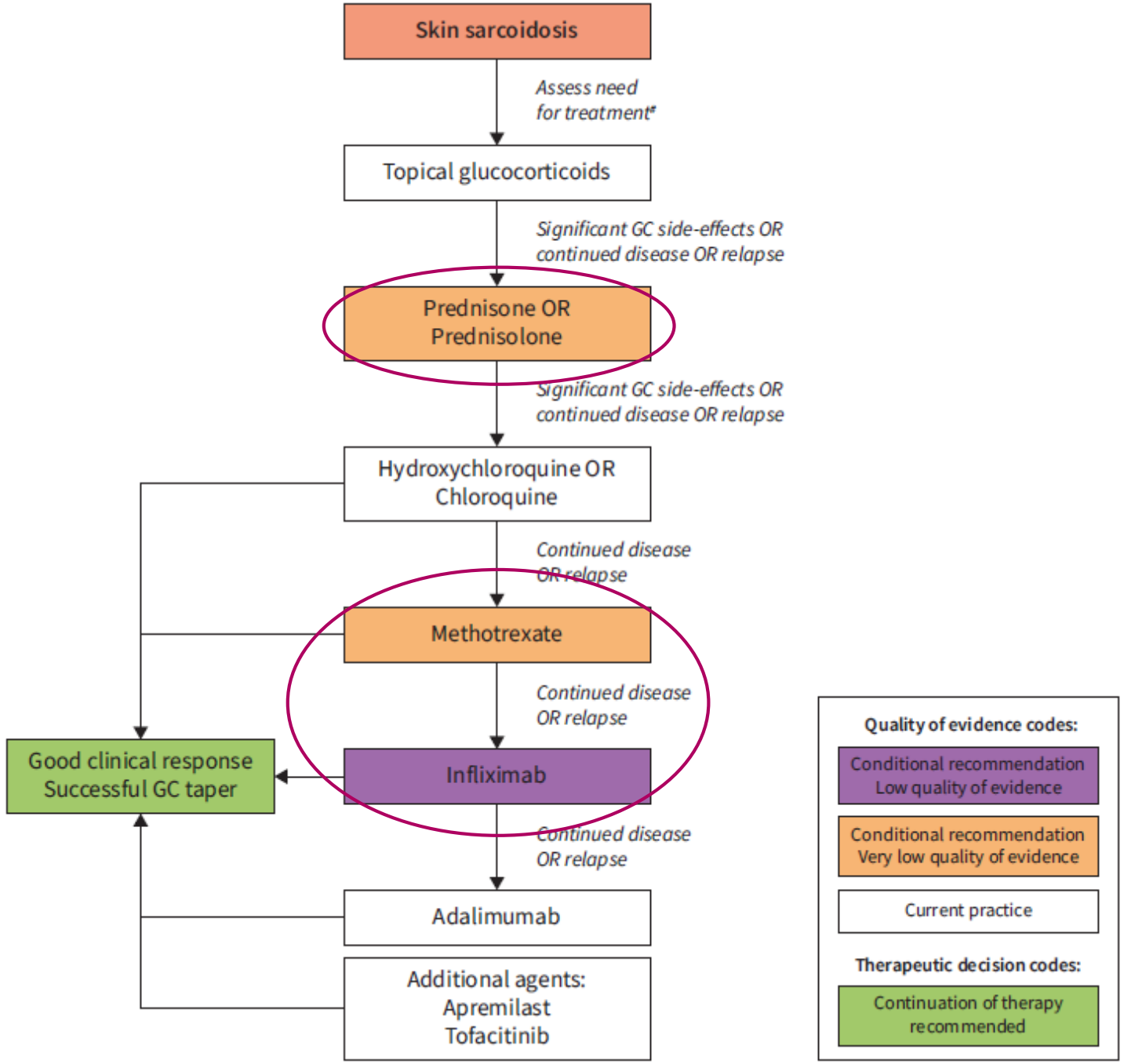
Kutane Sarkoidose

Wann?

- Normalerweise limitiert auf kosmetisch relevante Läsionen

Wie?

- Primär Therapieversuche lokal/intraläsional
- Systemische Steroide bei Versagen
  - Keine Dosisempfehlung der ESR
    - Uptodate: 0.5mg/kgKG
- MTX oder Infliximab (add-on)



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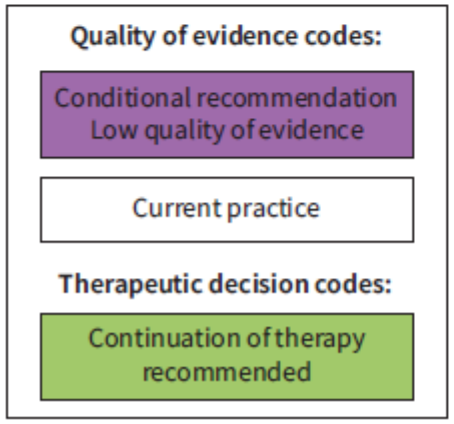
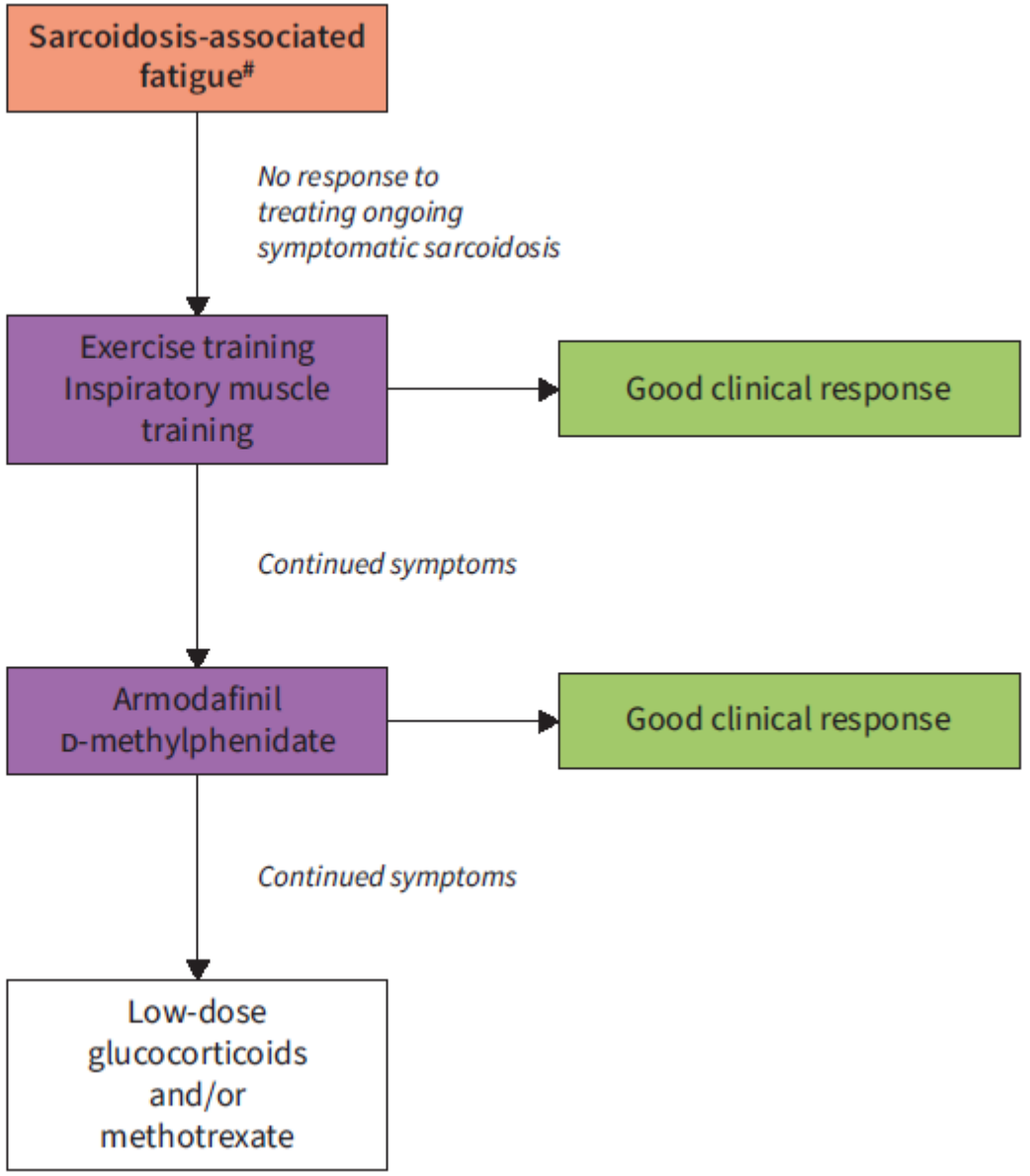
Therapie

Fatigue

Wann?

- Nach Ausschluss anderer DDs
- Bei Persistenz nach Behandlung aktiver granulomatöser Entzüdung
- Hinweise auch für low-dose Steroide aber unzureichend Evidenz





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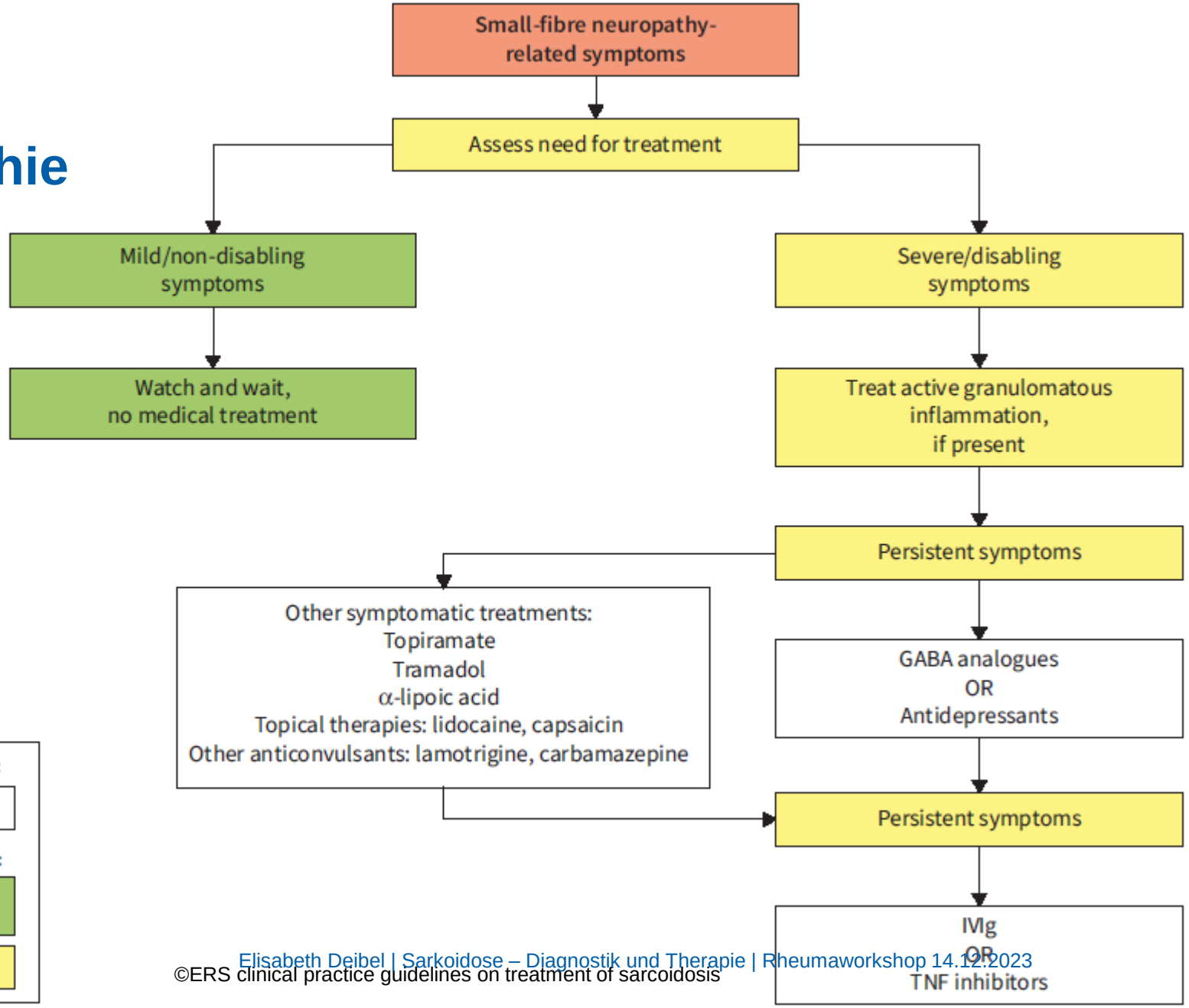
Therapie

Small-fiber Neuropathie

Keine Empfehlung hinsichtlich Einsatz immunsuppressiver Therapien, bei jedoch Einzelberichten hinsichtlich potentieller Effektivität von IVIG und/oder TNF-Hemmern



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Diagnostik

Table 1. Clinical Features Supportive of a Diagnosis of Sarcoidosis

	Highly Probable	Probable
History	Löfgren's syndrome*	Seventh cranial nerve paralysis Treatment-responsive renal failure Treatment-responsive CM or AVNB Spontaneous/inducible VT with no risk factors
Physical	Lupus pernio Uveitis Optic neuritis Erythema nodosum	Maculopapular, erythematous, or violaceous skin lesions Subcutaneous nodules Scleritis Retinitis Lacrimal gland swelling Granulomatous lesions on direct laryngoscopy Symmetrical parotid enlargement Hepato-/splenomegaly
Imaging	Bilateral hilar adenopathy (CXR, CT, and PET) Perilymphatic nodules (chest CT) Gadolinium enhancement on MRI (CNS) Osteolysis, cysts/punched-out lesion, trabecular pattern bone (X-ray, CT, and MRI) Parotid uptake (gallium and PET)	Upper lobe or diffuse infiltrates (CXR, CT, and PET) Peribronchial thickening (CT) Two or more enlarged extra thoracic nodes (CT, MRI, and PET) Increased inflammatory activity in heart (MRI, PET, and gallium) Imaging showing enlargement or nodules in liver or spleen (CT, PET, and MRI) Inflammatory lesions in bone (gallium, PET, and MRI)
Other testing	Hypercalcemia or hypercalciuria with abnormal vitamin D metabolism†	Reduced LVEF with no risk factors (echo and MRI) Elevated ACE level test‡ Nephrolithiasis with calcium stone, no vitamin D testing BAL lymphocytosis or elevated CD4:CD8 ratio Alkaline phosphatase greater than three times the upper limit of normal New-onset, third-degree AV block in young or middle-aged adults

Definition of abbreviations: ACE = angiotensin-converting enzyme; AV = atrioventricular; AVNB = atrioventricular node block; CM = cardiomyopathy; CNS = central nervous system; CT = computed tomography; CXR = chest X-ray; LVEF = left ventricular ejection fraction; MRI = magnetic resonance imaging; PET = positron emission tomography; VT = ventricular tachycardia.

*Löfgren's syndrome is defined as bilateral hilar adenopathy with erythema nodosum and/or periarticular arthritis.

†Abnormal vitamin D metabolism is defined as normal to low parathyroid hormone, normal to elevated 1,25-dihydroxyvitamin D, and normal to low 25-hydroxyvitamin D.

‡ACE elevated above 50% of the upper limit of normal was considered abnormal.

Diagnostik

Sarkoid-Myopathie

- Häufige Beteiligung wird vermutet; symptomatisch aber <3%
- 3 Formen:
  - Chronische Myositis (Bild Steroid-Myopathie)
  - Aktue Myositis (Bild akute Polymyositis)
  - Noduläre Myositis

- Diagnostisch:
  - Muskelenzyme erhöht bei akuter Myositis
  - ENMG pathologisch bei chronischer und akuter Myositis
  - MRI häufig positiv bei nodulärer Moysitis
  - PET sensitiv

Diagnostik

Sarkoid-Arthropathie

Arthritis

- **Aktue Arthritis i.R. Löfgren-Syndrom:**
  - Sonographisch v.a. Periarthritis mit Tenosynovitis
  - Synovialanalyse: Selten wirklich Synovitis → diagnostisch milde inflammatorisch
  - Synovialisbiopsie: keine Granulome

- **Chronische Arthritis**
  - Selten; häufig mit Hautbeteiligung. Häufiger: Tenosynovitiden, v.a. Extensorensehnen Handgelenke
  - Symmetrische Oligoarthritis der mittleren und grossen Gelenke; sehr selten destruierend
  - Synovialanalyse: weniger inflammatorisch als bei andere Polyarthritis; **lymphozytär**
  - Synovialbiopsie: histologisch nicht-verkäsende **Granulome**

Diagnostik

Sarkoid-Arthropathie

Axiale Beteiligung

- Bildgebung: Wirbelkörperbeteiligung sklerotisch, lytisch oder beides
  - ISG-Arthritis beschrieben, meist einseitig
- Histologie: Granulome

Daktylitis

- Konventionell radiologisch häufig zystische Läsionen
- Histologie: Granulome

Diagnostik

Ossäre Sarkoidose

- Röntgen/CT/MRI: Läsionen 3 Typen:
  - zystisch/lytisch (häufigste): Defekte in Kortikalis im Phalanxcaput, tlw. ausgestanzt
  - Sklerosierend: v.a. axial, ähnlich Metastasen
  - Motten-Frass Läsionen: Defekte in Kortikalis mit Weichteilschwellung
- Labor: meist normale Ca und AP