GRAPPA

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Sponsored by NOVARTIS

How To Manage?

Dalia Fayez

Prof of Int Med and Rheumatology

Ain Shams University

GRAPPA

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

EGYPT 2024

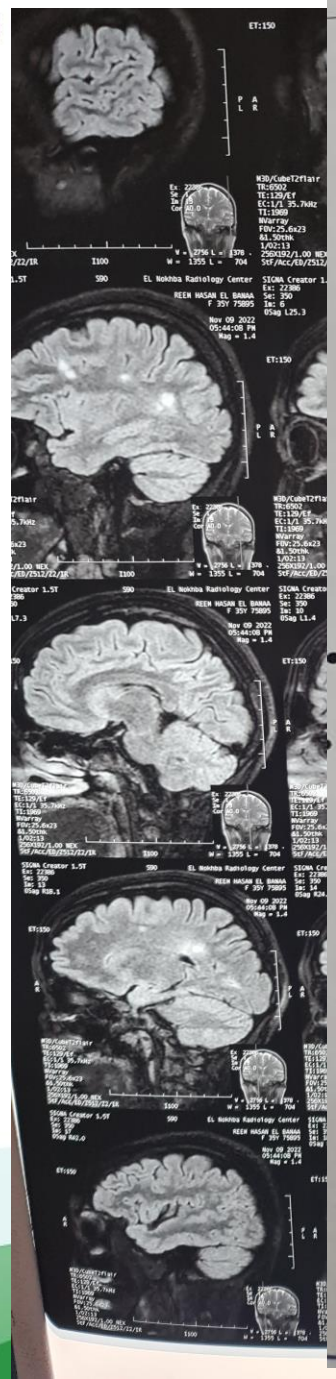
GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Case Scenario

- **Female** patient, 35 y.o married and has 3 children, **smoker**, works in Bank , with no method of contraception
- Her illness started in 2018 with **psoriatic skin lesions** on arms, legs and scaly scalp; she received local treatment
- 2 years later she developed **oligoarthritis** (knees and Lf wrist) , progressed to affect 2nd,3rd, 4th MCP of both hands , dactylitis and enthesitis of Rt Tendoachilles
- Rheumatologist advised her to take MTX; then add TNFi with improvement of skin and joint
- In 2022; she presented with blurring of vision, dizziness, followed by dysarthria, hypothesia of Rt UL, dysphagia and irritable bladder
- We asked for MRI brain and consult Neurologist

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

MRI Brain



Referred by :Prof.Dr :- دينا عبدالجواد زمزم
Date :- 9- 11 -2022

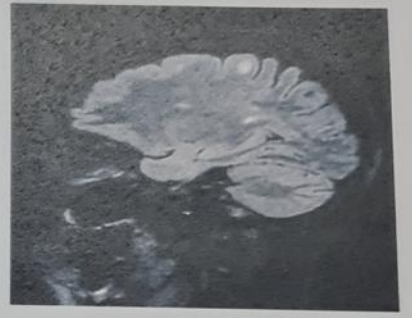
MRI OF THE BRAIN (CLOSED MRI 1.5 T)

Protocol:

- T1, T2, FLAIR, and DWI. of the brain using 1.5 Tesla closed MRI.

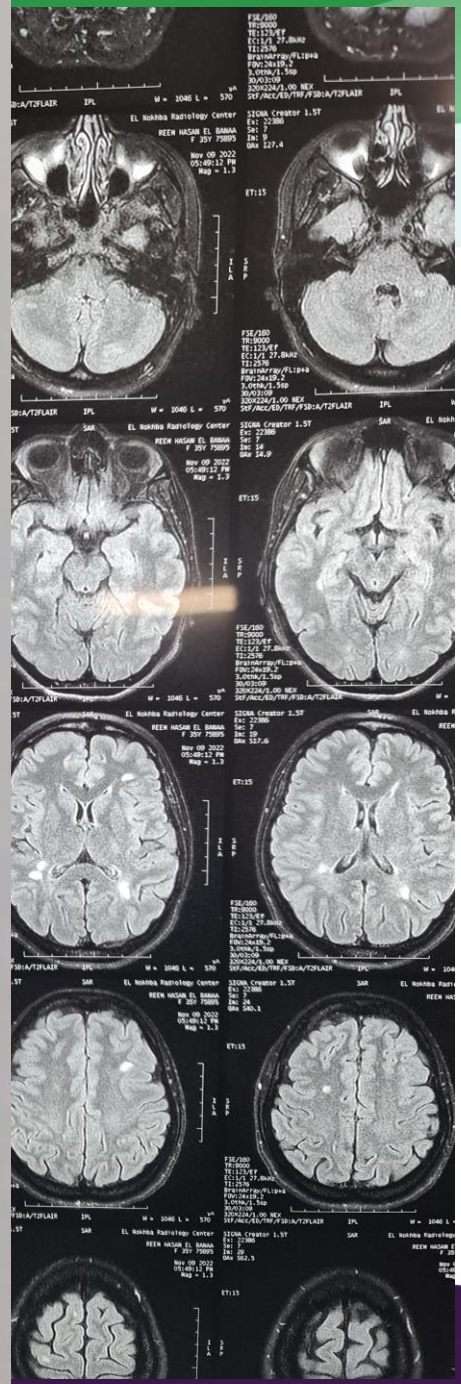
FINDINGS:

- **Multiple white matter foci of altered signal intensities are seen at the bilateral frontal, bilateral parietal, bilateral bilateral cereballar hemispheres and left side pons. These areas display low signal on T1WIs and bright signal on T2 and on FLAIR WIs with no mass effects or perifocal edema. No areas of abnormal diffusibility. Some of these lesions are patchy and some are linear. Affection of the juxtacorical and periventricular white matter is seen. ..... known case of MS.**



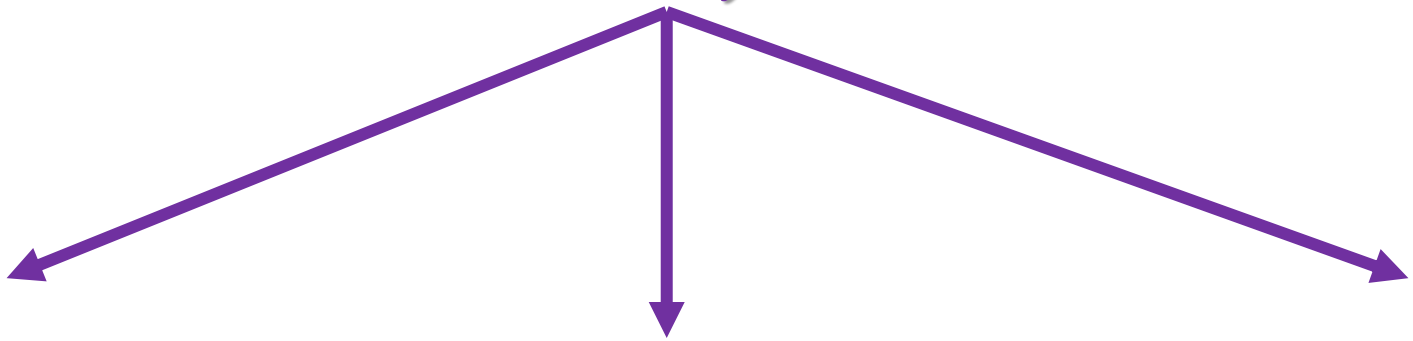
- Normal ventricular system with no evidence of displacement or deformity.
- Normal vascular channels.
- Normal appearance of cortical sulci.
- No mass lesions could be detected at the cerebellopontine angles.
- Normal appearance of the calvarial bones.
- Normal sellar & parasellar regions.
- Normal appearance of both orbits.

Dr. Mohamed El Sayed, MD



GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

What is the cause of brain lesion !?



TNFi induced demyelination

APL associated microthrombotic vasculopathy

Multiple Sclerosis with Psoriatic arthritis

Work Up

- ***Work up of Neurology***:

✓ MRI Brain; MRA, MRV

✓ CSF analysis : oligoclonal band…..

❑ Evoked potential tests

❑ confirmed diagnosis of MS

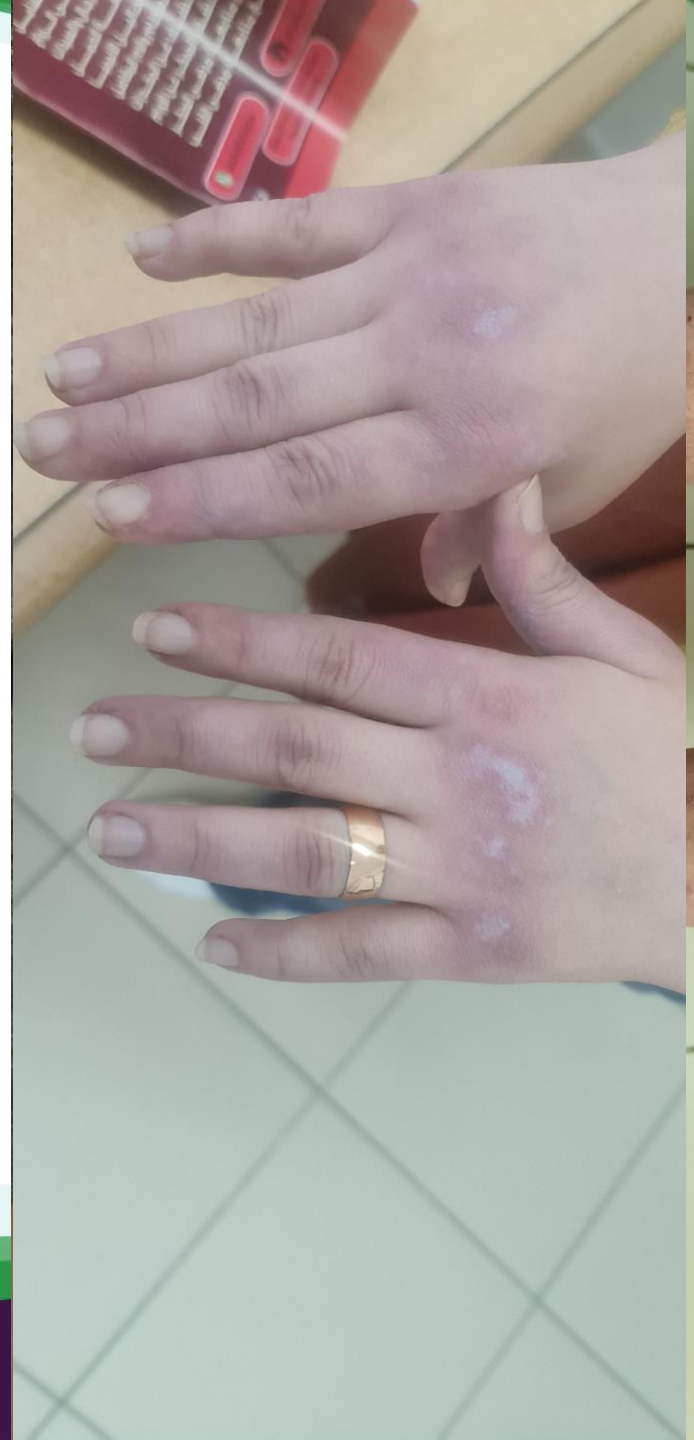
- ***Immunological investigation:***

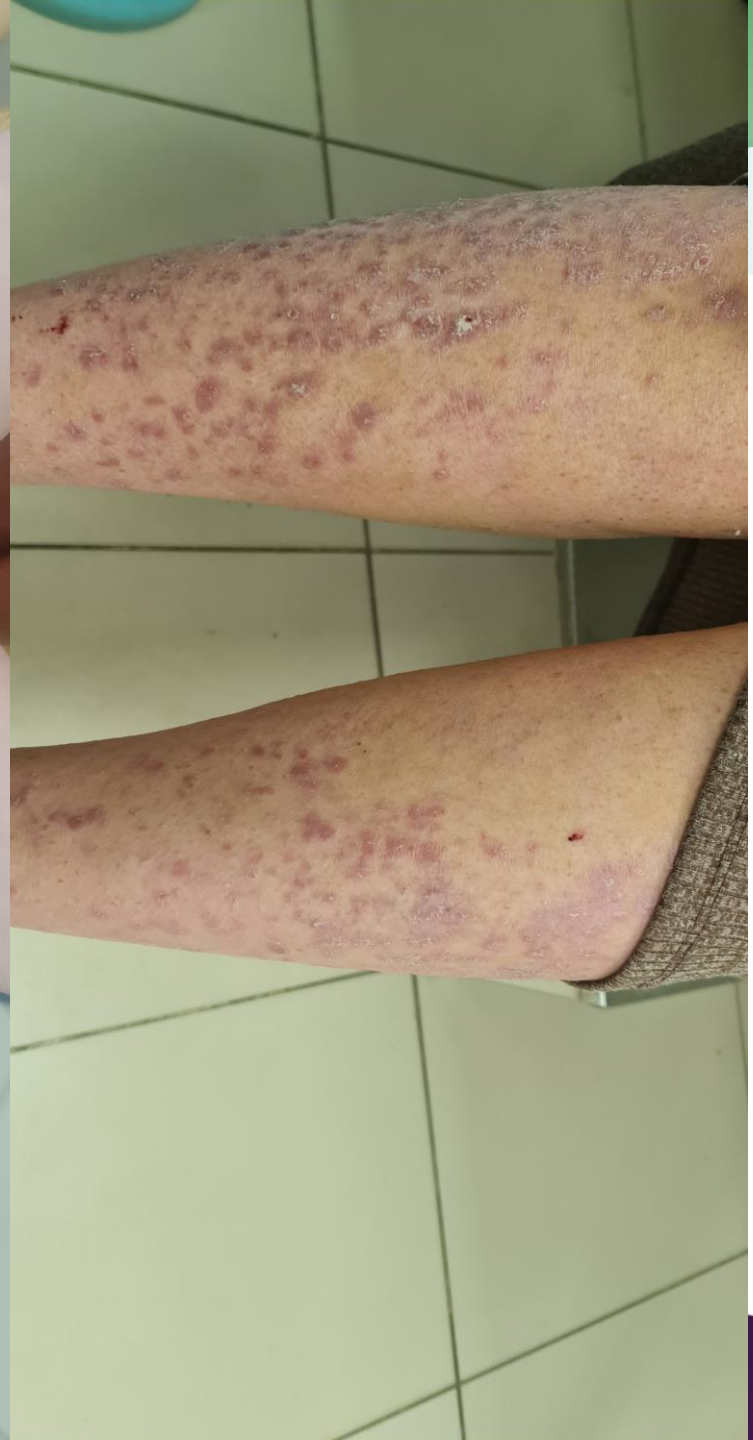
✓ ANA 1/160,

✓ ACL IgG +ve 23, IgM-ve , LA-ve

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

- We discontinued TNFi ,and patient was continued on MTX plus hydroxychloroquine
- She received treatment for MS…pulse steroids according to neurological protocol
- Unfortunately, after receiving treatment for MS (Fingolimod) there was a flare of psoriasis and psoriatic arthritis
- DAPSA: 22
- PASI: 15
- CRP: 24mg/dl





GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Case Scenario

- What is the next step in management ?
- What is the cause of patient flare ?
- Is there a relation between PSA and MS

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

- ✓ PsA is sometimes confused with MS.
- ✓ This is because it is a type of spondyloarthritis, an umbrella term for conditions that cause inflammation of the spine.
- ✓ Symptoms of spondyloarthritis can overlap with MS.

ARTHRITIS > PSORIATIC ARTHRITIS

Psoriatic Arthritis vs. Multiple Sclerosis: What Are the Differences?

By Lana Barhum | Published on November 30, 2021

Medically reviewed by David Ozeri, MD

It was found that 7% of MS diagnoses were actually spondyloarthritis conditions.
Kaisey M, et al., 2019

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Similarities

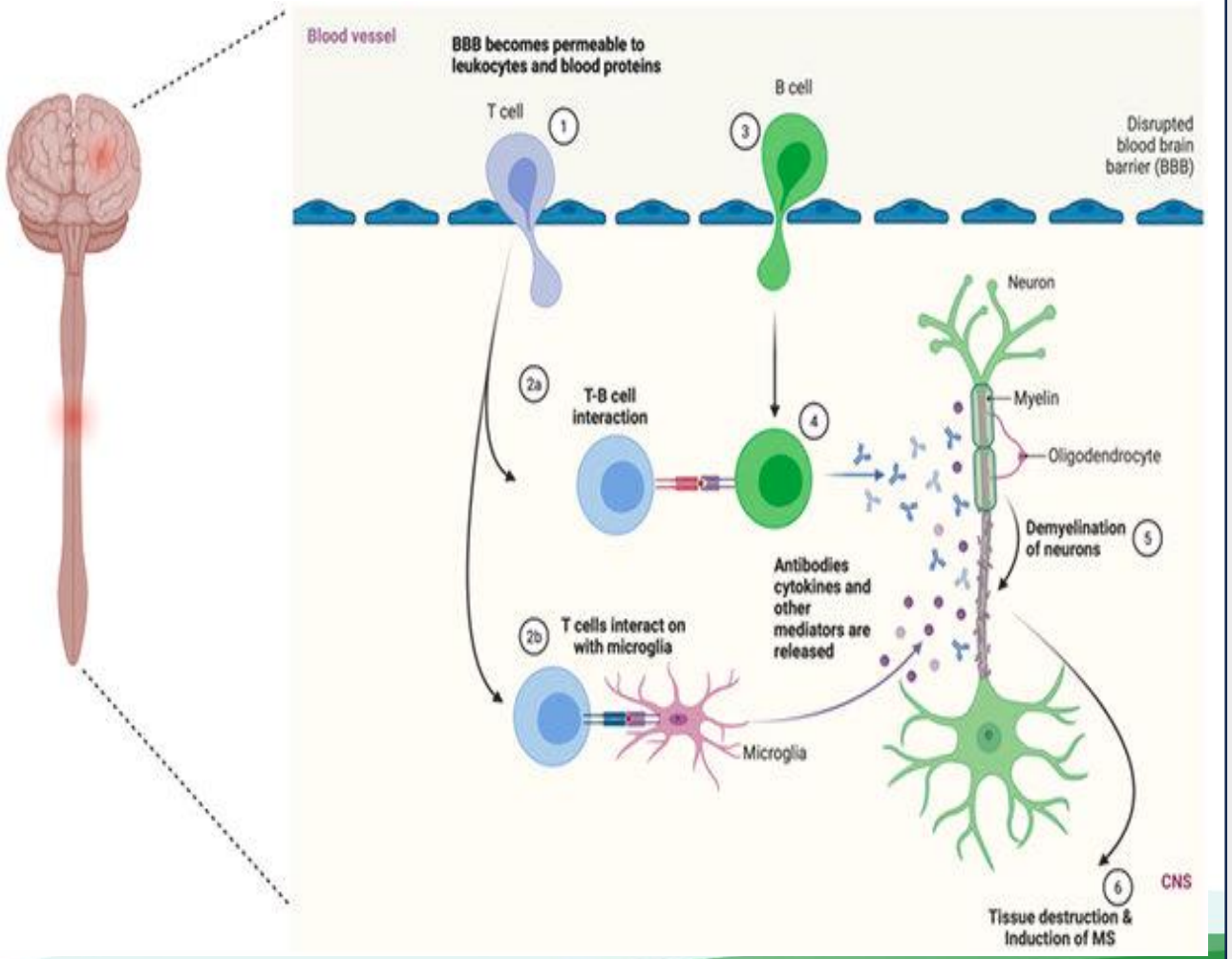
- ✓ PSA and MS are both autoimmune diseases.
- ✓ They occur when the immune system malfunctions and attacks healthy cells and tissue.
- ✓ With PsA, the immune system attacks the skin and joints.
- ✓ With MS, attacks focus on the protective coverings of nerve cells of the brain, spinal cord, and eyes.
- ✓ So , Some symptoms of PsA and MS are similar
- ✓ **Both have symptoms that come and go in the form of flare-ups and remission**

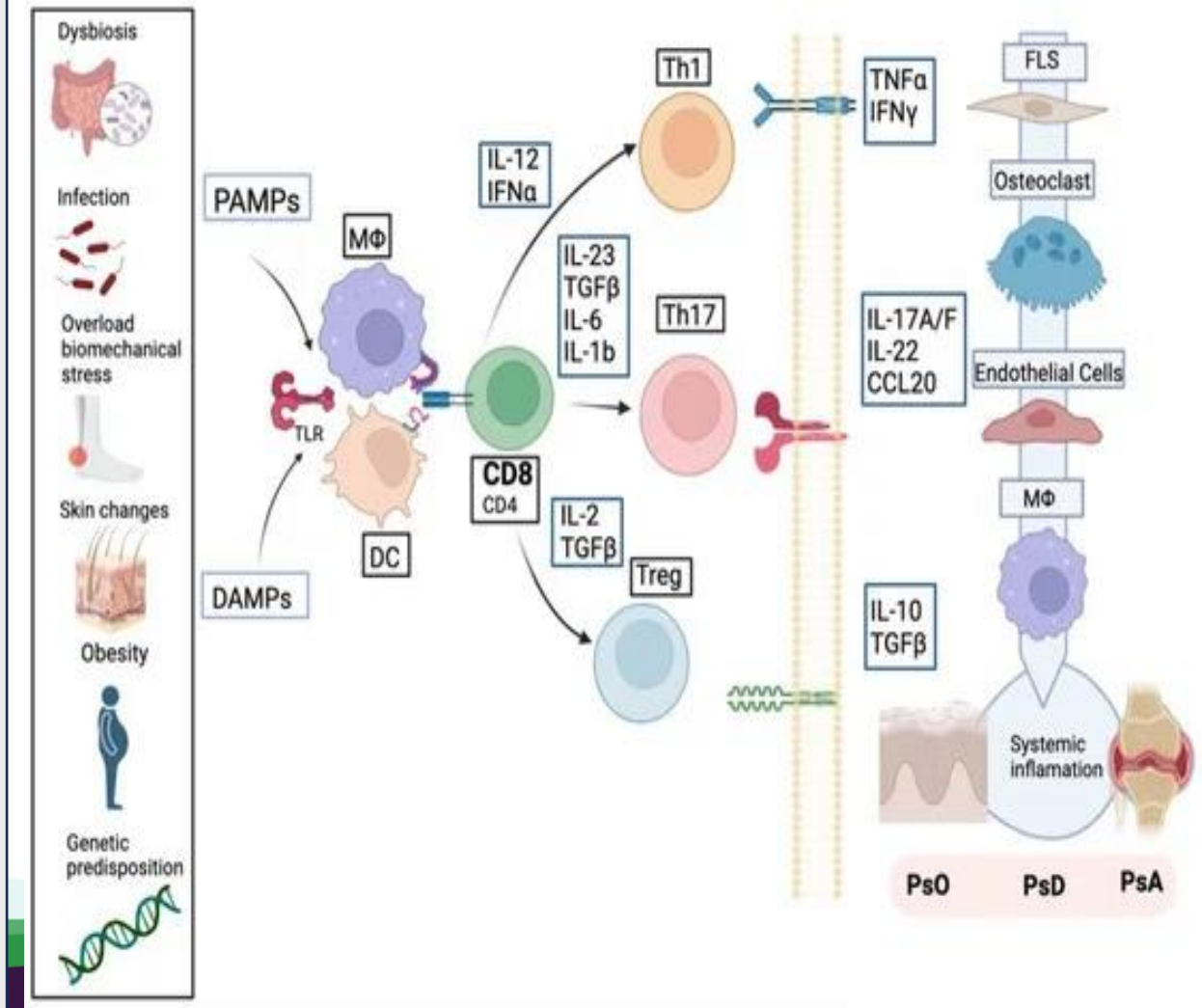
Course

Both PsA and MS are progressive diseases, which means they will get worse with time.
It is, therefore, important to get an early diagnosis and treatment to reduce the complications and damage these conditions can cause.

Mult Scler Int. 2021

Pathogenesis





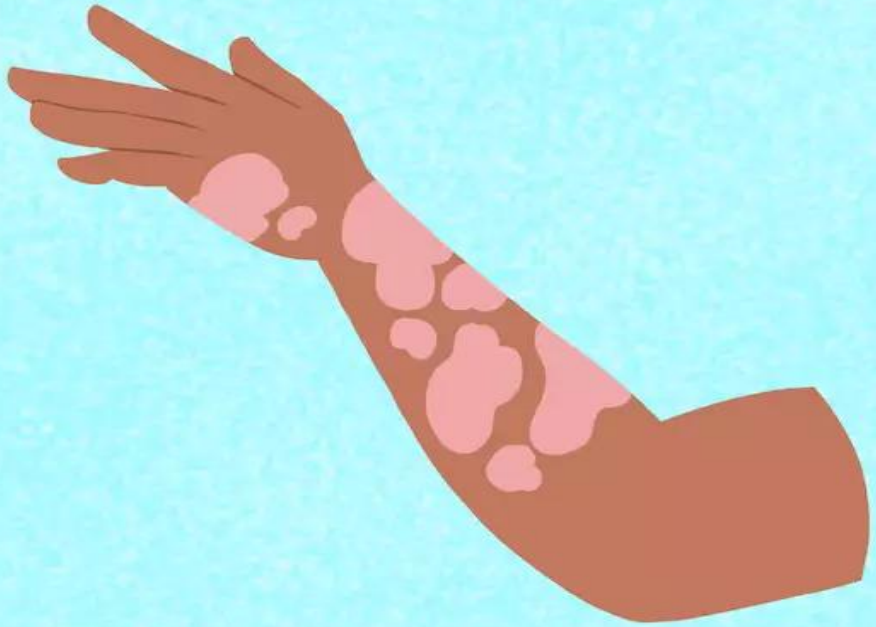
M. Lima et al.: CoVs ; Rev. Neurosci. 2022; 33(7): 703–720

Int. J. Mol. Sci. **2023**, *24*(14

Sponsored by NOVARTIS

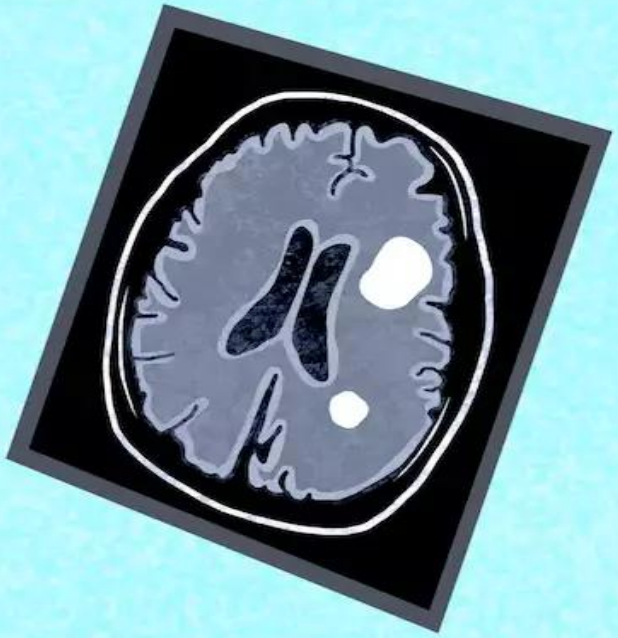
Risk Factors for Psoriatic Arthritis and Multiple Sclerosis

Psoriatic Arthritis



Physical trauma, environmental factors, stress, infection, and having a family member with PsA or psoriasis

Multiple Sclerosis



Lack of natural sunlight and vitamin D, gene variations or mutations, and immune system dysfunction

Clinical Presentation

Psoriatic Arthritis

- Arthritis : oligo, poly, symmetrical or asymmetrical
- Dactylitis
- Enthesitis
- Low back pain or sacroiliitis
- Thick, red patches of skin covered by silvery scales
- Nail changes: pitting, crumbling, and onycholysis
- Uveitis: eye pain and redness, and blurry vision, sometimes vision loss
- IBD

Multiple Sclerosis

- Numbness or weakness of the limbs on one side of the body
- Electric shock sensations with certain movement, especially when bending the neck
- Muscle stiffness and spasms
- Tremors
- Lack of coordination or an unsteady gait (walk)
- Partial or complete vision loss
- Pain with eye movement
- Double vision
- Fatigue, Dizziness, Blurry vision
- Slurred speech
- Tingling or pain in different body areas
- Problems with sexual, bowel, or bladder function

ORIGINAL ARTICLE

Risk of Multiple Sclerosis in Patients with Psoriasis: A Danish Nationwide Cohort Study

Alexander Egeberg[1,2], Lotus Mallbris[3], Gunnar Hilmar Gislason[1,4,5], Lone Skov[2] and Peter Riis Hansen[1]

Psoriasis and multiple sclerosis (MS) are inflammatory disorders with similarities in genetic risk variants and inflammatory pathways. Limited evidence is available on the relationship between the two diseases. We therefore investigated the risk of incident (new-onset) MS in patients with mild and severe psoriasis, respectively. All Danish citizens aged ≥ 18 years from 1 January 1997 to 31 December 2011 were identified by linkage of nationwide registries at the individual level. We estimated incidence rate ratios (IRRs) adjusted for age, gender, socioeconomic status, smoking, medication, comorbidity, and UV phototherapy by Poisson regression. There were 58,628 and 9,952 cases of mild and severe psoriasis, respectively, and 9,713 cases of MS. Incidence rates of MS per 10,000 person-years for the reference population, mild psoriasis, and severe psoriasis were 1.78, 3.22, 30) and 2.61 (95% CI, djustment for family pendent risk of MS. its potential clinical consequences.

❑ the findings suggest that psoriasis is an independent risk factor for MS

Journal of Investigative Dermatology (2016) 136, 93-98

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Treatment

Target

- ✓ Relief symptoms
- ✓ Slow down disease progression
- ✓ Prevent complications
- ✓ Improve patient's quality of life.

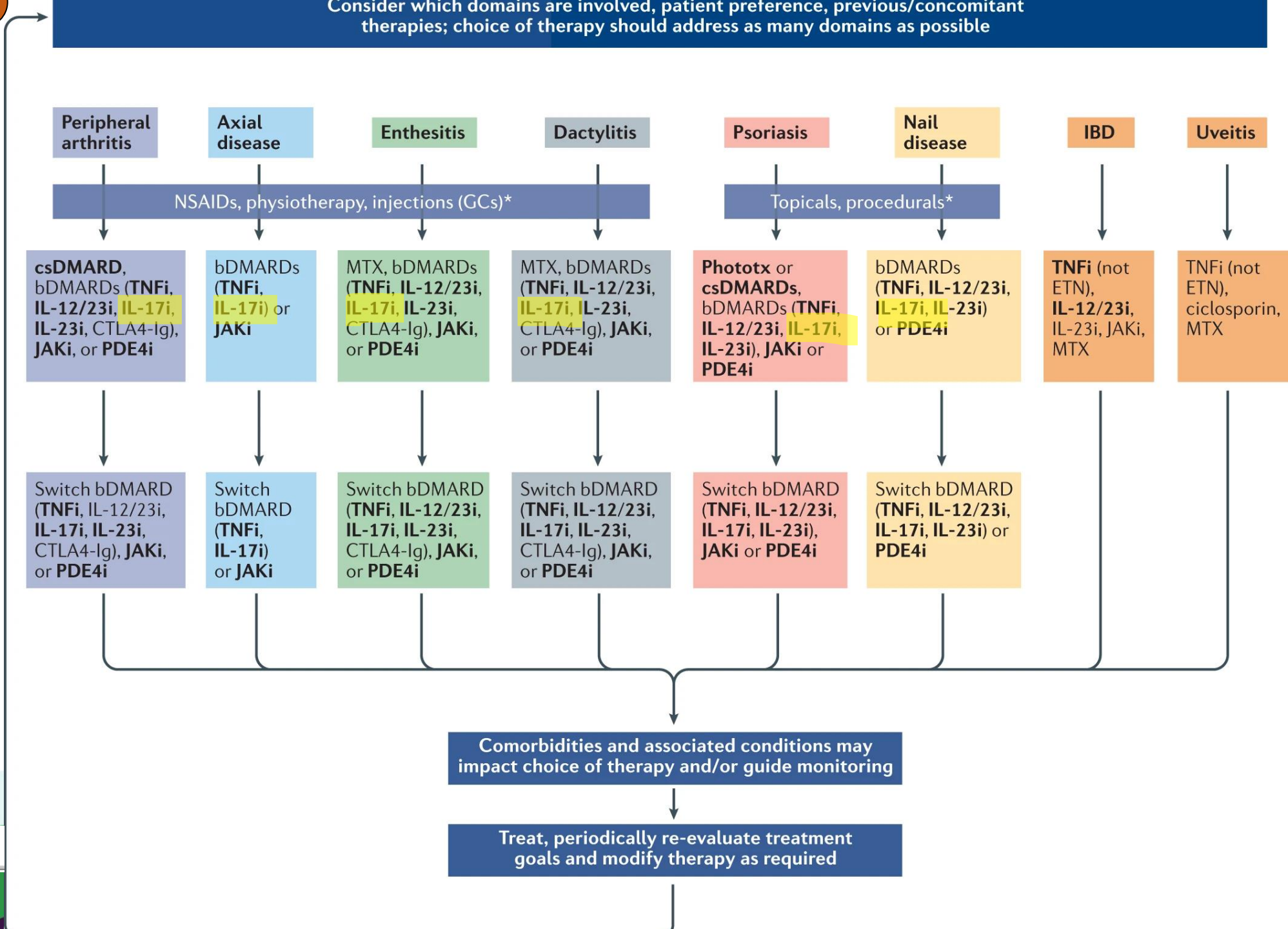
Psoriatic Arthritis

- NSAIDs
- sDMARD
- bDMARD
- JAKi
- Apremilast

Multiple Sclerosis

- Disease-modifying therapies (Prevent relapses and slow the accumulation of disability)
- Relapse management therapies (Shorten the duration and reduce the severity of acute disease exacerbations)
- Symptomatic treatments (Treat specific symptoms of MS, such as pain or fatigue)

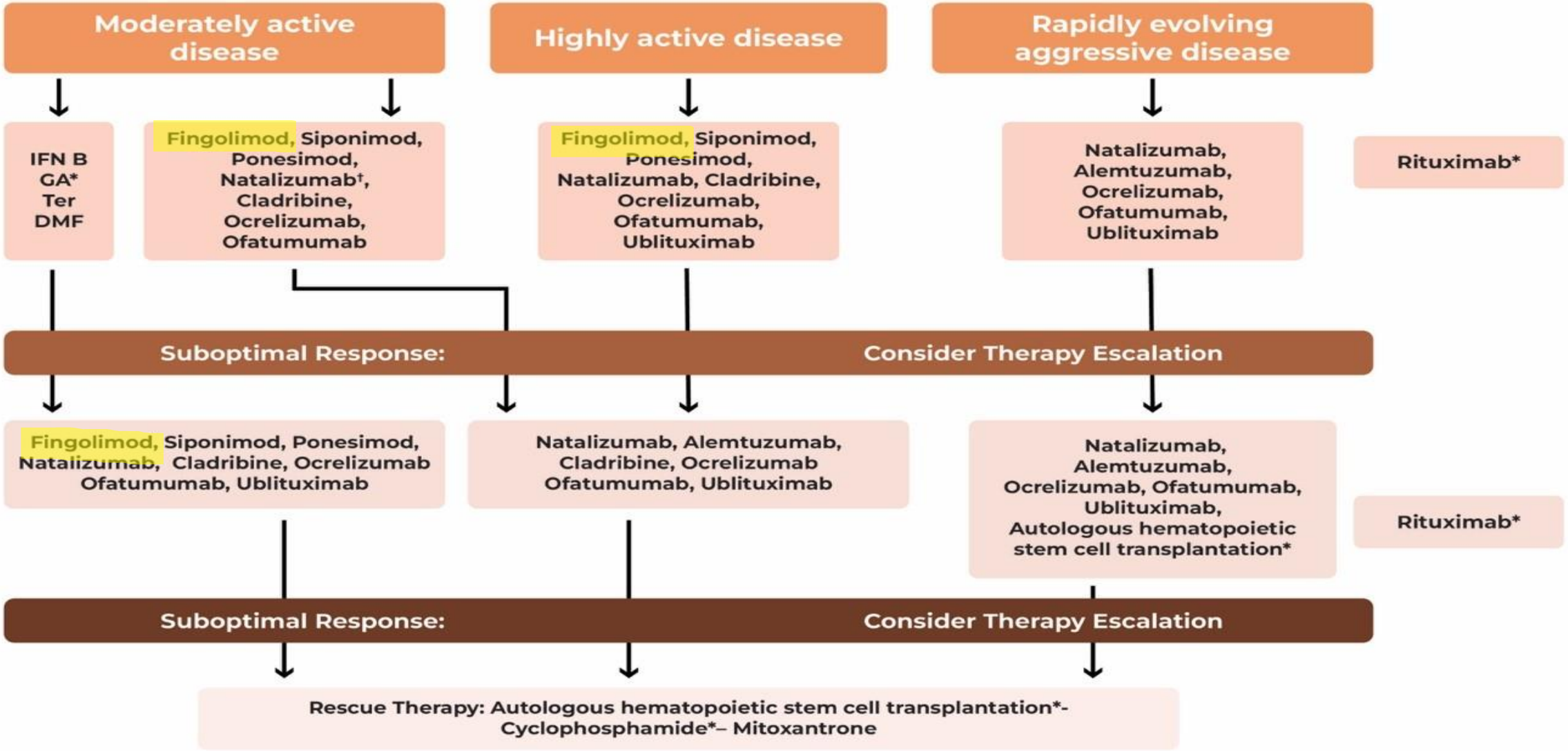
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021



Coates L, et al. Nat Rev Rheumatol 2022

18, pages465–479

MENACTRIMS 2023 Algorithm for Treatment of RRMS

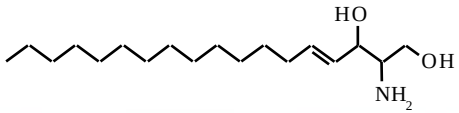


*Off label use
†JCV Ab negative

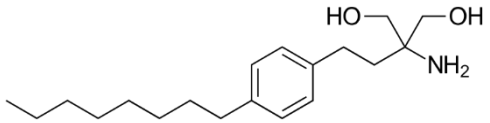
What is Fingolimod?

- Fingolimod is a structural analogue of natural sphingosine[1]
- Sphingosine 1-phosphate (S1P) is a naturally occurring bioactive sphingolipid that plays a key role in inflammation and repair.
- Both sphingosine and fingolimod are phosphorylated by ubiquitous intracellular sphingosine kinases to their active forms and act via S1P receptors2

Sphingosine

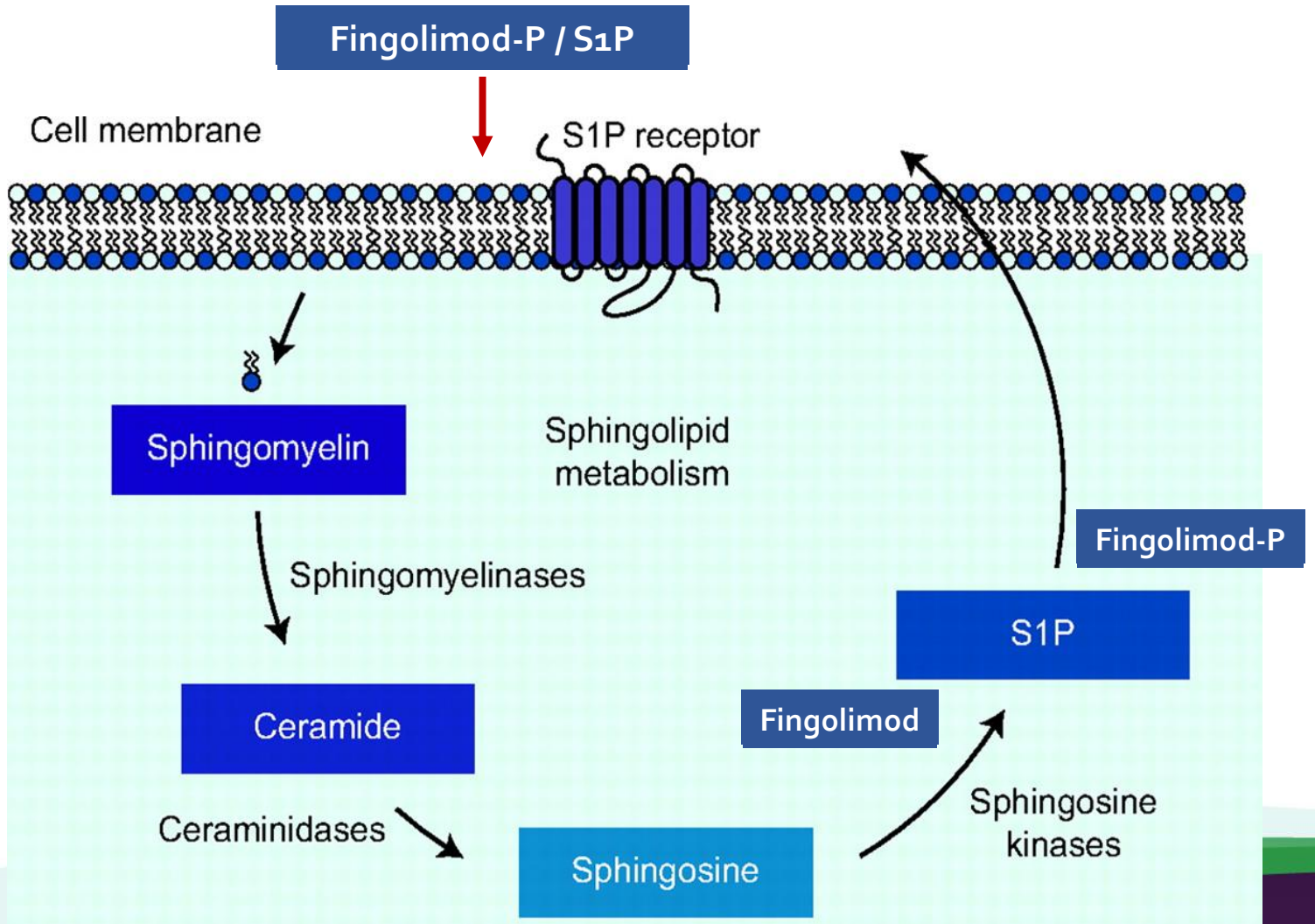


Fingolimod

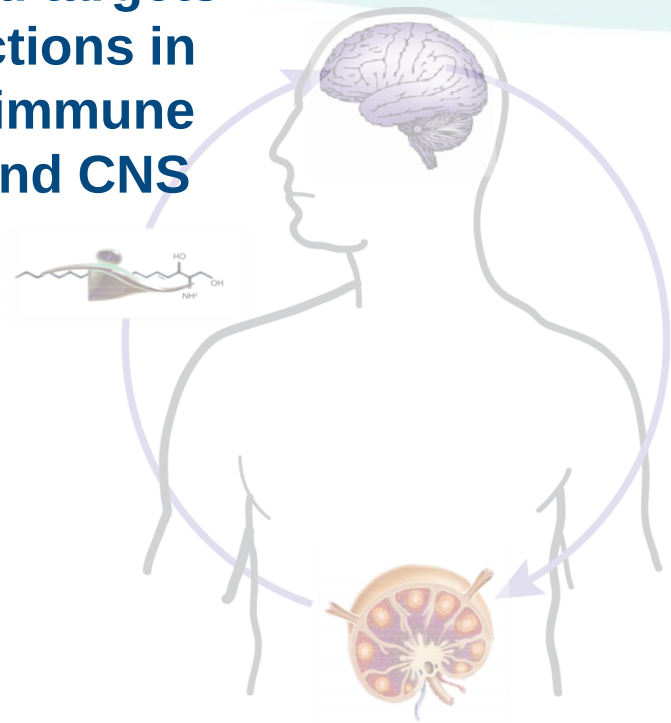


1. Brinkmann V & Lynch KR. *Curr Opin Immunol* 2002; 2. Anliker B & Chun J. *J Biol Chem* 2004; 3. An S *et al. FEBS Lett* 1997; 4. Lee MJ *et al. Science* 1998; 5. Zondag GC *et al. Biochem J* 199

Oral Fingolimod (FTY720)



Fingolimod targets MS via actions in both the immune system and CNS

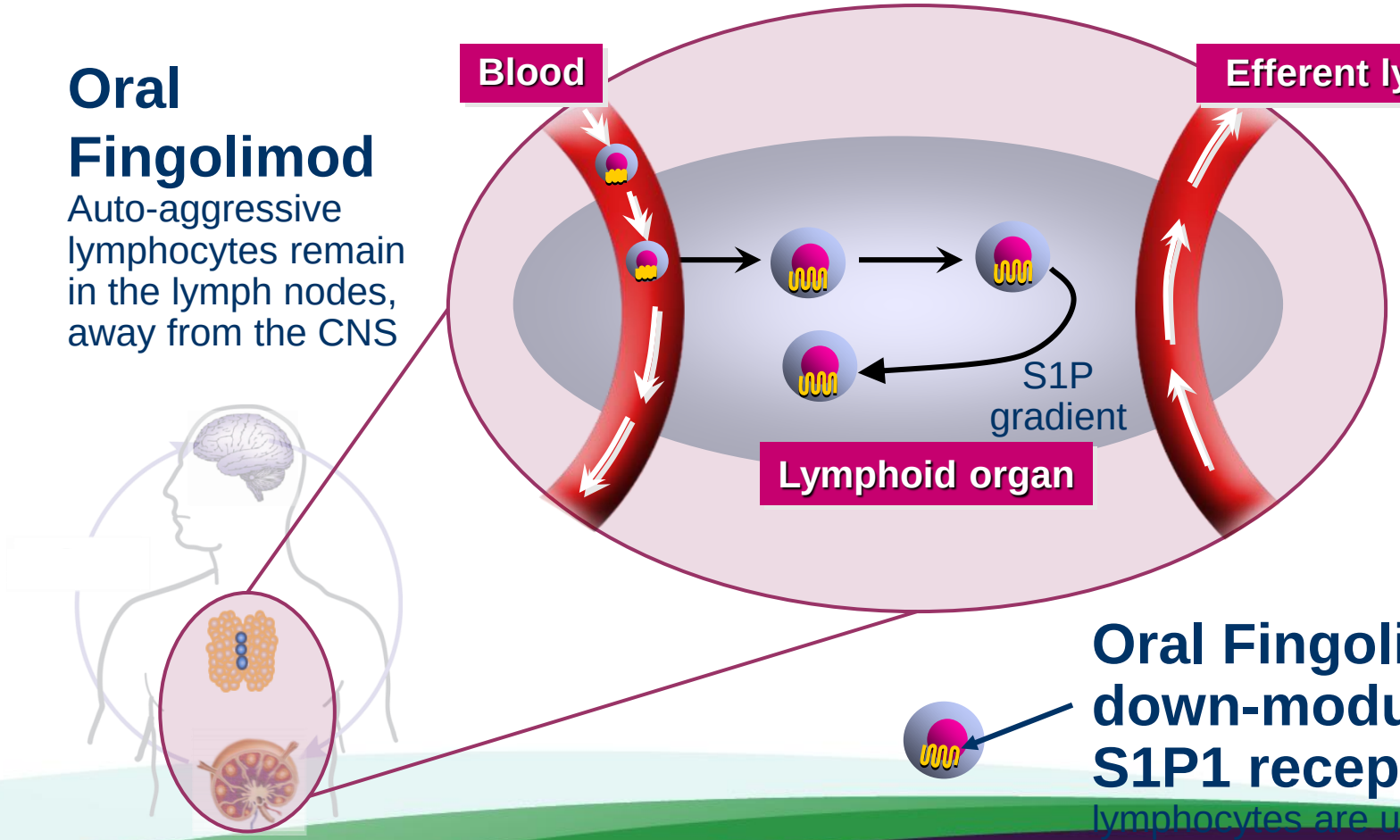


Fingolimod modulates Sphingosine 1-Phosphate receptors on Lymphocytes and Neural cells

Oral Fingolimod prevents lymphocyte egress from lymph nodes[1]

Oral Fingolimod

Auto-aggressive lymphocytes remain in the lymph nodes, away from the CNS

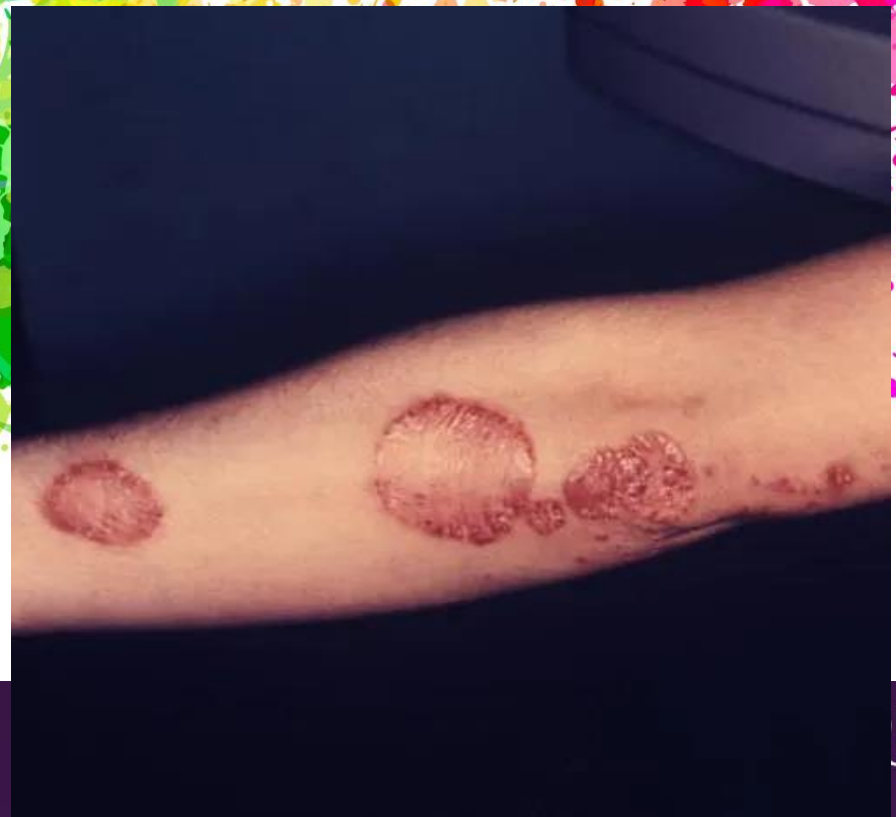


Oral Fingolimod down-modulates S1P1 receptor

lymphocytes are unable to egress

1. Brinkmann *et al. Am J Transplant* 2004;4:1019-25 CNS, central nervous system; S1P, sphingosine 1-phosphate

How to manage both disease ?
PsA with MS



Demylinating Disease
(Multiple Sclerosis)

Therapeutic Advances in Neurological Disorders 14

Treatment approaches to patients with multiple sclerosis and coexisting autoimmune disorders

Tobias Brummer, Tobias Ruck, Sven G. Meuth, Frauke Zipp and Stefan Bittner

Ther Adv Neurol Disord
2021, Vol. 14: 1–20
DOI: 10.1177/17562864211035542

Therapeutic Advances in Neurological Disorders

to disease severity in PsO and MS.[2,3] In fact, Th17 cells were initially described in the EAE model.[88,89] Secukinumab has demonstrated promising trends in a phase II trial with RRMS patients;[4] although the study's primary endpoint was not reached. Moreover, there are several case reports that describe a successful treatment of comorbid PsO/MS with secukinumab.[90–94] All patients described had a relapsing–remitting dis-

- Secukinumab may be one of the best therapeutic options for patients with PsO and coexisting RRMS.
- finally present which therapeutics can be utilized as a combinatory treatment, in order to 'kill two birds with one stone'

GRAPPA 2022 Safety Updates

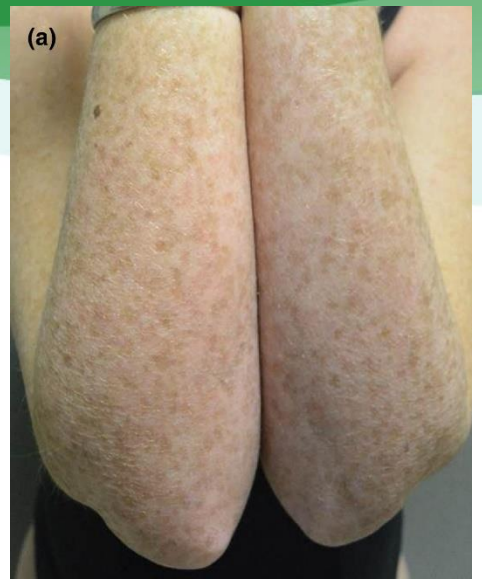
Table 4 | **Summary of recommendations for the treatment of PsA in the case of comorbidities**

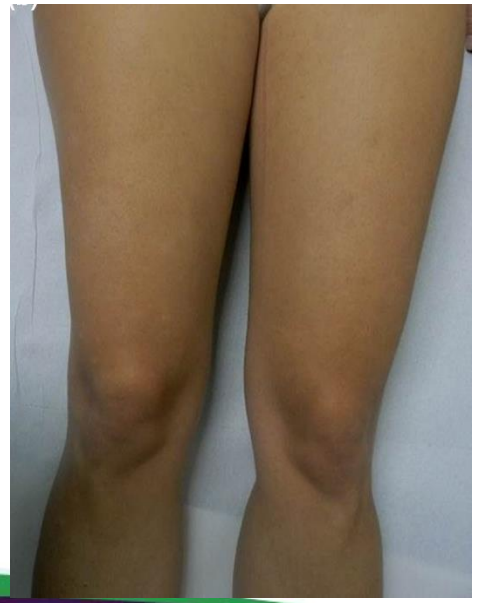
Comorbidity	NSAIDs	GCs	MTX and/or LEF	TNF inhibitor	IL-17 inhibitor	IL-12/23 inhibitor, IL-23 inhibitor	JAK inhibitor	PDE4 inhibitor
Elevated risk of CVD	Caution	–	–	–	–	–	Caution	–
Congestive heart failure[a]	–	Caution	–	Avoid	–	–	–	–
Elevated risk for VTE	–	–	–	–	–	–	Caution	–
Obesity	–	–	Caution	–	–	–	–	–
Fatty liver disease	–	–	Avoid	–	–	–	–	–
Active hepatitis B or C	–	–	Avoid	Caution	Caution	Caution	Caution	Caution
HIV	–	–	–	Caution	Caution	Caution	Caution	Caution
Tuberculosis	–	–	–	Caution	Caution	Caution	Caution	Caution
History of recent malignancy	–	–	–	Caution	Caution	Caution	Caution	Caution
MS and/or demyelinating disease	–	–	–	Avoid	–	–	–	–
Depression and/or anxiety	–	–	–	–	–	–	–	Caution

CVD, cardiovascular disease; GC, glucocorticoid; JAK, Janus kinase; LEF, leflunomide; MS, multiple sclerosis; MTX, methotrexate; PDE4, phosphodiesterase 4; PsA, psoriatic arthritis; VTE, venous thromboembolism. [a]Severe or advanced; class III or IV according to the New York Heart Association (NYHA) Functional Classification.

JEADV
Journal of The European Academy of Dermatology and Venereology
EADV

On February 2015, the articular and skin involvement were severe (PASI = 28), so that etanercept 25 mg (two times/week, subcutaneously) was restarted, in consideration of its previous partial efficacy in controlling the disease. Two months later, the patient reported a partial loss of vision in the left eye, pain during eye movements, paraesthesia of the right arm and urinary incontinence; ophthalmic examination revealed a central scotoma and MRI with gadolinium showed optic retrobulbar neuritis and high-density demyelinating areas in corpus callosum. These findings were diagnostic for MS. Etanercept was stopped and a systemic corticosteroid therapy was started. On January 2017, apremilast 30 mg (two times/day, orally) was introduced but 6 weeks later was discontinued for adverse events (i.e. nausea, diarrhoea, myalgia). Finally, secukinumab 300 mg (one time every 4 weeks, subcutaneously) was started, with a significant clinical improvement; PASI 75 was achieved after 4 weeks, PASI 90 after 6 weeks and PASI 100 after 12 weeks (Fig. 2). This result was still maintained after 24 months, at the last follow-up visit. Concerning MS, the disease remained stable over time; no other neurological symptoms were reported and MRI imaging did not show any sign of disease progression.





Case report

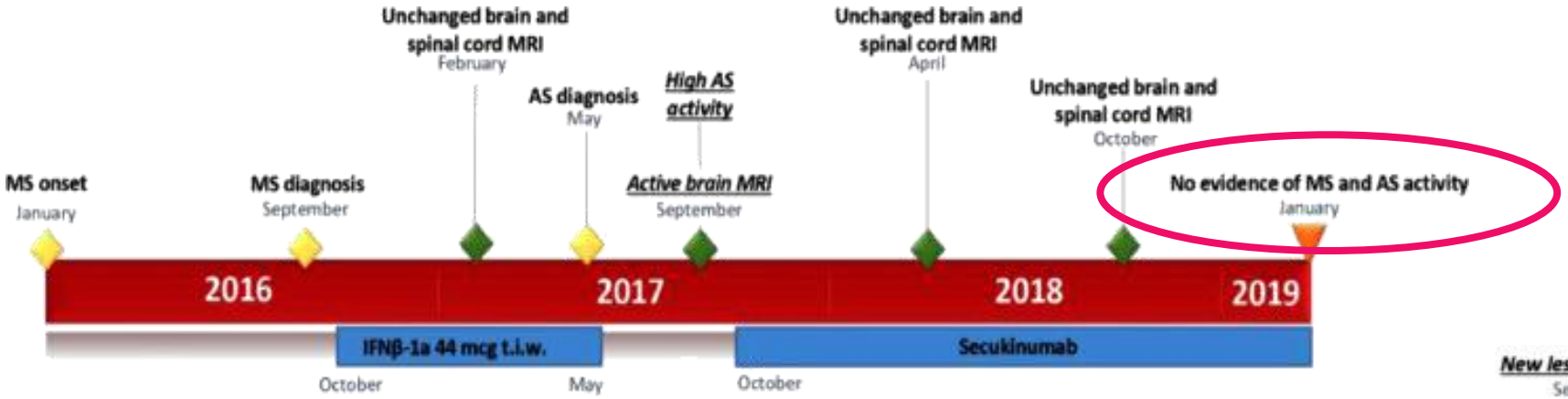
Secukinumab may be a valid treatment option in patients with CNS demyelination and concurrent ankylosing spondylitis: Report of two clinical cases

Antonio Cortese [a], Ramona Lucchetti [b], Alessio Altobelli [b], Antonella Conte [a, c], Marco Primavera [a], Guido Valesini [b], Enrico Millefiorini [a], Rossana Scrivo [b]

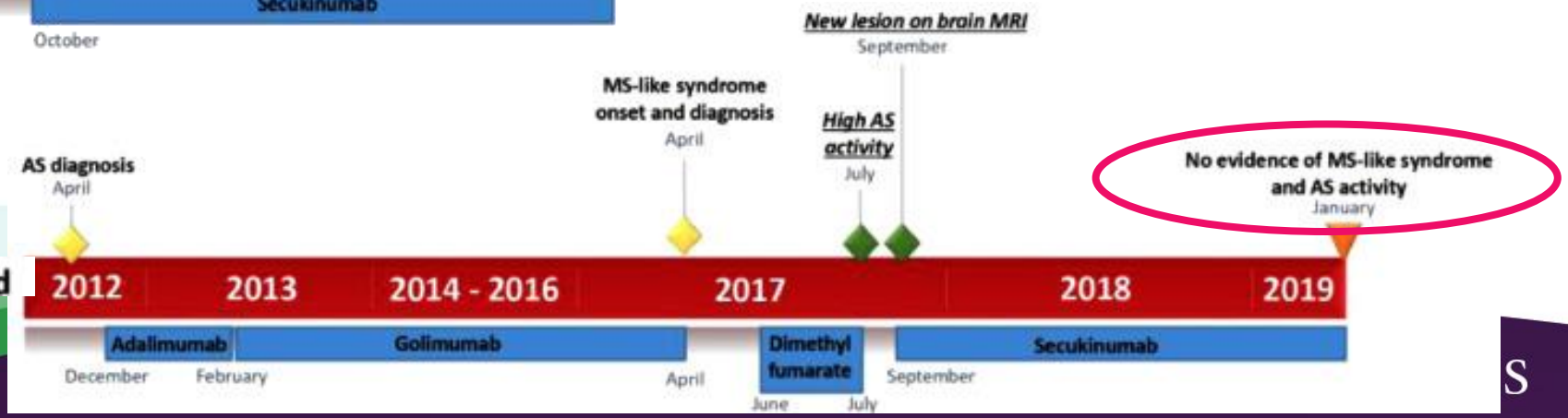
Volume 35, October 2019, Pages 193-195

Conclusion

We thus suggest that using secukinumab for treatment of CNS demyelination in patients with AS comorbidity may be efficacious for both conditions, and we recommend further studies on this topic (Figs.



Female, 37 years old



Female, 27 years old

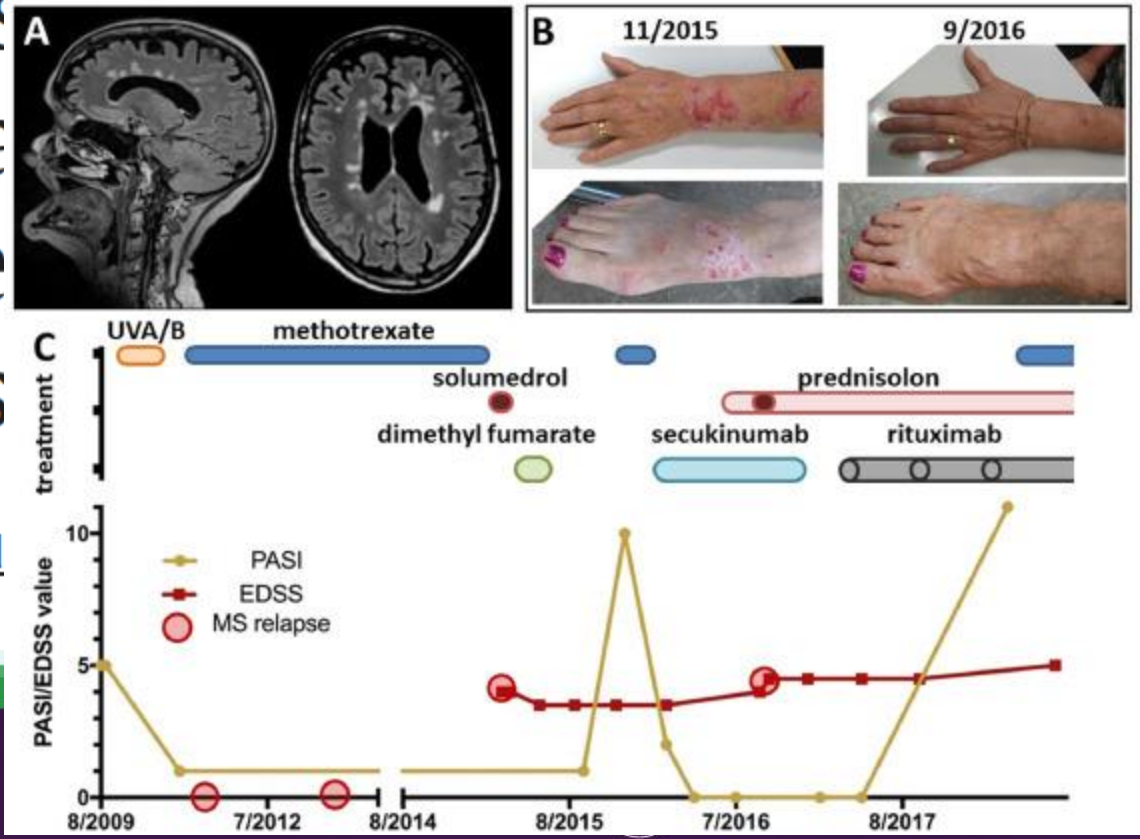
Multiple Sclerosis and Related Disorders

Volume 31, June 2019, Pages 38-40

Case report

A case of concomitant psoriasis and multiple sclerosis: Secukinumab and rituximab exert dichotomous effects in two autoimmune conditions

Martin Diebold [a], Simon Müller [b], Tobias Derfuss [a], Bernhard



GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

ELSEVIER

Neuroimmunology Reports
Volume 2, 2022, 100054

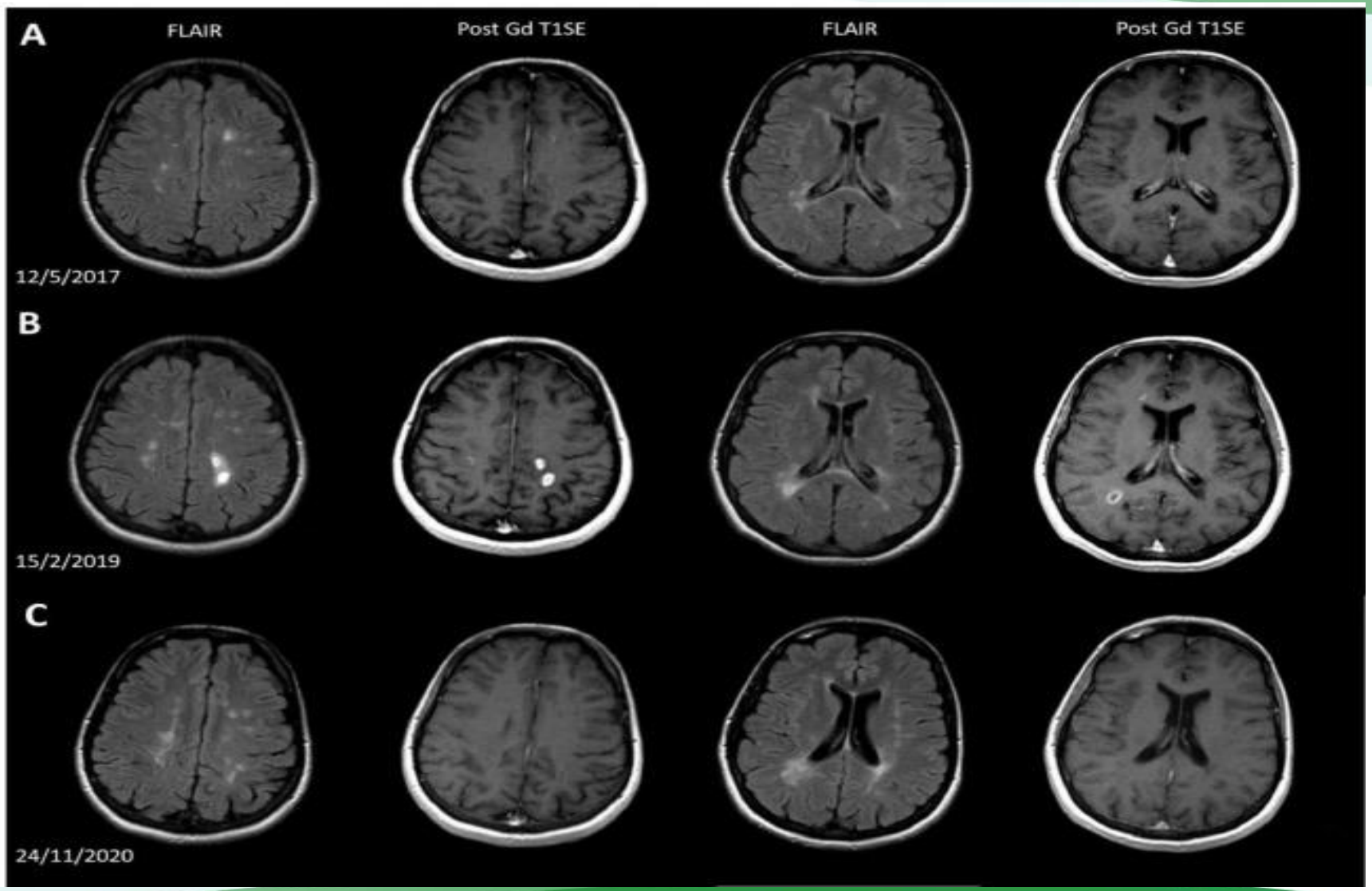
Successful treatment of highly active multiple sclerosis and psoriasis exacerbation with natalizumab and secukinumab combination. A case report and literature review

N. Kougkas [a], S. Kruger-Krasagakis [b], E. Papadaki [c d], V.C. Mastorodemos [e]

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Before Treatment

After Treatment



GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

Back to our patients

- Patients received her medication for MS (Oral Fingolimod) by Neurologist
- She received Secukinumab 300mg SC monthly after a loading dose
- There was improvement of skin and PSA
- PASI: 2; DAPSA: 5; crp: 0.5mg/dl
- No flare of neurological attacks and disease remained stable till this time

GRAPPA
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis

To Summarize

- Psoriatic arthritis and multiple sclerosis are both autoimmune diseases that result when the immune system malfunctions and attacks healthy tissues.
- In PsA, the immune system attacks skin and joints, and with MS, those attacks are directed toward the myelin sheath, the protective covering of nerve cells of the brain, spinal cord, and eyes.
- Psoriasis may confer a disease severity-dependent risk of MS development.
- Early diagnosis and aggressive treatment are vital to slowing down disease progression and reducing the potential for complications of these conditions.
- **secukinumab seems to be the only treatment which may be safely administered in patients with concomitant SpA and MS.**
- Secukinumab can be combined with different drugs used for MS even with Rituximab

THANK YOU

Sponsored by NOVARTIS