

Chief Report

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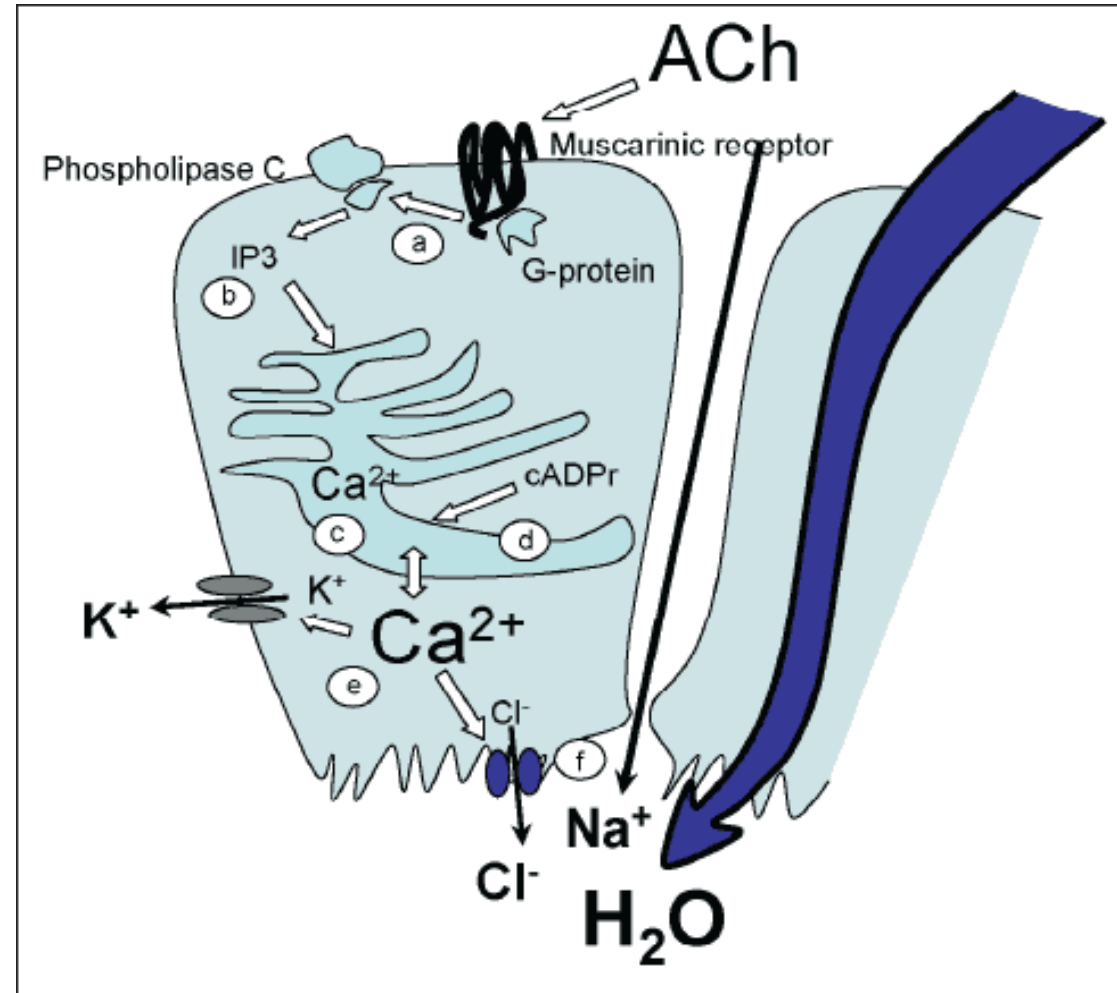


52 y o female: CC

- Dry mouth and dry eyes

Differential Diagnosis

- Medications



Differential Diagnosis

- Medications

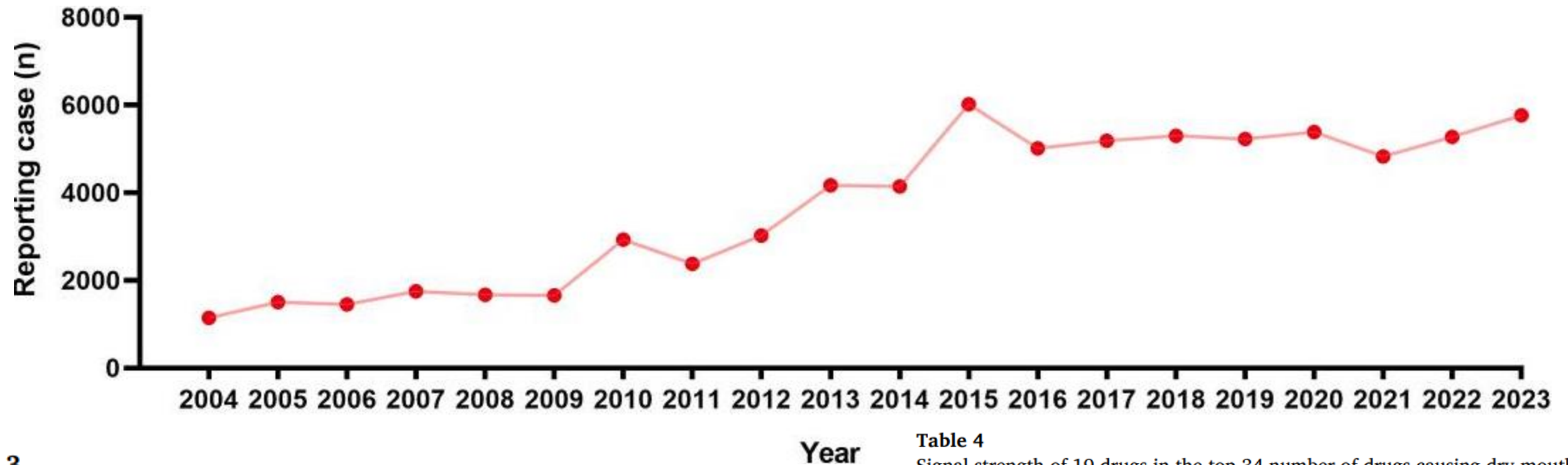


Table 3

Top 34 with the highest number of reported dry mouth.

Drug name	Total, n (%)
tiotropium bromide monohydrate	2080(6.06)
isotretinoin	1945(5.67)
pregabalin	1512(4.4)
solifenacin succinate	1416(4.12)
etanercept	1298(3.78)

Table 4

Signal strength of 19 drugs in the top 34 number of drugs causing dry mouth.

Drug name	ROR (95 % CI)	PRR (95 % CI)	χ^2
darifenacin	53.18(47.46, 59.59)	43.5(39.44, 47.98)	15187.76
solifenacin succinate	31.32(29.61, 33.12)	27.77(26.18, 29.45)	36015.1
fesoterodine fumarate	31.3(28.9, 33.9)	27.73(25.64, 29.99)	17666.39
tolterodine tartrate	29.51(26.55, 32.8)	26.31(23.85, 29.02)	9462.7

Differential Diagnosis

- Medications
- Radiation
- Primary Sjogren Syndrome
- Secondary Sjogren Syndrome
- Sarcoidosis
- IgG4 related disease
- HIV infection
- HCV infection
- Uncontrolled DM

52 y o female: Initial History

Dry Eyes Dry Mouth	Medical history: HTN HLD
HPI: Symptoms ongoing for 2 years Difficulty swallowing dry food and has to drink throughout the night Fatigue Pain in hands and wrists, particularly in the morning Stopped using contact lenses Episodes of swelling in the parotid glands over the last 2 years	Surgical history: Appendectomy (12 yrs ago)
Medications: Hydrochlorothiazide 25mg daily Atorvastatin 10mg daily	Social history: Smokes 4 cigarettes per day 3 glasses red wine per week No drug use

52 y o female: Physical Exam

Vitals T 36.1C BP 147/62 HR 90 RR 20 SpO2 95%	HEENT: Dry mouth Bilateral swelling of the parotid glands
Cardiac: Regular rate and rhythm No murmurs	Abdominal: Normal
Pulmonary: CTAB	MSK: Palpable purpura on bilateral legs Swelling on R wrist and L MCPs

52 y o female: Labs

- Cr 1.6 (from 0.7)
- WCC 9
- Neutrophil count 8
- Lymphocyte count 0.85
- ANA positive
- dsDNA negative
- RF positive
- Anti SSA Ab positive
- C4 low
- Cryoprecipitate formation/analysis negative
- Schirmer test of 3mm per 5min

Primary Sjogren Syndrome

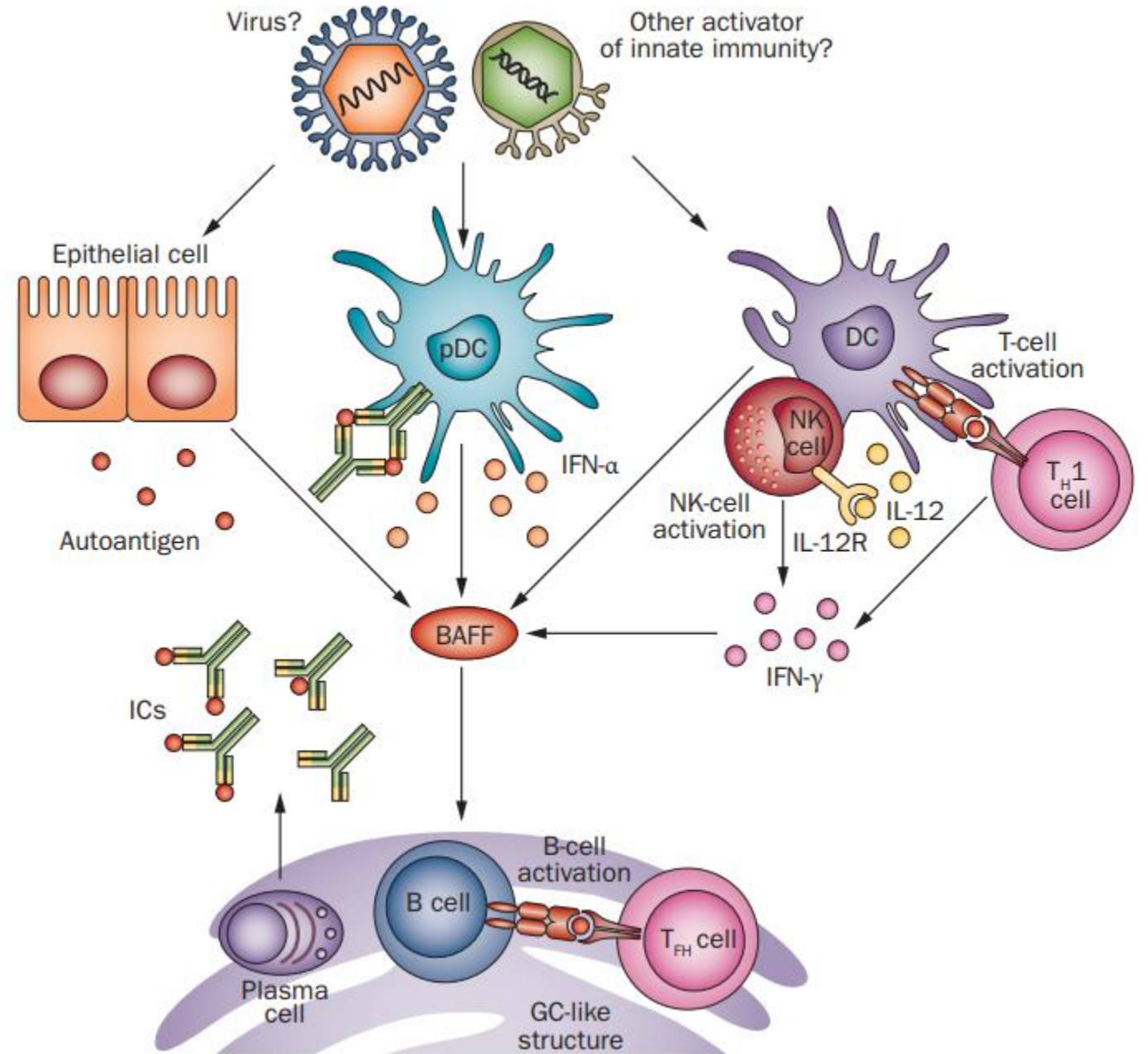
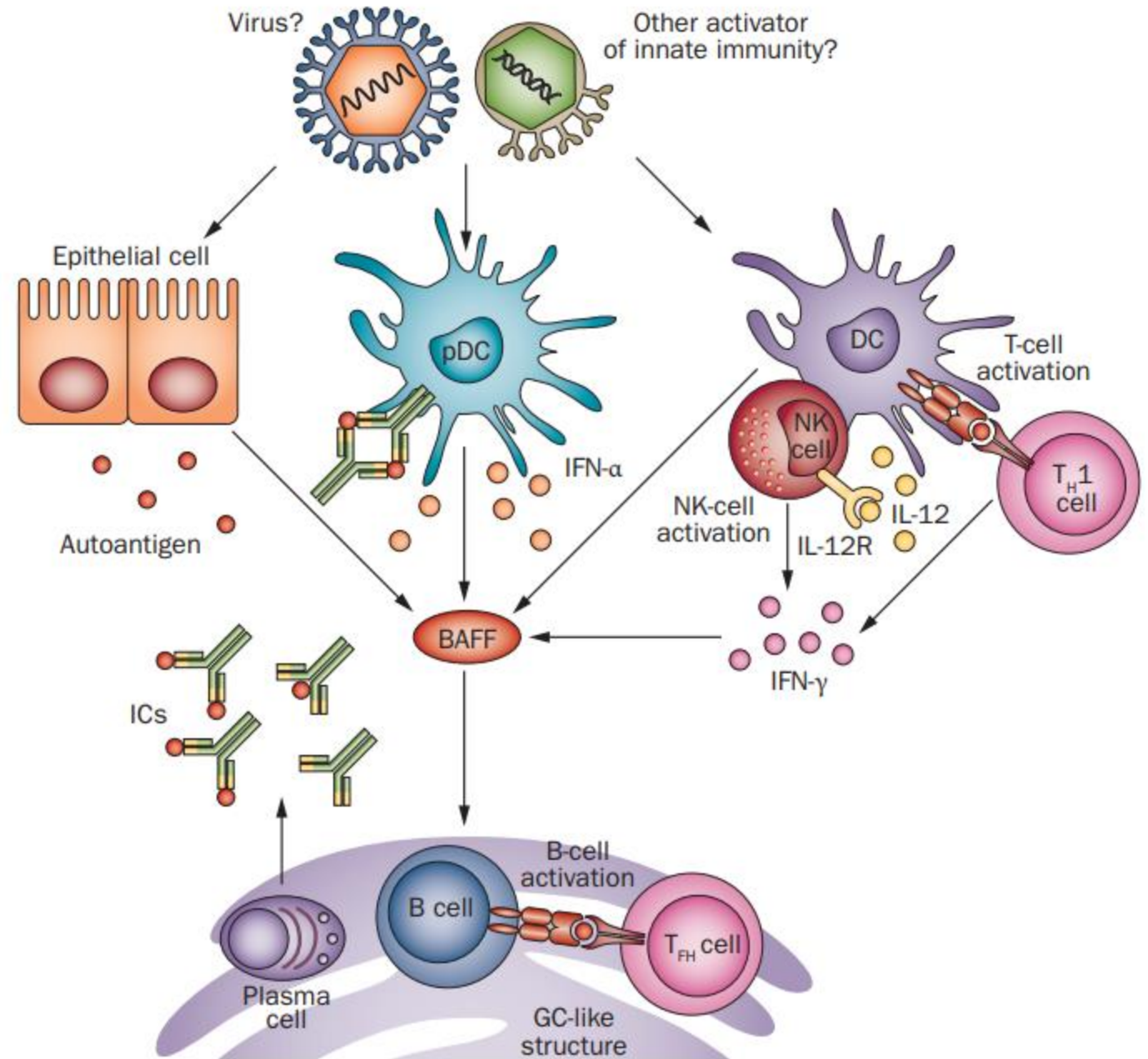


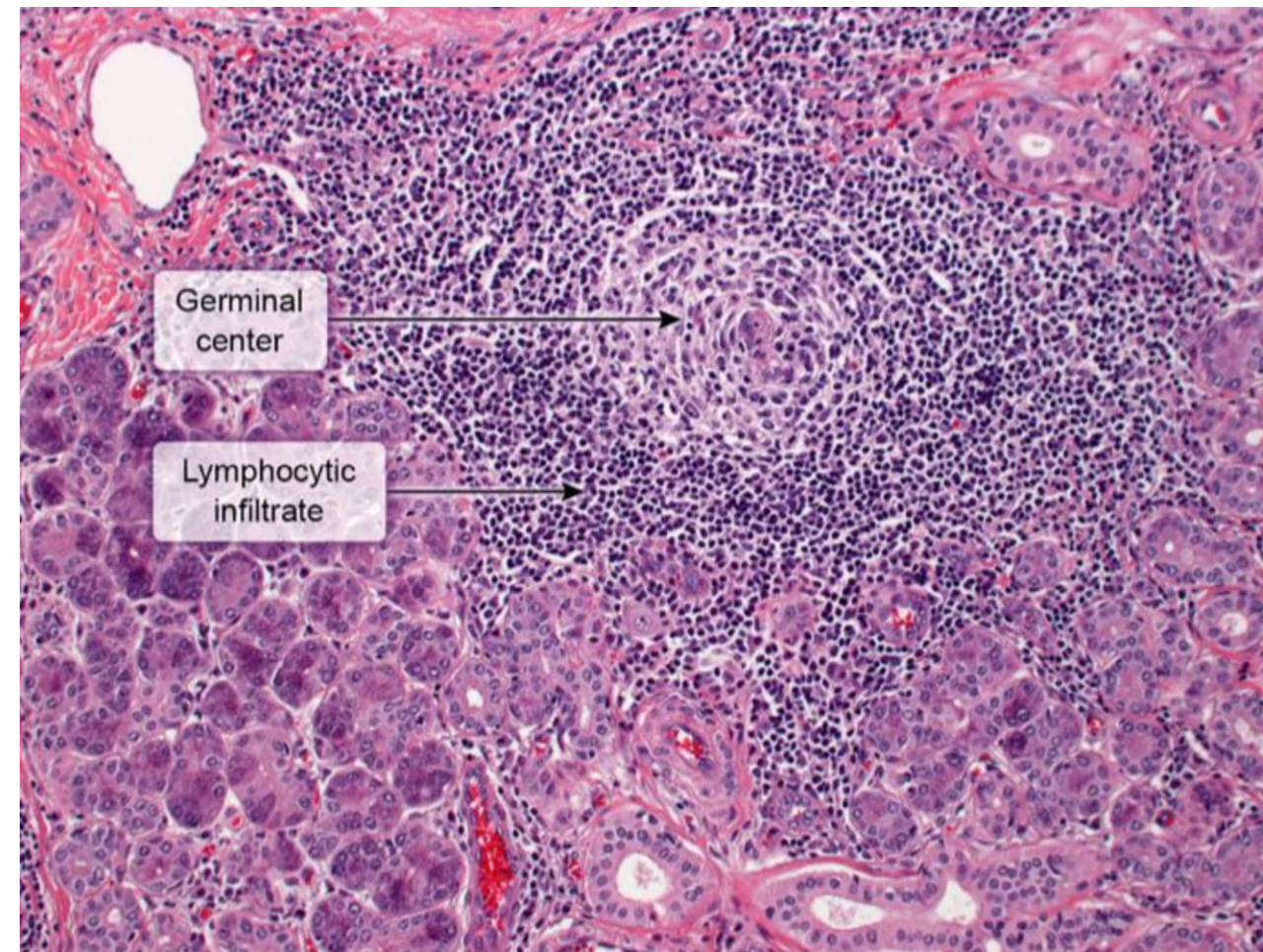
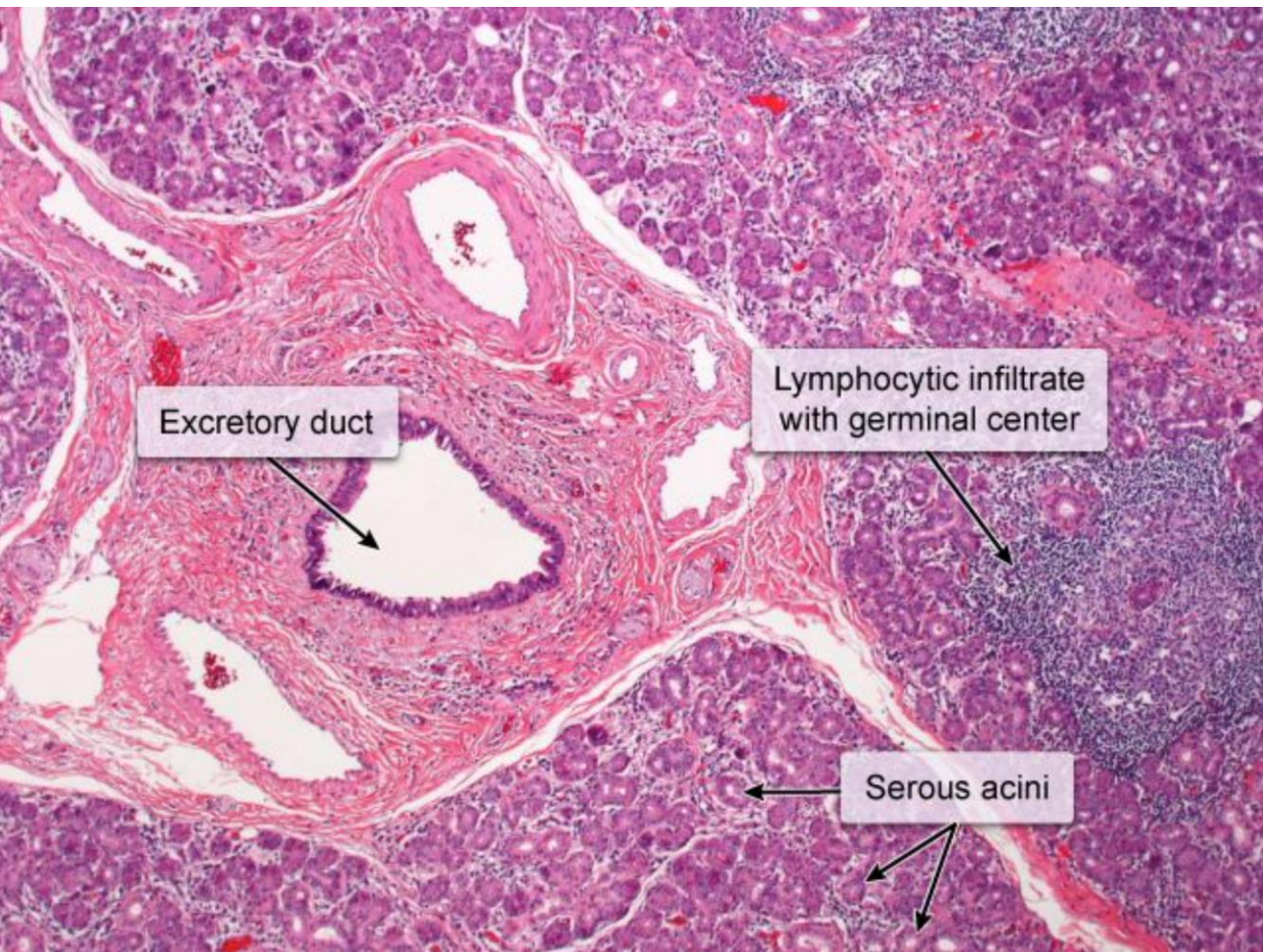
Table 1. 2017 ACR–EULAR Classification Criteria for Primary Sjögren’s Syndrome.*

Item	Description	Score
Focus score of ≥ 1	A score determined by the number of mononuclear-cell infiltrates containing ≥ 50 inflammatory cells per 4 mm^2 of minor labial salivary gland obtained on biopsy	3
Presence of anti-SSA antibodies†	Measured in serum; only anti-Ro60 antibodies have to be considered; isolated anti-Ro52 antibodies are not specific for Sjögren’s syndrome	3
SICCA ocular staining score of ≥ 5	A score determined by an ophthalmologist on the basis of examination with fluorescein and lissamine green staining; scores range from 0 to 12, with higher scores indicating greater severity	1
Schirmer test of $\leq 5 \text{ mm}$ per 5 min	An assay for measuring tear production by inserting filter paper on conjunctiva in the lower eyelid and assessing the amount of moisture on the paper	1
Unstimulated whole salivary flow of $\leq 0.1 \text{ ml}$ per min	An assay for measuring the rate of salivary flow by collecting saliva in a tube for at least 5 min after the patient has swallowed	1
Total score		9

Primary Sjogren Syndrome Pathophysiology

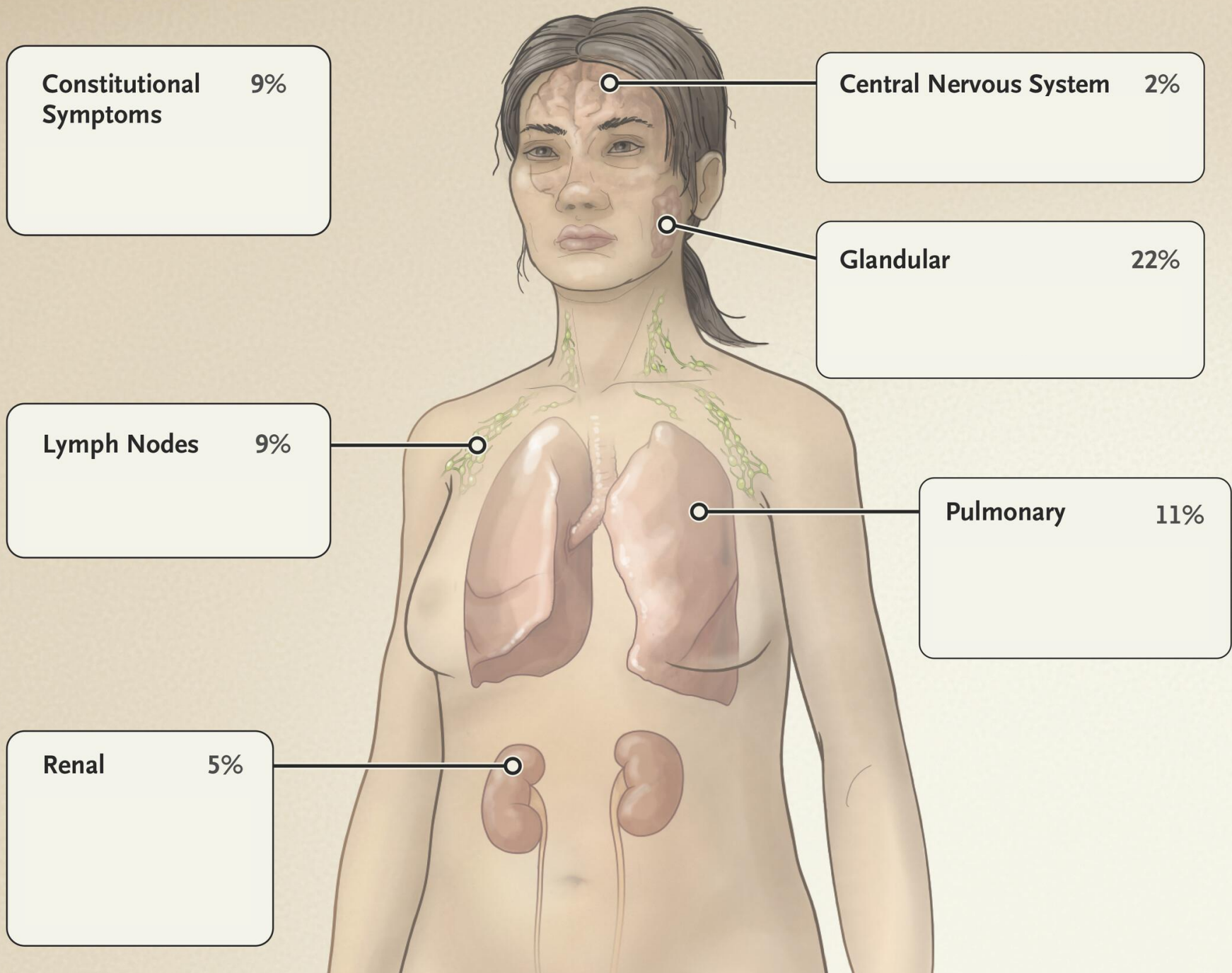
- Activation of mucosal epithelial cells
- Activation of innate and adaptive immune system
- GWAS show association with interferon pathways
- B-cell activating factor of the TNF family (BAFF) implicated

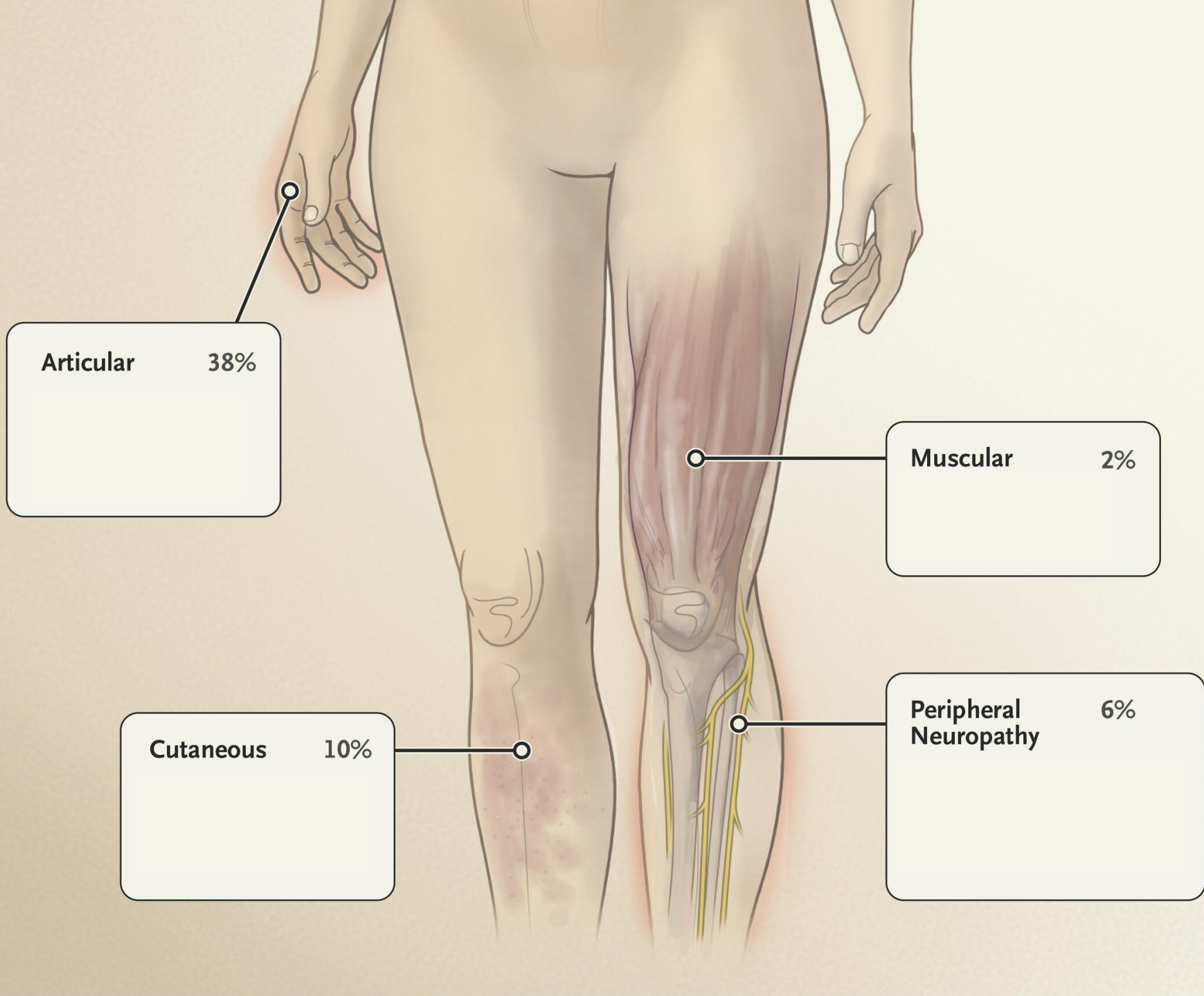




Systemic Manifestations of Primary Sjogren Syndrome

- Constitutional Symptoms
- CNS
- Lymph nodes
- Pulmonary
- Renal
- Articular
- Muscular
- Cutaneous
- Peripheral nerves



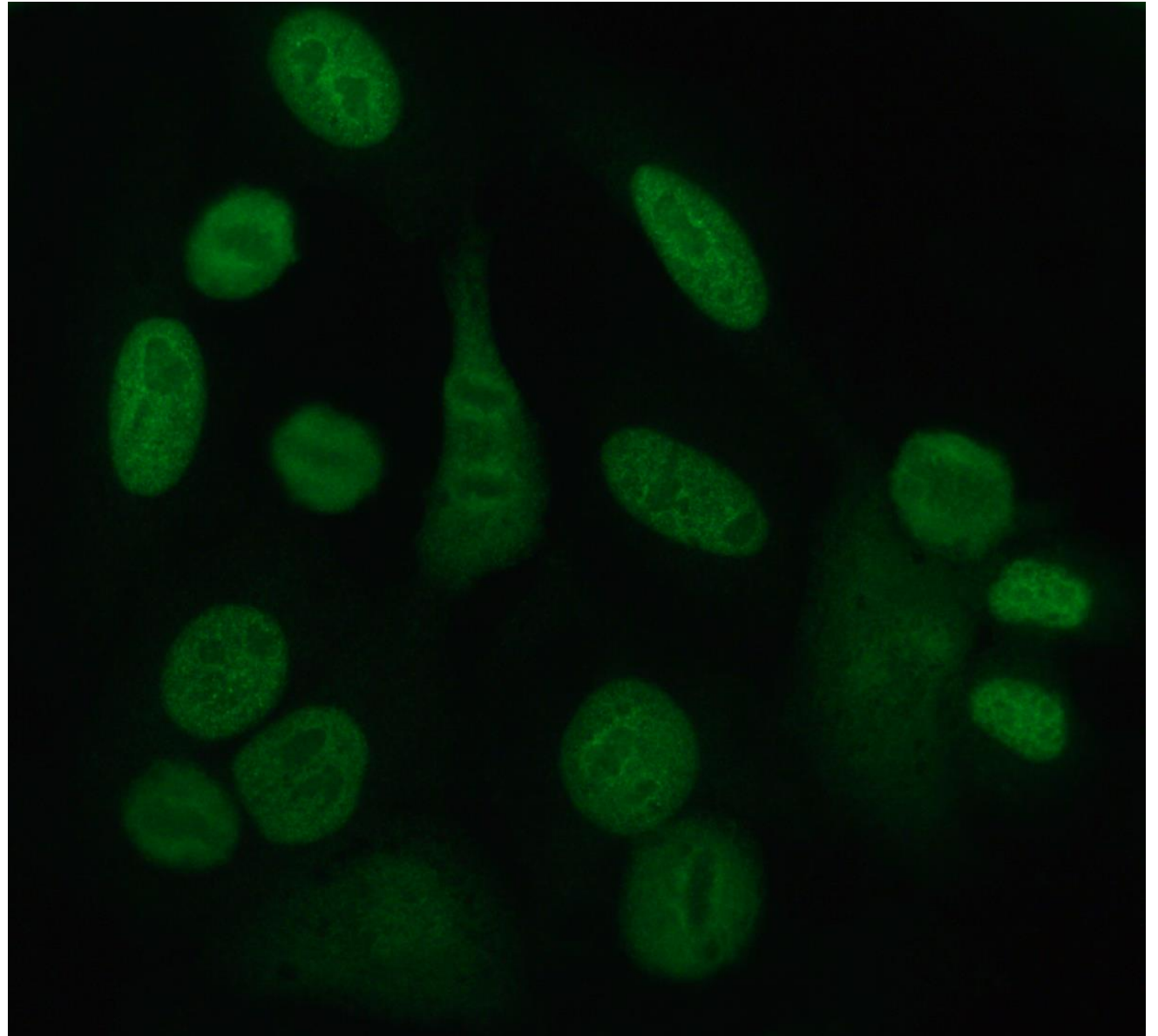


Learning point #1

- A diagnosis of primary Sjögren's syndrome is often made based on a classic triad of symptoms: dryness of the mouth and eyes, fatigue, and pain
- Systemic complications, which are present in 30 to 40% of patients, may provide the first clues to the disease

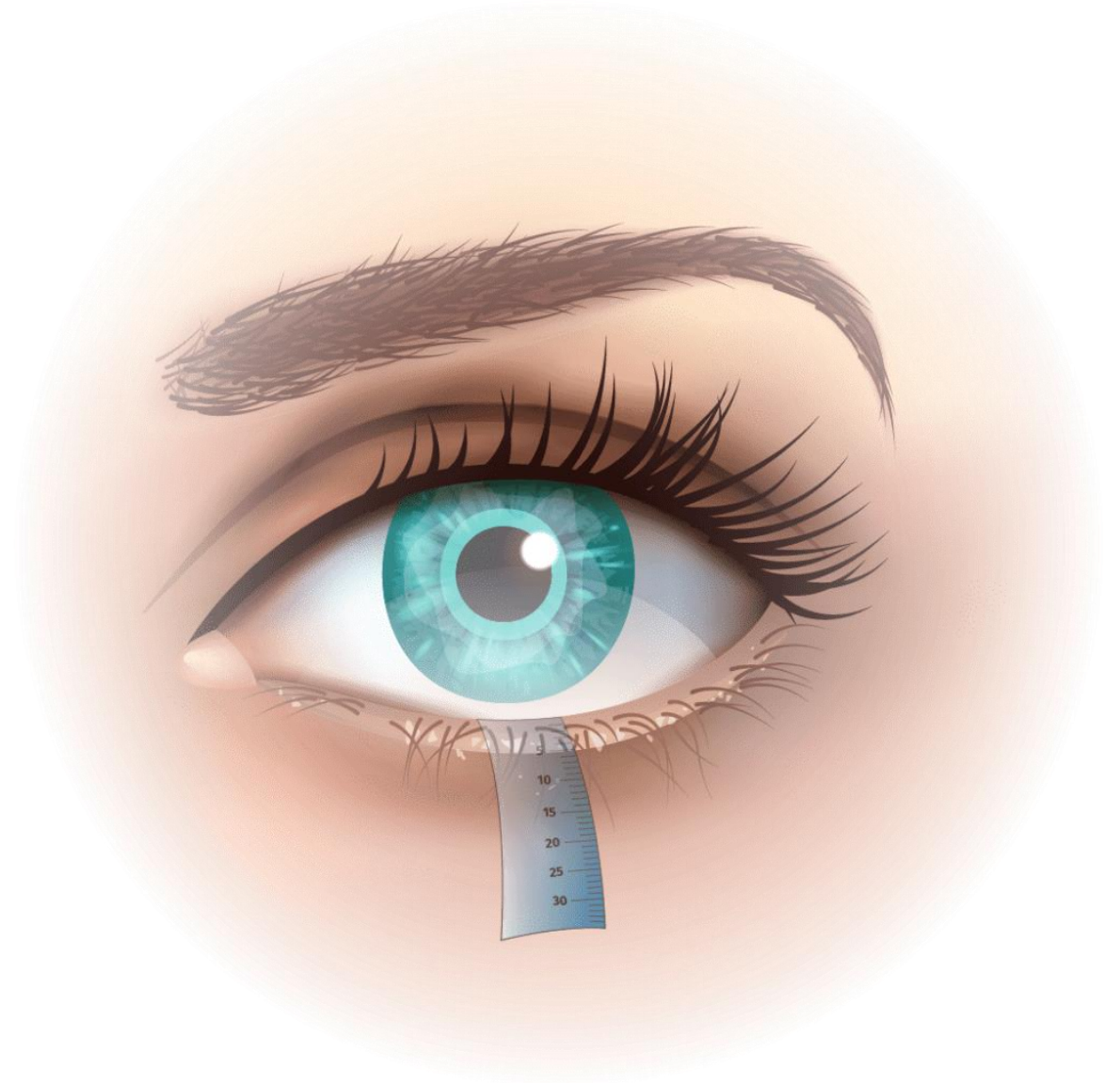
Laboratory Testing

- Anti-SSA antibodies
- Anti-SSB antibodies
- Rheumatoid Factor
- dsDNA
- Ocular dryness
- Oral dryness



Laboratory Testing

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MKSAP #1

- Our patient is evaluated at a follow-up visit. Chewing sugarless gum and taking frequent small sips of water are increasingly less helpful for oral dryness. Current medications are artificial tears and ophthalmic cyclosporine. She has no other concerning symptoms.
- On physical examination, vital signs are normal. Other than dry oral mucosa, the examination is normal

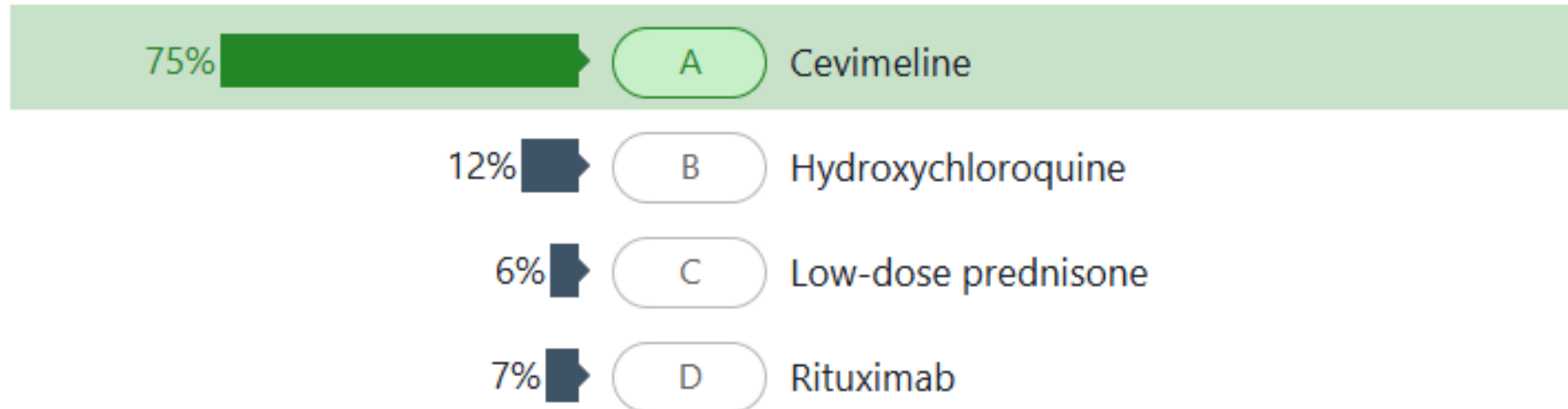
Which of the following is the most appropriate treatment?

- ☐ A Cevimeline
- ☐ B Hydroxychloroquine
- ☐ C Low-dose prednisone
- ☐ D Rituximab

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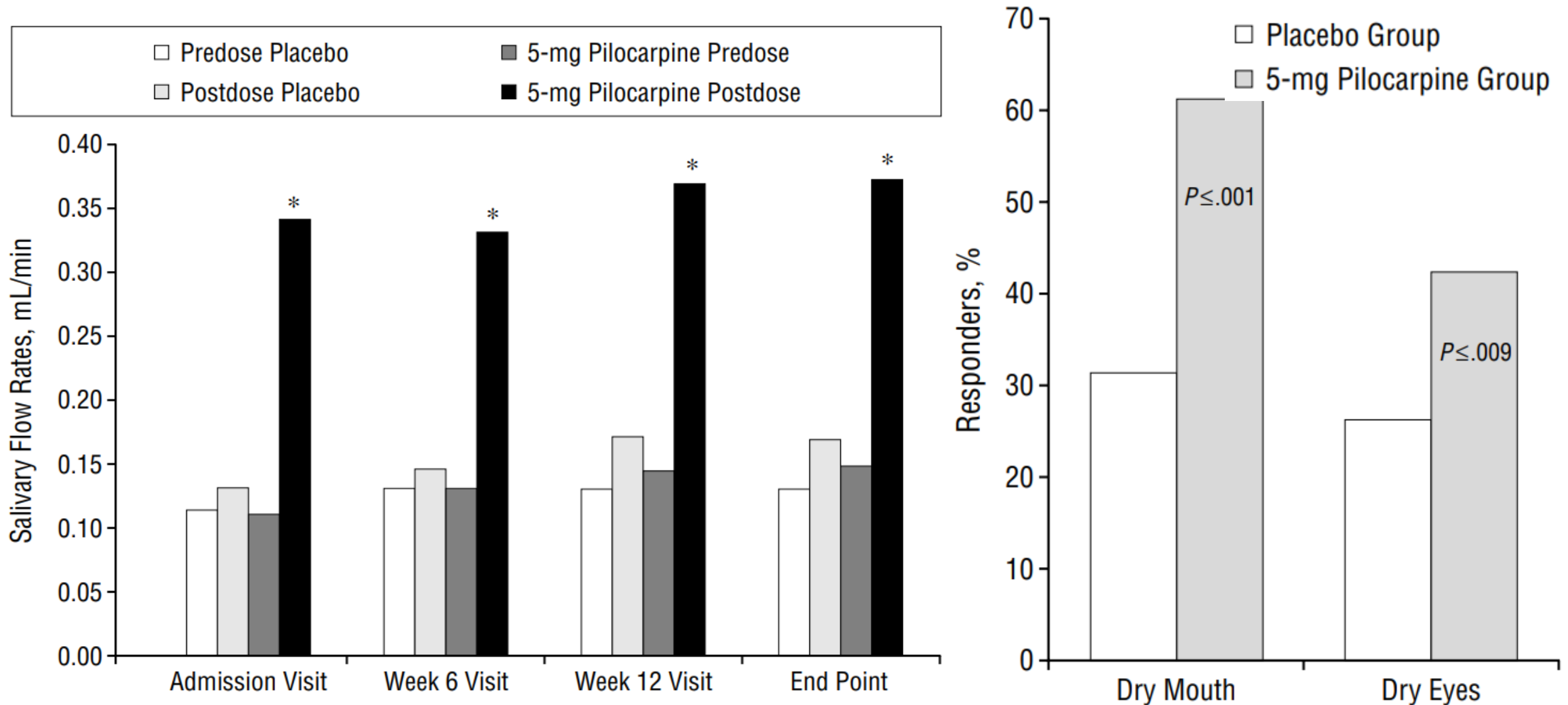
Which of the following is the most appropriate treatment?



Management

- Pilocarpine
- Cevimeline
- Topical cyclosporin eye drops
- Regular dental exams
- Oral hygiene

Pilocarpine for symptoms in pSS or sSS



Pilocarpine for symptoms in pSS or sSS

**Table 4. Incidence of Adverse Experiences
($\geq 10\%$ in Any Treatment Group)***

Adverse Experience	Placebo Tablets (n = 125)	Pilocarpine Tablets (n = 248)		Overall <i>P</i>
		2.5 mg (n = 121)	5 mg (n = 127)	
Sweating†	9 (7.2)	13 (10.7)	55 (43.3)	$\leq .001$
Headache	31 (24.8)	25 (20.7)	20 (15.8)	$\leq .20$
Flu syndrome	11 (8.8)	16 (13.2)	18 (14.2)	$\leq .38$
Nausea	11 (8.8)	15 (12.4)	15 (11.8)	$\leq .62$
Rhinitis	7 (5.6)	9 (7.4)	13 (10.2)	$\leq .38$
Dizziness	11 (8.8)	6 (5.0)	13 (10.2)	$\leq .29$
Urinary frequency†	2 (1.6)	13 (10.7)	12 (9.5)	$\leq .01$

Learning point #2

- Treatment relies on muscarinic agonists (pilocarpine and cevimeline). The main adverse effect of these agents is sweating, which can be minimized by gradual escalation of the dose

MKSAP #2

- Our patient is evaluated at a follow-up visit. For the past 4 weeks she has experienced arthralgia, unintentional weight loss, fever, and drenching night sweats. She has hypothyroidism. Current medications are levothyroxine, artificial tears, and ophthalmic cyclosporine suspension
- Parotid glands are enlarged, and the oropharynx is dry. No skin lesions or evidence of joint synovitis.
- Labs are shown. Immunofixation studies show a monoclonal IgM gammopathy (κ type)

Erythrocyte sedimentation rate 	73 mm/h
Hemoglobin 	10.2 g/dL (102 g/L)
C3  complement	102 mg/dL (1020 mg/L)
C4  complement	8 mg/dL (80 mg/L)
Thyroid-stimulating hormone 	3.0 µU/mL (3.0 mU/L)
Rheumatoid factor 	442 U/mL (442 kU/L)
Anti-cyclic citrullinated peptide antibodies	Negative
Anti-La/SSB antibodies	Negative
Anti-Ro/SSA antibodies	>8 U/L (normal, <1 U/L)
Urinalysis	0-1+ protein; no erythrocytes, leukocytes, or casts

Which of the following conditions is most likely responsible for her recent symptoms?

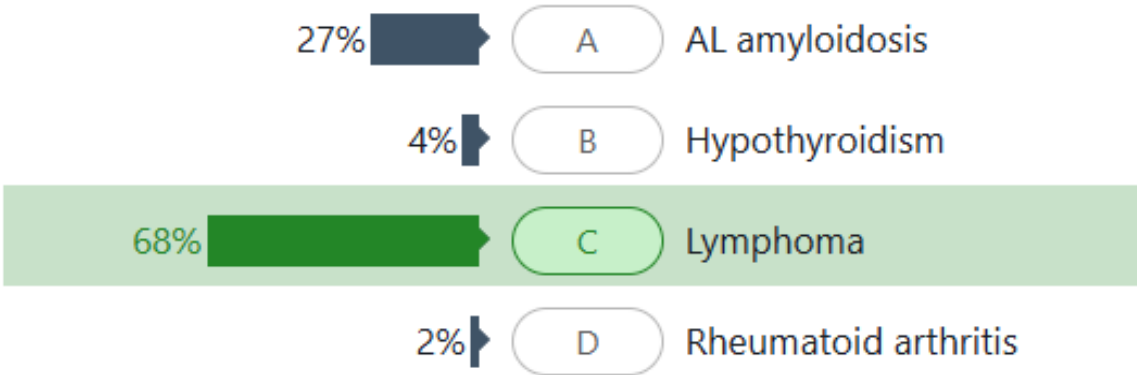
- ☐ A AL amyloidosis
- ☐ B Hypothyroidism
- ☐ C Lymphoma
- ☐ D Rheumatoid arthritis

MKSAP #2

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Risk of B-cell lymphoma

Table 2. Risk Factors for the Development of Lymphoma in Patients with Primary Sjögren's Syndrome.*

Risk Factor
Recurrent swelling of parotid glands
Splenomegaly, lymphadenopathy, or both
Purpura
Score of >5 on the ESSDAI†
Rheumatoid factor
Cryoglobulinemia
Low C4 level
CD4 T-cell lymphocytopenia
Presence of ectopic germinal centers
Focus score of >3‡
Germinal mutations in <i>TNFAIP3</i>

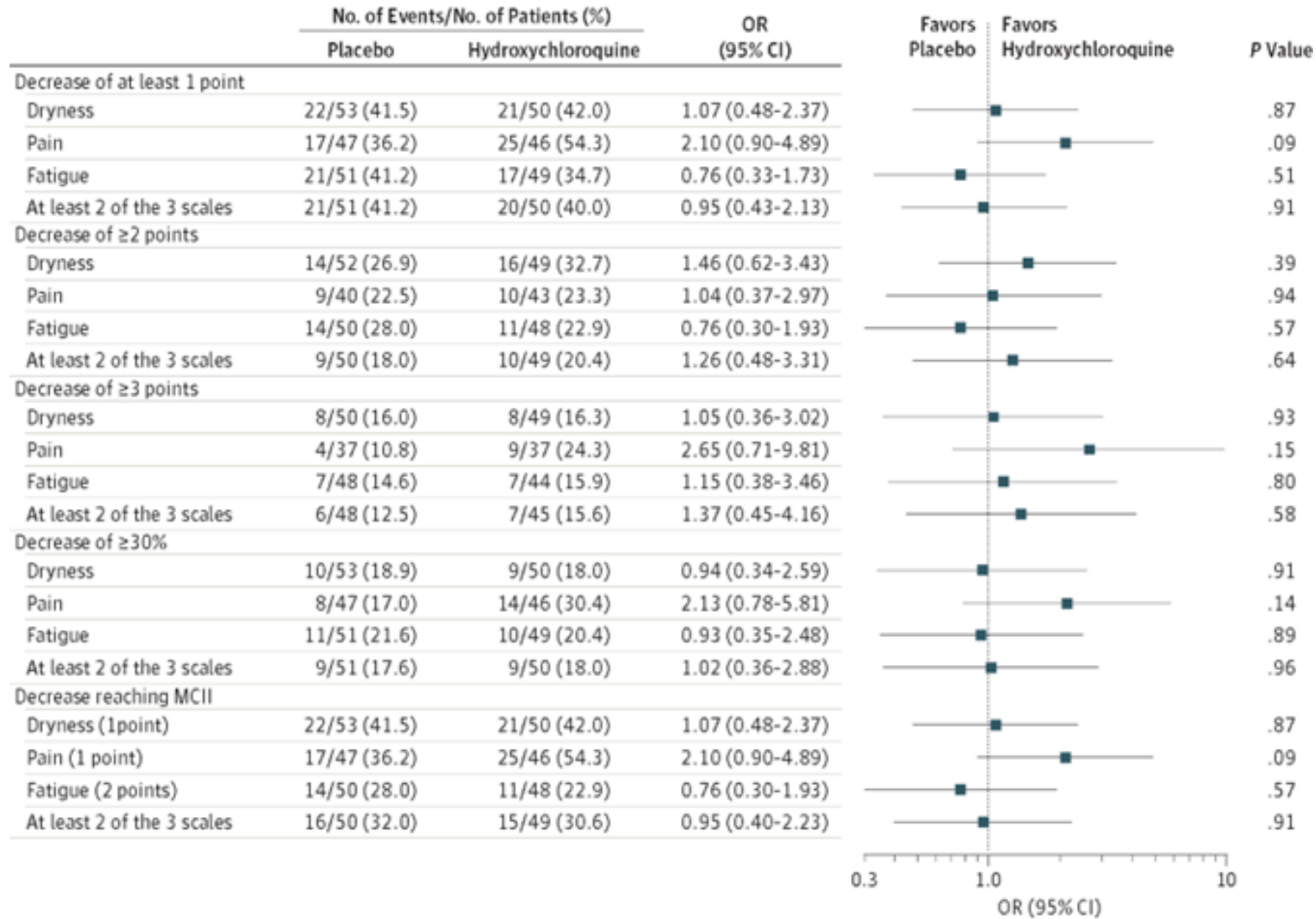
Learning point #3

- The risk of B-cell lymphoma is markedly increased (by a factor of 15 to 20) among patients with primary Sjögren's syndrome, as compared with the general population

Management – Organ Manifestations

- Treated in line with SLE or other CTDs
 - Hydroxychloroquine
 - Prednisone
 - Methotrexate
 - Mycophenolate
 - Azathioprine
 - Cyclosporin

Hydroxychloroquine for pSS



Learning point #4

- Hydroxychloroquine is often used for arthralgia with or without synovitis and purpura, although benefits have not been shown in a randomized, controlled trial
- In the absence of trials involving patients with pSS, severe organ manifestations are treated with immunosuppressive agents, in accordance with guidelines for SLE and other connective-tissue diseases.

Learning points

- Medications, particularly anti-cholinergics, are common causes of dry eyes/mouth
- A diagnosis of primary Sjögren's syndrome is often made based on a classic triad of symptoms: dryness of the mouth and eyes, fatigue, and pain
- Systemic complications, which are present in 30 to 40% of patients, may provide the first clues to the disease
- The risk of B-cell lymphoma is markedly increased (by a factor of 15 to 20) among patients with primary Sjögren's syndrome, as compared with the general population
- Treatment relies on muscarinic agonists (pilocarpine hydrochloride and cevimeline hydrochloride). The main adverse effect of these agents is sweating, which can be minimized by gradual escalation of the dose
- Hydroxychloroquine is often used for arthralgia with or without synovitis and purpura, although benefits have not been shown in a randomized, controlled trial
- In the absence of trials involving patients with pSS, severe organ manifestations are treated with immunosuppressive agents, in accordance with guidelines for SLE and other connective-tissue diseases.

References

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Thank You!