

# Atopic dermatitis predisposes dupilumab related conjunctivitis in prurigo nodularis patients

MD, PhD Piotr K Krajewski, MD, PhD Jacek C Szepietowski, Prof.

Division of Dermatology, Venereology and Clinical Immunology, Faculty of Medicine,  
Wroclaw University of Science and Technology

No conflict of interest to disclose

# Prurigo nodularis

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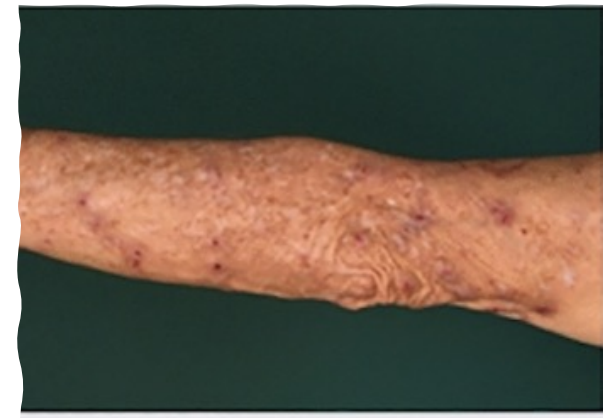
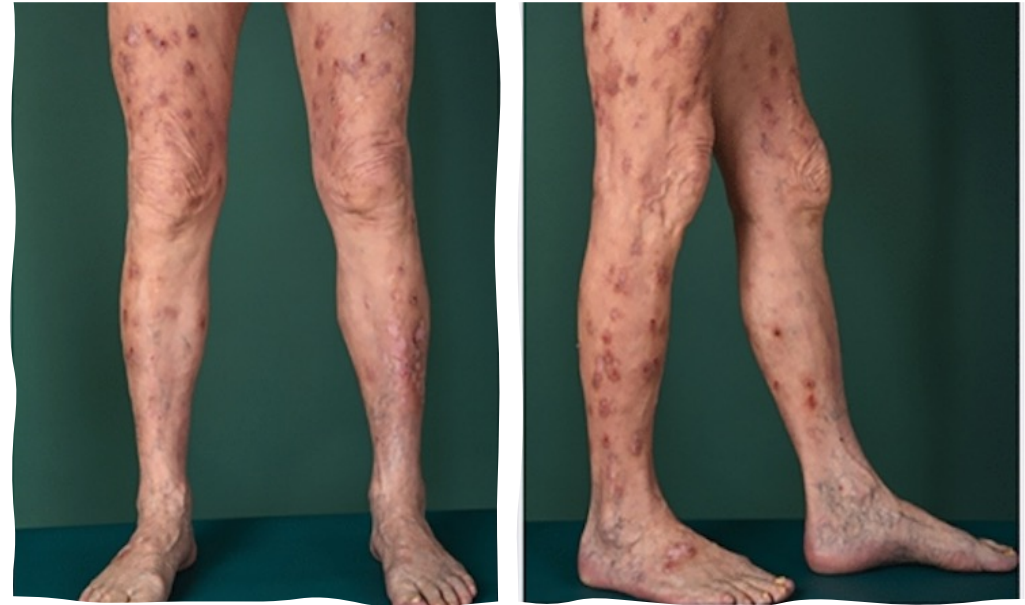
Debilitating chronic inflammatory skin disorder

Intensely pruritic nodules

Often associated with atopic predisposition

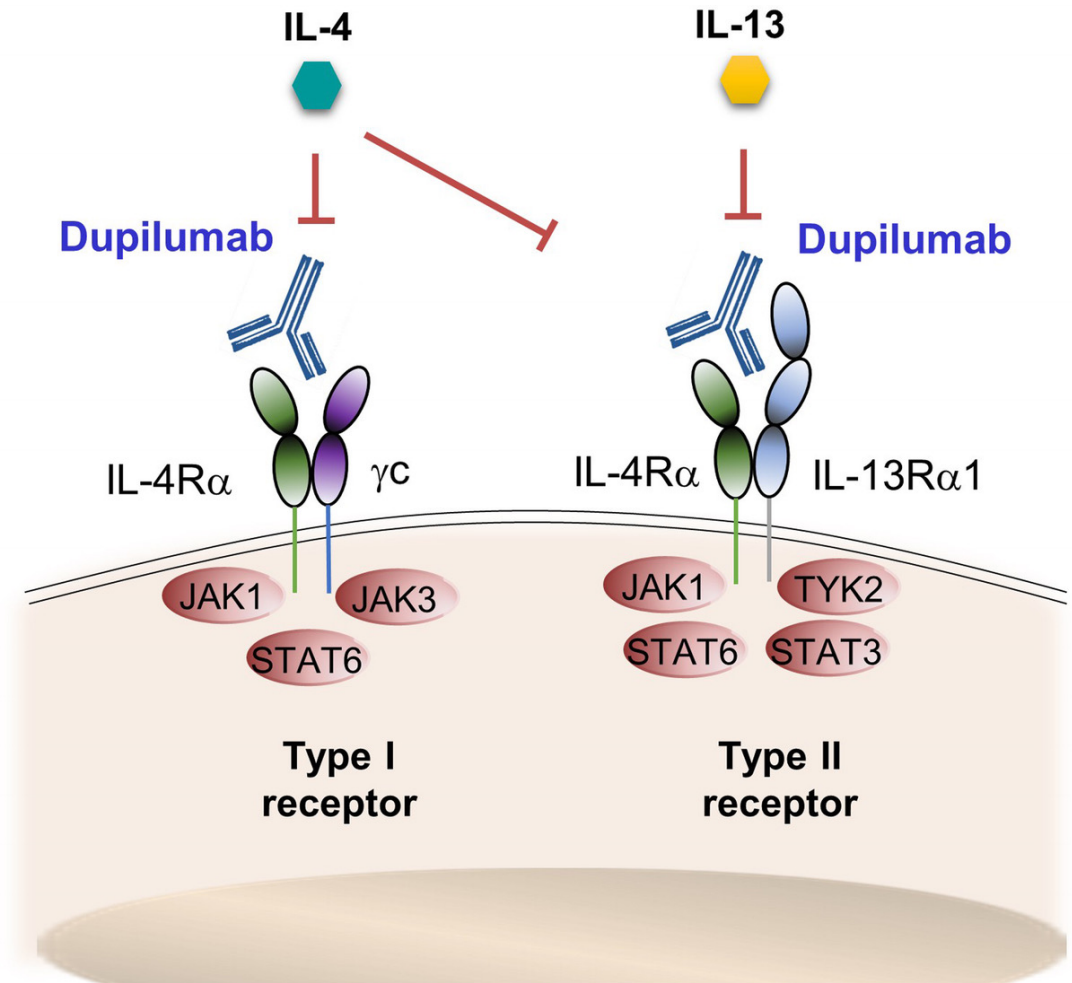
Prurigo nodularis reflects neuroimmune dysregulation

- Th2 cytokines (IL-4, IL-13, IL-31) sensitize cutaneous nerves
- Reduced intraepidermal nerve fibers
- Itch–scratch cycle, neuroplasticity, and dermal fibrosis



# Prurigo nodularis & Dupilumab

- Dupilumab, a monoclonal antibody targeting the IL-4 receptor  $\alpha$  subunit
- Robust efficacy in PN:
  - $\geq 4$ -point itch reduction
    - 60% vs 18% at week 24 (PRIME)
    - 37% vs 22% at week 12 (PRIME2)
  - Clear/almost-clear skin (IGA PN-S 0/1,  $\leq 5$  nodules) at week 24 in ~48%/45% vs 18%/16%



# Dupilumab associated conjunctivitis

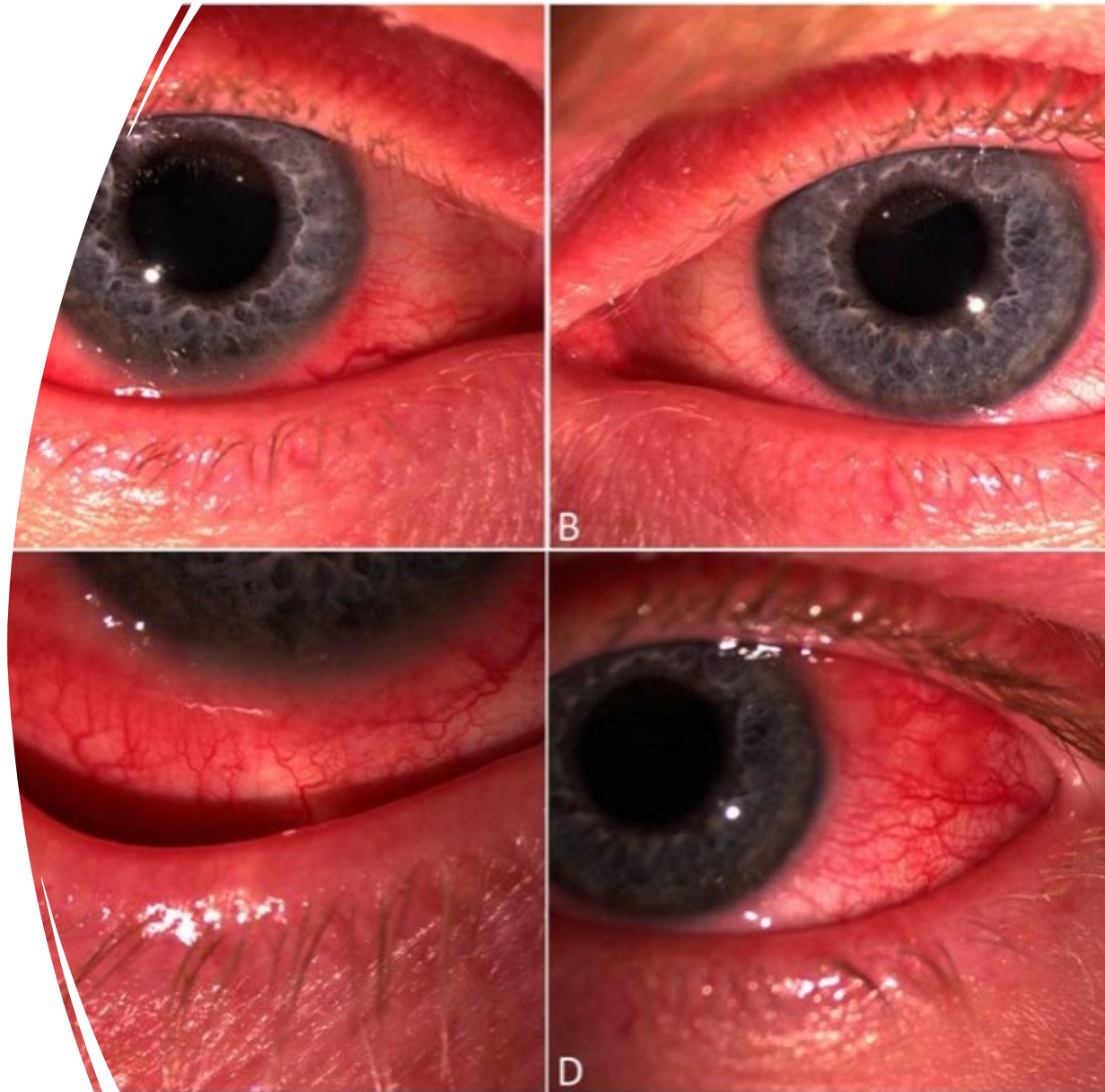
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- **Incidence:**

- Higher with dupilumab in AD ( $\approx 8\text{--}19\%$  in RCTs)
- Meta-analysis RR 1.9-2,4 vs placebo

- **Risk factors:**

- Prior ocular surface disease/conjunctivitis
- Facial/eyelid eczema
- Longer AD duration
- Possible roles of high IgE/eosinophilia.

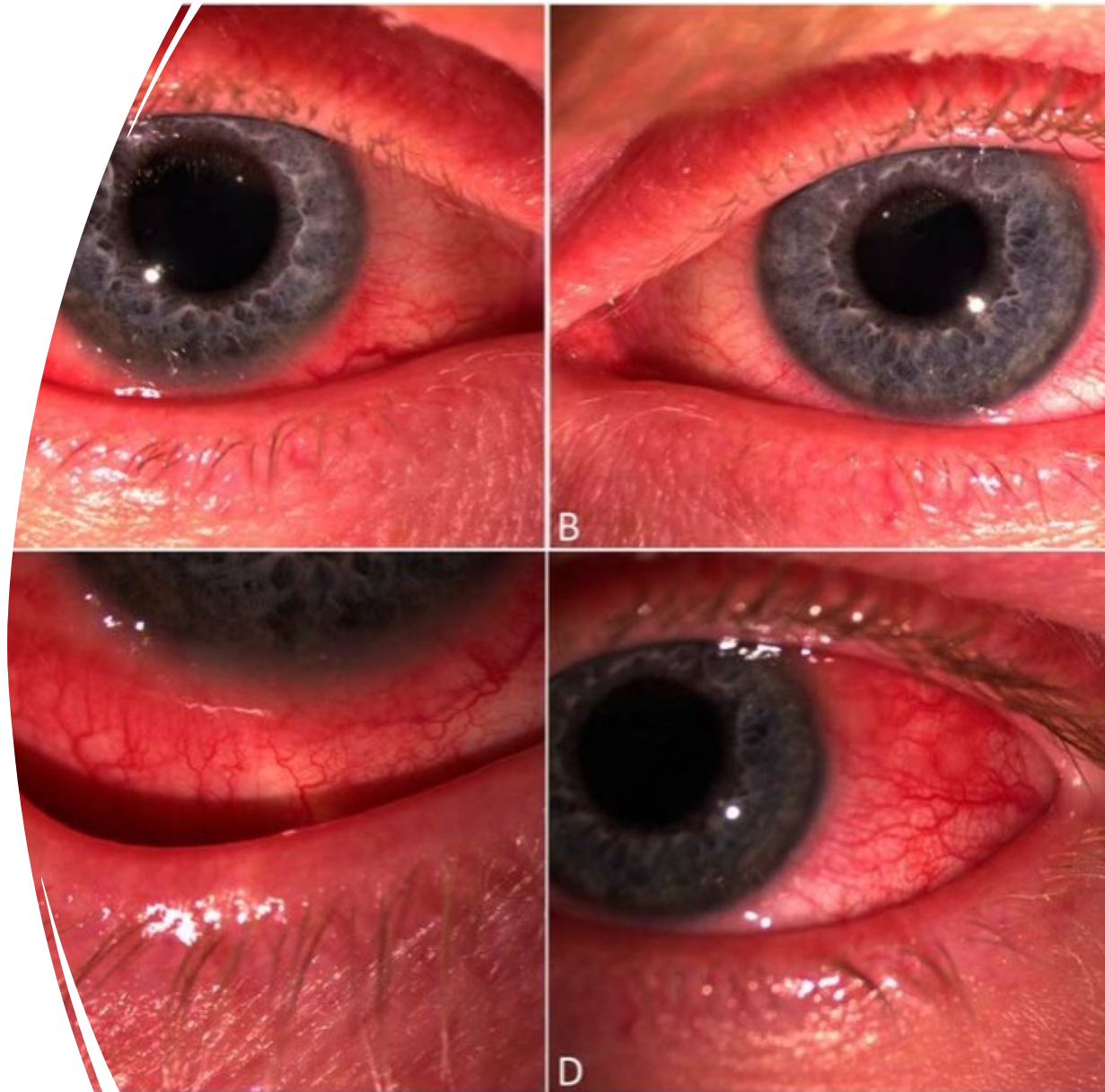





# Dupilumab associated conjunctivitis in PN

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- **Incidence:**
  - **AD:** 8–19% on dupilumab (significantly higher than placebo)
  - **PN:** ~3.9% on dupilumab overall
    - PRIME: 2.7% vs 2.7%;
    - PRIME2: 3.9% vs 0%—none serious, no discontinuations
- Prominent in AD
- Not consistently elevated vs placebo in non-AD indications (including PN)



A large orange shape on the left side of the slide, consisting of a rectangle with a quarter-circle cutout on its right side.

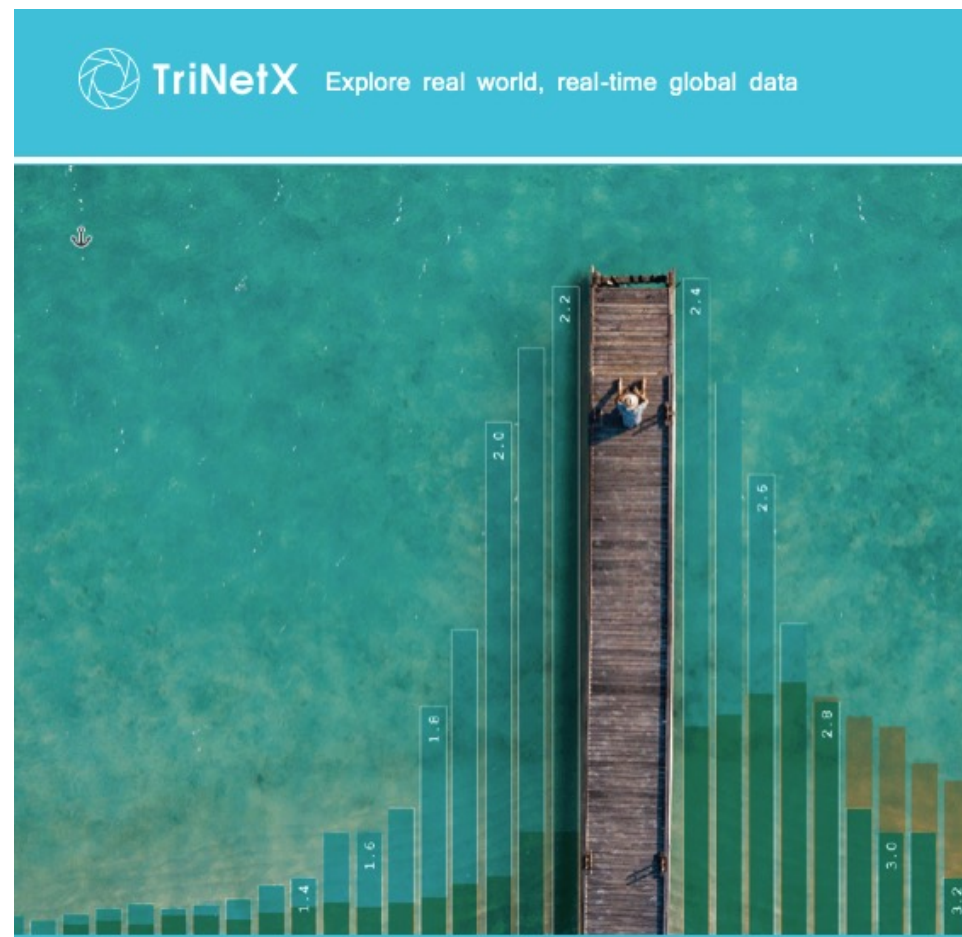
Atopic or  
disease-  
specific risk?

It remains unclear whether this risk is driven  
by  
underlying “**atopic diathesis**”  
or  
specifically by **atopic dermatitis itself**

A blue dashed line in the bottom right corner, composed of four curved segments that follow a diagonal path from the bottom left towards the top right.

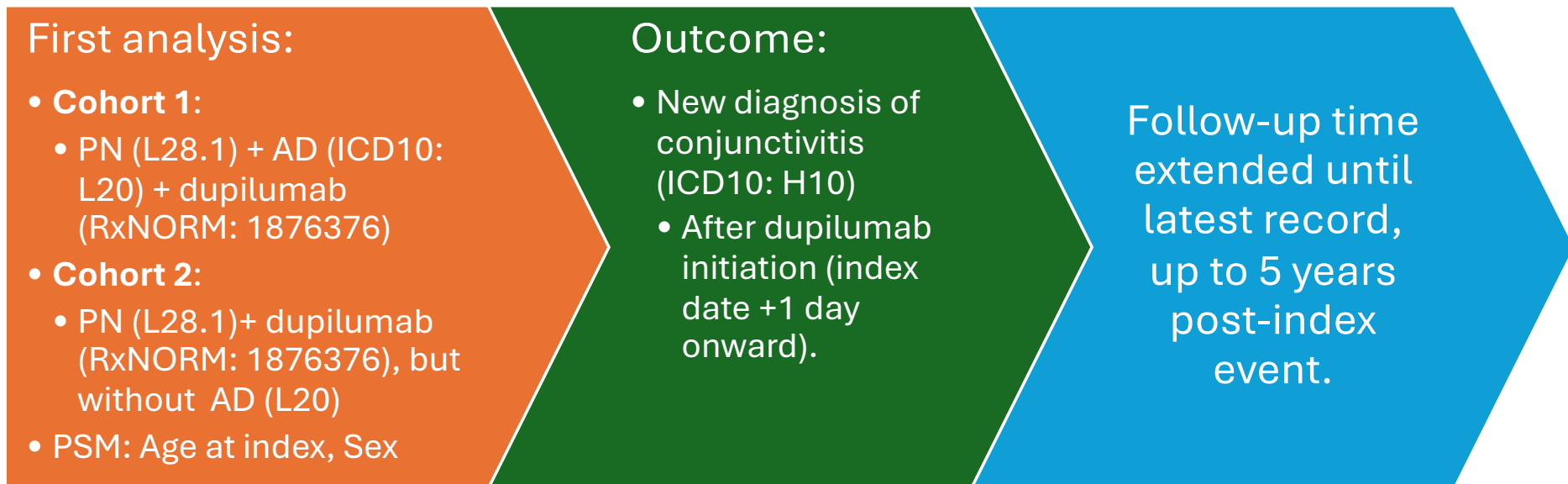
# Rationale, clinical importance

- Defining risk factors:
  - Crucial for patient risk stratification
  - Monitoring
  - Preventive strategies
- We conducted a large, multi-center, propensity-matched cohort study
- Assess the actual contribution of atopic dermatitis and related atopic comorbidities to the risk of conjunctivitis in patients with PN treated with dupilumab.



# First analysis – general influence

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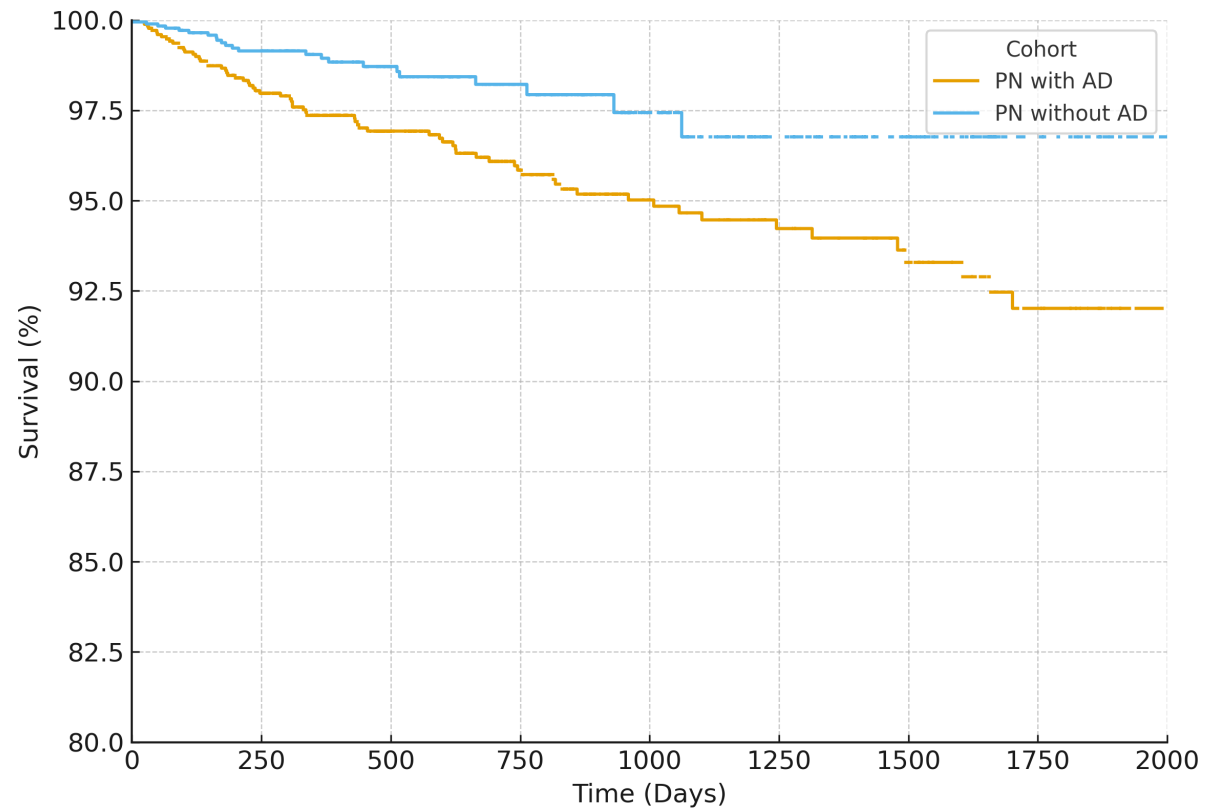
# Matching

		Before Matching					After Matching				
▼ Demographics		Mean ± SD	Patients	% of Cohort	P-Value	Std diff.	Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
AI	Age at Index	56.1 ± 18.2	2,744	100%	< 0.0001	0.2912	60.6 ± 14.9	2,132	100%	0.6998	0.0118
		60.9 ± 14.5	2,188	100%			60.5 ± 14.4	2,132	100%		
F	Female		1,596	58.163%	< 0.0001	0.1282		1,333	62.523%	0.4852	0.0214
			1,409	64.397%				1,355	63.555%		
M	Male		1,148	41.837%	< 0.0001	0.1282		799	37.477%	0.4852	0.0214
			779	35.603%				777	36.445%		

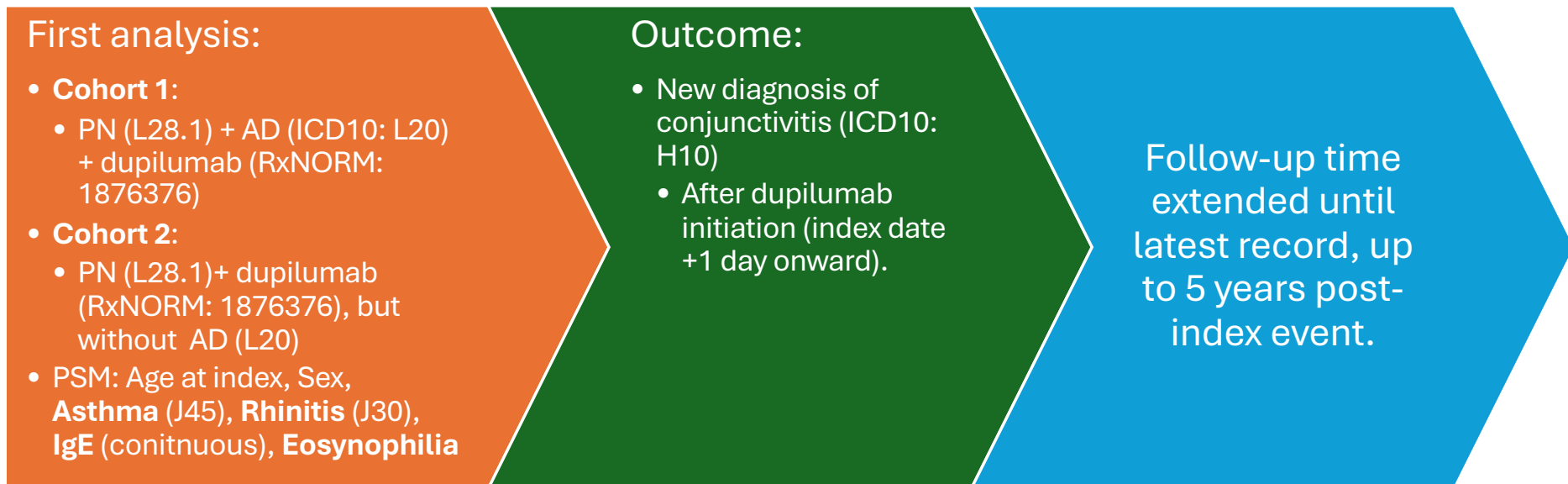
# First analysis - results

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- Conjunctivitis risk
  - PN with AD **4,1%**
  - PN without AD **1,2%**
- Time to event analysis
  - **HR 2.26**
  - **95% CI: 1.405-3.634)**
  - **p<0.001**



# Second analysis – pure AD influence



# Matching

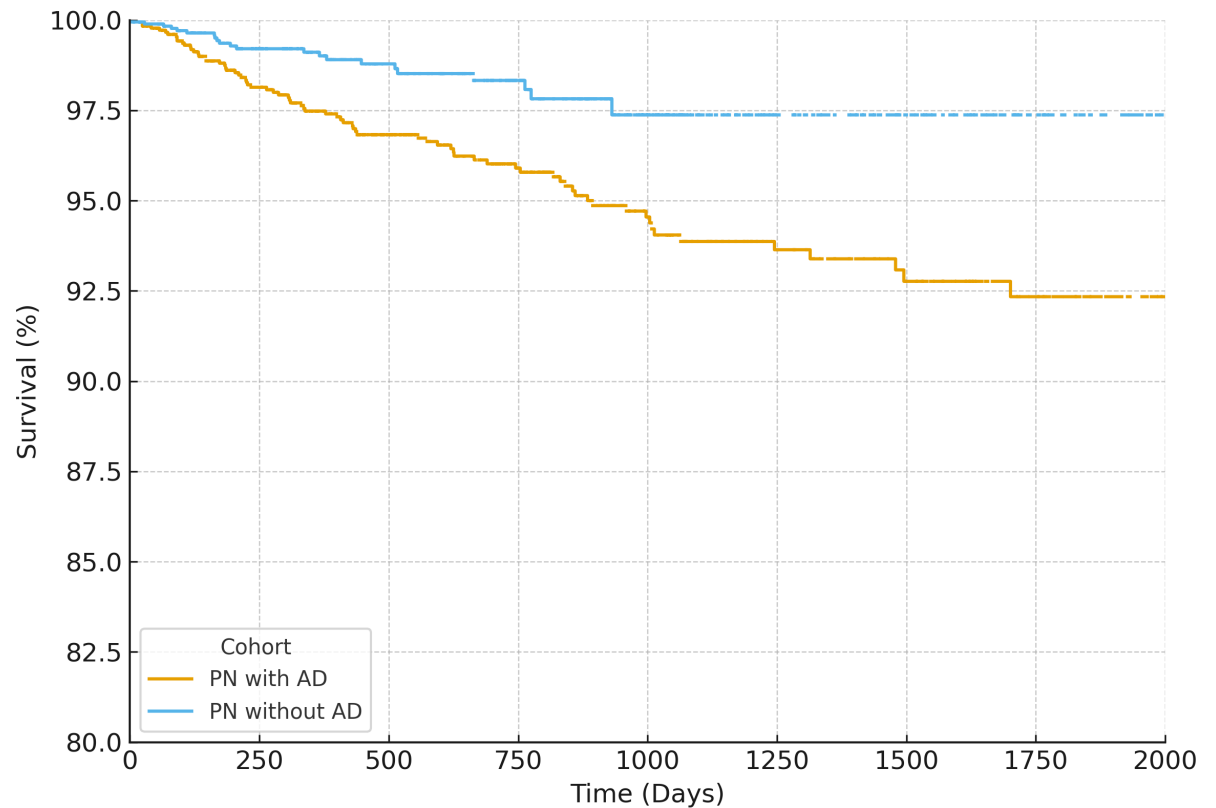
Before Matching							After Matching					
Demographics			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.	Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
AI	Age at Index		55.7 ± 18.5 60.7 ± 14.6	2,717 2,228	100% 100%	< 0.0001	0.3003	60.3 ± 15.9 60.1 ± 14.5	2,127 2,127	100% 100%	0.6193	0.0152
F	Female			1,568 1,439	57.711% 64.587%	< 0.0001	0.1414		1,312 1,347	61.683% 63.329%	0.2677	0.0340
M	Male			1,149 789	42.289% 35.413%	< 0.0001	0.1414		815 780	38.317% 36.671%	0.2677	0.0340
Diagnoses				Patients	% of Cohort	P-Value	Std diff.		Patients	% of Cohort	P-Value	Std diff.
ICD-10-CM	J45	Asthma		787 565	28.966% 25.359%	0.0046	0.0812		525 544	24.683% 25.576%	0.5018	0.0206
ICD-10-CM	J30	Vasomoto...		771 512	28.377% 22.98%	< 0.0001	0.1238		502 500	23.601% 23.507%	0.9424	0.0022
Labs			Mean ± SD	Patients	% of Cohort	P-Value	Std diff.	Mean ± SD	Patients	% of Cohort	P-Value	Std diff.
TNX Curated	LG32849-8	Eosinophil...	0.949 ± 7.23 0.633 ± 5.64	1,909 1,546	70.261% 69.39%	0.1598	0.0487	0.873 ± 6.8 0.65 ± 5.75	1,498 1,485	70.428% 69.817%	0.3339	0.0354
				1,929 1,560	70.997% 70.018%	0.4521	0.0215		1,509 1,498	70.945% 70.428%	0.7110	0.0114
TNX Curated	LG5901-6	IgE [Units/...	2,277 ± 6,095 469 ± 1,045	345 177	12.698% 7.944%	0.0001	0.4136	1,014 ± 3,827 471 ± 1,047	167 176	7.851% 8.275%	0.0712	0.1933
				345 177	12.698% 7.944%	< 0.0001	0.1567		167 176	7.851% 8.275%	0.6123	0.0155



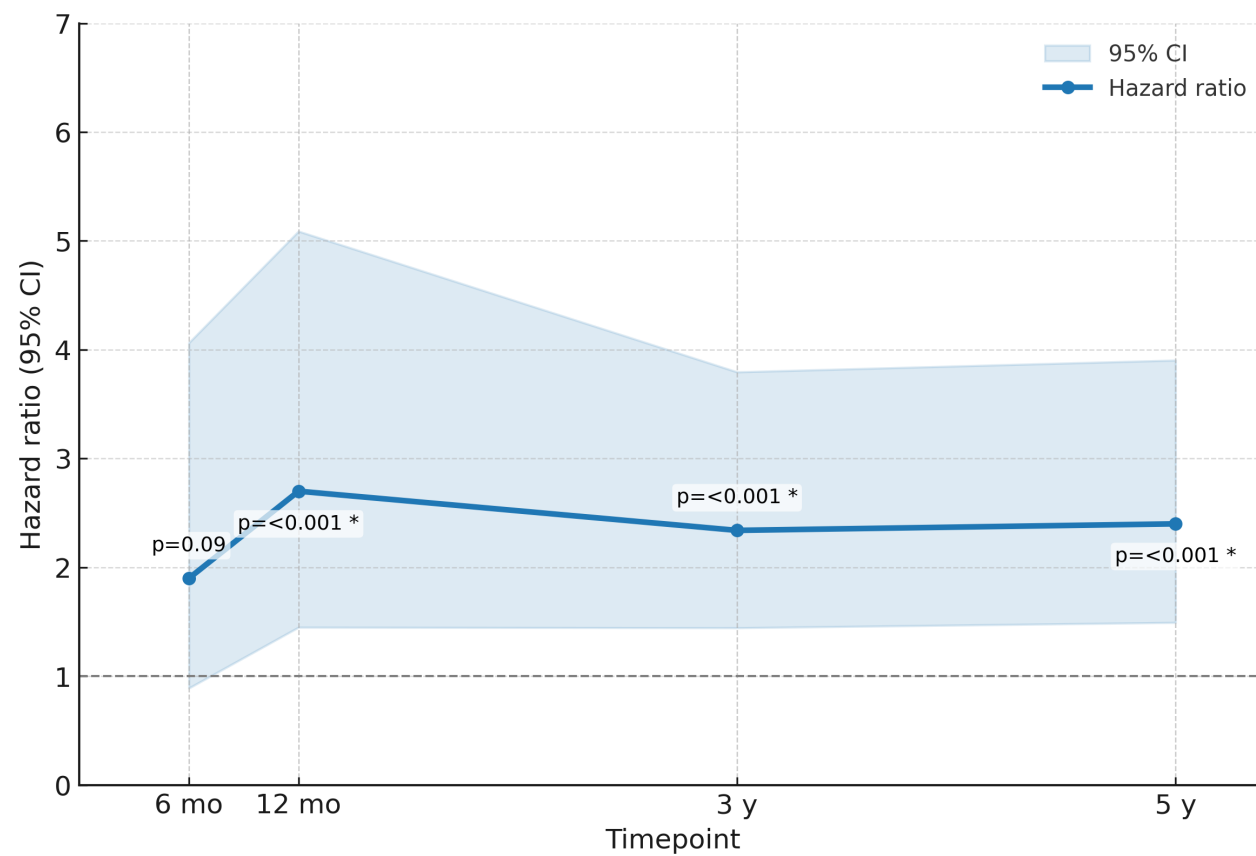
## Second analysis - results

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- Conjunctivitis risk
  - PN with AD **4,3%**
  - PN without AD **1,2%**
- Time to event analysis
  - **HR 2.47**
  - **95% CI: 1.534-3.634)**
  - **p<0.001**



## Time to event analysis





# Subgroup Analyses

Too few conjunctivitis cases in subgroups for robust HR calculation

No evidence for statistically significant effect modification by sex (descriptive risk trends similar for males/females)

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# Maybe it is not only AD?

1b : Kaplan-Meier Analysis Excluding Patients with Outcome Prior to the Time Window

Cohort	Patients in Cohort	Patients with Outcome	Cohort Statistics		Log-Rank Test		
			Median Survival (Days)	Survival Probability at End of Time Window	$\chi^2$	df	p
1 PN & asthma	1,110	48	-	79.315%	0.713	1	0.3986
2 PN w/o asthma	1,227	44	-	86.219%			

\* 269 patients in Cohort 1 and 152 patients in Cohort 2 were excluded from results because they had the outcome prior to the time window.

[Learn More](#)

Hazard Ratio		Proportionality		
Hazard Ratio	95 % CI	$\chi^2$	df	p
1.192	(0.792,1.795)	0.02	1	0.8887

1.19 (NS)

1b : Kaplan-Meier Analysis Excluding Patients with Outcome Prior to the Time Window

Cohort	Patients in Cohort	Patients with Outcome	Cohort Statistics		Log-Rank Test		
			Median Survival (Days)	Survival Probability at End of Time Window	$\chi^2$	df	p
1 PN & rhinitis	1,111	57	3,072	39.871%	15.139	1	< 0.0001
2 PN w/o rhinitis	1,311	29	-	91.482%			

\* 319 patients in Cohort 1 and 119 patients in Cohort 2 were excluded from results because they had the outcome prior to the time window.

[Learn More](#)

Hazard Ratio		Proportionality		
Hazard Ratio	95 % CI	$\chi^2$	df	p
2.372	(1.514,3.716)	0.088	1	0.7662

2.372



# Multivariable Analysis - sensitivity

Predictor	Hazard Ratio (95% CI)	p-value
<b>Atopic Dermatitis</b>	1.39 (1.29–1.50)	<0.001
Asthma	1.52 (1.44–1.61)	<0.001
Allergic Rhinitis	2.10 (2.00–2.21)	<0.001
Male Sex	0.88 (0.84–0.92)	<0.001
Baseline IgE	1.00 (1.00–1.00)	NS
Baseline Eosinophils	1.00 (0.99–1.01)	NS



## Key results

Exposure	HR (95% CI)	p-value	
<b>Atopic dermatitis</b>	2.40 → 1.30	<0.001	Independent risk; stable after adjustment
<b>Asthma</b>	1.19 → 1.52	<0.001	Mild, significant only in multivariable model
<b>Allergic rhinitis</b>	2.37 → 2.10	<0.001	Strongest and most consistent association



## Key results

### Time-dependent pattern:

- 6 mo: HR 1.9 (NS)
- 12 mo: HR 2.7 ( $p < 0.001$ )
- 3–5 yrs: HR  $\sim 2.4$  ( $p < 0.001$ )  $\rightarrow$  stable effect over time

### Cumulative incidence:

- PN + AD:  $\sim 4\%$
- PN – AD:  $\sim 1\%$

# Conclusions and clinical implications

Atopic dermatitis and allergic rhinitis independently increase the risk of dupilumab-associated conjunctivitis.

Both AD and AR increase DCA; **AR is the strongest *independent* predictor**, while **AD drives the largest *absolute* increase** in the matched population

Asthma shows only a modest contribution after adjustment.

The risk peaks within the first year of therapy and remains stable long-term.

## Clinical implications:

- Baseline ophthalmologic screening for patients with AD or AR before dupilumab.
- Preventive measures (artificial tears, eyelid hygiene).
- Early recognition and management of ocular symptoms during treatment.



A nighttime photograph of a historic European city square. The central focus is a large, ornate Gothic building, likely a town hall, with multiple spires and a prominent clock face. The building is illuminated from within, casting a warm glow. To the left, a row of colorful, multi-story buildings lines the street, also lit up. In the foreground, a horse-drawn carriage is visible, with a person standing nearby. The sky is dark with some clouds, and the overall atmosphere is serene and historic.

Thank you for your  
attention

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