



# Updates on Pruritic Skin Disorders

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Pennsylvania Academy of Dermatology and Dermatologic Surgery 55<sup>th</sup> Annual Scientific Meeting

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## Disclosures



Advisory board member/consultant: Abbvie, Amgen, Arcutis Biotherapeutics, Aslan Pharmaceuticals, Cara Therapeutics, Castle Biosciences, Celldex Therapeutics, Galderma, Incyte Corporation, Johnson & Johnson, Leo Pharma, Novartis Pharmaceuticals Corporation, Pfizer, Regeneron Pharmaceuticals, and Sanofi

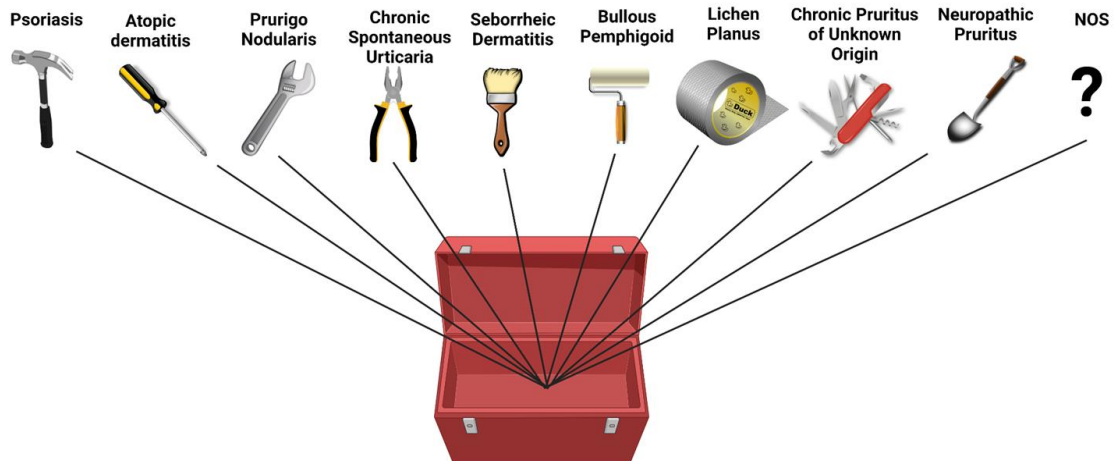
Investigator: Galderma, Incyte, Pfizer, and Sanofi.

National Secretary/Treasurer for the Skin of Color Society

National Eczema Society Scientific and Medical Advisory Council Member

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# Our treatment toolbox expands



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**Prurigo nodularis**

**Atopic dermatitis**

**Chronic pruritus of unknown origin**

**Neuropathic itch**

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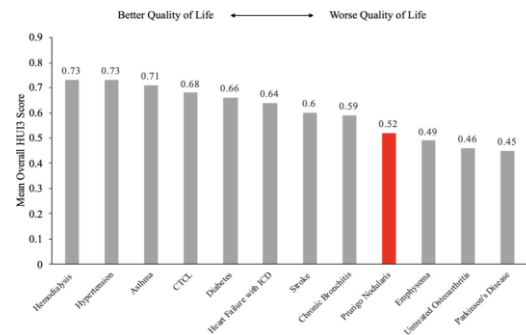
## Prurigo nodularis

Atopic dermatitis

Chronic pruritus of unknown origin

Neuropathic itch

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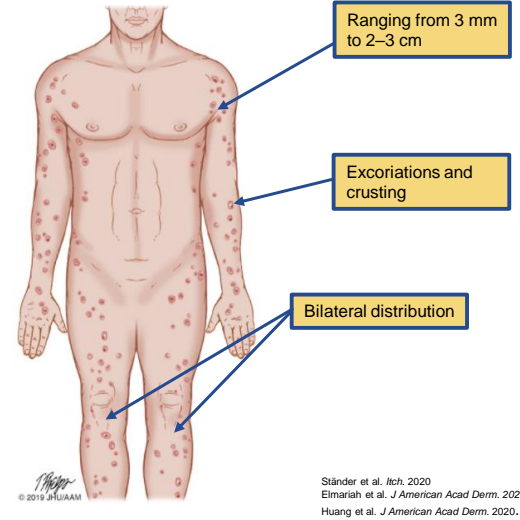
Whang et al. *J Am Acad Dermatol.* 2022.  
 Photos courtesy of Dr. Shawn Kwatra, MD

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# What is Prurigo Nodularis (PN)?

Table 1. Core symptoms and common additional features	
Variable	Description
Core symptoms	<ul style="list-style-type: none"> <li>• Presence of firm, nodular lesions</li> <li>• Pruritus lasting <math>\geq 6</math> weeks</li> <li>• History and/or signs of repeated scratching, picking, or rubbing</li> </ul>
Common additional features	<p>Signs and symptoms</p> <ul style="list-style-type: none"> <li>• Nodules are usually symmetrically distributed on areas of the skin accessible to scratching</li> <li>• Face, palms, soles, scalp, and genitals are rarely affected</li> <li>• Additional lesions induced by scratching/picking/rubbing may be present (eg, lichenified plaques, excoriations, ulcerations, and/or scars)</li> <li>• Pruritus may be accompanied by additional burning, stinging, pain, and other sensations</li> </ul> <p>Burden of disease</p> <ul style="list-style-type: none"> <li>• Impaired quality of life, sleep deprivation, missed work/school, emotional impact (depression, anxiety, anger, shame, helplessness), and social isolation</li> <li>• Associated comorbidities include impaired liver, renal, or thyroid function, diabetes, HIV or hepatitis B/C virus, and malignancy</li> </ul>

Table 2 - Diagnostic Criteria	
Core Symptoms (Major)	Chronic pruritus (≥ 6 weeks)
History and/or signs	Localized or generalized nodules and/or plaques, often with excoriations and crusting
Associated Criteria	Clinical signs
Range of clinical manifestations	Symptoms
Function	Emotions



Ständer et al. *Itch*. 2020  
 Elmanah et al. *J American Acad Derm.* 2021  
 Huang et al. *J American Acad Derm.* 2020.

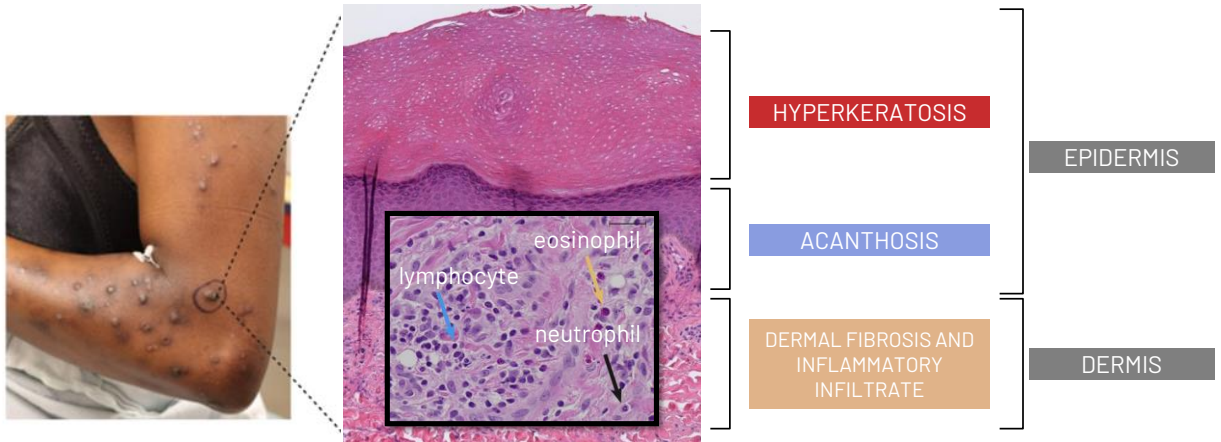
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Photos courtesy of Shawn Kwatra, MD

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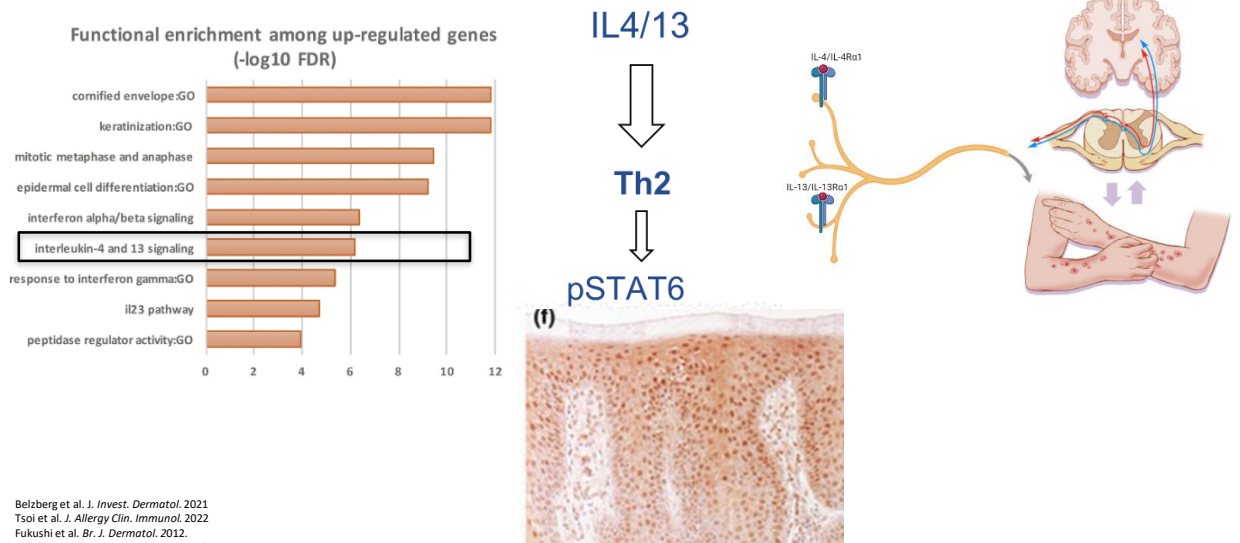
# Histologic Features of PN



Wiegelt et al. *J Cutan Pathol.* 2010.  
Belzberg et al. *J Invest Dermatol.* 2021.

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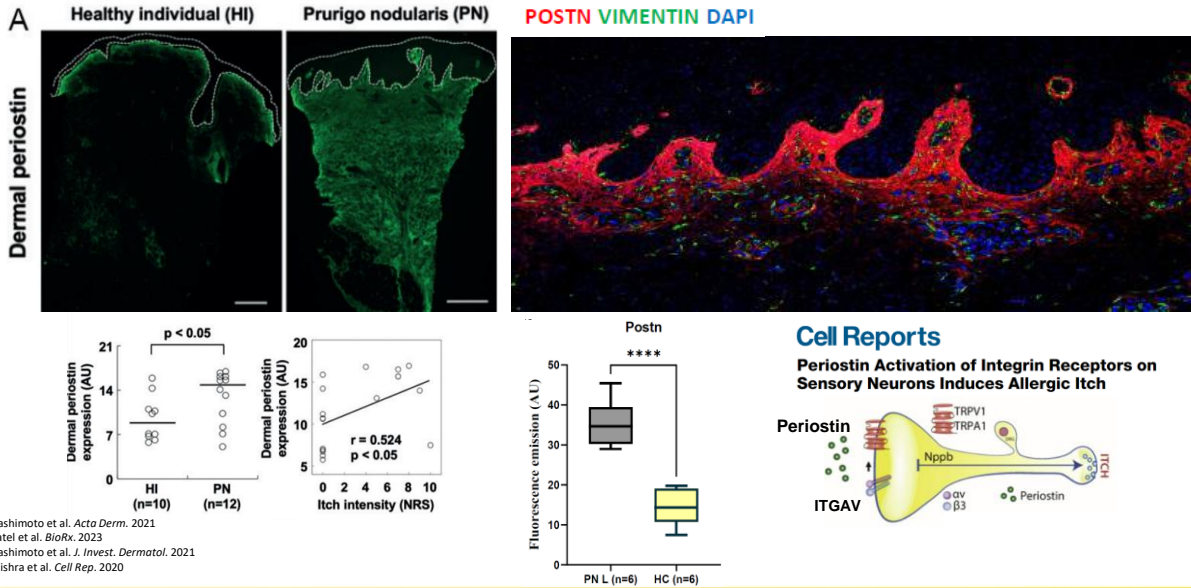
# Th2 - IL-4/IL-13



Belzberg et al. *J. Invest. Dermatol.* 2021  
Tsoi et al. *J. Allergy Clin. Immunol.* 2022  
Fukushi et al. *Br. J. Dermatol.* 2012.  
Gandhi et al. *Expert Rev. Clin. Immunol.* 2017

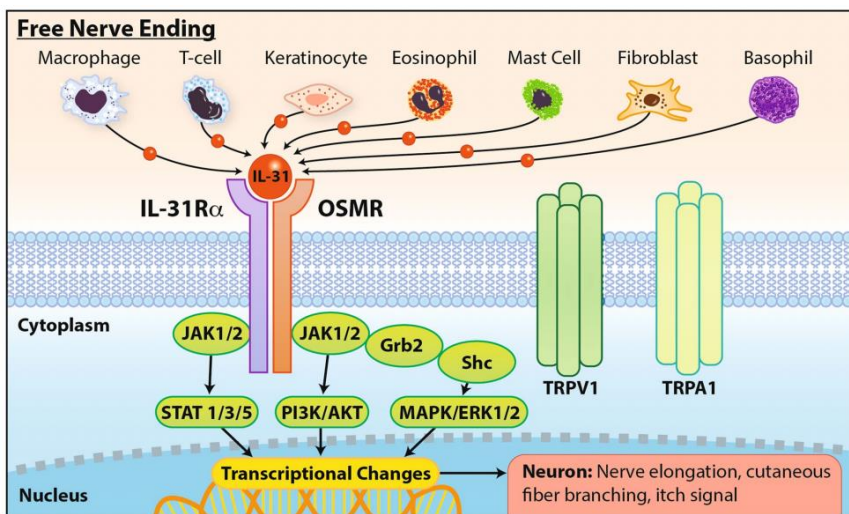
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# Periostin



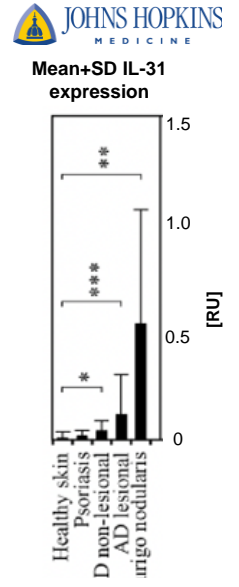
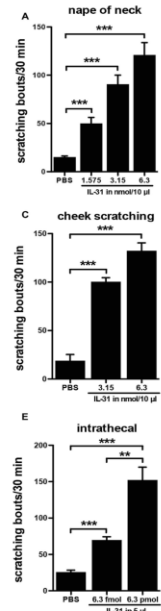
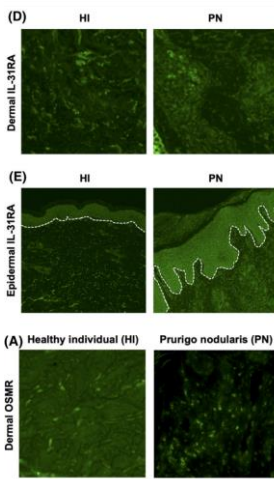
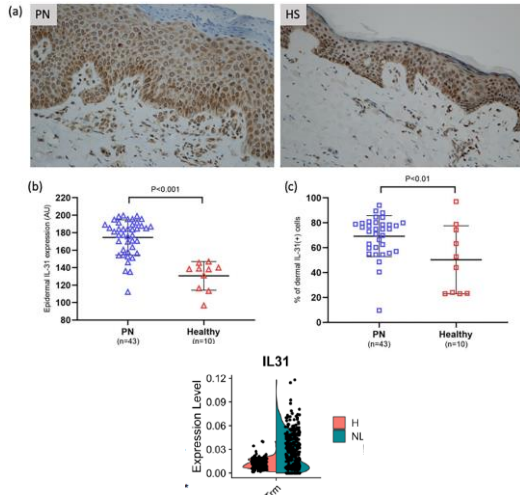
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# IL-31



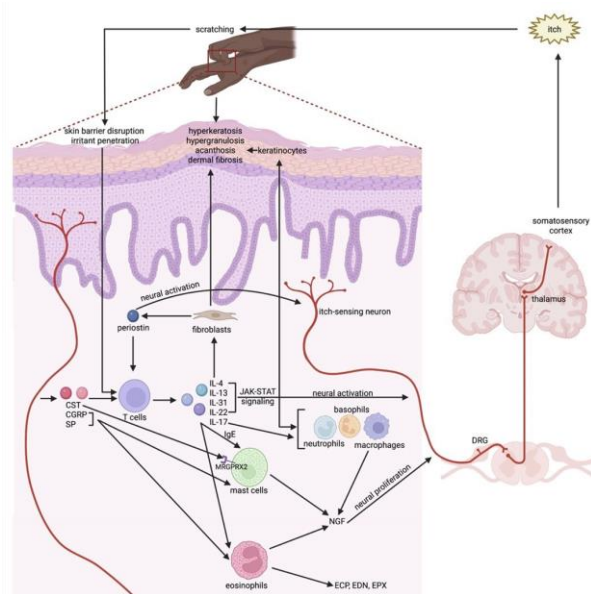
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# IL-31

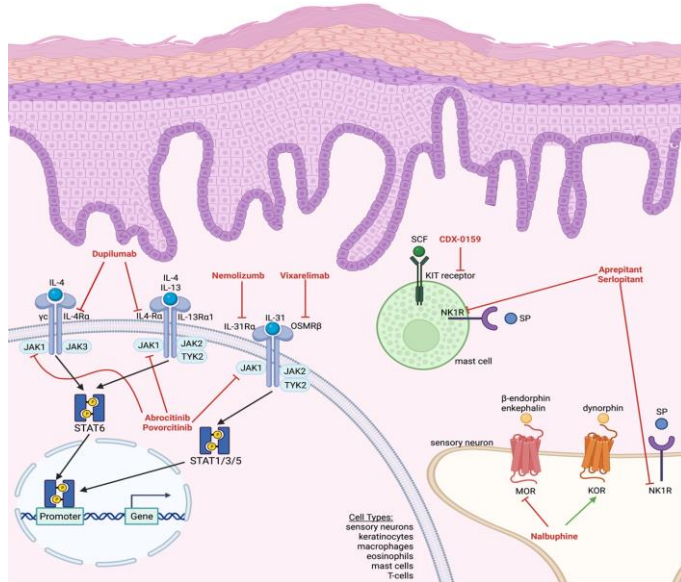


Chaowattapanit et al. *Ther. Adv. Chronic Dis.* 2022.  
 Hashimoto et al. *Experimental Dermatology.* 2020.  
 Sankoly et al. *J. Allergy Clin. Immunol.* 2006.  
 Cevikbas et al. *J. Allergy Clin. Immunol.* 2014.  
 Patel et al. *BioRx.* 2023.

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# Treatment for prurigo nodularis

	Candidate	Pre-clinical	Phase 1	Phase 2	Phase 3	Approved
Biologic Drugs	Dupilumab	[Progress bar from Pre-clinical to Approved]				
	Nemolizumab	[Progress bar from Pre-clinical to Phase 3]				
	Vixarelimab	[Progress bar from Pre-clinical to Phase 2]				
	CDX-0159	[Progress bar from Pre-clinical to Phase 1]				
NK1R Antagonist	Aprepitant	[Progress bar from Pre-clinical to Phase 2, then X]				
	Serlopitant	[Progress bar from Pre-clinical to Phase 3, then X]				
Opioid Receptor Antagonist	Nalbuphine	[Progress bar from Pre-clinical to Phase 3]				
JAK Inhibitor	Abrocitinib	[Progress bar from Pre-clinical to Phase 2]				
	Povorcitinib	[Progress bar from Pre-clinical to Phase 2]				

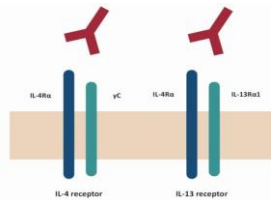
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# Biologics for PN

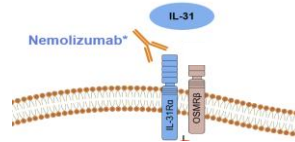
## Dupilumab

MAb binding shared alpha subunit of the IL-4 receptor to inhibit IL-4 and IL-13 signal transduction



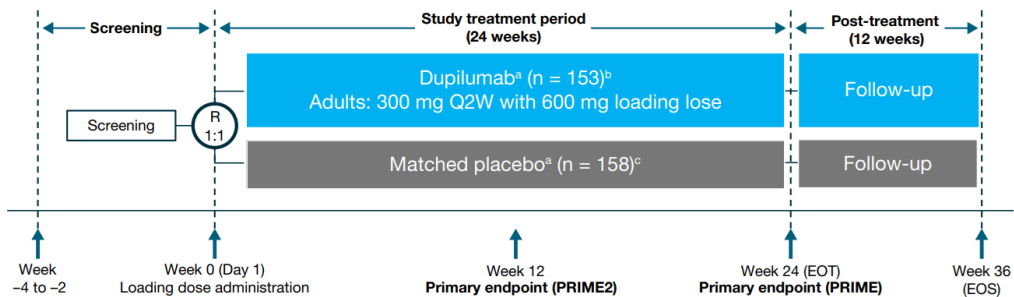
## Nemolizumab

MAb antibody targeting the alpha subunit of the IL-31 receptor



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# Dupilumab in PN study design



### Key inclusion criteria

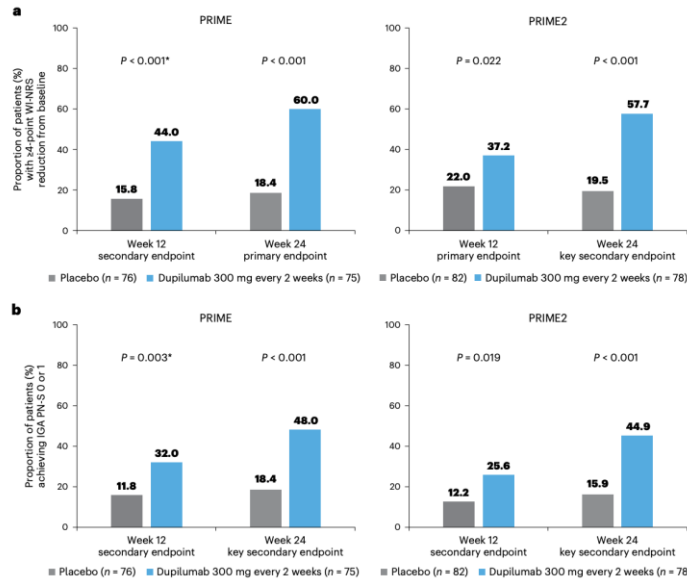
- Aged ≥ 18 to 80 years
- PN diagnosis for ≥ 3 months
- Average WI-NRS score ≥ 7 in the 7 days prior to Day 1 (daily assessed)
- ≥ 20 PN lesions at screening and Day 1
- History of failing a 2-week course of medium-to-superpotent TCS, or TCS not medically advisable
- 10% of mild active atopic dermatitis was allowed in the atopic population

### Key exclusion criteria

- Severe renal conditions
- Active chronic or acute infection (except HIV infection)
- Known or suspected immunodeficiency
- Active malignancy or history of malignancy within 5 years before baseline
- Skin morbidities (except for PN and mild AD)
- PN secondary to medications
- PN secondary to medical conditions such as neuropathy or psychiatric disease

Yosipovitch et al. Presented at RAD 2022 Virtual Conference.

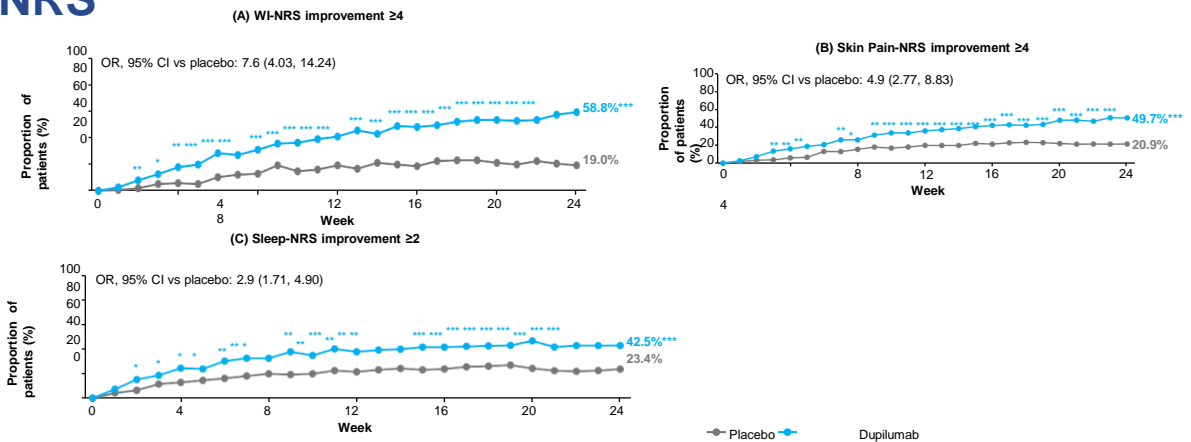
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Yosipovitch G, et al. *Nat Med.* 2023

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# Significant difference starting at Week 2 for WI-NRS and Sleep-NRS, and Week 3 for Skin Pain-NRS



\* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . OR presented at Week 24. CI, confidence interval; OR, odds ratio; WI-NRS, worst itch numerical rating scale.

Kwatra et al. Presented at AAD 2023 Meeting, New Orleans, LA.

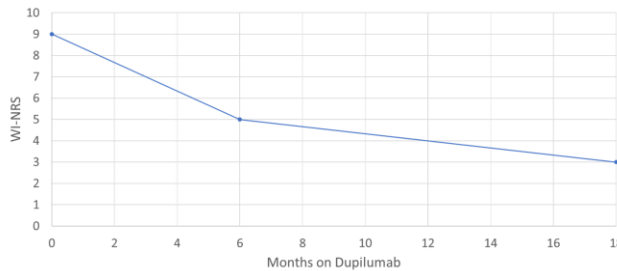
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- **HPI:** 66-year-old Asian (Indian) male with prurigo nodularis for 1.5 years
- **Severity:** WI-NRS 9, IGA 3
- **PMH:** T2DM, obesity, HLD, acute MI, systolic heart failure
- **Labs:** Eos 8.2%, IgE 614
- **Previous treatments:** triamcinolone 0.1% ointment, antihistamines
- Started on dupilumab 600 mg as initial dose → 300 mg q2wks



Photos courtesy of Shawn Kwatra, MD

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Photos courtesy of Shawn Kwatra, MD

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# Real-world experience

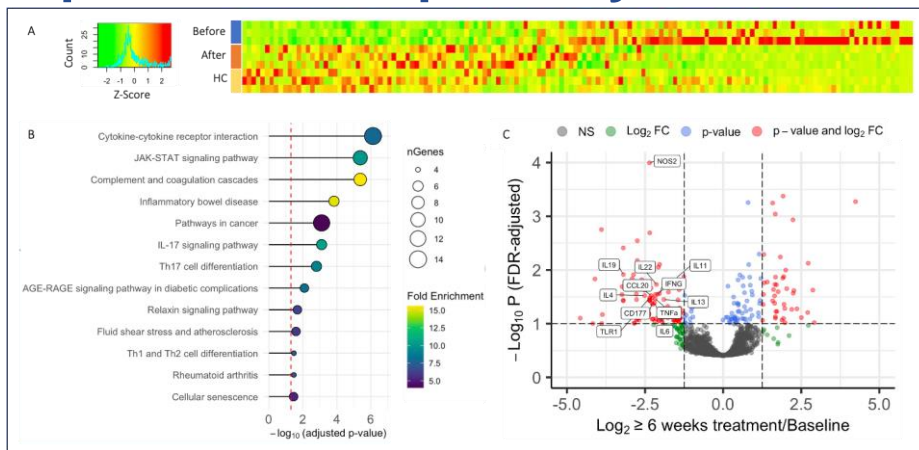


Characteristic	Patient 1	Patient 2	Patient 3
Age	66	58	52
Sex	Asian	Caucasian	Asian
Race	Male	Female	Male
Baseline WI-NRS	9	10	10
After WI-NRS	3	3	1
Baseline IGA	3	3	4
After IGA	1	1	1
Eosinophil Percentage (%)	8.2	3.8	5.9
Abs Eosinophil count (K/ $\mu$ L)	0.67	0.3	0.49
Baseline IgE (kU/L)	614	310	94
Months on dupilumab	18	54	19

Unpublished data

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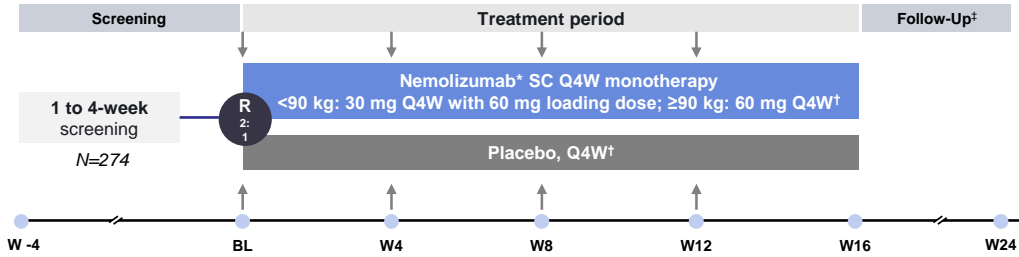
# Effect of dupilumab on cytokine protein expression and pathway enrichment in PN



Unpublished data

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# Nemolizumab Olympia 2 Study Design

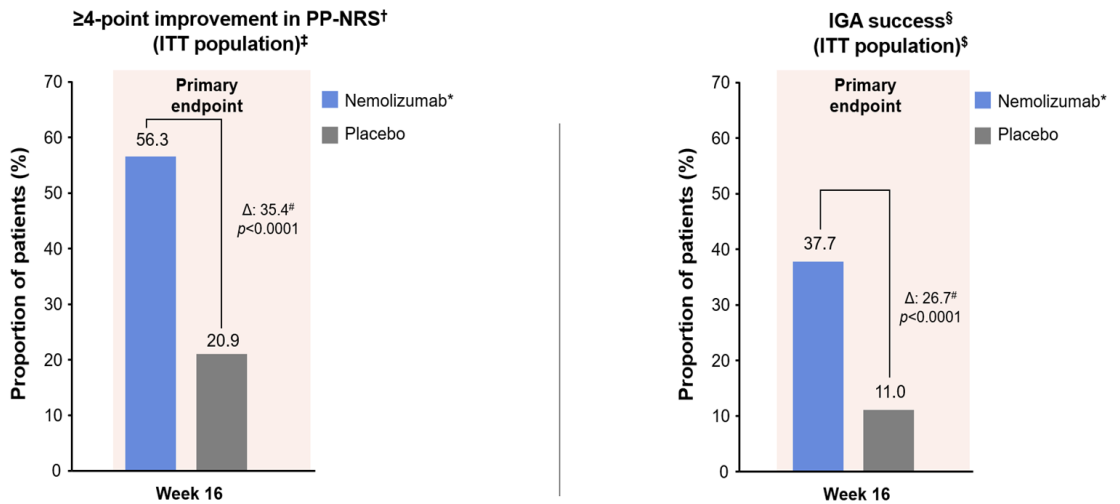


### Selected eligibility criteria

- Inclusion criteria
  - Adults (≥18 years) with prurigo nodularis for ≥6 months
  - Average PP-NRS ≥7
  - ≥20 nodules on the body with a bilateral distribution
  - IGA ≥3
- Exclusion criteria
  - Chronic pruritus resulting from another active condition other than prurigo nodularis
  - Neuropathic and psychogenic pruritus
  - Active atopic dermatitis

Kwatra et al. Presented at AAD 2023 Meeting, New Orleans, LA.

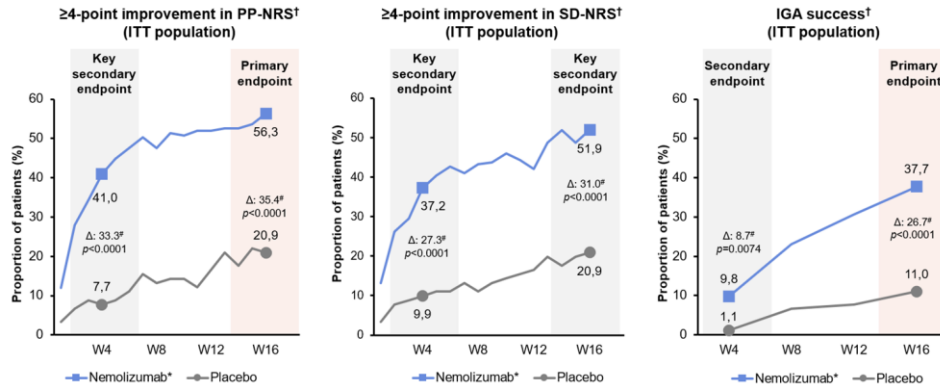
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Kwatra et al. Presented at AAD 2023 Meeting, New Orleans, LA.

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# Significant Improvements in itch, sleep disturbance and skin lesions at Weeks 4 and 16



Kwatra et al. Presented at AAD 2023 Meeting, New Orleans, LA.

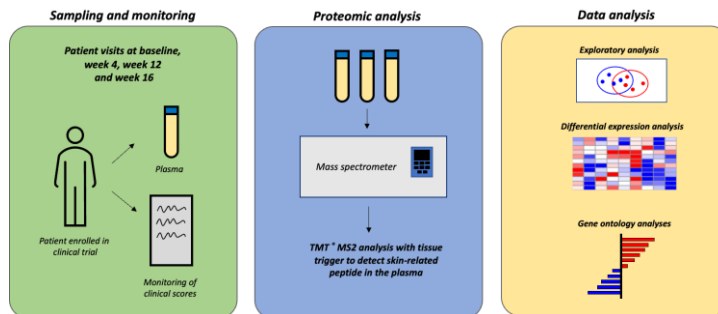
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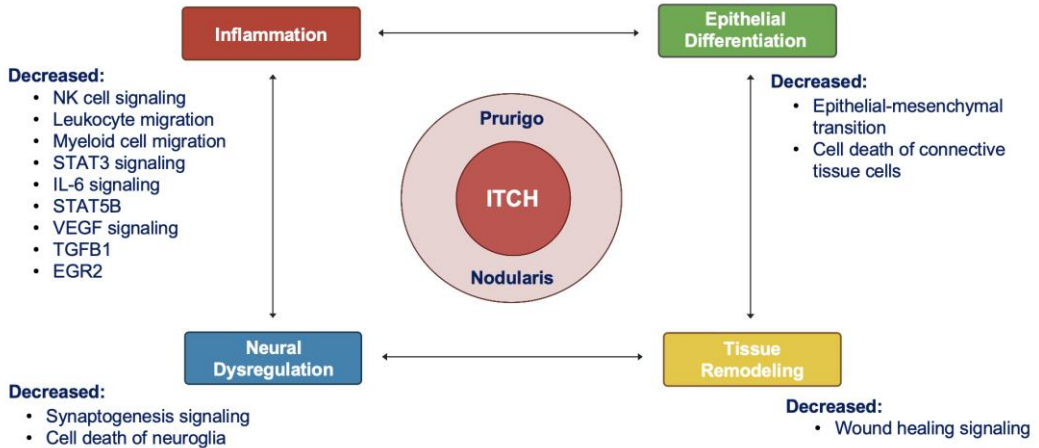
JAMA Dermatology | Original Investigation

## Modulation of Neuroimmune and Epithelial Dysregulation in Patients With Moderate to Severe Prurigo Nodularis Treated With Nemolizumab

Junwen Deng, MD; Viviane Liao, BA; Varsha Parthasarathy, MD; Hannah L. Cornman, BA; Anusha Kambala, BS; Madan M. Kwatra, PhD; Sonja Ständer, MD; Christophe Picketty, MD, PhD; Prasad Chaskar, PhD; Jayendra Kumar Krishnaswamy, PhD; Valerie Julia, PhD; Shawn G. Kwatra, MD

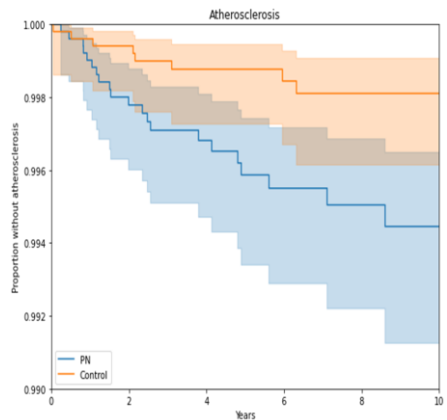


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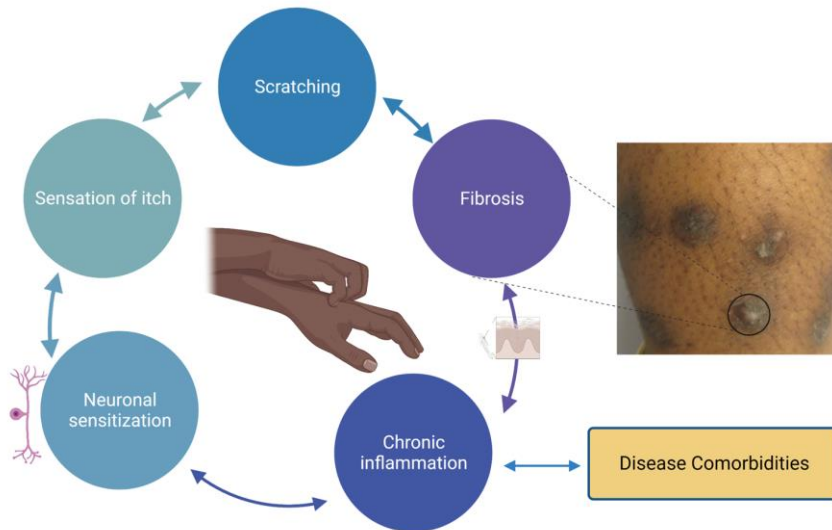
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	PN				AD				Psoriasis			
	2016	2017	2018	2019	2016	2017	2018	2019	2016	2017	2018	2019
MI (%)	1.5	2.1	2.6	3.0	0.3	0.4	0.4	0.6	1.0	1.4	1.7	2.1
CHF (%)	7.5	8.2	9.6	11.0	1.6	1.8	2.1	2.3	4.1	4.8	5.7	6.7
Peripheral Vascular Disease (%)	9.7	12.9	15.0	17.3	2.5	2.9	3.4	4.0	6.4	8.0	9.4	11.1
Cerebrovascular Disease (%)	7.6	10.1	12.5	14.2	1.9	2.4	2.8	3.3	5.0	6.8	8.0	9.2
Dementia (%)	2.9	3.3	3.9	4.1	0.7	0.7	0.8	0.8	1.2	1.4	1.5	1.8
Pulmonary Disease (%)	20.8	24.9	27.5	30.7	24.6	27.5	29.6	30.9	16.2	19.9	22.3	24.5
Connective Tissue Disease (%)	3.9	5.0	5.7	6.5	1.2	1.4	1.6	1.8	9.5	10.0	10.8	11.7
Peptic Ulcer Disease (%)	1.6	2.0	2.5	2.8	0.3	0.6	0.7	0.8	1.0	1.5	1.9	2.2
Mild Liver Disease (%)	6.6	9.6	11.7	13.6	1.4	2.0	2.7	3.3	7.2	9.2	11.2	12.8
DM (without complications) (%)	22.9	24.3	25.7	27.6	4.6	5.0	5.6	6.3	18.1	19.6	20.6	21.9
DM (with complications) (%)	8.8	10.9	12.1	14.0	1.5	1.7	2.0	2.4	5.9	6.8	8.0	9.1
Hemiplegia (%)	0.8	1.1	1.1	1.1	0.3	0.3	0.4	0.5	0.6	0.8	0.9	1.1
Renal Disease (%)	9.3	10.3	11.6	13.6	1.9	1.9	2.2	2.6	5.1	6.0	6.7	7.7
Cancer (%)	8.9	11.0	12.2	13.6	2.3	2.4	2.8	3.2	6.7	7.6	8.3	9.2
Severe Liver Disease (%)	0.7	0.7	0.7	0.8	0.0	0.1	0.1	0.1	0.6	0.7	0.7	0.8
Metastatic Disease (%)	0.9	1.1	1.3	1.7	0.2	0.3	0.4	0.4	0.9	1.1	1.2	1.3
HIV/AIDS (%)	0.8	0.9	0.6	0.7	0.1	0.1	0.2	0.2	0.3	0.4	0.4	0.4



Wongvibulsin et al. *Br J Dermatol*. 2021. Unpublished data

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## Lingering Questions about PN **JOHNS HOPKINS** MEDICINE

### • Why?

**ORIGINAL ARTICLE**

### A Polygenic Risk Score for Predicting Racial and Genetic Susceptibility to Prurigo Nodularis

Chirag Vasavda<sup>1,2,9</sup>, Guihong Wan<sup>3,4,9</sup>, Mindy D. Szeto<sup>2</sup>, Melika Marani<sup>2</sup>, Nishadh Sutaria<sup>2</sup>, Ahmad Rajeh<sup>3</sup>, Chenyue Lu<sup>3,4</sup>, Kevin K. Lee<sup>2</sup>, Nga T.T. Nguyen<sup>3</sup>, Waleed Adawi<sup>2</sup>, Junwen Deng<sup>2</sup>, Varsha Parthasarathy<sup>2</sup>, Zachary A. Bordeaux<sup>2</sup>, Matthew T. Taylor<sup>2</sup>, Martin P. Alphonse<sup>2</sup>, Madan M. Kwatra<sup>5</sup>, Sewon Kang<sup>2</sup>, Yevgeniy R. Semenov<sup>3,10</sup>, Alexander Gusev<sup>6,7,10</sup> and Shawn G. Kwatra<sup>2,8,10</sup>

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# Lingering Questions about PN

- Is all PN the same?

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## Is all PN the same?



African American

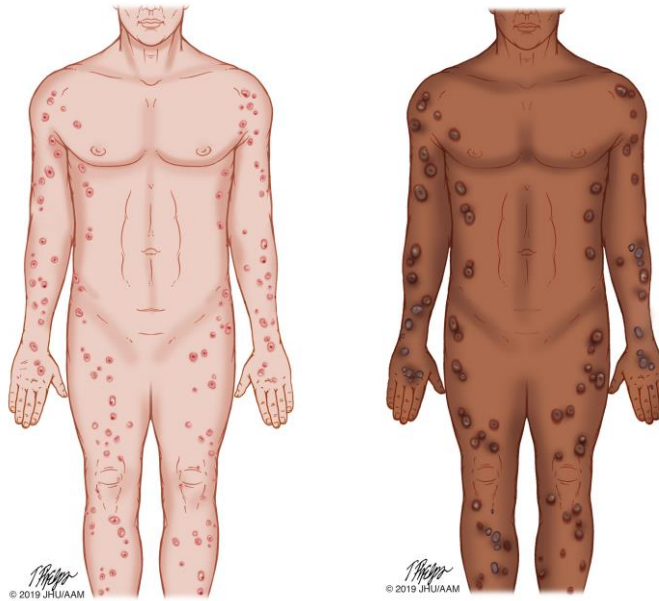


Caucasian

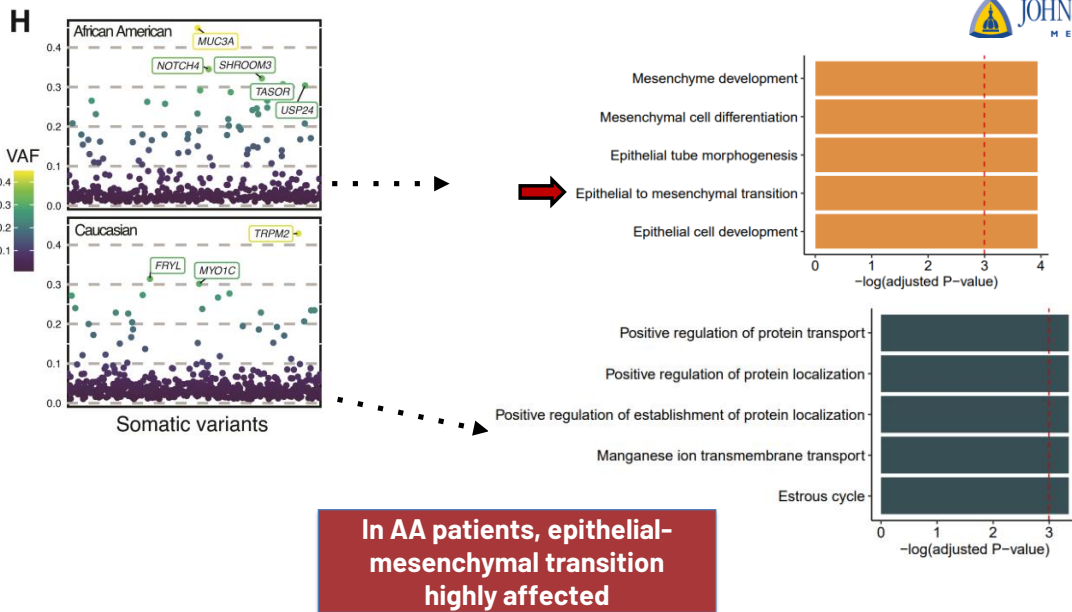


Photos courtesy of Dr. Shawn Kwatra, MD

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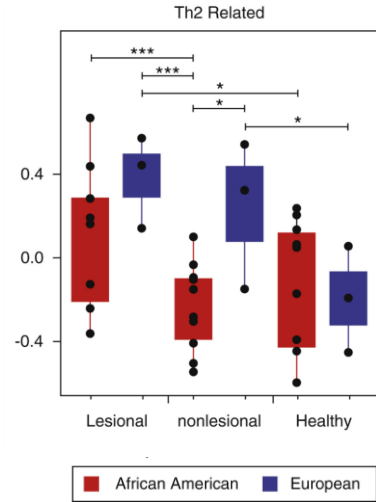
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Rajah et al. Under review.

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# Endotypes in PN



Sutaria et al. *J Invest Dermatol.* 2021.  
Belzberg et al. *J Invest. Dermatol.* 2021

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# Endotypes in PN

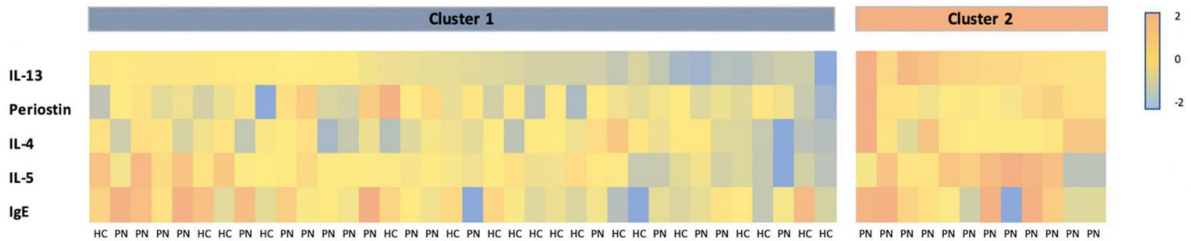
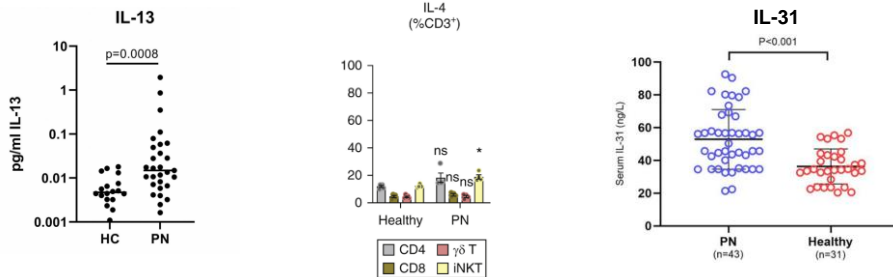


Cluster	Race	WI-NRS	DLQI	Myelopathy
1	33% AA	8.3 ± 1.2	13.0 ± 4.1	67%
2	87% AA	9.5 ± 0.9	21.9 ± 6.9	18%
	<b>P = 0.0227</b>	<b>P = 0.0359</b>	<b>P = 0.0152</b>	<b>P = 0.0227</b>

Sutaria et al. *J Invest Dermatol.* 2021.

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# Type 2 inflammation in blood



Parthasarathy et al. *Front. Med.* 2022  
 Hashimoto et al. *Exp. Dermatol.* 2021  
 Belzberg et al, *J Invest. Dermatol.* 2021

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ORIGINAL ARTICLE

## The blood proteomic signature of prurigo nodularis reveals distinct inflammatory and neuropathic endotypes: A cluster analysis

Varsha Parthasarathy, BS,<sup>1</sup> Karen Cravero, PhD,<sup>2</sup> Lillian Xu, BA,<sup>3</sup> Junwen Deng, BA,<sup>3</sup> Zhe Sun, PhD,<sup>3</sup> Sarah M. Engle, MS,<sup>3</sup> Jonathan T. Sims, MD,<sup>3</sup> Angela J. Okragly, MS,<sup>3</sup> and Shawn G. Kwatra, MD<sup>3</sup>

**Background:** Prurigo nodularis (PN) is an extremely pruritic, chronic inflammatory skin disease. Little is known about systemic inflammation in PN.

**Objective:** To characterize plasma inflammatory biomarkers in patients with PN and investigate the presence of disease endotypes.

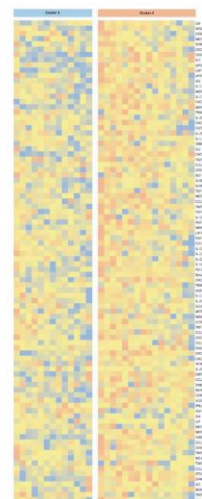
**Methods:** In this cross-sectional study, Olink proteomic analysis was performed on plasma samples from patients with PN (n = 29) and healthy controls (n = 18).

**Results:** Patients with PN had increased levels of 8 circulating biomarkers compared to controls, including tumor necrosis factor, C-X-C Motif Chemokine Ligand 9, interleukin-12B, and tumor necrosis factor receptor superfamily member 9 (P < .05). Two PN clusters were identified in cluster 1 (n = 13) and cluster 2 (n = 16). Cluster 2 had higher levels of 25 inflammatory markers than cluster 1. Cluster 1 had a greater percentage of patients with a history of myelopathy and spinal disc disease compared with cluster 2 (69% vs 25%, P = .05). Patients in cluster 2 were more likely to have a history of atopy (38% in cluster 2 vs 8% in cluster 1, P = .09).

**Limitations:** Small sample size precludes robust subgroup analyses.

**Conclusion:** This study provides evidence of neuroimmune-biased endotypes in PN and can aid clinicians in managing patients with PN that are nonresponsive to traditional therapies. (*J Am Acad Dermatol* <https://doi.org/10.1016/j.jaad.2023.01.042>.)

**Key words:** clustering; endotypes; itch; multiplex; Olink; proteomic; pruritus; prurigo nodularis.



Parthasarathy et al. *J Am Acad Dermatol.* 2023.

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**Prurigo nodularis**

**Atopic dermatitis**

**Chronic pruritus of unknown origin**

**Neuropathic itch**

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- HPI: 29 yo female with AD flaring at visit 2 years ago with BSA 40%, IGA 4, and WI-NRS 10/10
- Previously managed with topical steroids, tacrolimus, NBUVB
- PMHx: none



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One year later, the patient improved on dupilumab from WI-NRS 10/10 to WI-NRS 3/10 and from IGA 4 to IGA 2.



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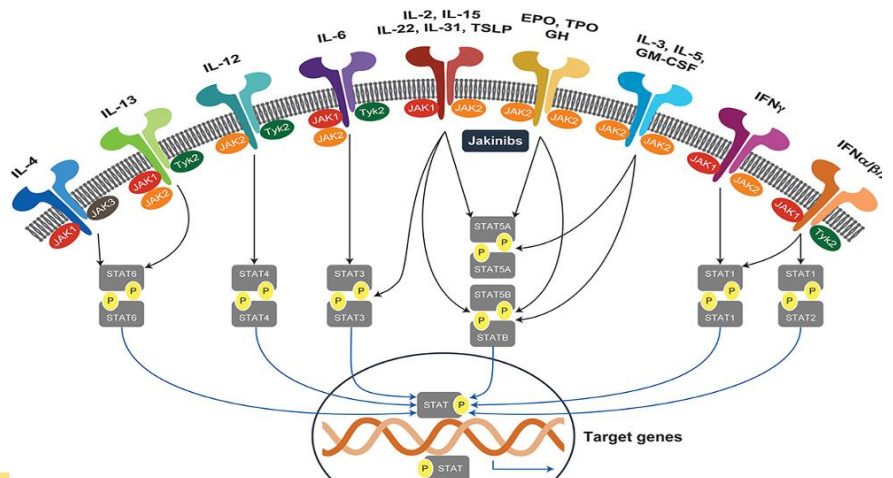
- 38-year-old African American Female presents with AD since childhood
- Failed to improve with topical corticosteroids and NB-UVB
- Had initial relief with biologic therapy, but by one year she had more flares
- At time of presentation, she had been using dupilumab 300mg q2w for 35 months. WI-NRS 10/10, IGA 3.
- Eosinophil %: 2.3 (normal)
- Eosinophil (abs): 0.16 K cells/ $\mu$ L (normal)



Photos courtesy of Dr. Shawn Kwatra, MD

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- Improved significantly after 6 months on upadacitinib 15 mg daily
- BSA <1%
- IGA 0
- NRS 0



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- **HPI:** 58-year-old Asian male
- **Severity:** WI-NRS 10, IGA 4
- **PMH:** None
- **Labs:** Eos **9.1%**
- **Previous treatments:** triamcinolone, betamethasone, clobetasol
- **Biopsy:** psoriasiform epidermal hyperplasia with confluent parakeratosis containing neutrophils and a thinned granular layer



Photos courtesy of Shawn Kwatra, MD

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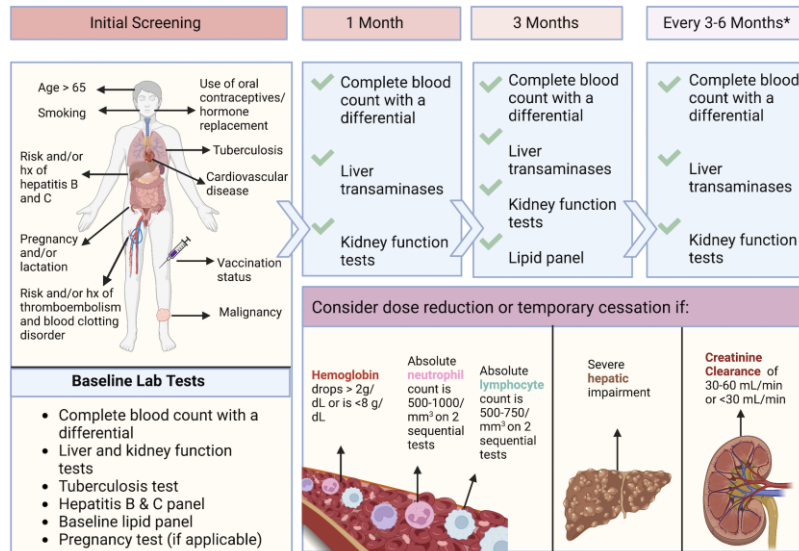
- 35-year-old Asian male presents with AD (50% BSA)
- Developed allergic conjunctivitis on biologic therapy
- WI-NRS: 7/10
- **Eosinophil %: 7.9 (elevated)**
- **IgE: 27 (elevated)**
- **Eosinophil (normal): 0.35 K cells/ $\mu$ L (elevated)**
- Started on JAK inhibitor abrocitinib 100 mg daily > 6 months later, 24hr WI-NRS is now 1/10



Photos courtesy of Dr. Shawn Kwatra, MD

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Samuel et al. *Dermatol Ther.* 2023.

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# Agenda

Prurigo nodularis

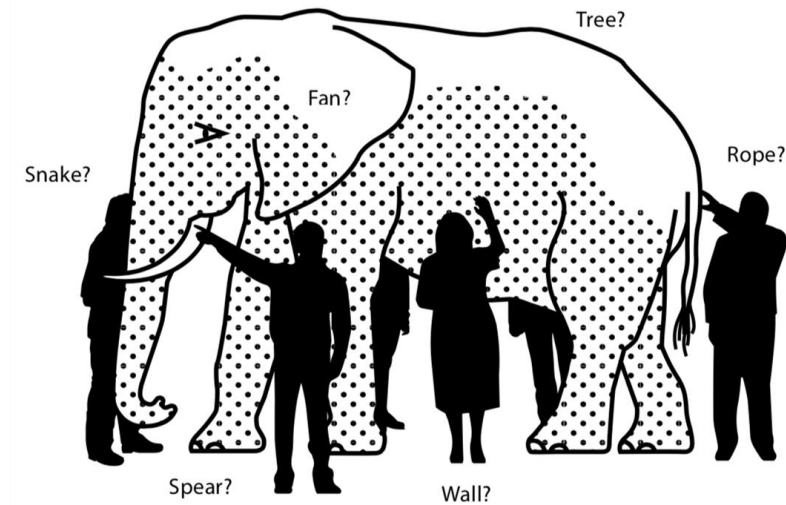
Atopic dermatitis

Chronic pruritus of unknown origin

Neuropathic itch

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# What are we even talking about?



<https://fs.blog/elephant/>

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## What is CPUO?



Open Access | Review

### Pathophysiology and Treatment of Pruritus in Elderly

by [Bo Young Chung](#) <sup>1</sup>, [Ji Young Um](#) <sup>1</sup>, [Jin Cheol Kim](#), [Seok Young Kang](#), [Chun Wook Park](#) and [Hye One Kim](#)\*

### Chronic Pruritus in the Elderly: Pathophysiology, Diagnosis and Management

[Rodrigo Valdes-Rodriguez](#), [Carolyn Stull](#) & [Gil Yosipovitch](#)

### A Literature Review of Senile Pruritus: From Diagnosis to Treatment

Caroline-Jade CLERC and Laurent MISERY  
Department of Dermatology, University Hospital of Brest, Brest, France

### Pruritus in the Older Patient A Clinical Review

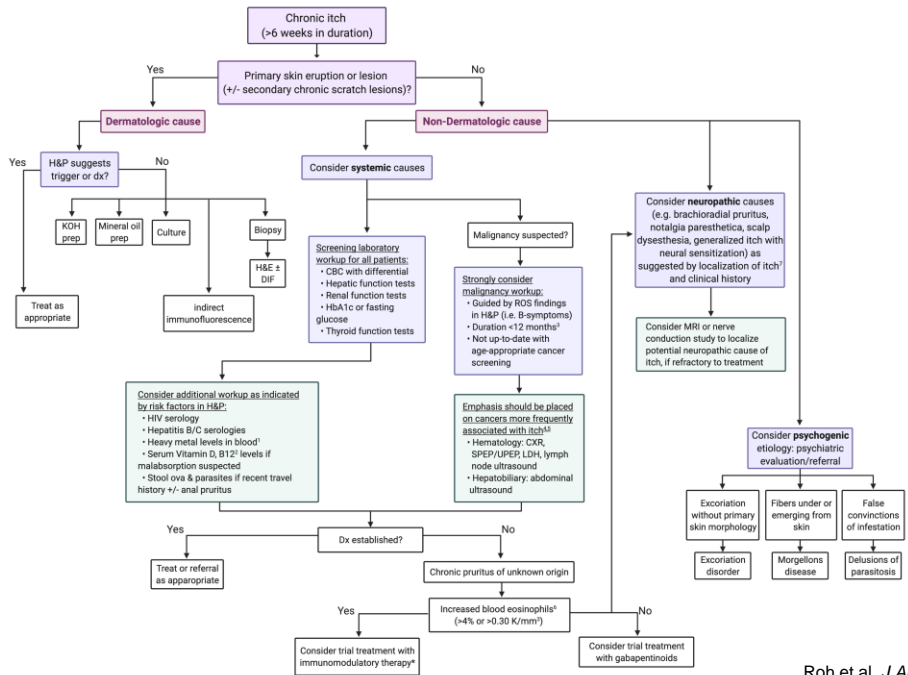
Timothy G. Berger, MD<sup>1</sup>; Melissa Shive, MD, MPH<sup>2</sup>; G. Michael Harper, MD<sup>3</sup>

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Photos courtesy of Shawn Kwatra, MD

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Roh et al. *J Am Acad Dermatol.* 2022.

54

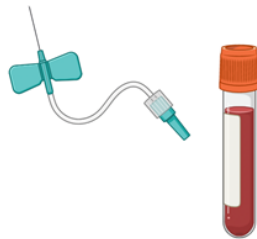
# Workup

## All Patients

- ✓ CBC with differential
- ✓ Liver function tests
- ✓ Renal function tests
- ✓ Thyroid function testing

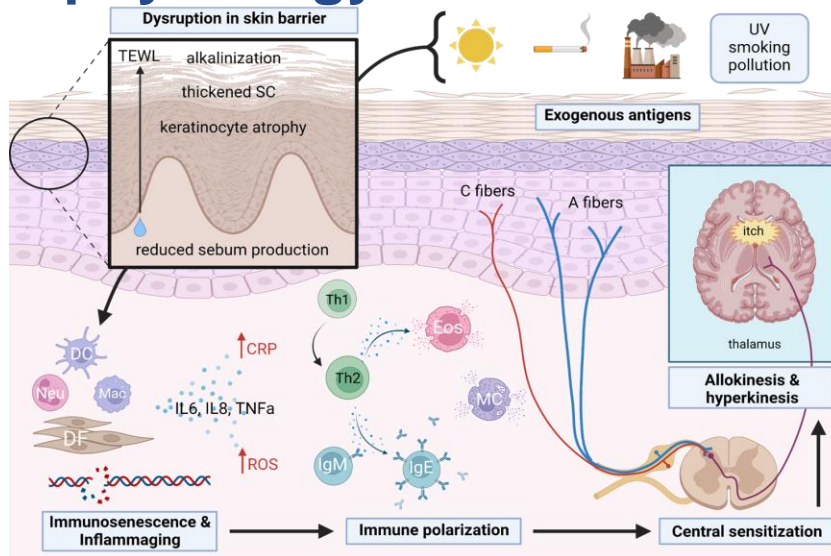
## As Indicated

- ✓ Targeted malignancy workup
- ✓ Chest x-rays
- ✓ Evaluation for gammopathies
- ✓ HIV testing
- ✓ Bullous pemphigoid testing
- ✓ Stool exam for ova and parasites
- ✓ Hepatitis B and C serologies



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# Pathophysiology



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- **HPI:** 81-year-old white female with total body itch for 2 years.
- **Severity:** WI-NRS 10
- **PMH:** CKD stage 3, depression, T2DM, CVA, HLD, HTN, gout, afib, allergic rhinitis
- **Previous treatments:** MTX, topical steroids, prednisone
- Tx off-label dupilumab 600 mg as initial dose → 300 mg q2wks



Photos courtesy of Shawn Kwatra, MD

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At 1 month of treatment, patient reported satisfactory improvement in itch and skin appearance, WI-NRS 2



Photos courtesy of Shawn Kwatra, MD

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- **HPI:** 78-year-old African American female with total body itch for 20 years
- **Severity:** WI-NRS 10
- **PMH:** lower back pain
- **Labs:** eos wnl
- **Previous treatments:** topical steroids, doxepin, hydroxyzine
- Started gabapentin 100mg TID



Photos courtesy of Shawn Kwatra, MD

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At 8 months of treatment, patient reported satisfactory improvement in itch and skin appearance, WI-NRS 0.



Photos courtesy of Shawn Kwatra, MD

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# Chronic Pruritus of Unknown Origin – role of increased blood eosinophils

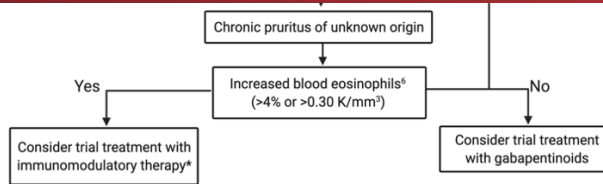
*The Journal of Allergy and Clinical Immunology:*  
**In Practice**

CLINICAL COMMUNICATIONS | ARTICLES IN PRESS

Circulating blood eosinophils as a biomarker for variable clinical presentation and therapeutic response in patients with chronic pruritus of unknown origin

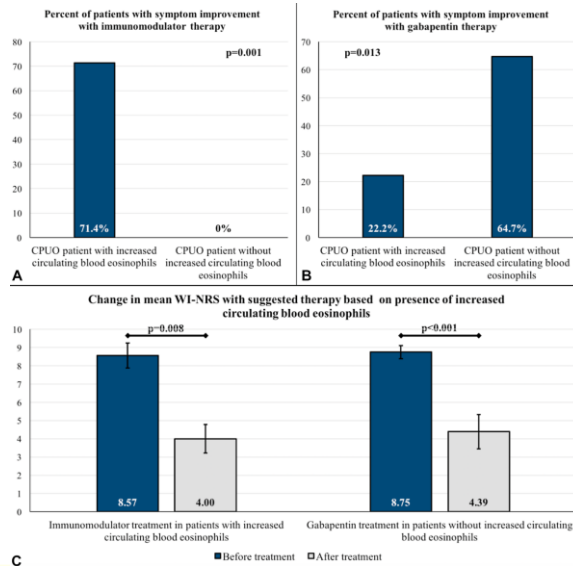
Youkyung S. Roh, BA \* • Raveena Khanna, BA \* • Sagar P. Patel, MD • ... Martin P. Alphonse, PhD • Madan M. Kwatra, PhD • Shawn G. Kwatra, MD • Show all authors • Show footnotes

Pub



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## CPUO endotypes



Roh YS et al. *J Allergy Clin Immunol Pract.* 2021

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**Prurigo nodularis**

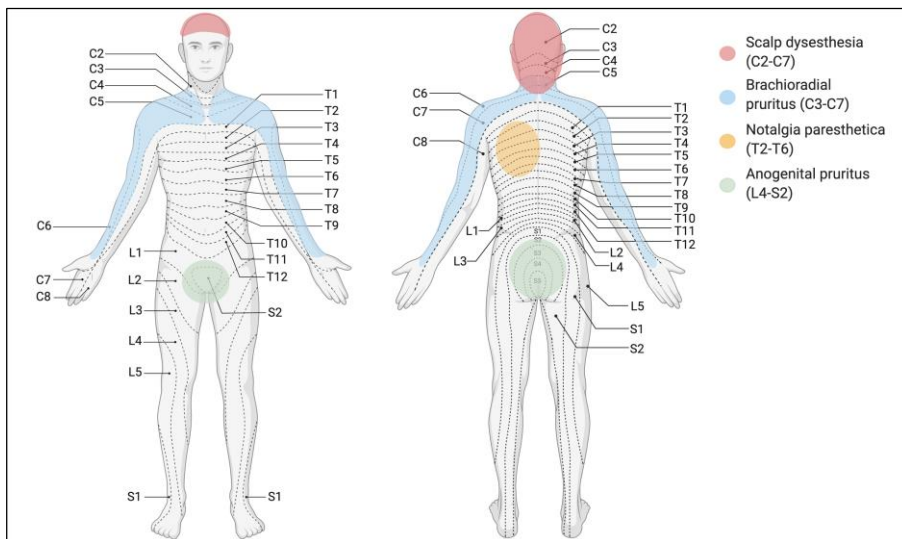
**Atopic dermatitis**

**Chronic pruritus of unknown origin**

**Neuropathic itch**

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# Neuropathic etiologies of Itch

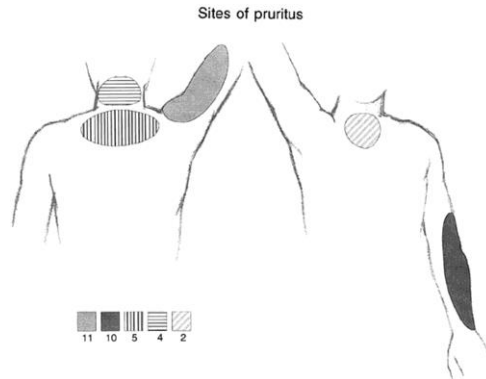


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# Brachioradial pruritus

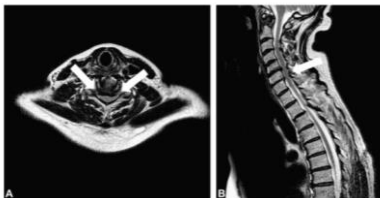
- Localized pruritus in the dorsolateral area of the arm can extend to the back and chest.



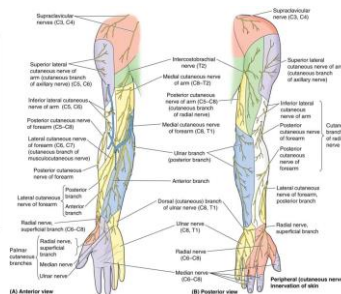
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# Brachioradial pruritus

- Stenosis of intervertebral foramen or protrusions of cervical disc C5-C7.
- Photo aggravated: tennis players
- Ice pack sign- Bernhard



Marziniak et al. *JAAD*. 2011.  
Cohen et al. *JAAD*. 2003 48: 825-8.  
Goodkin et al. *JAAD*. 2003 48: 521-4.



66

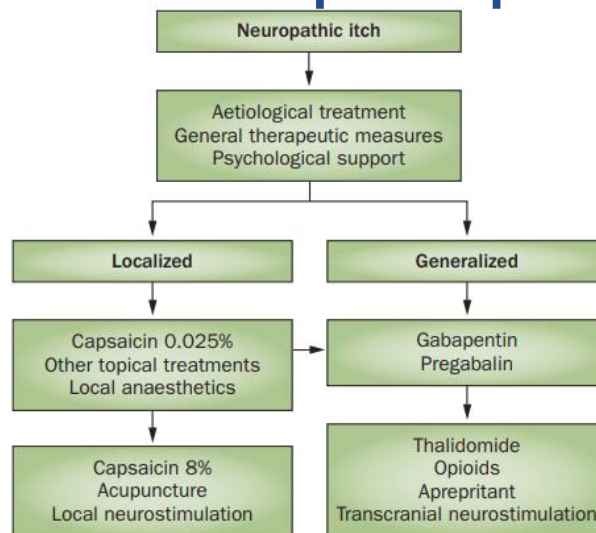
# Notalgia Paresthetica

- Localized, unilateral pruritus of the medial upper back
- Hyperpigmentation representing macular amyloidosis from chronic scratching
- Thought to be due to spinal nerve entrapment of the posterior rami of nerves arising from T2-T6
- Treatment similar to brachioradial pruritus – topical capsaicin, topical anesthetics, gabapentin, pregabalin, transeletrical nerve stimulation
- Clinical trial ongoing with oral difelikefalin (kappa opioid agonist)

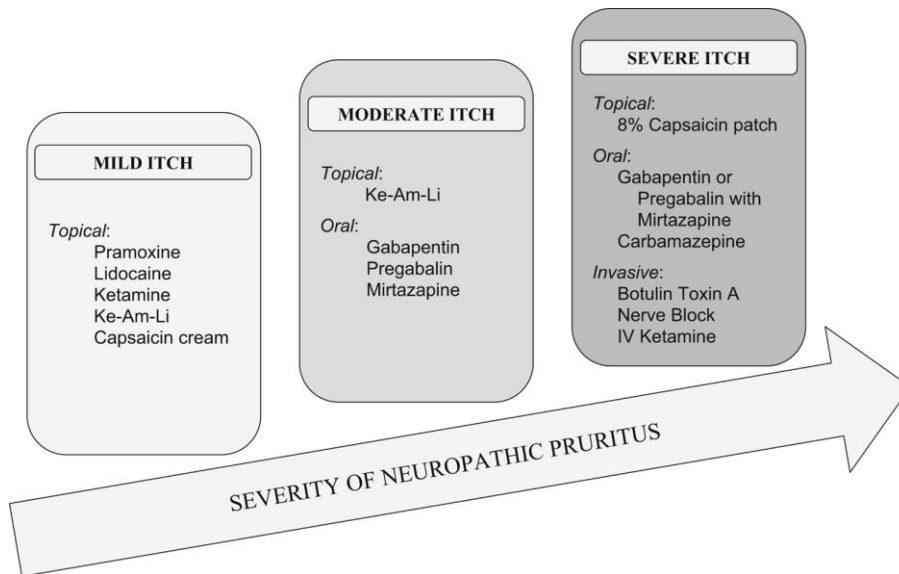


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# Treatment for neuropathic pruritus

Misery et al. *Nat Rev Neurol.* 2014.

68

Rosen et al. *Dermatologic Clinics*. 2018.

69

### REVIEW

## Gabapentin and pregabalin for the treatment of chronic pruritus

Kazuki M. Matsuda, BM,<sup>a</sup> Divya Sharma, BS,<sup>b</sup> Ariel R. Schonfeld, MD,<sup>c</sup> and Shawn G. Kwatra, MD<sup>d</sup>  
*Tokyo, Japan; Newark, New Jersey; and Baltimore, Maryland*

### CAPSULE SUMMARY

- Gabapentin 100-3600 mg daily - 300 mg 3x daily, up to 3600 mg daily (start with 100 mg dose for elderly)
- Most common SE: dizziness, drowsiness, lower extremity edema
- Dose adjusted in pt's with poor renal function

- Chronic pruritus is a distressing condition that is often difficult to manage.
- Multiple studies have demonstrated that gabapentin and pregabalin are effective for several forms of pruritus, in particular uremic pruritus and that of neural origin.
- Gabapentin and pregabalin are promising therapeutic options for pruritus refractory to conventional treatment.

- Pregabalin 75-300 mg daily (average 75 mg)
- Administer in 2-3 divided doses/day
- Most common SE: dizziness, somnolence, dry mouth, peripheral edema, weight gain

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## Antidepressants



- Paroxetine 20-30 mg daily
- Mirtazapine 7.5-15 mg nightly
- Amitriptyline 25-150 mg (divided in 1-3 doses per day)
- Sertraline 25-100 mg/daily (cholestatic pruritus)
- Doxepin 10-25 mg/qhs
- Combination paroxetine 20 mg/day and doxepin 10 mg nightly
- SE: drowsiness, dizziness somnolence most common

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JAMA  
Dermatology



## Ketamine Infusions for Treatment-Resistant Neuropathic Pruritus

Shawn G. Kwatra, MD<sup>1</sup>; Anusha Kambala, BS<sup>1</sup>; Hannah Cornman, BS<sup>1</sup>; Sriya V. Reddy, BS<sup>1</sup>; Steven P. Cohen, MD<sup>2</sup>

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*JAMA Dermatol.* Published online August 2, 2023. doi:10.1001/jamadermatol.2023.1772

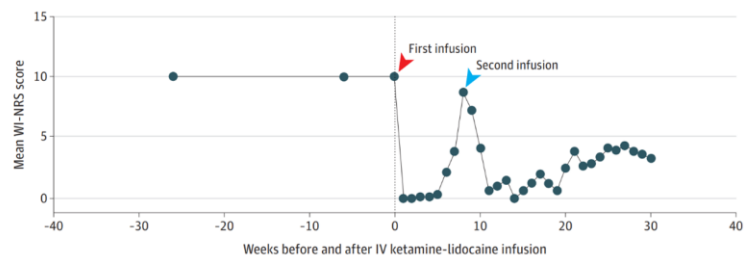
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- **HPI:** 56-year-old female with brachioradial pruritus/notalgia paresthetica for 3-4 years
- **Severity:** WI-NRS 10
- **Previous treatments:** No relief with butorphanol, topical steroids, topical pramoxine, gabapentin 1800 mg daily, exercises and stretches. Only ice packs provide relief.



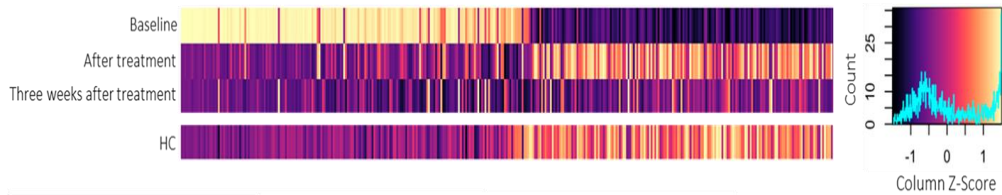
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- Received infusion of IV **ketamine** 125 mg and **lidocaine** 100 mg, along with a field block of 25 mL **bupivacaine** 0.25% injected in the bilateral forearms and posterior neck  
 → **WI-NRS 1/10** within one hour, sustained for 5 weeks.
- Repeated infusion with IV ketamine 100 mg and lidocaine 100 mg, and field block with 28 mL bupivacaine after 2 months  
 → Sustained itch reduction for **30 weeks**.



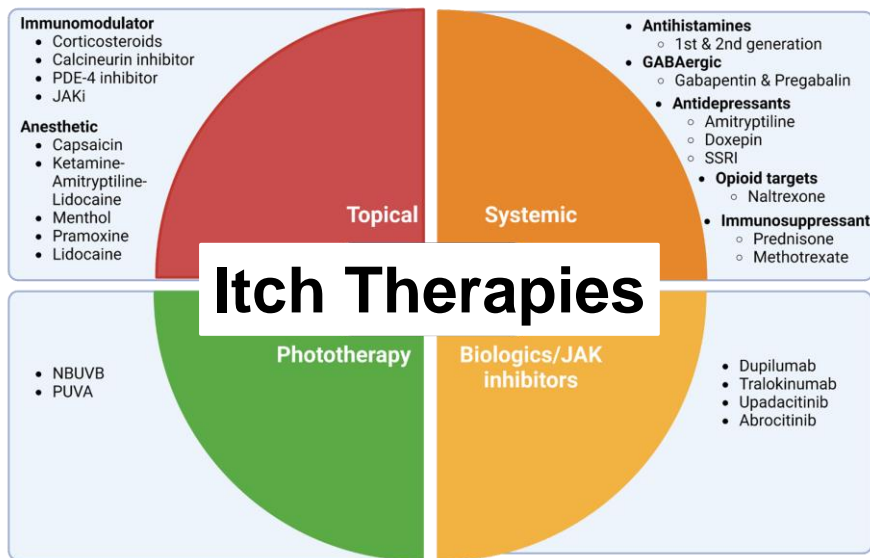
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# Ketamine infusion affected on the molecular blood signature in neuropathic pruritus



Unpublished data

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## Next Steps...



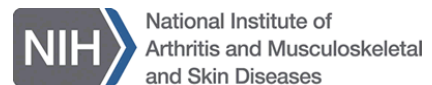
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