Comparison between dupilumab and oral Janus kinase inhibitors in the treatment of prurigo nodularis with or without atopic dermatitis in a tertiary care center in Singapore

To the Editor: Prurigo nodularis (PN) is a highly pruritic chronic skin disease with unknown pathophysiology. New evidence has suggested that antagonists of T-helper 2 cytokines and Janus kinase (JAK) inhibitors could be used as treatment.[1] Dupilumab has recently been approved for treatment of PN but evidence remained limited.[2,3] reports of oral JAK-inhibitors for PN are also uncommon. We therefore aim to assess and compare the treatment efficacy of dupilumab and oral JAK-inhibitors for PN with or without atopic dermatitis (AD) in a real-world clinical cohort.

Patients diagnosed having PN (with or without AD) by dermatologists and received either dupilumab or oral JAK-inhibitors at a tertiary skin center in Singapore from 01 January, 2018 to 30 September, 2022 were analyzed. Demographics, comorbidities, treatment regimen, prior treatment details, body surface area (BSA), Worst Itch Numerical Rating Scale (WI-NRS), and retrospective charting of Investigator's Global Assessment for PN-Stage (IGA PN-S) according to number of nodules were recorded. Response was defined as a WI-NRS reduction of ≥4 or IGA PN-S score of 0 or 1 assessed at Week 12 to 16.[2] Subjective improvements were documented (Table I).

Thirty-six PN patients received dupilumab (300 mg fortnightly) and 13 patients had oral JAK-inhibitors. Ten patients had baricitinib (2-4 mg daily) while the remaining 3 had upadacitinib (15 mg daily). Overall, mean age of patients was 45.6 ± 20.0 years. Majority were male (63.3%) and ethnic Chinese (91.8%). Most PN cases (75.5%) also had concurrent AD. Patients on dupilumab were significantly more likely to have atopy but less likely to have previous oral immunosuppressants than those on JAK-inhibitors (Table I). While baseline BSA and itch scores differed, both groups achieved similar response targets. At week 12-16, the ≥4-point reduction in WI-NRS of the dupilumab group was achieved by 60.0%, versus 58.3% in the JAK-inhibitors group ($P = .921$). An IGA PN-S score of 0 or 1 was achieved by 40.0% in the dupilumab

Table I. Comparison of prurigo nodularis patients treated with dupilumab or oral JAK inhibitors

	Dupilumab (n = 36)	Oral Jak inhibitors (n = 13)	P value
Age (mean, years)	42.7 ± 20.6	53.7 ± 16.4	.087
Female (%)	27.8	61.5	***.045***
Race (%)			
Chinese	88.9	100	.455
Malays	8.3	0	
Indians	2.8	0	
With atopic dermatitis (%)	77.8	69.2	.708
Atopy history (%)	63.9	30.8	***.040***
Duration of disease (years)	14.8 ± 12.1	14.6 ± 7.37	.954
Previous treatments (%)			
Potent topical steroids	100	100	1.00
Oral prednisolone pulses	94.4	100	1.00
Intralesional steroids	22.2	30.8	.539
Liquid nitrogen	16.7	15.4	.915
Phototherapy (NBUVB, UVA1)	63.9	84.6	.293
Methotrexate	27.8	69.2	***.009***
Ciclosporin	33.3	84.6	***.001***
Azathioprine	8.3	76.9	***8.00E-06***
Mycophenolate mofetil	5.6	46.2	***.003***
Dupilumab	-	23.1	-
Others (eg, thalidomide, aprepitant, apremilast, adalimumab, acitretin, isotretinoin)	8.3	53.8	***.002***
Duration of treatment (weeks)	40.3 ± 39.8	18.5 ± 11.1	***.005***
Time to first response (weeks)	10.7 ± 13.4	3.65 ± 2.27	***.004***
Baseline BSA* (%)	19.2 ± 20.3	10.7 ± 4.57	***.023***
BSA* at Week 12-16 (%)	7.31 ± 10.5	5.92 ± 4.15	.648
Baseline itch score† (out of 10)	7.39 ± 1.20	8.46 ± 1.20	***.008***
Itch score† at Week 12-16 (out of 10)	3.31 ± 2.32	4.46 ± 2.15	.123
Itch score† reduction of ≥ 4 at Week 12-16 (%) (n = 42)	60	58.3	.921
Investigator's Global Assessment for PN-stage (IGA PN-S) at baseline (%)			.846

Continued

Table I. Cont'd

	Dupilumab (n = 36)	Oral Jak inhibitors (n = 13)	P value
0 (no nodules)	0	0	
1 (1-5 nodules)	5.6	0	
2 (6-19 nodules)	5.6	7.7	
3 (20-99 nodules)	75	76.9	
4 (over 100 nodules)	13.9	15.4	
IGA PN-S at Week 12-16 (n = 42) (%)			.381
0 (no nodules)	10	8.3	
1 (1-5 nodules)	30	16.7	
2 (6-19 nodules)	43.3	33.3	
3 (20-99 nodules)	16.7	41.7	
4 (over 100 nodules)	0	0	
IGA PN-S of 0 or 1 (%) at Week 12-16 (n = 42) (%)	40.0	25.0	.485
Adverse effects (%)	22.2	23.1	.950
Patients' subjective improvement (%)‡	72.2	76.9	.742
AD flare (%)	2.8	7.7	.464
Eye symptoms (%)	11.1	0	.562
Skin infections (Herpes, impetigo) (%)	2.8	15.4	.168
Head and neck dermatitis (%)	5.6	0	1.00

P value of less than .05 are bold and italic.
*BSA: Body surface area of prurigos and dermatitis (if any); NBUVB: narrow band UVB.
†Worst Itch Numerical Rating Scale.
‡Subjective improvements in itch or flattening of nodules.

group versus 25.0% in the JAK-inhibitors group (P = .485). However, those on oral JAK-inhibitors have a faster first response than dupilumab (3.65 ± 2.27 vs 10.7 ± 13.4 weeks; P = .004), after adjusting for confounders (P = .042). Both have similar adverse effects risk, but disease flare and skin infections seemed more common in the JAK-inhibitors group.

Our study showed good clinical improvements in itch and nodules for both treatments. These responses were higher than the LIBERTY-PN-PRIME trials which had 40.5% patients having a ≥4-point reduction in itch scores and 28.8% patients achieving IGA-PN-S score of 0 or 1 at Week 12.[2] This could be attributed to concurrent use of potent topical or intralesional steroids. This study is among the first to compare dupilumab with oral JAK-inhibitors in treating PN. It is, however, limited by a small sample size and its retrospective nature. Further insights could be extrapolated from recent head-to-head studies of dupilumab and JAK-inhibitors in the treatment of AD (Heads Up and JADE COMPARE trials).[4,5] Oral JAK-inhibitors were found be more superior than dupilumab in treatment of AD.[4,5] However, more studies could be performed to compare efficacy of these agents in PN patients only.

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Conflicts of interest

None disclosed.

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