

Association Between an Itch-Free State in Atopic Dermatitis Treated With Ruxolitinib Cream and Systemic Inflammatory Mediators

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Introduction

- Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by substantial pruritus
- Pruritus is known to substantially disrupt quality of life
- Ruxolitinib cream (selective Janus kinase [JAK]1/2 inhibitor) previously demonstrated significant therapeutic benefit in a phase 2b trial of patients with AD amenable to topical treatment

Objective

- To evaluate proteomic changes in patients with AD, eligible for topical therapy, achieving an itch-free state compared with those who do not

Methods

Patients

- 307 adults 18–70 years of age who met the inclusion and exclusion criteria were enrolled in the NCT03011892 study
 - Diagnosed with AD for ≥2 years
 - Investigator's Global Assessment of 2 or 3
 - Affected body surface area of 3–20%
- Patient-reported itch was assessed daily using a numeric rating scale (NRS; 0–10), and an itch-free state was defined as an NRS score of 0/1 at week 8
- Data and sera from 89 patients with available itch and protein data were analyzed

Samples

- A semiquantitative, broad proteomic panel of 1012 proteins was conducted using a proximity extension assay

Principal Component Analysis

- A principal component analysis (PCA) was conducted on available proteins. Patients were plotted on the first 2 dimensions of the PCA. Patients were grouped by week 8 itch score

Differential Expression

- Fold change from baseline to week 8 of 1012 proteins was evaluated for each patient, and comparisons were made between itch-free and non-itch-free patients using a 2-sample *t* test. Raw *t* test *P* values were reported
- Volcano plots show the values that were significantly differentially expressed using fold change cutoffs
- The heatmap shows values that are differentially expressed at a raw *P* value of 0.05

Figure 1. Percentage of Patients Achieving an Itch-Free State by Treatment (n = 230)

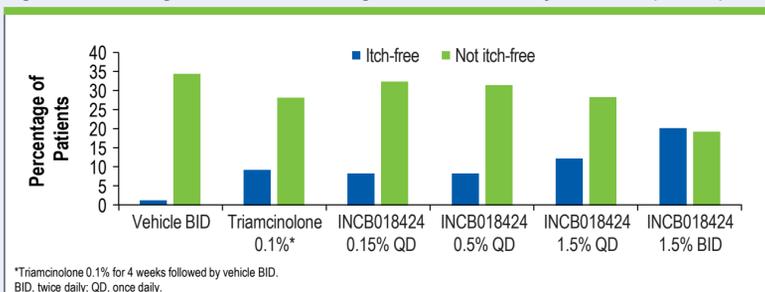
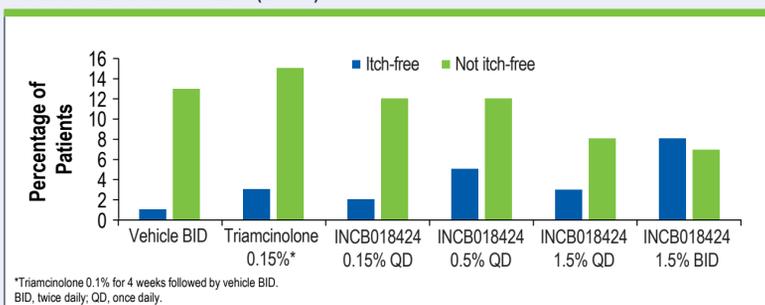


Figure 2. Percentage of Patients Achieving an Itch-Free State by Treatment With Available Serum for Broad Proteomics (n = 89)



Results

- Results of large-scale proteomics (PCA) of all 1012 proteins are shown in Figures 3A and 3B
- Patients are graphed against the 2 major dimensions of the PCA. Colors and ellipses indicate whether patients achieved itch resolution (A) and by treatment group (B)

Figure 3. Principal Component Analysis

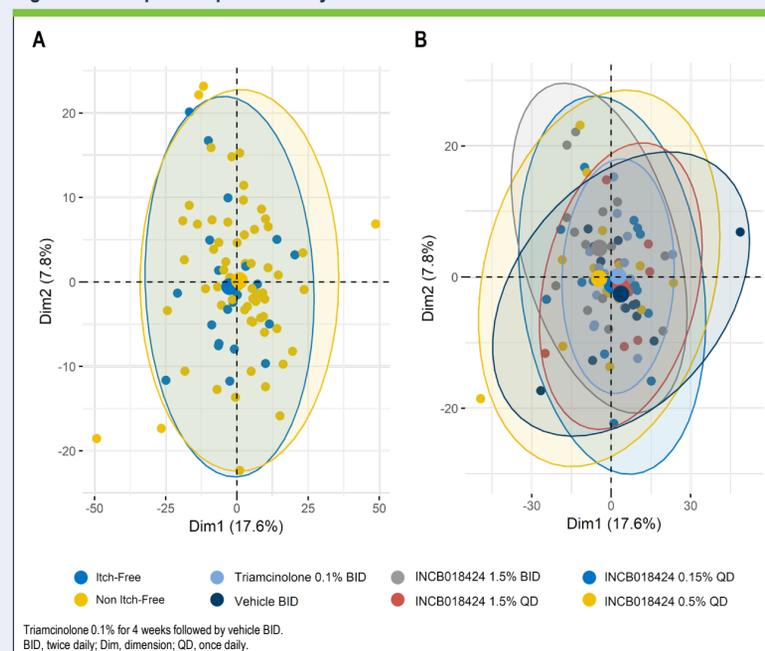


Figure 4. Volcano Plot of Differentially Expressed Proteins

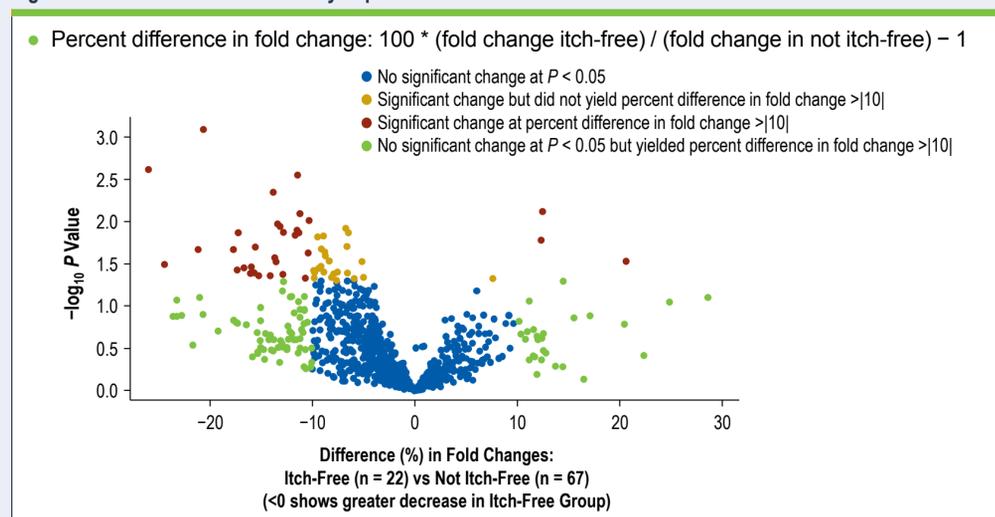


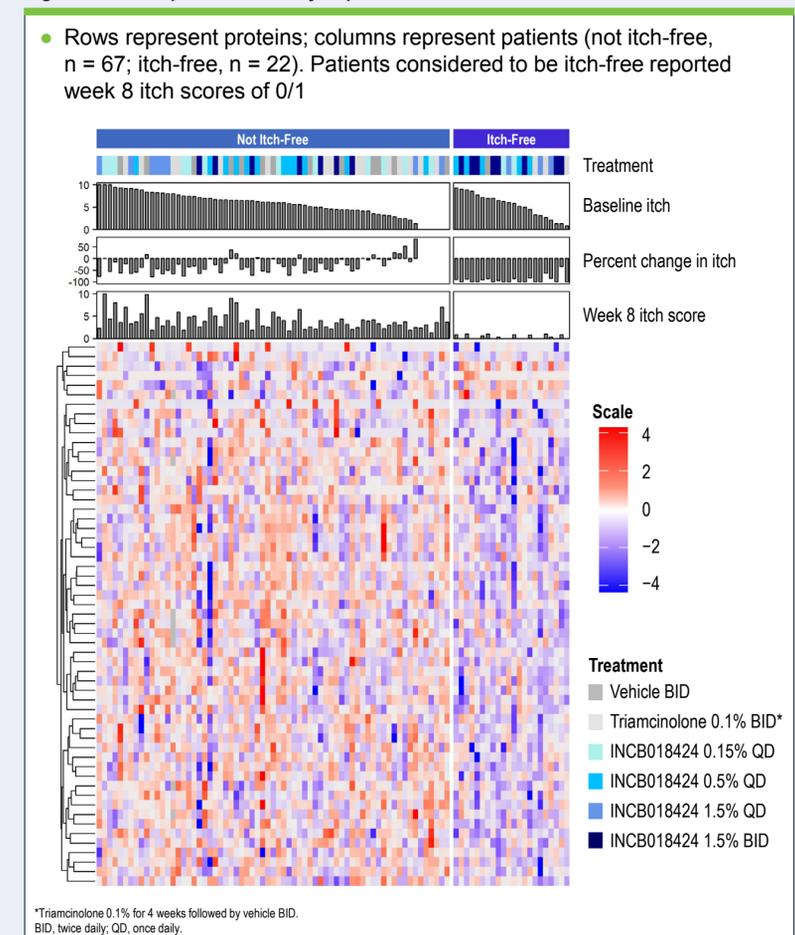
Table 1. Top 10 Differentially Expressed Proteins

Proteins	Not Itch-Free Mean Fold Change (Week 8 NRS >1)	Itch-Free Mean Fold Change (Week 8 NRS 0/1)	Raw P Value
ALDH3A1	0.82	1.11	0.002
CES2	0.78	1.03	0.031
TMPRSS15	0.83	1.05	0.021
NTF4	1.12	0.93	0.030
TYMP	0.74	0.93	<0.001
LEP	0.85	1.03	0.021
FOXO1	0.81	0.98	0.037
ALDH1A1	0.80	0.96	0.014
FADD	0.81	0.97	0.035
NPPC	0.84	1.00	0.041

NRS, numeric rating scale.

- Most significantly differentially expressed proteins from baseline to week 8 in patients achieving an itch-free state (NRS 0/1) versus those who did not (NRS >1) are presented in Table 1
- No proteins met the threshold for false discovery rate *P* value correction
- Neurotrophin-4 was the top protein listed to experience more up-regulation in itch-free patients

Figure 5. Heatmap of Differentially Expressed Proteins



*Triamcinolone 0.1% for 4 weeks followed by vehicle BID. BID, twice daily; QD, once daily.

- 53 proteins were more down-regulated in itch-free patients (n = 22) compared with those with NRS itch scores >1 at week 8 (n = 67), whereas 4 were more up-regulated

Conclusions

- Understanding the relationships between itch and proteins is of interest to patients and clinicians because it significantly impacts quality of life
- The greatest percentage of patients achieving itch-free state occurred in the 1.5% twice-daily cohort, followed by the 1.5% once-daily cohort
- Additional studies with larger numbers of patients are needed to further characterize the relationship between pruritus and inflammation

Disclosures

All authors: Employment and stock ownership – Incyte Corporation.

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