

# The 487-gene expression profile test guides systemic therapy selection to improve outcomes for patients with atopic dermatitis: Results from a prospective, multi-center trial

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## Background

Atopic dermatitis (AD) is an inflammatory skin disease driven by complex interplay between T helper (Th) type 1, 2, and 17 pathways.<sup>1</sup> Systemic therapies, including targeted biologics that target the Th2 inflammatory pathway (Th2-targeted therapies) and small molecules targeting multiple inflammatory pathways (JAK inhibitors, JAKi), have improved care for AD.<sup>2,3,4</sup> However, current therapy selection involves trial and error without considering the patient's underlying biology, resulting in inadequate disease control for up to half of patients taking systemic therapies.<sup>5</sup> An objective test measuring a patient's underlying disease biology to guide therapy selection with the goal of reducing the trial-and-error phase of therapy selection should lead to earlier treatment responses and higher proportions of patients achieving adequate disease control.

## Methods

A prospective observational study enrolled patients with AD or psoriasis. Samples were acquired via non-invasive skin scraping from affected skin lesions and analyzed by RNA sequencing. Therapy use, eczema area and severity index (EASI) outcomes, worst itch in 7 days on a 5-point Likert scale (PROMIS® Itch questionnaire) and flare frequency data were collected. A neural network ensemble algorithm (AdvanceAD-Tx, 487-GEP test) was developed using 12 inflammatory and cutaneous biology pathways containing a total of 487 genes. A training set of n=192 patients was used to create the 487-GEP, which identified patients with a Th2 Molecular Profile or a JAKi Responder Profile. The test was then validated in an independent validation cohort of patients age 12 and older receiving Th2-targeted therapies or JAKi for AD (n=112 patients). A 3-month (up to 15 weeks) endpoint was assessed.

### Figure 1. Non-invasive skin sampling technique

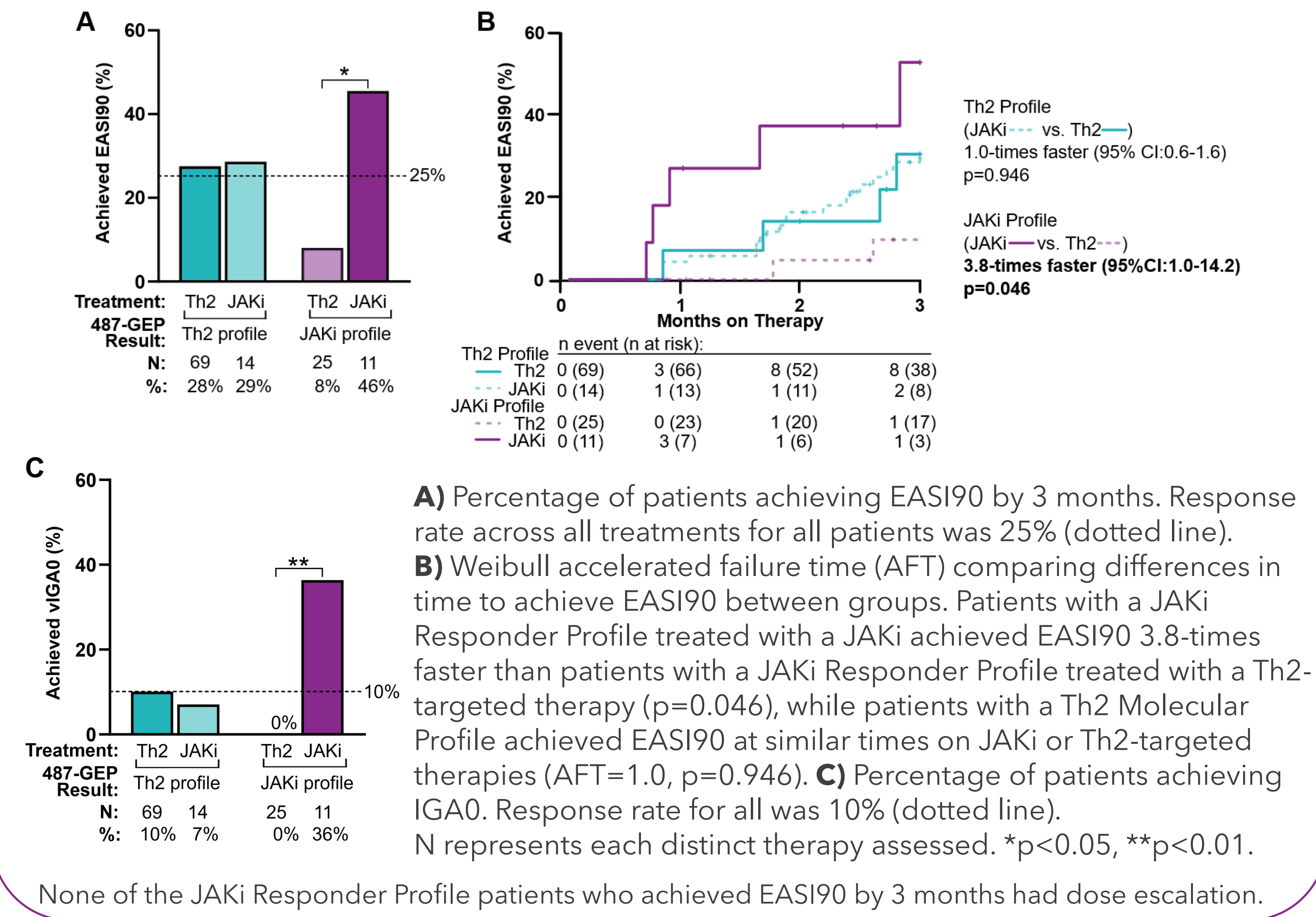


After preparation of lesion to be sampled with an alcohol swab, gently scrape the lesion with the blunt end of a curette ten times followed by a quality check to ensure the sample was collected and sample storage in RNA preserving buffer without requirement for freezing

## Objective

Develop and validate a non-invasive GEP test to guide systemic therapy selection for AD to improve health outcomes.

**Figure 2. AD patients with a JAKi Responder Profile treated with a JAKi had significantly higher rates of achieving EASI90 and IGA0 by 3 months and responded faster than those treated with a Th2-targeted therapy**



## Conclusions

In patients with AD, the 487-GEP test is predictive of **rapid** and **deep** response to systemic JAK inhibitors, thereby identifying a clinically meaningful group of patients with AD who are significantly more likely to benefit from JAK inhibitors than Th2-targeted therapies.

## References

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## Acknowledgments & Disclosures

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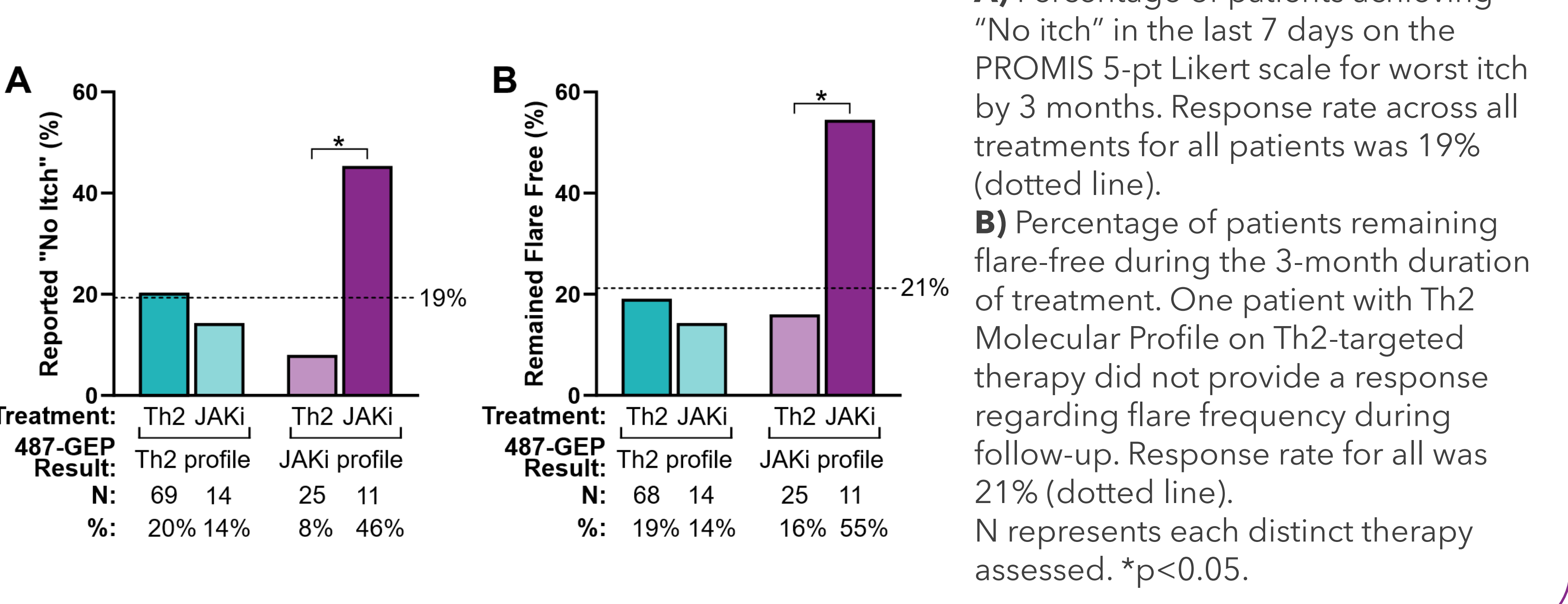
## Results

**Table 1. Patient Demographics**

Descriptor	Development (n=321)	Training Subset (n=192)	Validation (n=112)
Age, median (range) years	52 (3-84)	51 (3-84)	32 (12-79)
Sex, n (%)			
Female	159/321 (49.5%)	85/192 (44.3%)	54/112 (48.2%)
Male	162/321 (50.5%)	107/192 (55.7%)	58/112 (51.8%)
Race, n (%)*			
Asian	29/321 (9.0%)	14/192 (7.3%)	14/112 (12.5%)
Black/African American	28/321 (8.7%)	18/192 (9.4%)	12/112 (10.7%)
East/South Asian Indian	11/321 (3.4%)	8/192 (4.2%)	3/112 (2.7%)
Multiracial	9/321 (2.8%)	4/192 (2.1%)	5/112 (4.5%)
White	231/321 (72.0%)	141/192 (73.4%)	72/112 (64.3%)
Unknown/other/unspecified	13/321 (4.0%)	7/192 (3.6%)	6/112 (5.4%)
Ethnicity, n (%)			
Hispanic	37/321 (11.5%)	27/192 (14.1%)	16/112 (14.3%)

\*American Indian/Native Alaskan, Latinx, and Native Hawaiian/Pacific Islander had less than 5 each per cohort and are included in Unknown/other/unspecified.

**Figure 3. AD patients with a 487-GEP JAKi responder profile treated with a JAKi were significantly more likely to achieve "No itch" and remain flare-free**



## Clinical Impact

Use of the 487-GEP identifies systemic therapy response and clinical use may lead to improved individual patient outcomes and satisfaction.