Treatment with the oral CCR4 antagonist RPT193 results in meaningful changes in cutaneous biomarkers detected by transcriptomic profiling of tape-strips

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INTRODUCTION

- Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by cytokine activation and barrier dysfunction driven by Th2 inflammation.
- RPT193 is an oral CCR4 antagonist, inhibiting the migration and subsequent activation of Th2 T-cells.
- Here, we present biomarker data collected during a double-blinded phase 1b study evaluating the safety and efficacy of RPT193 as monotherapy.

OBJECTIVE

- To further characterize the mechanism of action of RPT193
- To assess changes in the skin transcription profile using tape-strips in RPT193- or placebo-treated AD subjects

METHODS

Study Design

Using tape-strips, we analyzed the effect of RPT193 on skin biomarkers in 30 subjects with moderate-to-severe AD subjects receiving either RPT193 400mg once daily (n=20) or placebo (n=10) for 4 weeks. Tape-strips were collected from lesional and non-lesional skin at baseline and on day 29 and analyzed with RNA-seq.

RESULTS

At baseline, 4,446 genes (1,452 up; 2,994 down) were differentially expressed between lesional and non-lesional skin across treatment arms. By Day 29, RPT193 improved expression of a subset of 174 immune genes by 45%, compared to 2.38% with placebo.

CONCLUSIONS

RPT193 induced significant changes in AD-related biomarkers in tape-stripped AD skin after 4 weeks of treatment. Transcriptional changes correlated with biopsy RNA-seq data (data not shown) and improved clinical metrics.

These data suggest that RPT193 treatment improves the AD skin transcriptome, consistent with observed clinical efficacy and with decreases in CCR4 expression in the skin and on circulating Th2 cells. A phase 2 study investigating the safety and efficacy of RPT193 in patients with moderate-to-severe AD is ongoing (NCT05399368).

REFERENCES