RPT193, a novel CCR4 inhibitor, improves clinical severity of atopic dermatitis and modulates the transcriptomic profile of lesional skin

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Emma Guttman, MD, PhD

S026- Late-breaking Research: Clinical Trials

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Disclosures:

Research support, consulting or lecture fees on atopic dermatitis from Regeneron, Sanofi, Pfizer, Galderma, Celgene, Leo Pharma, Janssen, Medimmune, Dermira, Anacor, AnaptysBio, Glenmark, Novartis, Abbvie, GSK, Sun Pharma, Mitsubishi Tanabe, Vitae, Almirall, Asana Biosciences, Amgen, Immune, Gilead, Concert, Kyowa Kirin, DS Biopharma, Ralexar, Eli Lilly, UCB, Escalier, Boehringer, Botanix, Incyte, Sienna, Innovaderm, Cara Therapeutics, Dermavant, Union Therapeutics, Kiniksa, Arena, RAPT Therapeutics, Target

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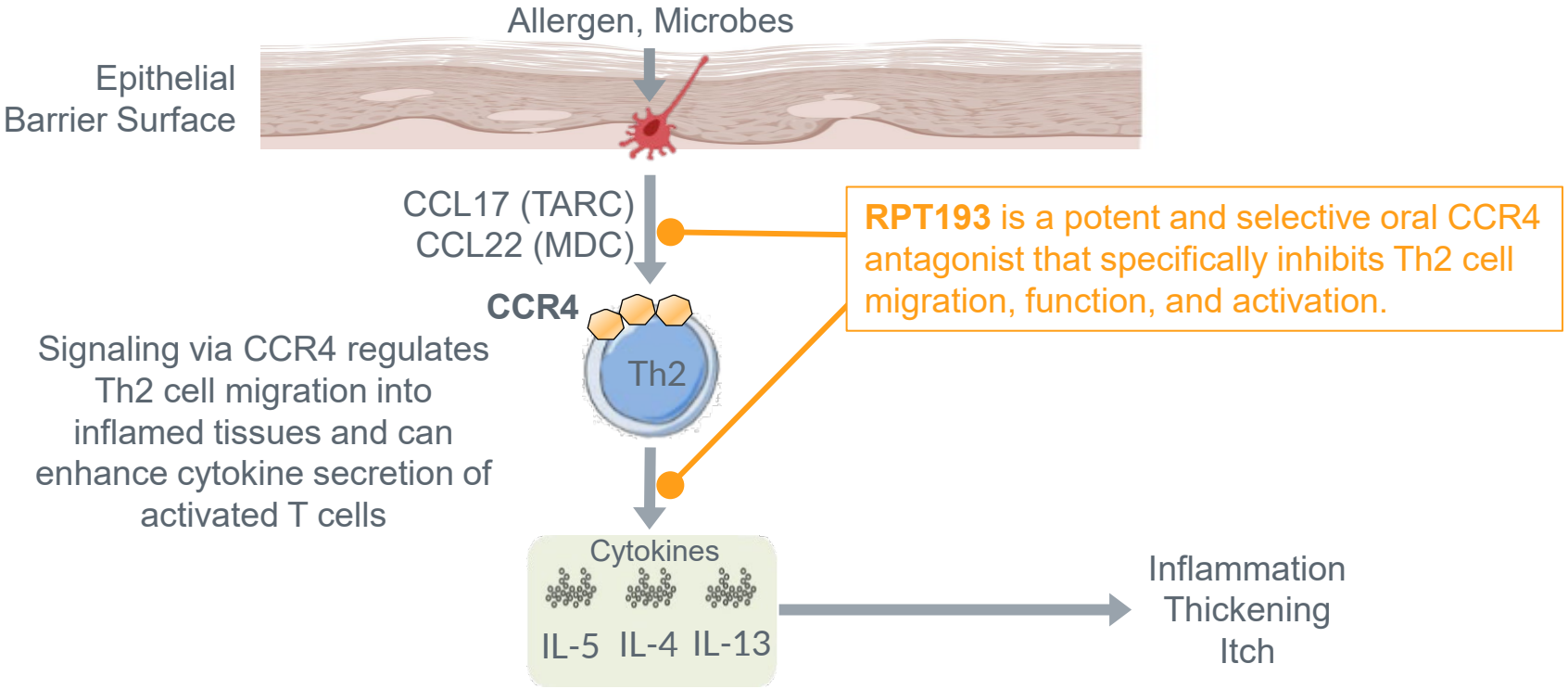
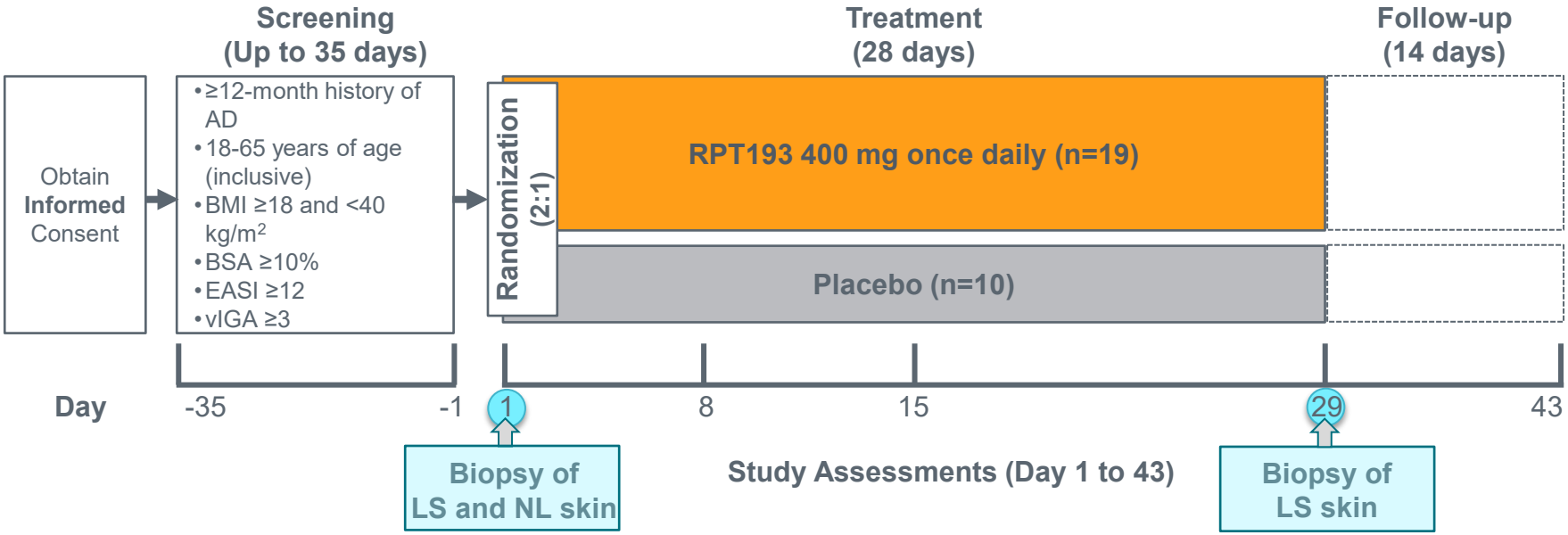
RPT193 Acts on a Well Validated Pathway in Atopic Dermatitis and Asthma

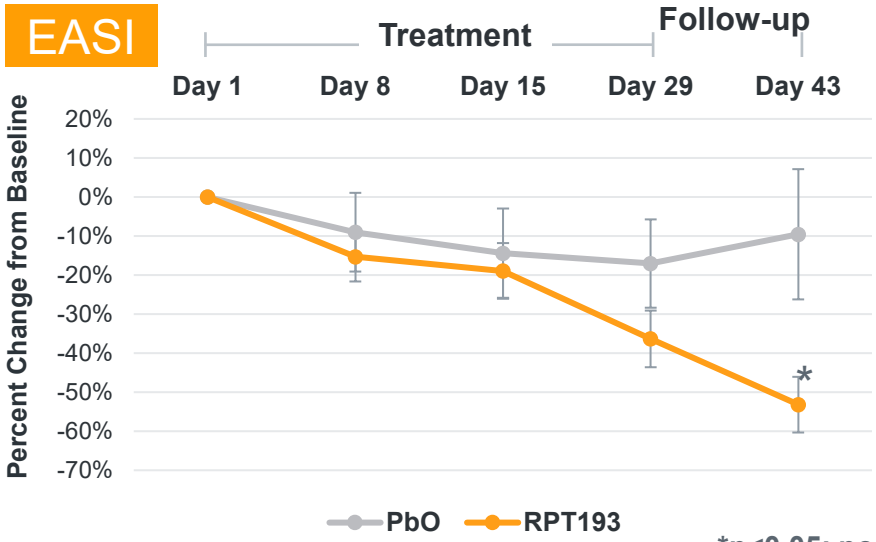


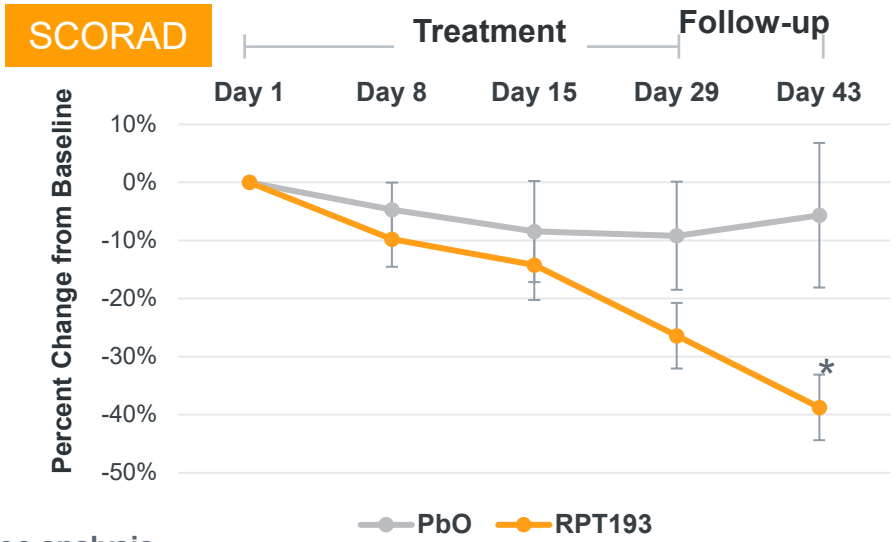
Phase 1b Trial Explored RPT193 Activity in Subjects with Moderate-to-Severe Atopic Dermatitis



- Phase 1b trial part of a broader study including healthy volunteers to investigate single and multiple doses of RPT193
- Double-blind, randomized, monotherapy study
- Primary and secondary endpoints were safety and PK
  - Trial was not powered for clinical endpoints (EASI and SCORAD were exploratory endpoints)
- In addition to skin biopsies, plasma and whole-blood biomarker assessments were performed (data not shown)

RPT193: Previously Reported Phase 1b Data





*p<0.05; post-hoc analysis

RPT193 demonstrated improvement compared to Placebo in EASI and SCORAD at Day 29 with further deepening of response at Day 43

Once-daily, oral RPT193 was generally well tolerated after 28 days of dosing

Study Population And Methods

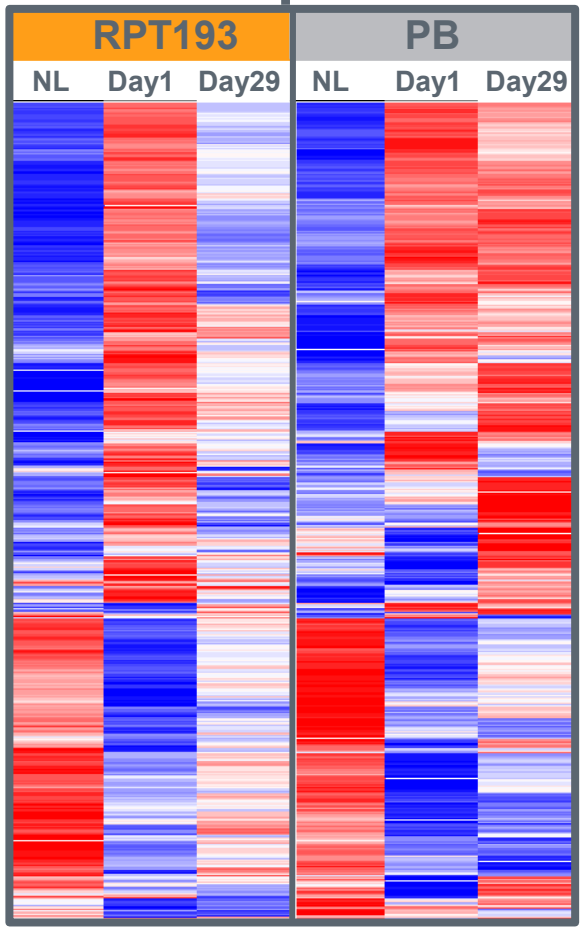
Characteristic	Placebo n=10	RPT193 n=19	P-value
Gender	F (4); M (6)	F (12); M (7)	0.27
Age (mean)	35.80	41.11	0.34
Race	AA (5); W (5); O (0)	AA (7); W (10); O (2)	0.73
EASI (mean)	21.07	17.96	0.27
SCORAD (mean)	56.62	56.44	0.97

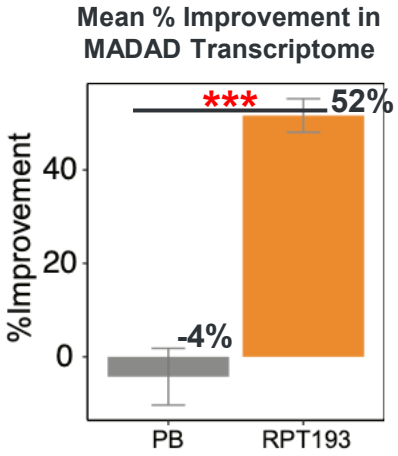
Methods:

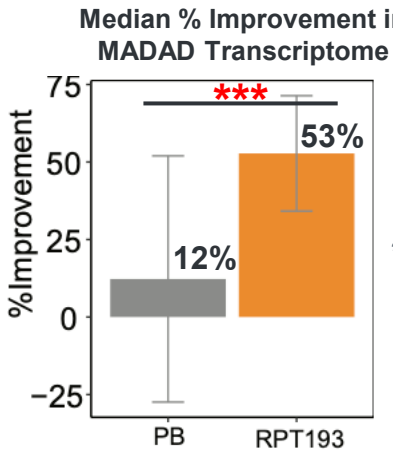
- Gene expression was evaluated using RNA-sequencing
- Pathway analysis was performed using GSVA
- Spearman correlations were used to correlate biomarkers and clinical scores

F, female; M, male; AA, African-American; W, white; O, other; EASI, Eczema Area and Severity Index; SCORAD, SCORing Atopic Dermatitis

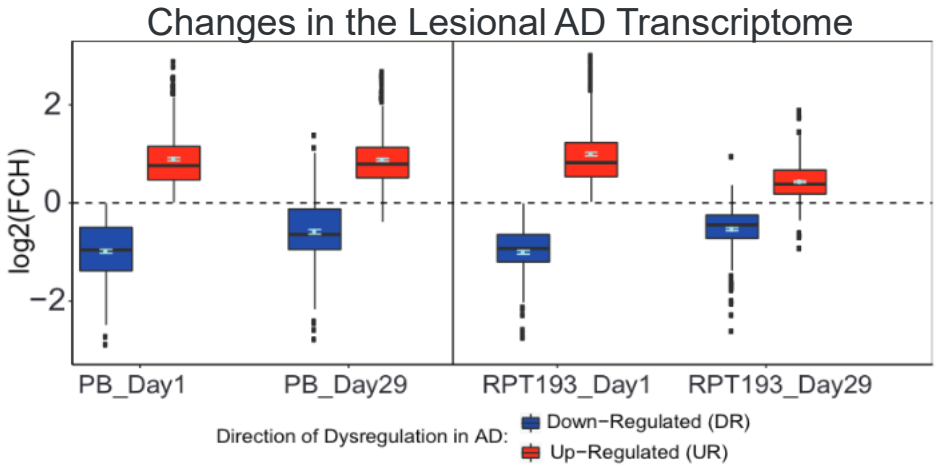
RPT193-Treated Subjects Exhibit Improvement in MADAD Transcriptome





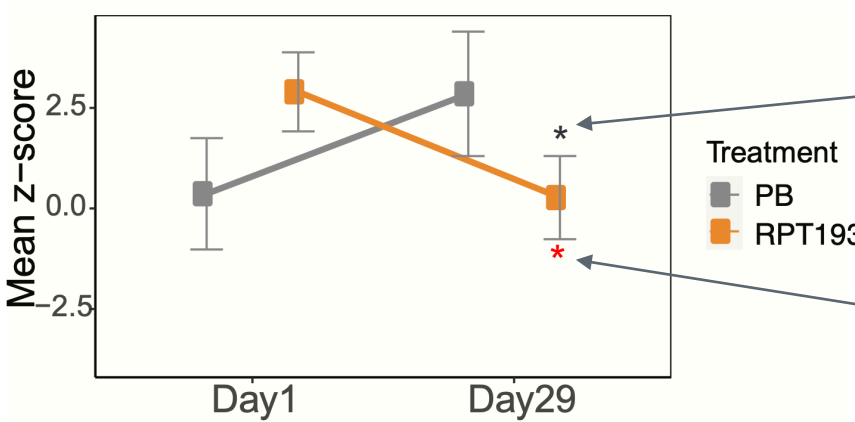


***(p<0.001)



MADAD, Th2, Th22 and Th1 Immune Pathways Show Decreases

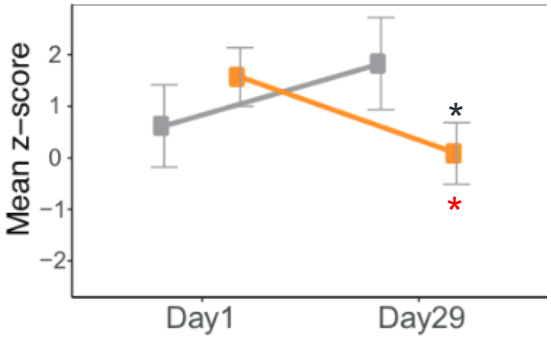
MADAD Immune Gene Set



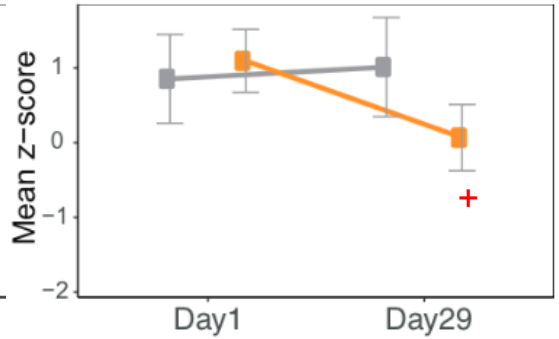
Black * indicates significance relative to baseline (same group)

red * or + indicates significance vs placebo

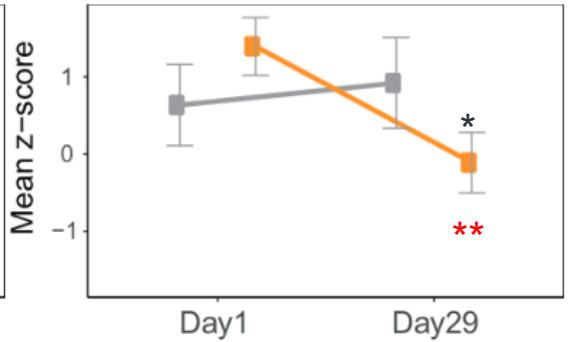
Th1



Th2



Th22



*** (p<0.001), **(p<0.01), *(p<0.05), +(p<0.1)

Changes In Th2-, Th22- And Th1-Related Genes Correlate With Decreased Disease Severity

Correlations with EASI

EASI	R value	P value
CXCR3	0.53	0.01
S100A7	0.53	0.01
S100A9	0.52	0.02
S100A8	0.50	0.02
CCR8	0.49	0.03
IL12B	0.42	0.06
CCL3	0.42	0.06
CCL11	0.41	0.07
IL22	0.39	0.08

Correlations with SCORAD

SCORAD	R value	P value
CXCR3	0.66	0.00
CD27	0.51	0.02
LCK	0.50	0.02
IL12/23p40	0.48	0.03
CCR2	0.48	0.03
CXCL13	0.46	0.04
ITGB2	0.46	0.04
CCR8	0.46	0.04
IL23p19	0.44	0.05
CD3D	0.41	0.07
TNFRSF4 (Ox40)	0.40	0.07
STAT2	0.40	0.08
CCR9	0.39	0.08
CD3E	0.39	0.08
CCL4	0.38	0.09
ICOS	0.38	0.09

RPT193 Demonstrated Efficacy And Helped Normalize The Skin Transcriptome

- In this Phase 1b study, RPT193 improved EASI score at the end of treatment (Day 29) with further decrease at Day 43 (vs. placebo)
- Significant decreases in the AD gene signature (MADAD) were seen in RPT193-treated compared to placebo-treated subjects
- RPT193-treated subjects exhibited decreases in gene signatures associated with Th2, Th22, and Th1 immune pathways
- Changes in AD related biomarkers show significant correlations with clinical efficacy in RPT193-treated subjects
- **Future Clinical Investigations:**
  - A dose-ranging, Phase 2b trial to further assess efficacy and safety of RPT193 in AD subjects
  - A Phase 2a trial in asthma