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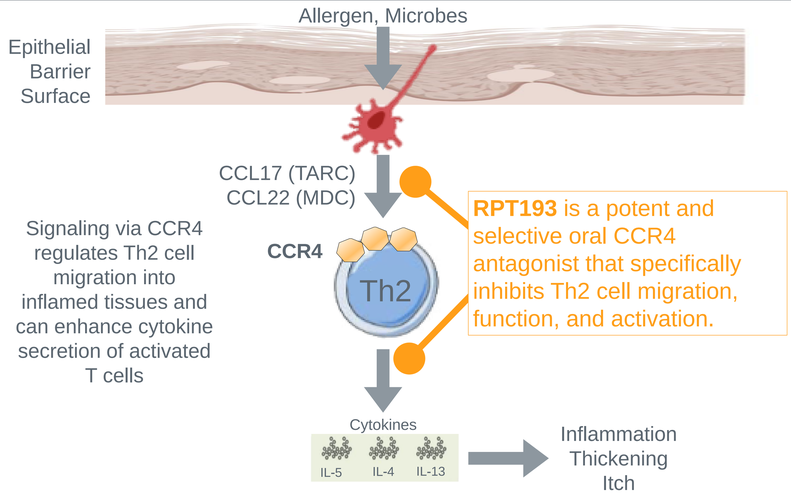
Abstract 88

RPT193, an oral CCR4 inhibitor: Efficacy results from a randomized, placebo-controlled Phase 1b monotherapy trial in patients with moderate-to-severe atopic dermatitis

Robert Bissonnette[1], Joshua Rulloda[2], Nadine Lee[2], Paul Kassner[2], Jasmina Jankicevic[2], William Ho[2], Laurence Cheng[2], Emma Guttman-Yassky[3]
[1]Innovaderm Research Inc., Montreal, Quebec, Canada, [2]RAPT Therapeutics, Inc., South San Francisco, CA, USA, [3]Icahn School of Medicine at Mount Sinai, New York, NY, USA

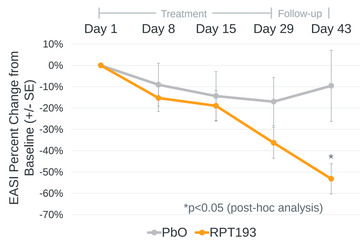
BACKGROUND[1,2]

RPT193 Targets Th2 Activity Responsible for Allergic Inflammation in Atopic Dermatitis, Asthma, and Other Diseases



KEY DATA PREVIOUSLY PRESENTED[3]

Clinical Efficacy



Proportion of Patients		Placebo	RPT193
EASI-50	Day 29	10.0%	42.9%
	Day 43	20.0%	61.9%*
EASI-75	Day 29	10.0%	4.8%
	Day 43	0.0%	28.6%
EASI-90	Day 29	0.0%	4.8%
	Day 43	0.0%	9.5%
vIGA	Day 29	0.0%	4.8%
	Day 43	0.0%	14.3%

- PK of RPT193 demonstrates dose-linearity for C_{max}, steady-state trough, and AUC after multiple 50-400 mg once daily doses[4]
- At the End of Treatment (Day 29), RPT193 showed improvement in EASI, EASI-50, vIGA, and proportion of patients achieving a 4-pt drop in pruritus NRS
- At the End of Study (Day 43), RPT193 showed further deepening of response in EASI and improvement compared to placebo-treated patients in EASI-50/75/90, and vIGA
  - Improvement in EASI and EASI-50 at Day 43 demonstrated statistical significance in a post-hoc analysis

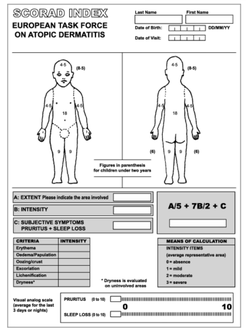
Clinical Safety

Clinical Safety	Placebo	RPT193
Number of subjects with treatment emergent AE (TEAE), n (%)	2 (20.0%)	9 (42.9%)
Number of SAEs reported, n (%)	0 (0.0%)	0 (0.0%)
TEAEs observed in 2 or more subjects		
Nausea, n (%)	0 (0.0%)	3 (14.3%)

- RPT193 was generally well-tolerated
- All TEAEs were mild or moderate
- All TEAEs in the RPT193 arm resolved with most resolving during treatment
- Only one TEAE reported by more than one patient
  - 3 patients (14.3%) in the RPT193 arm reported nausea
  - Nausea also observed in 12.5% of HV in the placebo arm of the MAD portion of the Phase 1
- No laboratory safety signals, ECG changes, or vital sign changes of clinical significance noted
- No serious infections, acne, conjunctivitis, or hematologic AEs observed

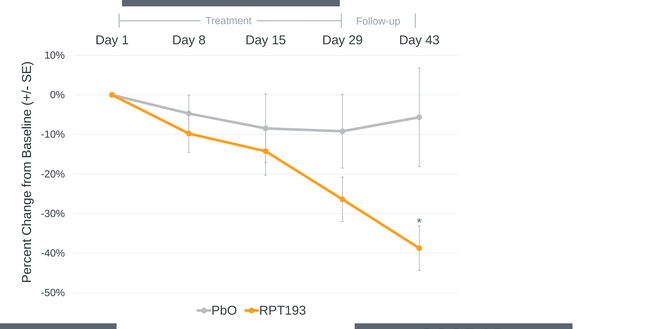
RPT193 SIGNIFICANTLY DECREASES THE TOTAL SCORAD AND SUB-DOMAINS WITH CONTINUED IMPROVEMENT AFTER CESSATION OF TREATMENT

SCORAD Background

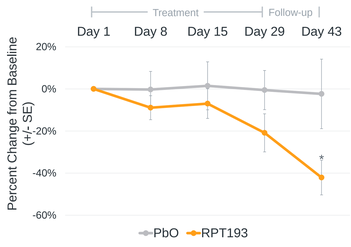


- Developed in 1993[5]
- Score range from 0-103 with objective, investigator-assessed and subjective, patient-reported elements
- Objective
  - Six criteria signs are used to assess intensity or lesion severity
  - Extent of BSA affected by AD
- Subjective
  - Sleep loss and pruritus assessed individually
  - Patients rate average for sleep loss and pruritus over the past 3 days using a visual analog scale

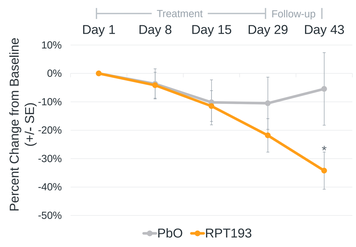
Total SCORAD



SCORAD Extent



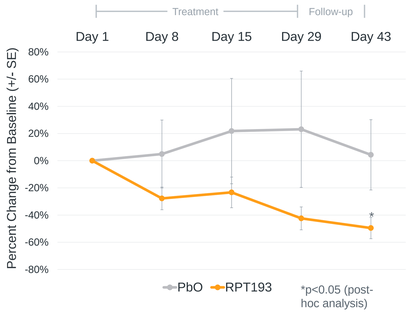
SCORAD Intensity/Severity



*p<0.05 (post-hoc analysis)

RPT193 SIGNIFICANTLY DECREASES TWO KEY SYMPTOMS OF AD

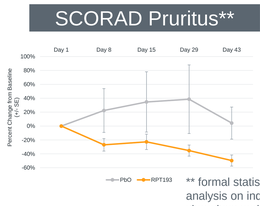
SCORAD Pruritus and Sleep Loss



*p<0.05 (post-hoc analysis)

SCORAD Sleep Loss**

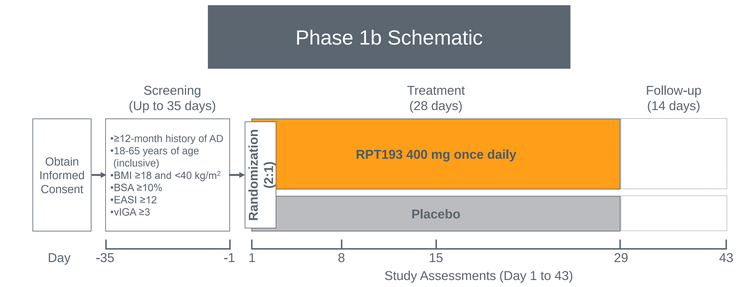
SCORAD Pruritus**



** formal statistical analysis on individual sleep loss and pruritus data not yet performed

METHODS

Phase 1b Schematic



Key Trial Design Elements

- Phase 1b trial part of a broader study conducted in healthy volunteers (HV) to investigate single and multiple doses of RPT193
- 400 mg dose selected based on safety, tolerability, PK and PD data from HV
- Double-blind, randomized, monotherapy study
- Primary and secondary endpoints were safety and PK, respectively
  - Trial was not powered for any specific endpoint
  - This poster focuses on SCORAD data
- Modified Intent to Treat (mITT) dataset with arithmetic means and standard error for continuous endpoints presented

Baseline Patient Demographics and Characteristics

	Placebo	RPT193
N	10	21
Age, Mean (Range)	35.8 (22-64)	41.1 (19-63)
Female, n (%)	4 (40.0%)	12 (57.1%)
Hispanic or Latino Ethnicity, n (%)	3 (30.0%)	3 (14.3%)
Race		
White, n (%)	5 (50.0%)	12 (57.1%)
Asian, n (%)	0 (0%)	2 (9.5%)
Black or African American, n (%)	5 (50.0%)	7 (33.3%)
Baseline AD Characteristics		
Total SCORAD (Range)	56.62 (41.0-81.4)	56.98 (36.6-82.4)
SCORAD Subj (Range)	10.77 (2.0-16.3)	11.99 (5.0-18.0)
EASI, Mean (Range)	21.07 (13.6-45.5)	18.49 (12-30)
BSA, Mean (Range)	24.50 (10-61)	23.29 (11-55)
vIGA 3, n (%)	8 (80.0%)	18 (85.7%)

CONCLUSIONS

- This is the first reported study of a CCR4 antagonist that showed a positive efficacy signal on both the signs and symptoms of AD
- Once-daily, oral RPT193 was generally well tolerated after 28 days of dosing
- At the End of Treatment (Day 29) and compared to Placebo, RPT193 showed greater decrease in total SCORAD and all sub-domains
- At the End of Study (Day 43), RPT193 showed further decreases in total SCORAD and sub-domains, including pruritus and sleep loss, compared to Day 29
  - Change in total SCORAD and all sub-domains at Day 43 demonstrated statistical significance in a post-hoc analysis
- Further improvement after cessation of dosing could be consistent with unique kinetics associated with targeting Th2 cell migration and activation through CCR4 inhibition
- A dose-ranging Phase 2b trial is planned to further investigate RPT193's efficacy and safety in patients with AD

REFERENCES AND ACKNOWLEDGEMENTS

References

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5. ETFAD, Dermatology (1993)

Acknowledgments

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