Society for Investigative Dermatology 2026, ID # 0483

Stanford MEDICINE
School of Medicine

Immunologic and Clinical Activity of Soquelitinib, a Selective ITK Inhibitor, in Atopic Dermatitis

Kavita Sarin, MD, PhD
Professor of Dermatology
Stanford University Medical Center

Kavita Sarin[1], Albert Chiou[1], Michael Cameron[2], Jennifer L. Parish[3], Dan Li[4], Lih-Yun Hsu[4], Drew Hotson[4], Sinem Bagci[4], Suresh Mahabhashyam[4], Richard Miller[4]

[1]Stanford University, Palo Alto, CA, United States; [2]Equity Medical LLC, New York, NY, United States; [3]Paddington Testing Co Inc, Philadelphia, PA, United States; [4]Corvus Pharmaceuticals Inc, So. San Francisco, CA, United States

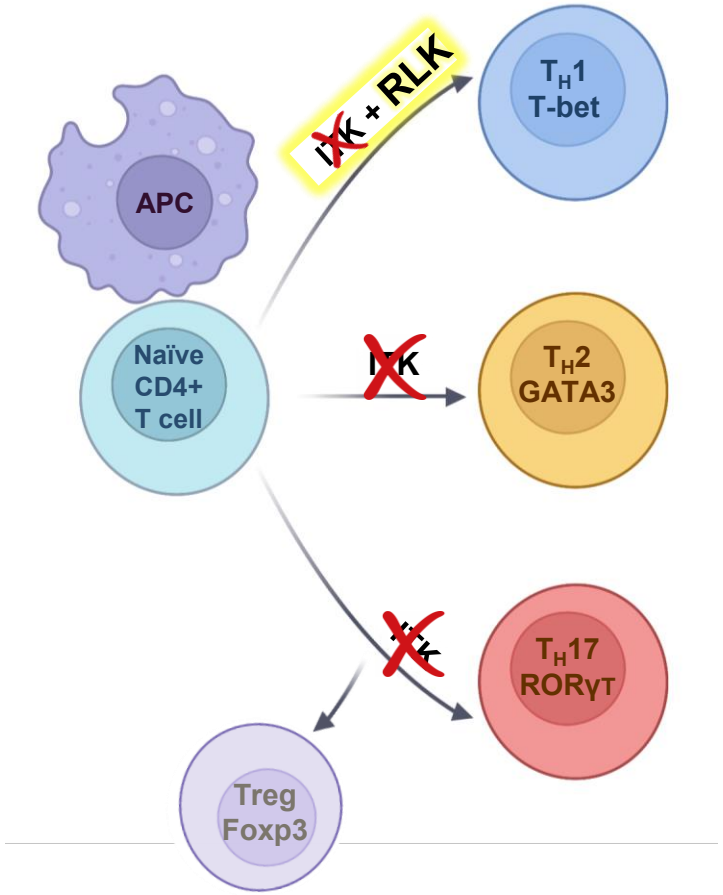
Chiou et al, Abstract ID # LB1154
Soquelitinib, an ITK inhibitor, Produces Prolonged Drug-Free Remissions in Atopic Dermatitis

Disclosures

Consultant for Nflection Therapeutics, Biossil, Springworks, Color Health, Kamal Therapeutics.

Corvus Pharmaceuticals is the sponsor of the soquelitinib clinical trial (CPI-818-003).

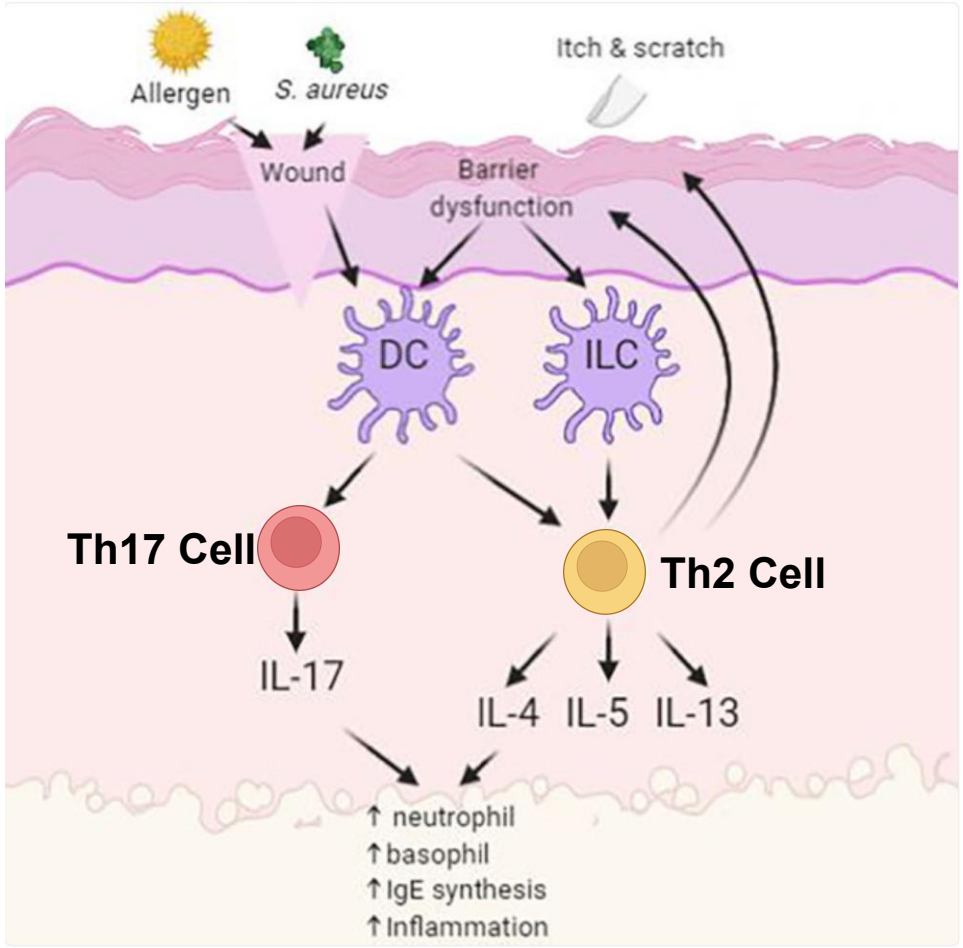
ITK is an Immune Regulator



- Interleukin-2-inducible T cell kinase (ITK) is expressed in T, NK and ILC-2 cells
- ITK is involved in TCR signaling and cell differentiation: inhibition leads to
  - Decreased Th2 and Th17
  - Th1 skewing (via RLK sparing)
  - Th17→ Treg switch
- Soquelitinib is an oral selective ITK inhibitor

Sci Signal 17:1, 2024 (DOI: 10.1126/scisignal.adh2381)
PLOS ONE 14 (4): 1, 2019 (DOI: 10.1371/journal.pone.0215963)

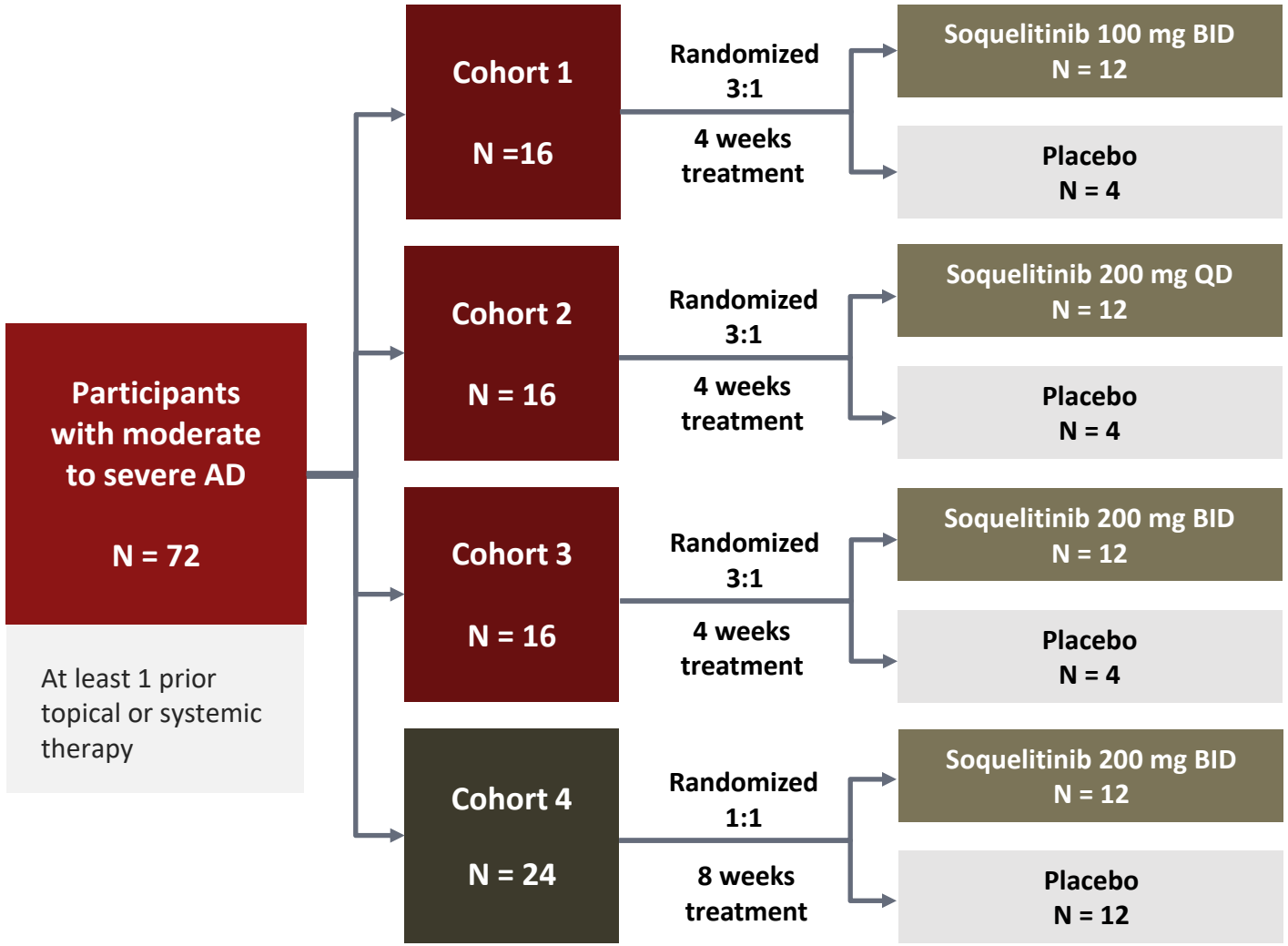
Why This Matters in Atopic Dermatitis



Front Pharm. 2020 Jul 31;11:1086. (DOI: 10.3389/fphar.2020.01086)

- AD is primarily Th2-driven disease
- Current therapies suppress inflammation
- ITK inhibition can lead to upstream immune reprogramming

Atopic Dermatitis Placebo Control Phase 1 Design



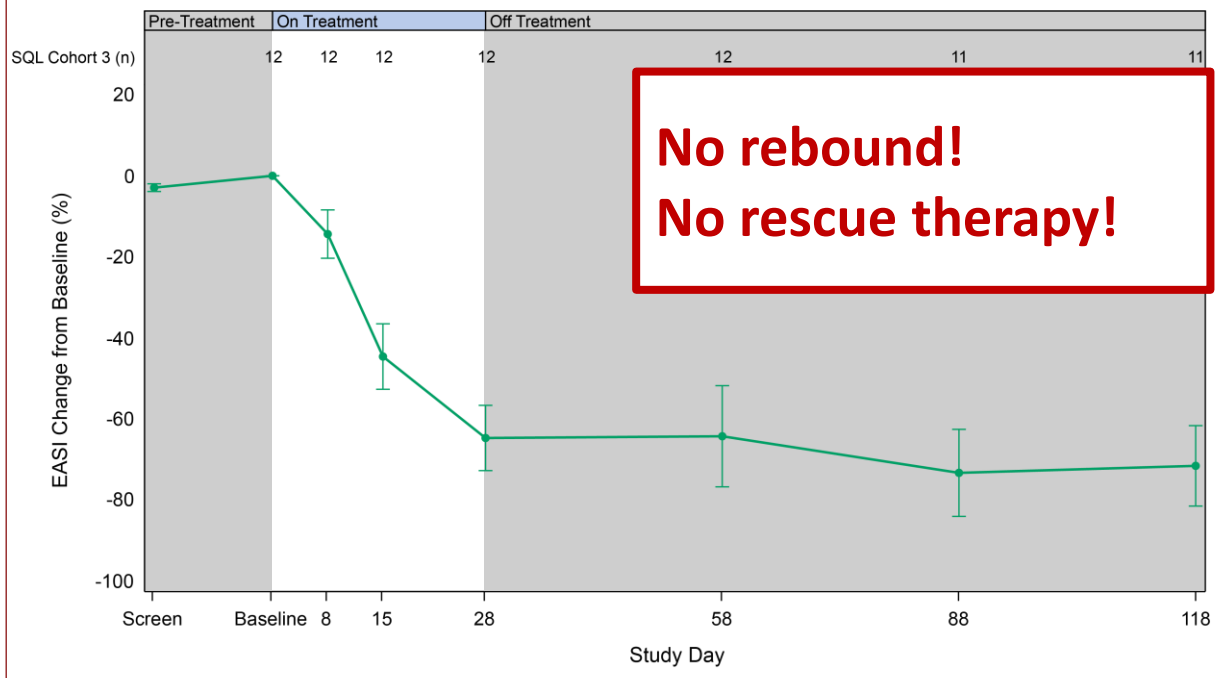
Clinical Trial Design

- N = 72, moderate–severe atopic dermatitis
- Randomized, placebo-controlled
- 4–8 weeks treatment
- All cohorts had 30–90 days of **off-treatment follow-up**

Chiou et al, Abstract ID # LB1154
Soquelitinib, an ITK inhibitor, Produces Prolonged Drug-Free Remissions in Atopic Dermatitis

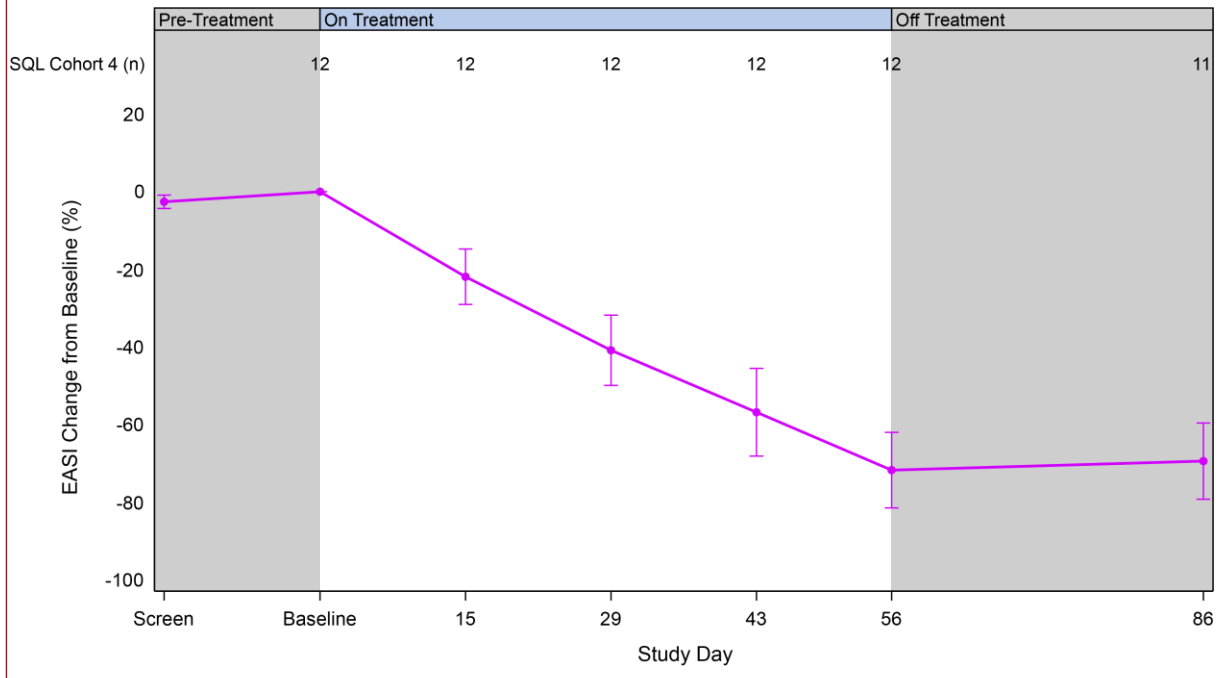
Durable Responses After Drug Withdrawal

4-week Treatment Regimen



No rebound observed ≥90 days of follow-up
No patients received rescue meds

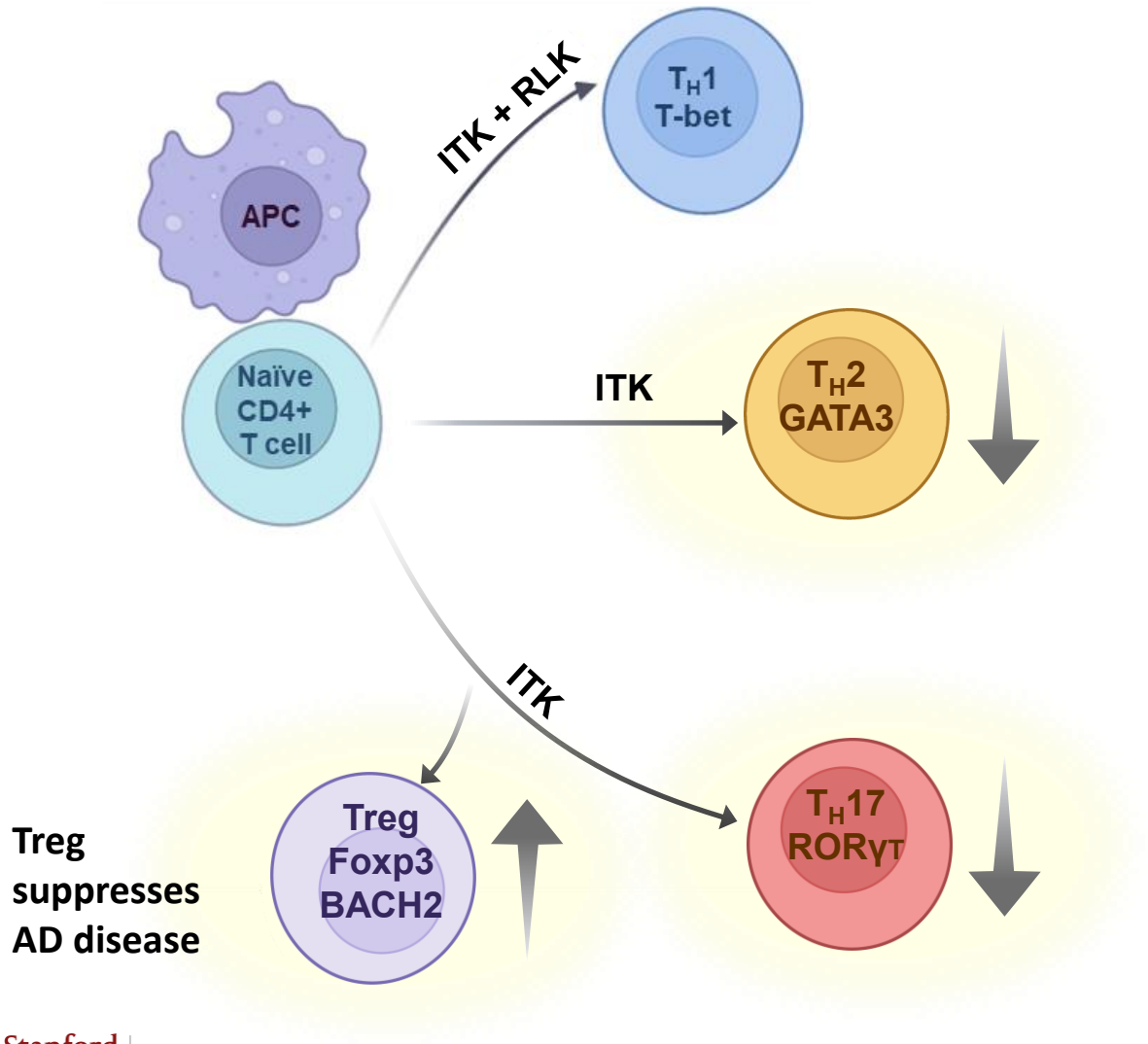
8-week Treatment Regimen



No rebound observed ≥30 days of follow-up
No patients received rescue meds

Improvement persists ≥30–90 days off therapy

Mechanism-Driven Biomarker Strategy



Biomarker Assessments

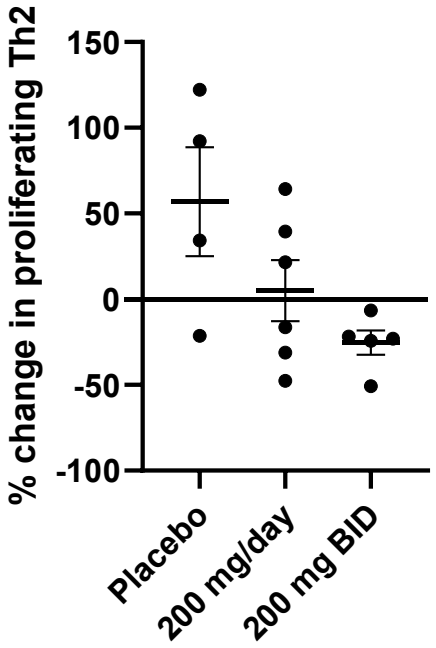
Based on MOA, we evaluated effects on **Th1, Th2, Th17, and Tregs**:

- Serum cytokines (MSD)
- Blood flow cytometry (Foxp3)
- PBMC single cell RNAseq

Effects on Th2 Related Immunology

Th2 drives AD disease

Dose-dependent Reduction in Proliferating Th2*

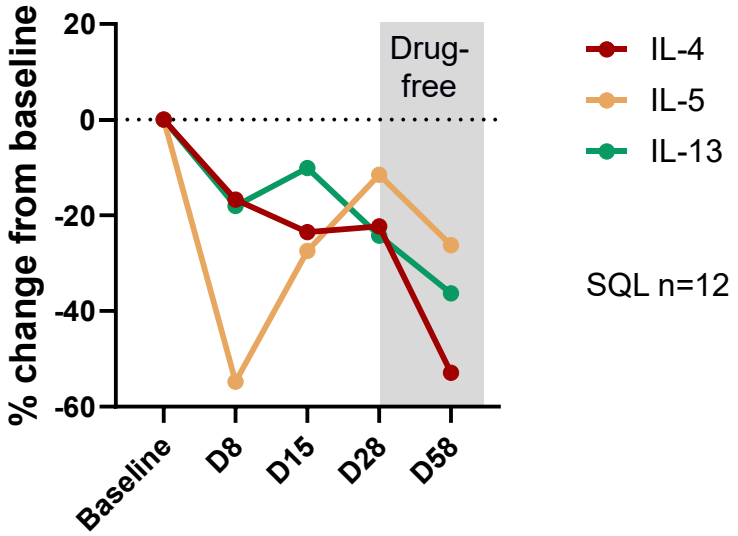


Ki-67-high Th2 cells (GATA3, STAT6, c-MAF, CCR4, PTGDR2)

Significant reduction in IL-4, IL-5, IL-13 and TARC

Cohort 3

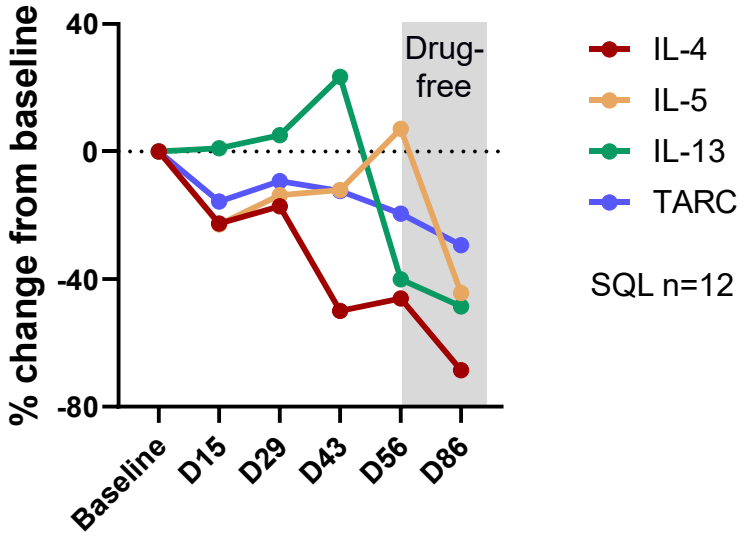
200 mg BID for 28 days



p=0.006 in IL-4 at D58 vs. Baseline
p=0.05 in IL-5 at D58 vs. Baseline

Cohort 4

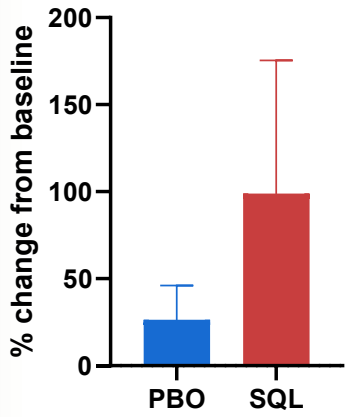
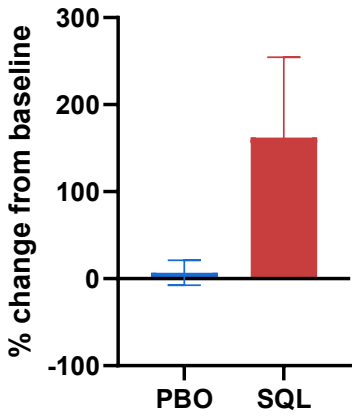
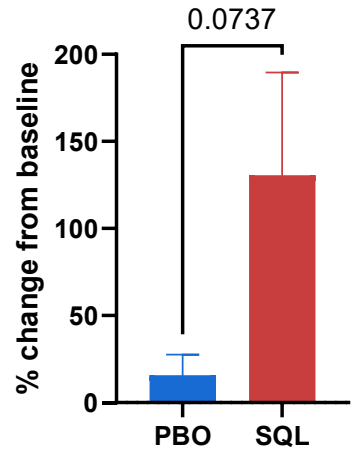
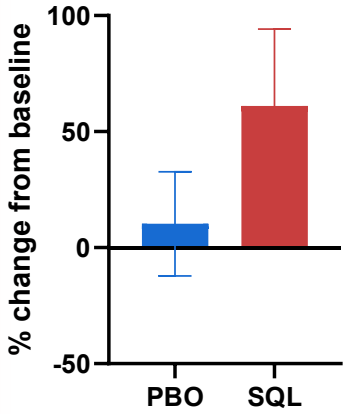
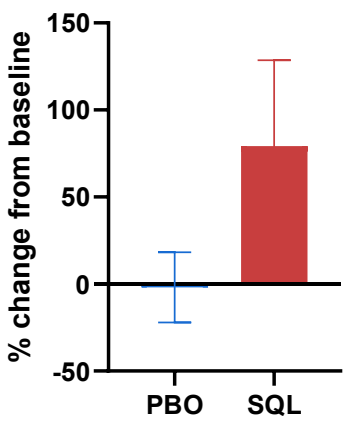
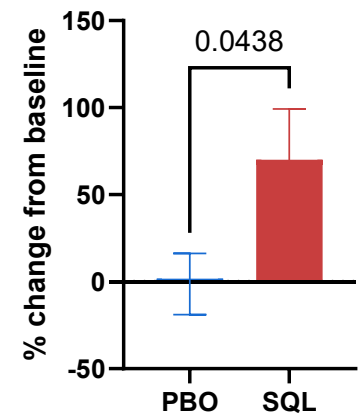
200 mg BID for 56 days



p=0.02 in IL-4 at D56 vs. Baseline
p=0.007 in IL-13 at D56 vs. Baseline
p=0.04 in TARC at D56 vs. Baseline

Soquelitinib Treatment Leads to Increase in Persistent Tregs

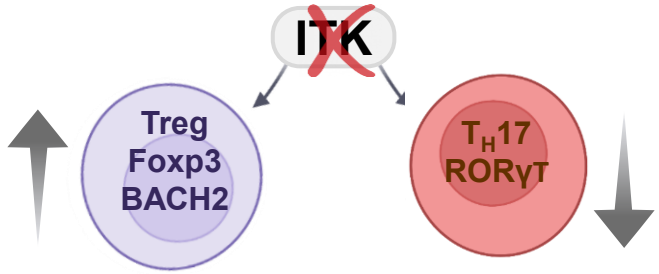
Tregs ($CD4^+$, $CD25^{hi}$, $Foxp3^+$) persist beyond treatment

	Cohort 3 – 200 mg BID	Cohort 4 – 200 mg BID	Cohort 3+4* – 200 mg BID
28 Days on Drug			
30-day Drug-free Period			

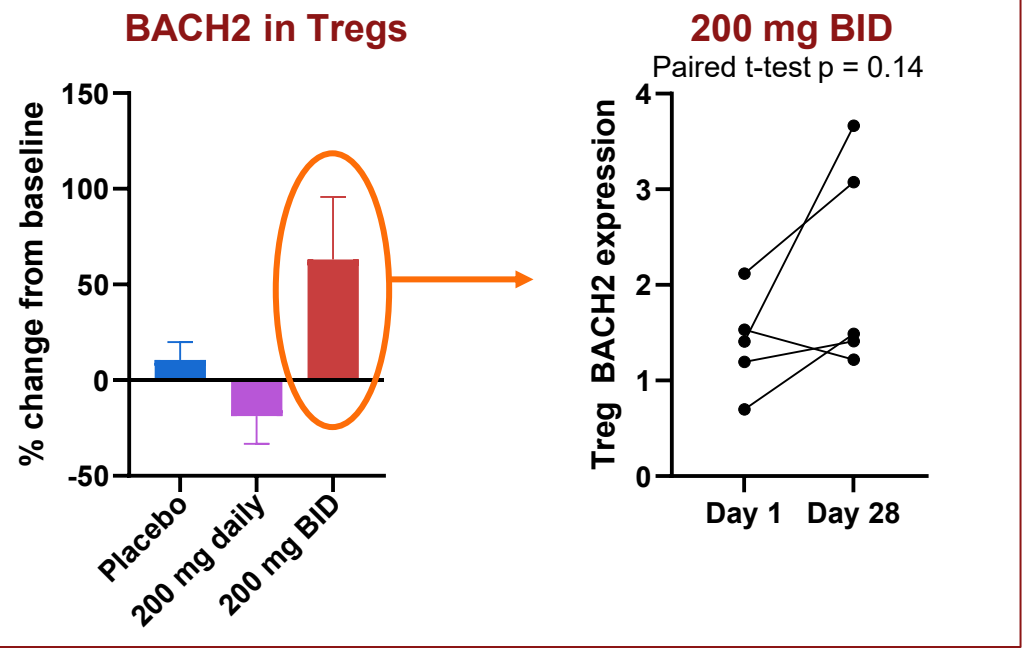
*Placebo (PBO) n=23, soquelitinib (SQL) n=24

Inhibiting ITK Regulates Switch to Treg from Th17

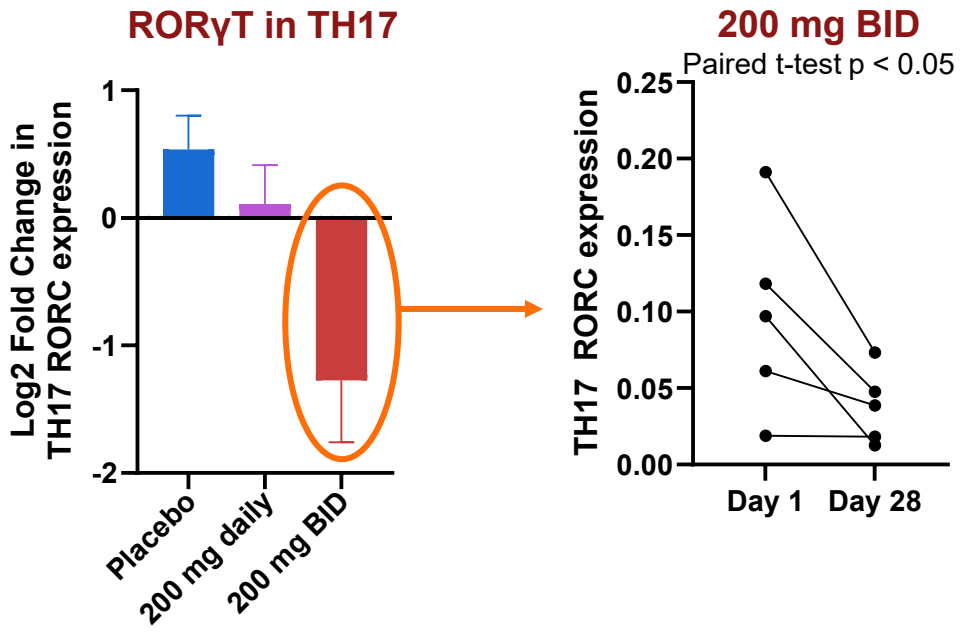
Increased BACH2 and reduced RORγT expression



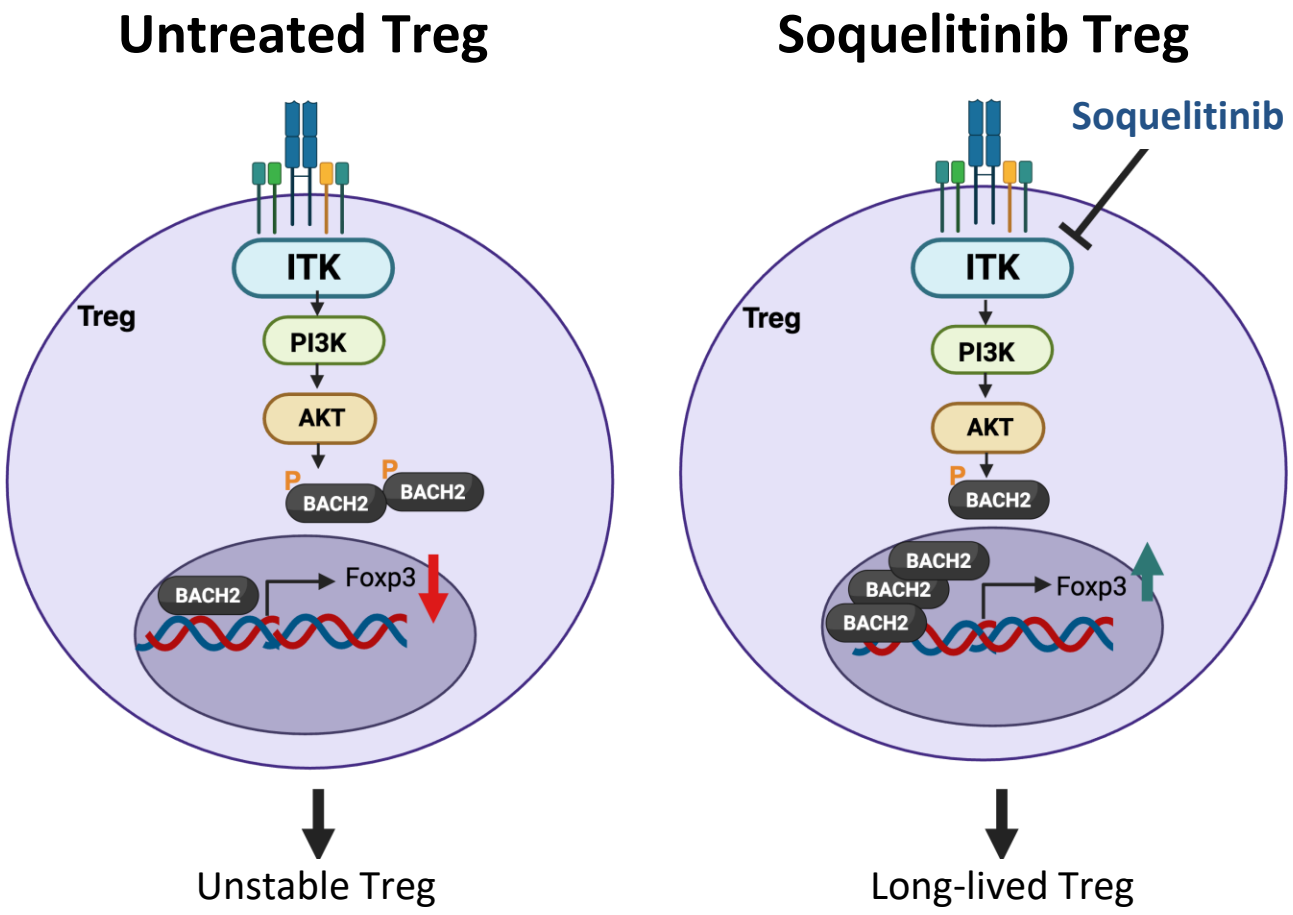
Treg BACH2 increases at 200 mg BID dose



RORγT decreases at 200 mg BID dose



Potential Mechanism of Treg Stabilization

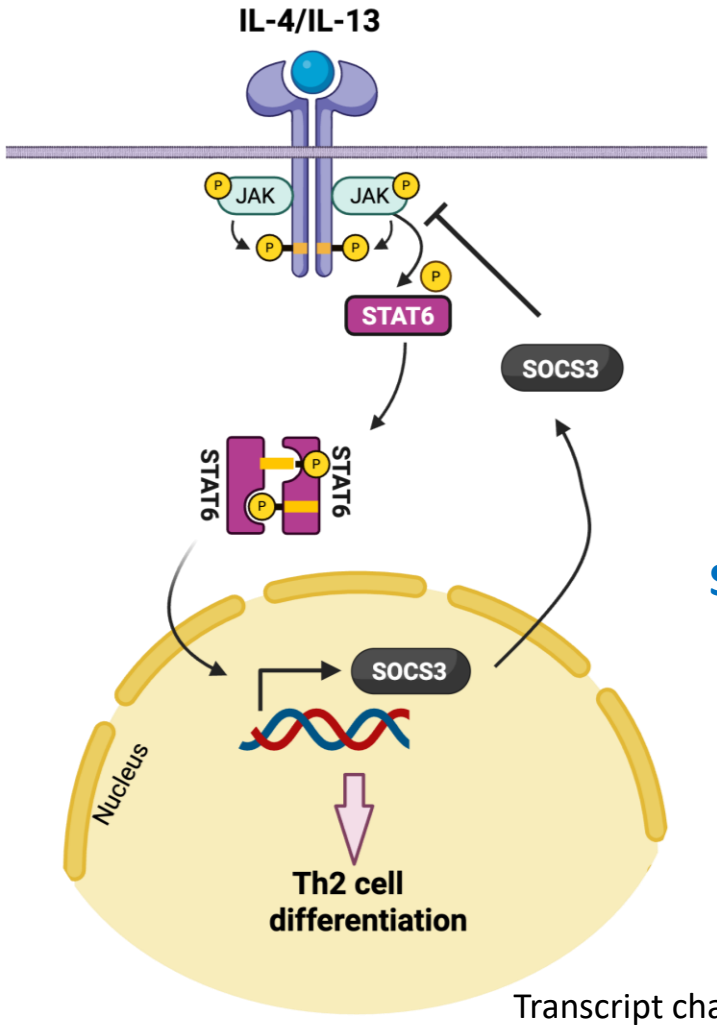


- Increased BACH2 expression promotes Treg survival
- ITK signaling prevents nuclear localization of BACH2
- ITK inhibition promotes BACH2 nuclear localization and activation of Foxp3 gene

Cells 13(11):891, 2024. DOI: 10.3390/cells13110891
Nat Commun 11(1):252, 2020. DOI: 10.1038/s41467-019-14112-2

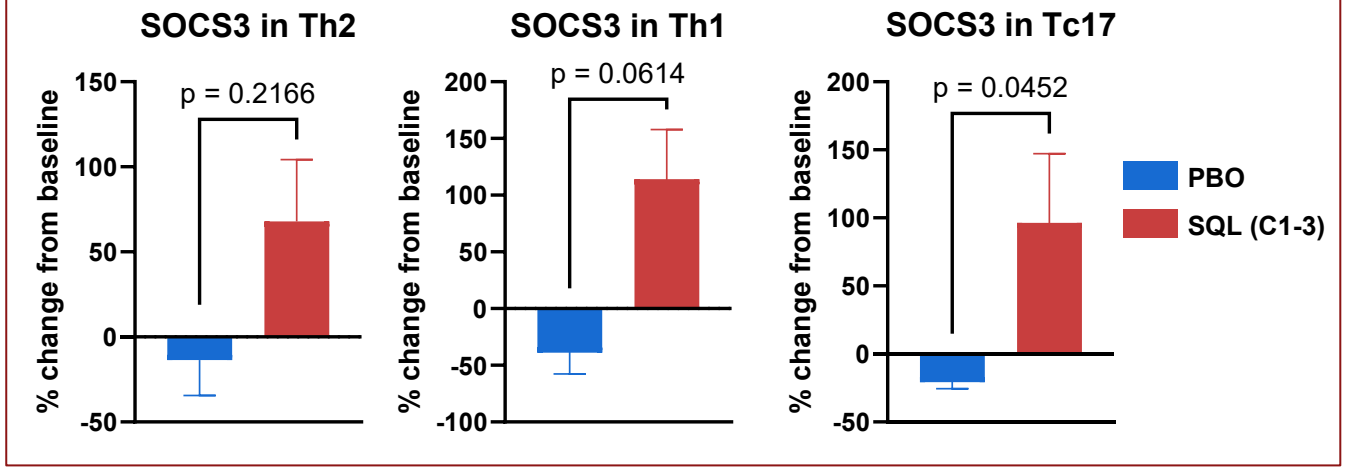
Soquelitinib Upregulates SOCS3 and Reduces JAK1 in T helper Cells

Modulation of the JAK-STAT Pathway

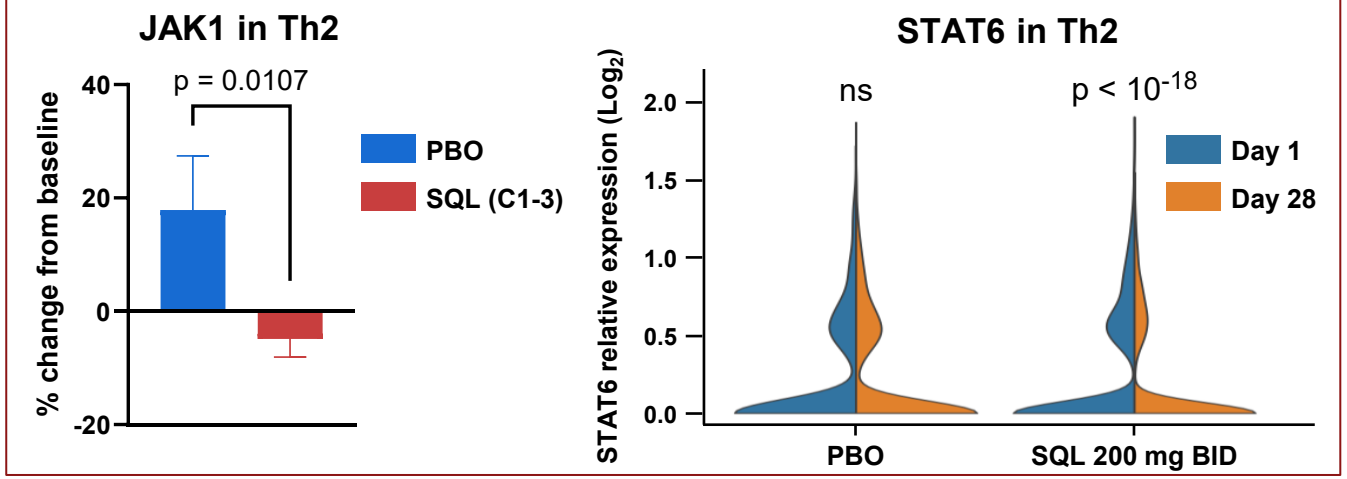


SQL ↑ SOCS3 ↓ JAK1 ↓ STAT6

SOCS3 increases in circulating T cells



JAK1 and STAT6 decreases in circulating Th2 cells



Transcript change from baseline at Day 28 (n=11 SQL, n=4 placebo); STAT6 (n=5 SQL, n=4 placebo)

Stanford MEDICINE | School of Medicine

Conclusions

Soquelitinib: Immune Reprogramming for Durable Control of Atopic Dermatitis

Targeted Mechanism

Soquelitinib is a **selective**, covalent **ITK inhibitor**

Blocks Th2/Th17

Immune Reprogramming

Treg rebalancing:

- Th2/Th17 reduced inflammatory signaling
- Increased Tregs

Shifts from inflammatory Th2/Th17 responses toward regulatory Treg responses

Pathway Modulation

Soquelitinib modulates the JAK-STAT pathway in T cells

↑ SOCS3 and ↓ JAK1 reduce STAT signaling and inflammatory cytokine production

Clinical Impact

Durable Remissions
Continued improvement after treatment discontinuation

Favorable Safety Profile
Well tolerated in Phase 1

Potential for Broad Utility
In AD and other immune-mediated diseases

A new paradigm: Target upstream. Reprogram immunity. Achieve ***durable*** control.

We thank the clinical trial participants and collaborating sites:

Apex Clinical Research, Arkansas Research Trials, Best Skin Research, Cahaba Dermatology and Skin Health Research Center, Center For Dermatology Clinical Research, Empire Clinical Research, Equity Medical - New York and Kentucky, Noble Clinical Research, Paddington Testing Company, Progressive Clinical Research, Sadick Research Group, Santos Research Center, and SUNY Downstate Medical Center.