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Soquelitinib, an ITK inhibitor, Produces Prolonged Drug-Free Remissions in Atopic Dermatitis

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Disclosures

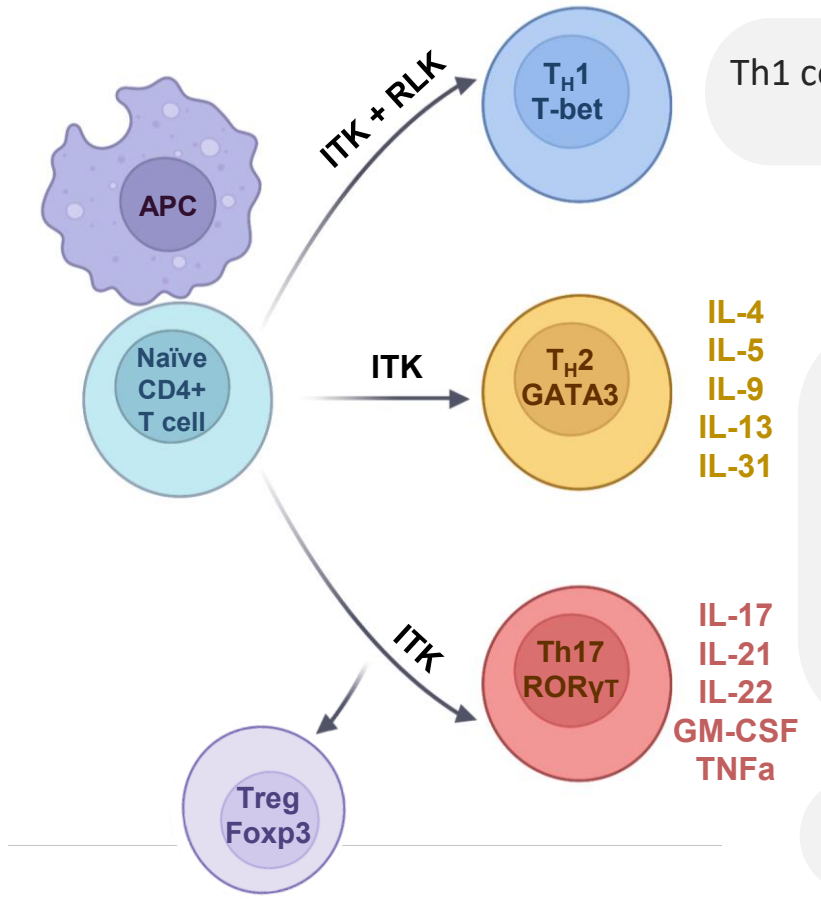
Corvus Pharmaceuticals – Investigator (Grants/Research Funding/Clinical Advisory Board); AbbVie – Investigator (Grants/Research Funding); Abeona Therapeutics – Investigator (Grants/Research Funding); Eli Lilly and Company – Investigator (Grants/Research Funding); Phoenix Tissue Repair – Investigator (Grants/Research Funding); Sanofi/Regeneron – Investigator (Grants/Research Funding)

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

Background

- ITK (interleukin-2-inducible T cell kinase) is expressed in T, NK and ILC-2 cells
- Soquelitinib is an oral, selective covalent inhibitor of ITK
  - Nanomolar binding to ITK while sparing RLK
  - Inhibits Th2 and Th17 differentiation and inhibits the production of IL-4, 5, 13, 17, 31, etc.
- Blocking ITK results in a switch from Th17 to Tregs
  - Soquelitinib increases Tregs
- Active in animal models of atopic dermatitis, asthma, psoriasis, GVHD, and systemic sclerosis
- A phase 2 trial in AD and a phase 3 trial in T cell lymphoma are ongoing

ITK blockade leads to reduction in Th2, Th17 "Th1 skewing"



Th1 cells play a role in cancer cell and viral elimination

Th2 and Th17 cells are involved in autoimmune, inflammatory, fibrotic and allergic diseases

Treg suppresses inflammation

Background

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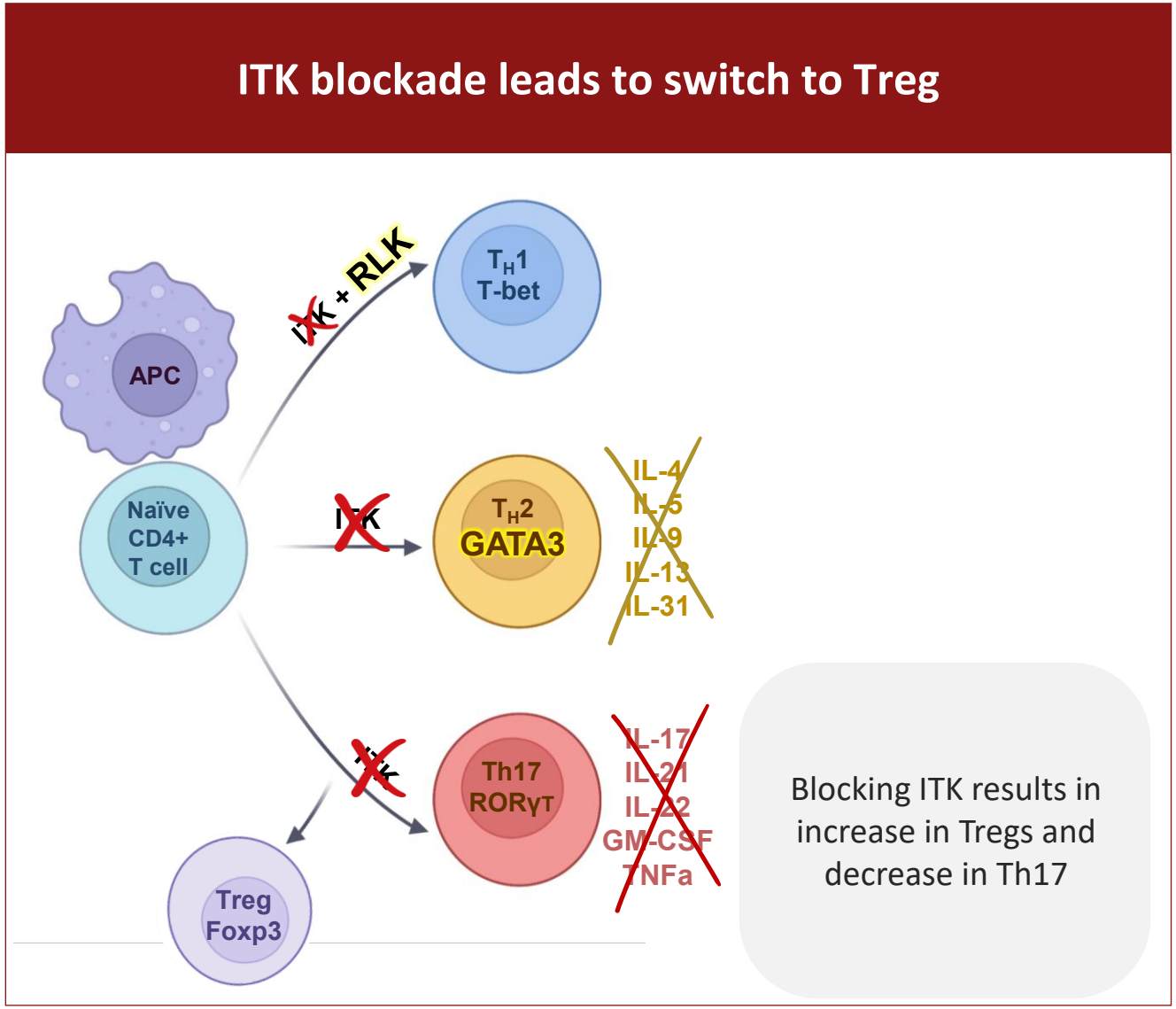
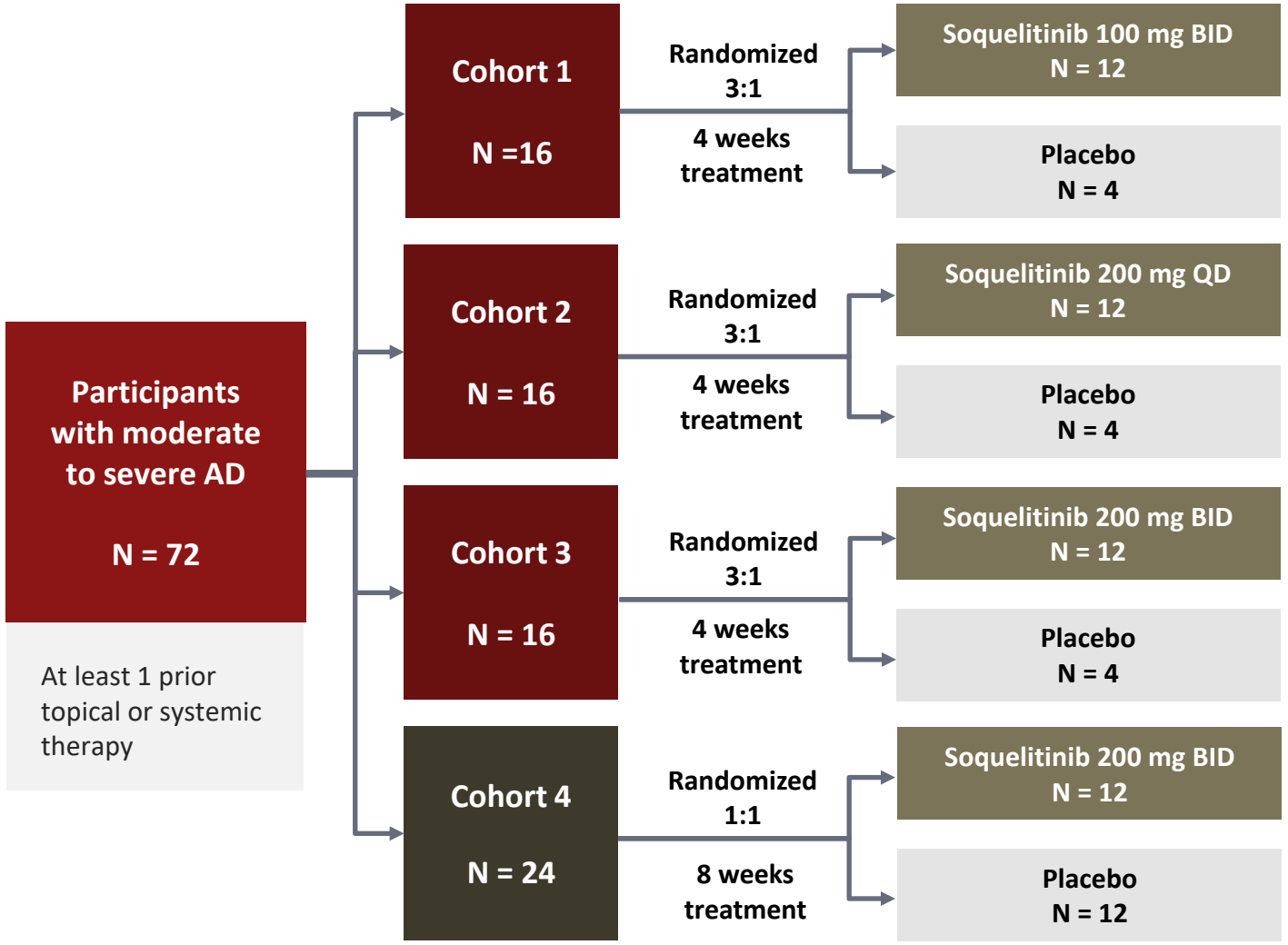


Sci Signal 17:1, 2024 (DOI: 10.1126/scisignal.adh2381)
PLOS ONE 14 (4): 1, 2019 (https://doi.org/10.1371/journal.pone.0215963)

Atopic Dermatitis Placebo Control Phase 1 Design



Study Design

- Endpoints:
  - Primary: safety
  - Secondary: % change in EASI, EASI75, EASI90, IGA 0 or 1
- Design
  - Blinded with placebo
  - No concomitant topical steroids
  - 28 day treatment for cohorts 1-3 (3:1 randomization)
  - 56 day treatment for cohort 4 (1:1 randomization)
  - Off treatment follow up
- Prior systemic therapy allowed
- 14 sites all U.S.

Patient Baseline Characteristics

	4-week			8-week	
	Cohorts 1 and 2	Cohort 3	Cohorts 1–3	Cohort 4	
	Soquelitinib 100 mg BID or 200 mg QD (n=24)	Soquelitinib 200 mg BID (n=12)	Placebo (n=12)	Soquelitinib 200 mg BID (n=12)	Placebo (n=12)
Age, mean (range), yrs	44.4 (21–66)	46.4 (25–71)	38.8 (20–62)	40.5 (18–69)	42.3 (21–67)
Gender, male n (%)	14 (58.3)	4 (33.3)	7 (58.3)	6 (50)	7 (58.3)
Race/ethnicity, n (%)					
Asian	2 (8.3)	0 (0)	1 (8.3)	3 (25)	2 (16.7)
Black or African American	13 (54.2)	5 (41.7)	5 (41.7)	5 (41.7)	5 (41.7)
White	4 (16.7)	4 (33.3)	2 (16.7)	3 (25)	2 (16.7)
Hispanic or Latino	5 (20.8)	2 (16.7)	4 (33.3)	1 (8.3)	3 (25)
Not Reported	0 (0)	1 (8.3)	0 (0)	0 (0)	0 (0)
Baseline EASI, mean (range)	19.9 (14.7–46.6)	27.2 (18.0–41.5)	21.2 (14.4–46.6)	25.7 (16.6–64.7)	21.9 (16.4–32.9)
Baseline IGA 4, n (%)	2 (8.3)	1 (8.3)	2 (16.7)	2 (16.7)	1 (8.3)
Prior AD therapies, n (%)					
Topical corticosteroids	24 (100)	12 (100)	12 (100)	12 (100)	12 (100)
Systemic therapies	6 (25)	4 (33.3)	3 (25)	5 (41.7)	7 (58.3)
Dupilumab	2 (8.3)	2 (16.7)	2 (16.7)	2 (16.7)	3 (25)
JAK inhibitor	0 (0)	1 (8.3)	0 (0)	1 (8.3)	2 (16.7)
Other	4 (16.7)	4 (33.3)	2 (16.7)	5 (41.7)	6 (50)

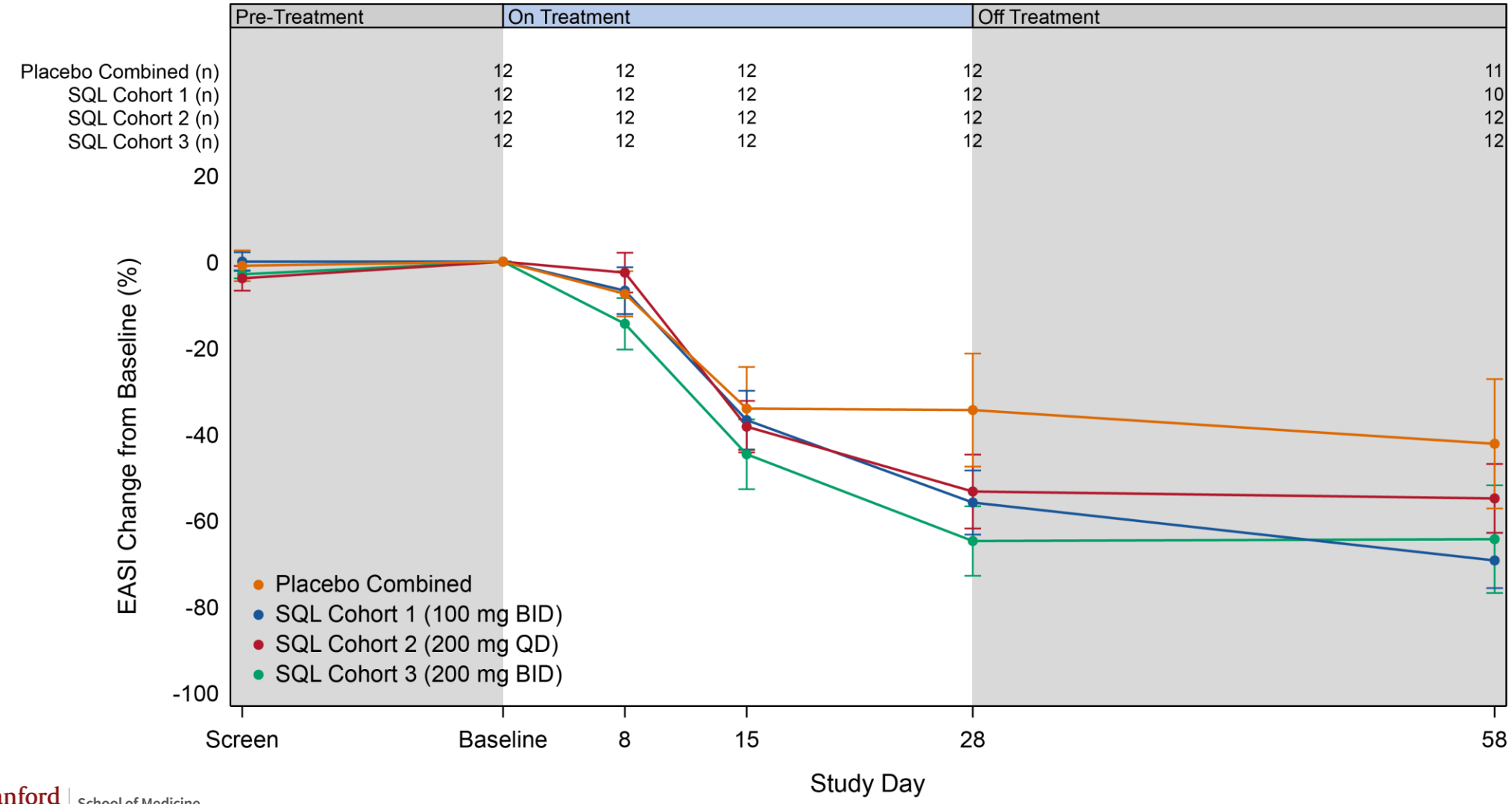
Efficacy Results at 4 Weeks

Cohorts 1–3

	Soquelitinib		Placebo
	Cohorts 1 and 2 (N=24)	Cohort 3 (N=12)	Combined (N=12)
EASI 75 (%pts)	29	50	0
IGA 0 or 1 (%pts)	21	25	0
EASI 50 (%pts)	75	83	58
EASI 90 (%pts)	4	8	0
Change EASI Mean % Reduction	54.6	64.8	34.4

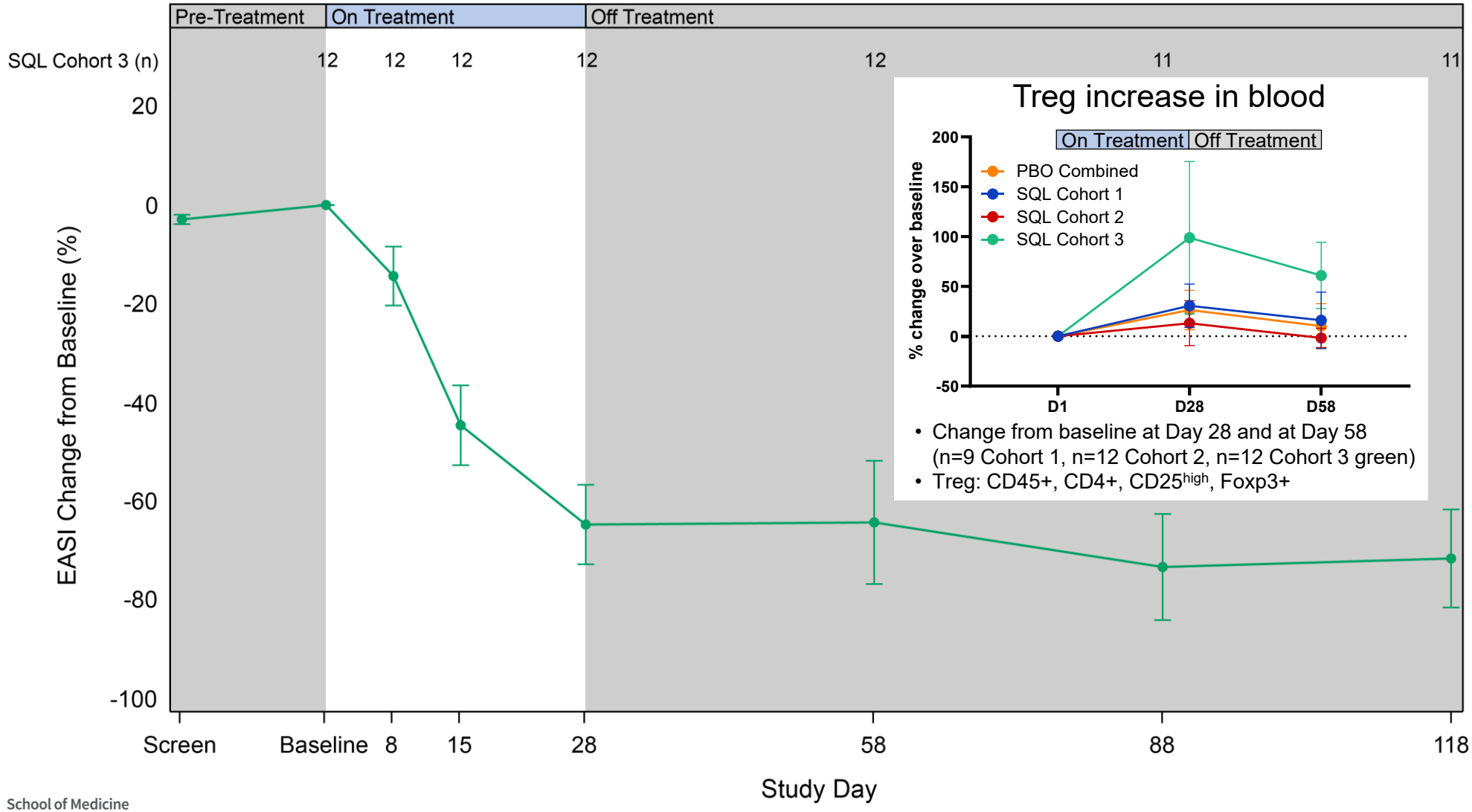
Mean Percent Reduction in EASI

Cohorts 1, 2, and 3



Immune Rebalance

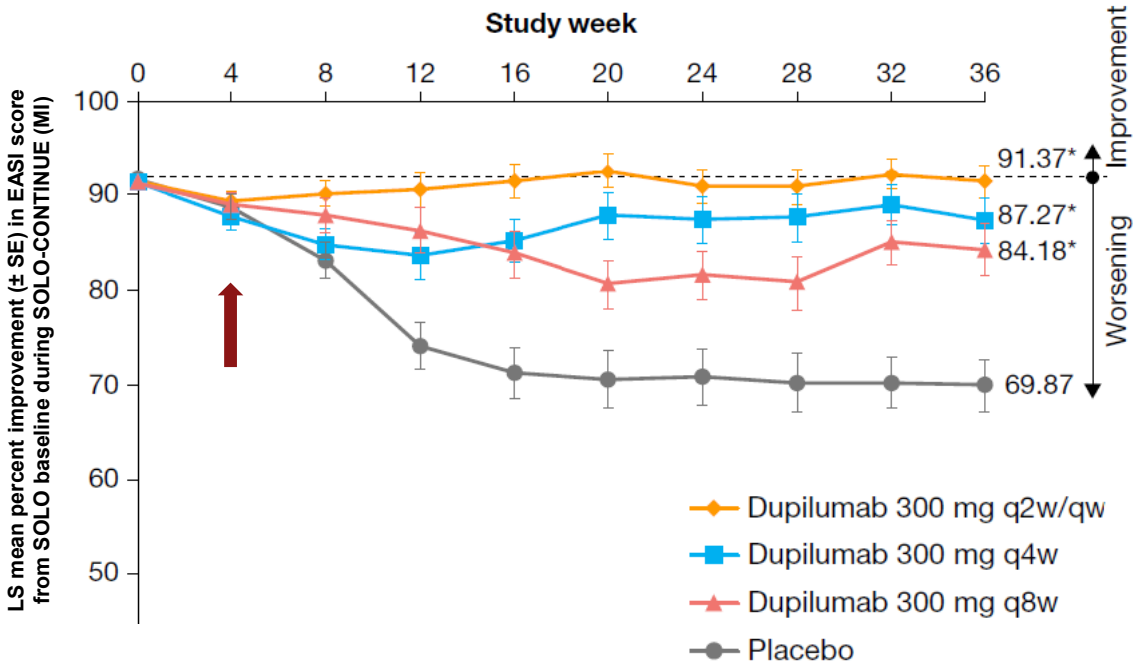
Durable remission with increase in Tregs in Cohort 3



Rebound Following Dupilumab and JAKi

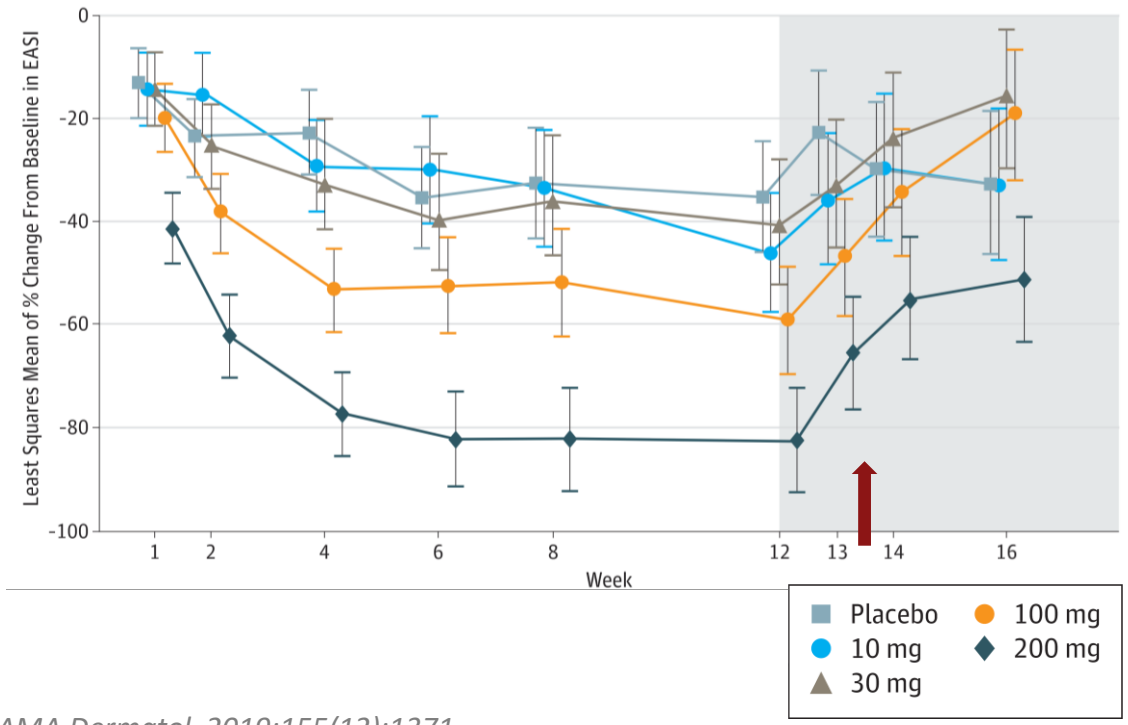
Worsening within 4 weeks of stopping therapy

Dupilumab



JAMA Dermatol. 2020;156(2):131

Abrocitinib



JAMA Dermatol. 2019;155(12):1371

Efficacy Results at 8 Weeks

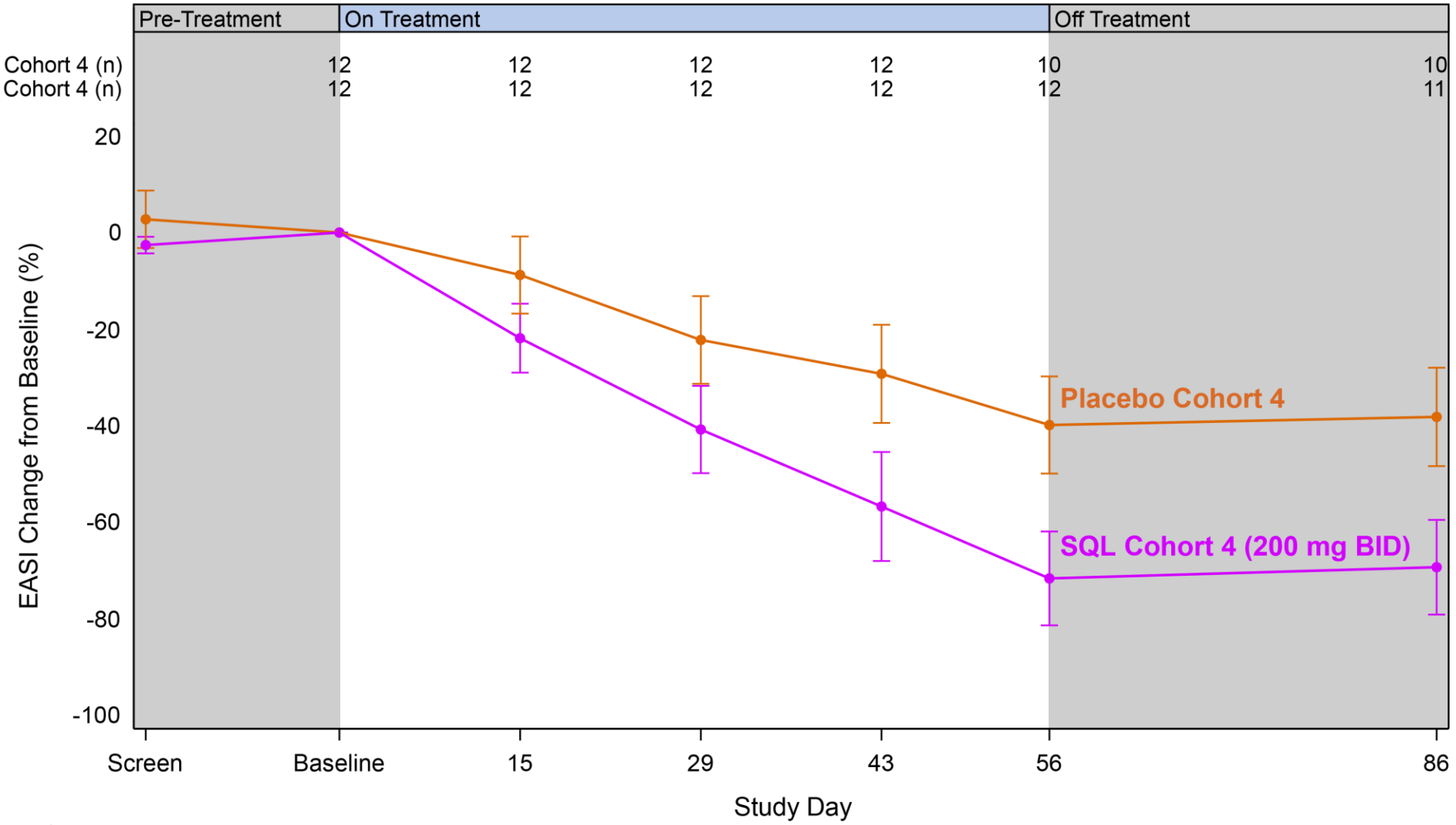
Cohort 4 achieved 75% EASI 75

	Cohort 4 (200 mg BID)	
	8-week	
	Soquelitinib (N=12)	Placebo (N=12)
EASI 75 (%pts)	75	20*
IGA 0 or 1 (%pts)	33	0
EASI 50 (%pts)	92	30*
EASI 90 (%pts)	25	0
Change EASI Mean % Reduction	72	40*
Flare *(requiring rescue meds)* (%pts)	0	17

**2 placebo patients missed the Day 56 visit and are not included. They did return for later visits and did not achieve EASI 75 at any time point. If included in the placebo analysis the 8-week EASI 75 is 17%.*

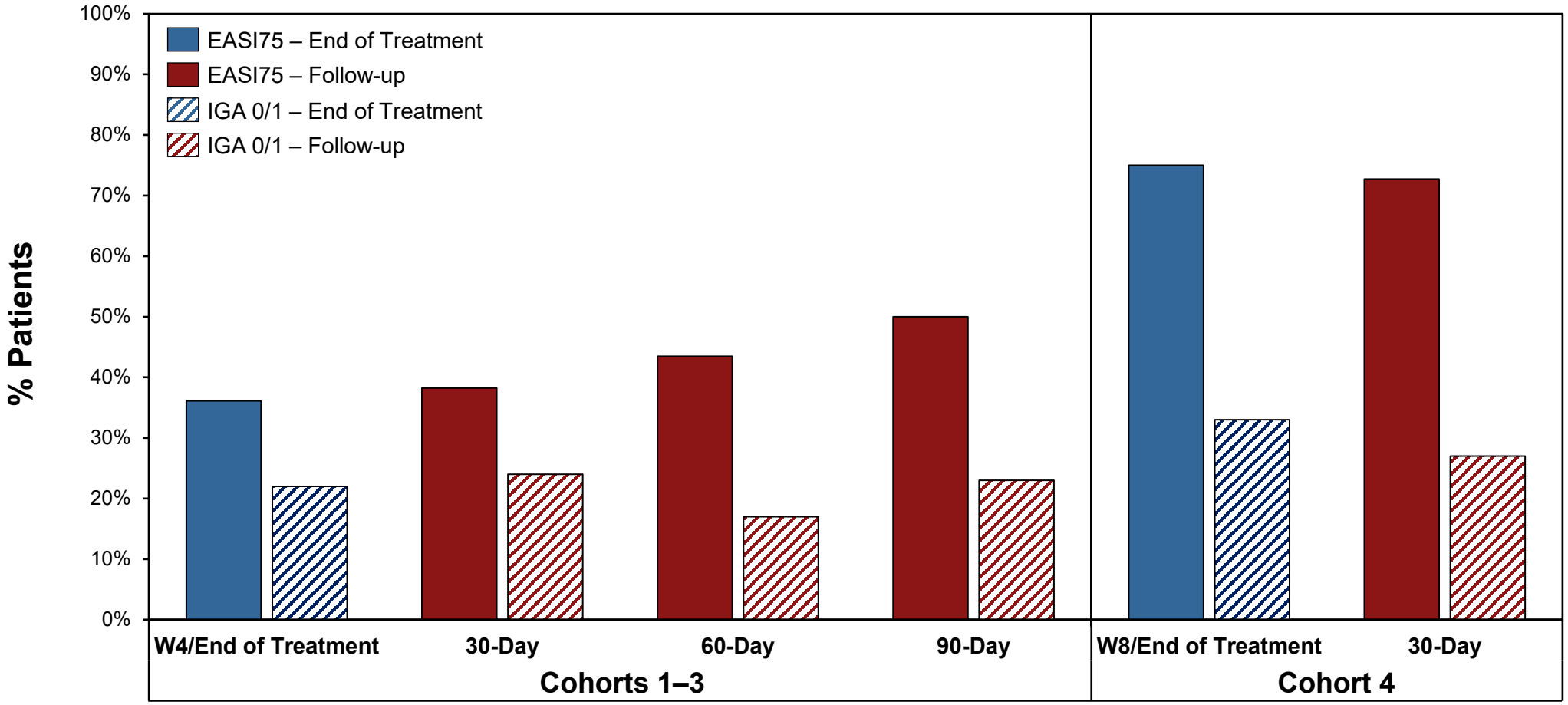
Mean Percent Reduction in EASI Cohort 4

Increased efficacy with longer duration of treatment (8 weeks)



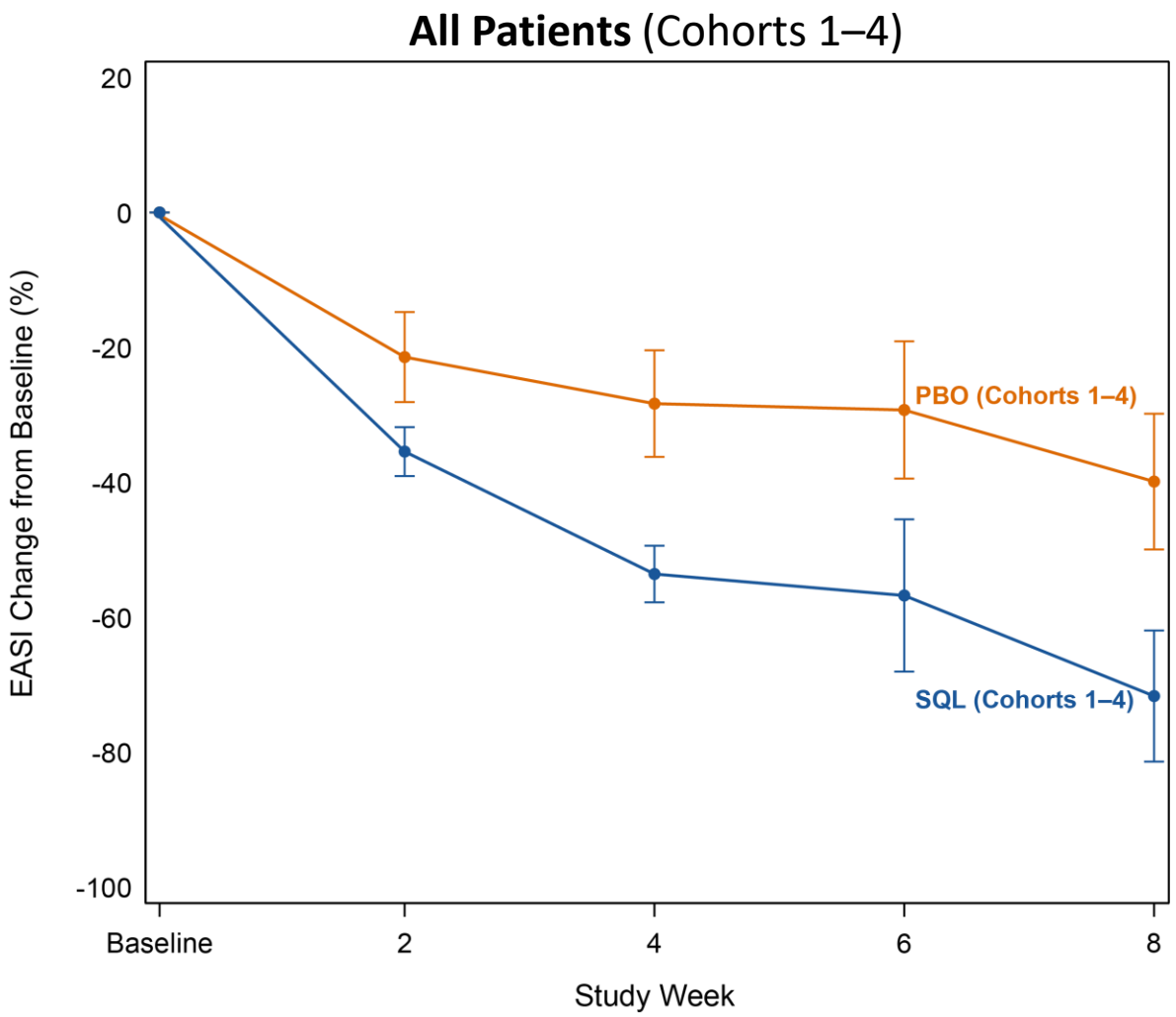
Percentage Patients Achieving EASI75 and IGA 0/1

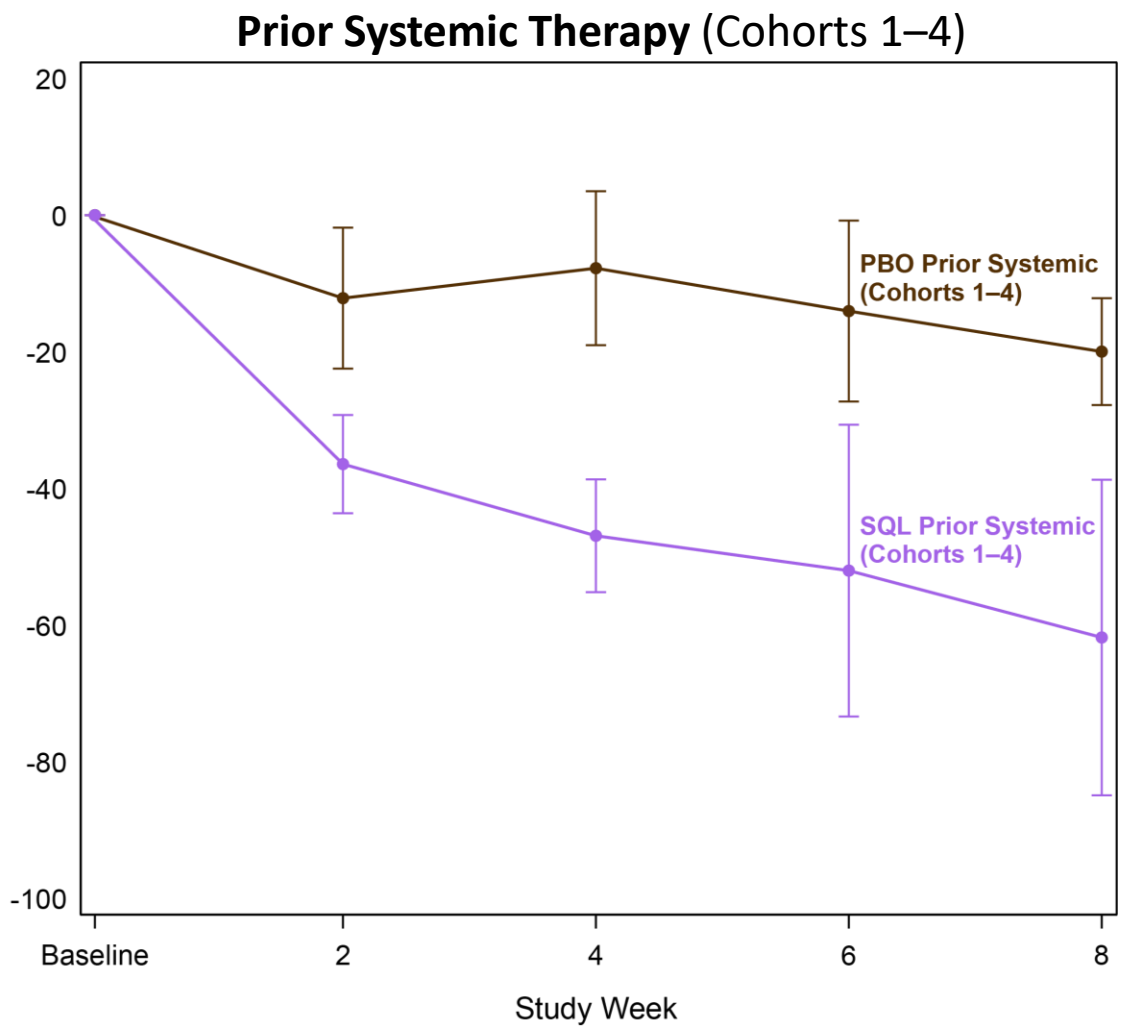
Responses maintained in drug-free follow up



Efficacy in Patients with Prior Systemic Therapy (Cohorts 1–4)

Comparable efficacy in patients with prior systemic therapy





Response in Systemic Treatment Resistant Patients

Cohorts 3 & 4

Study Treatment	Age/Gender	Prior Treatment Resistant	Baseline EASI	% EASI change
Soquelitinib	60/F	Dupilumab	24.6	–91%
Soquelitinib	18/M	Dupilumab, anti-OX40L	23.8	–96%
Soquelitinib	52/M	Dupilumab, methotrexate, upadacitinib	41.5	–27%
Soquelitinib	34/M	Dupilumab, anti-OX40, abrocitinib	23.9	29%
Placebo	37/M	Dupilumab, upadacitinib	17.2	Flare (Rescue Meds)
Placebo	26/F	Dupilumab, upadacitinib	32.9	Flare (Rescue Meds)

Safety Summary

	4-week		8-week	
	Cohorts 1–3		Cohort 4	
	Soquelitinib (n=36)	Placebo (n=12)	Soquelitinib (n=12)	Placebo (n=12)
Subjects with AEs*	15 (41.7%)	4 (33.3%)	5 (41.7%)	6 (50%)
Severe (Grade ≥3) AEs	0	0	0	0
Serious AEs	0	0	0	0
AEs leading to study drug discontinuation	0	0	0	0

**All Grade 1-2 AEs not requiring dose modifications. No clinically significant lab abnormalities. No AEs of conjunctivitis.*

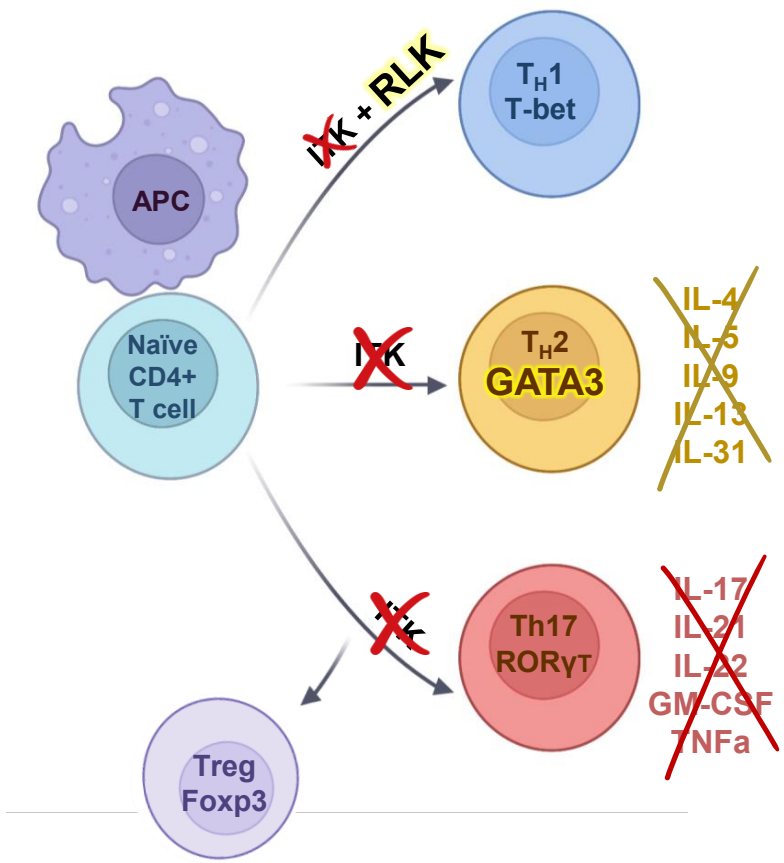
Safety Summary

All reported AEs

	Cohorts 1–3		Cohort 4	
	SQL (n=36), n (%)	PBO (n=12), n (%)	SQL (n=12), n (%)	PBO (n=12), n (%)
Subjects with any TEAE	**15 (41.7)**	**4 (33.3)**	**5 (41.7)**	**6 (50)**
Headache	4 (11.1)	1 (8.3)	4 (33.3)	0 (0)
Abdominal pain upper	1 (2.8)	0 (0)	0 (0)	1 (8.3)
Nausea	1 (2.8)	1 (8.3)	0 (0)	0 (0)
Upper respiratory tract infection	1 (2.8)	1 (8.3)	0 (0)	0 (0)
Worsening of AD	0 (0)	0 (0)	0 (0)	2 (16.7)
Anemia	1 (2.8)	0 (0)	0 (0)	0 (0)
Eosinophilia	1 (2.8)	0 (0)	0 (0)	0 (0)
Diarrhea	0 (0)	0 (0)	1 (8.3)	0 (0)
Food poisoning	0 (0)	0 (0)	1 (8.3)	0 (0)
COVID-19	1 (2.8)	0 (0)	0 (0)	0 (0)
Cellulitis	0 (0)	1 (8.3)	0 (0)	0 (0)
Nasopharyngitis	1 (2.8)	0 (0)	0 (0)	0 (0)
Skin bacterial infection	0 (0)	0 (0)	0 (0)	1 (8.3)
Staphylococcal infection	0 (0)	0 (0)	1 (8.3)	0 (0)
Increased appetite	0 (0)	0 (0)	0 (0)	1 (8.3)
Arthralgia	0 (0)	0 (0)	0 (0)	1 (8.3)
Muscle spasms	0 (0)	0 (0)	0 (0)	1 (8.3)
Basal cell carcinoma	0 (0)	0 (0)	0 (0)	1 (8.3)
Neck pain	1 (2.8)	0 (0)	0 (0)	0 (0)
Somnolence	1 (2.8)	0 (0)	0 (0)	0 (0)
Insomnia	0 (0)	1 (8.3)	0 (0)	0 (0)
Menstruation irregular	1 (2.8)	0 (0)	0 (0)	0 (0)
Lower respiratory tract congestion	1 (2.8)	0 (0)	0 (0)	0 (0)
Skin neoplasm excision	0 (0)	0 (0)	0 (0)	1 (8.3)

Conclusions

Immunologic effects of soquelitinib



- Soquelitinib is a first-in-class selective oral ITK inhibitor that suppresses Th2 and Th17 inflammatory responses and increases Tregs
- Clean safety profile with no infection signal and no lab abnormalities
- Early and deep response with short dosing period
- Durable treatment effects with no evidence of rebound flare with cessation
- Activity seen in prior systemic therapy resistant patients
- Treatment of autoimmune/inflammatory diseases based on rebalancing of immunity could reduce need for chronic therapy

We thank the clinical trial participants and collaborating sites:

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