P0231

Rapid Reduction of Symptoms Reported in Daily Diaries in Patients With Atopic Dermatitis Treated With Baricitinib Plus Topical Corticosteroids: Results From 2 Phase 3 Trials

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BACKGROUND

- Itch, sleep disturbance, and skin pain (eg, discomfort or soreness) are highly burdensome symptoms in atopic dermatitis (AD)[1,2]
- Baricitinib is an oral, selective Janus kinase (JAK)1/JAK2 inhibitor[3] in development for the treatment of moderate-to-severe AD
- BREEZE-AD7 (NCT03733301) and BREEZE-AD4 (NCT03428100) are multicenter, randomized, double-blind, placebo-controlled, Phase 3 studies evaluating the efficacy and safety of baricitinib in combination with topical corticosteroids (TCS) in adults with:
  - Moderate-to-severe AD who had an inadequate response to topical therapies (BREEZE-AD7)[4]
  - Moderate-to-severe AD who had an inadequate response to topical therapies and either experienced failure, were intolerant to, or had a contraindication to cyclosporine (BREEZE-AD4)

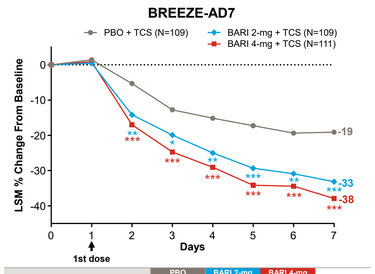
OBJECTIVE

- To examine the effect of baricitinib on patient-reported outcomes, including itch, sleep disturbance, and skin pain, in the first week of treatment in adults with moderate-to-severe AD in BREEZE-AD7 and BREEZE-AD4

KEY RESULTS

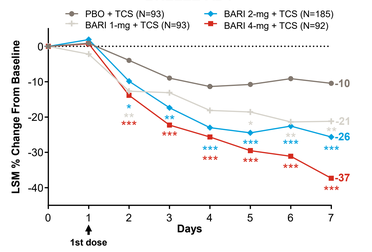
Percent Reduction in Itch NRS From Baseline Was Greater in BARI Groups Compared to PBO

BREEZE-AD7



	PBO + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	7.4 (1.7)	7.0 (2.1)	7.0 (2.0)	7.1 (2.0)
Day 7 change from baseline, LSM (SE)	-1.4 (0.2)	-2.4 (0.2)***	-2.7 (0.2)***	-

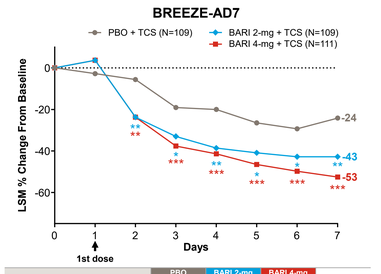
BREEZE-AD4



	PBO + TCS	BARI 1-mg + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	7.1 (1.9)	6.7 (2.3)	6.7 (1.9)	6.7 (2.3)	6.8 (2.1)
Day 7 change from baseline, LSM (SE)	-0.7 (0.2)	-1.4 (0.2)**	-1.7 (0.1)***	-2.5 (0.2)***	-

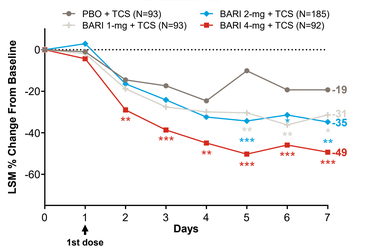
Percent Reduction in ADSS Item 1[a] From Baseline Was Greater in BARI Groups Compared to PBO

BREEZE-AD7



	PBO + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	2.3 (1.1)	2.1 (1.1)	2.1 (1.0)	2.2 (1.1)
Day 7 change from baseline, LSM (SE)	-0.5 (0.1)	-0.9 (0.1)**	-1.1 (0.1)***	-

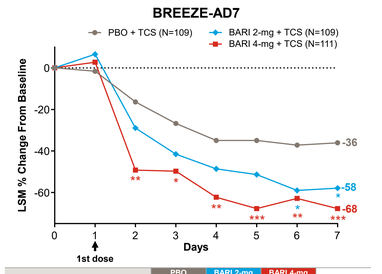
BREEZE-AD4



	PBO + TCS	BARI 1-mg + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	2.2 (1.1)	2.2 (1.1)	2.0 (1.1)	2.0 (1.2)	2.1 (1.1)
Day 7 change from baseline, LSM (SE)	-0.4 (0.1)	-0.7 (0.1)*	-0.7 (0.1)**	-1.0 (0.1)***	-

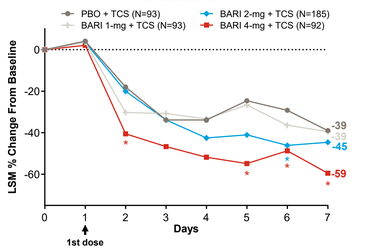
Percent Reduction in ADSS Item 2[a] From Baseline Was Greater in BARI Groups Compared to PBO

BREEZE-AD7



	PBO + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	1.8 (2.0)	1.9 (2.3)	1.8 (2.3)	1.8 (2.2)
Day 7 change from baseline, LSM (SE)	-0.7 (0.1)	-1.1 (0.1)*	-1.2 (0.1)***	-

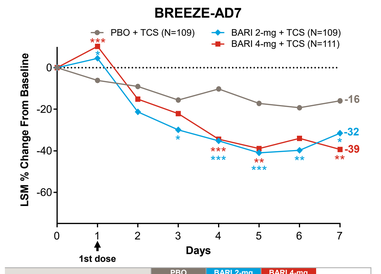
BREEZE-AD4



	PBO + TCS	BARI 1-mg + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	1.6 (1.6)	2.2 (2.7)	1.9 (3.1)	2.1 (1.8)	2.0 (2.5)
Day 7 change from baseline, LSM (SE)	-0.8 (0.1)	-0.8 (0.1)	-0.9 (0.1)	-1.2 (0.1)*	-

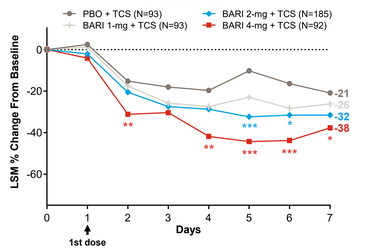
Percent Reduction in ADSS Item 3[a] From Baseline Was Greater in BARI Groups Compared to PBO

BREEZE-AD7



	PBO + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	2.5 (0.9)	2.4 (1.0)	2.4 (0.8)	2.4 (0.9)
Day 7 change from baseline, LSM (SE)	-0.4 (0.1)	-0.8 (0.1)*	-1.0 (0.1)**	-

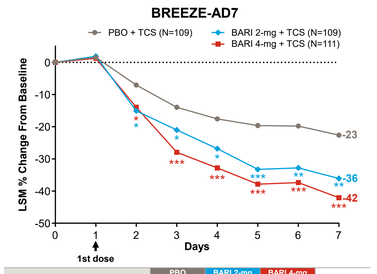
BREEZE-AD4



	PBO + TCS	BARI 1-mg + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	2.4 (1.0)	2.6 (0.9)	2.4 (0.9)	2.5 (1.0)	2.4 (0.9)
Day 7 change from baseline, LSM (SE)	-0.5 (0.1)	-0.6 (0.1)	-0.8 (0.1)	-0.9 (0.1)*	-

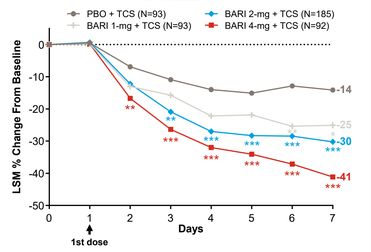
Percent Reduction in Skin Pain NRS From Baseline Was Greater in BARI Groups Compared to PBO

BREEZE-AD7



	PBO + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	6.8 (2.3)	6.3 (2.5)	6.0 (2.5)	6.4 (2.5)
Day 7 change from baseline, LSM (SE)	-1.4 (0.2)	-2.3 (0.2)**	-2.7 (0.2)***	-

BREEZE-AD4



	PBO + TCS	BARI 1-mg + TCS	BARI 2-mg + TCS	BARI 4-mg + TCS	Total
Baseline, mean (SD)	6.5 (2.3)	6.3 (2.7)	6.1 (2.4)	6.1 (2.6)	6.2 (2.5)
Day 7 change from baseline, LSM (SE)	-0.9 (0.2)	-1.6 (0.2)*	-1.9 (0.2)***	-2.6 (0.2)***	-

* p≤0.05, ** p≤0.01, *** p≤0.001 vs. PBO

* p≤0.05, ** p≤0.01, *** p≤0.001 vs. PBO; [a] Difficulty falling asleep due to itch (0=not at all; 4=very difficult)

* p≤0.05, ** p≤0.01, *** p≤0.001 vs. PBO; [a] Number of awakenings due to itch (frequency score 0-29)

* p≤0.05, ** p≤0.01, *** p≤0.001 vs. PBO; [a] Difficulty getting back to sleep due to itch (0=not at all; 4=very difficult)

* p≤0.05, ** p≤0.01, *** p≤0.001 vs. PBO

CONCLUSIONS

- In 2 Phase 3 trials of baricitinib plus TCS for the treatment of moderate-to-severe AD, significant improvements (vs. placebo) were observed, as early as Day 2, for:
  - Itch severity and skin pain (BREEZE-AD7 and BREEZE-AD4)
  - Falling asleep and awakening (BREEZE-AD7 and BREEZE-AD4)
  - Getting back to sleep (BREEZE-AD4)

REFERENCES

1. Vakharia PP, et al. *Ann Allergy Asthma Immunol.* 2017;119:548-522.
2. Silverberg JI, et al. *J Invest Dermatol.* 2015;135:56-66.
3. Fridman JS, et al. *J Immunol.* 2010;184:5298-5307.
4. Reich K, et al. *JAMA Dermatol.* 2020; doi:10.1001/jamadermatol.2020.3260.

ABBREVIATIONS

AD=atopic dermatitis; ADSS=Atopic Dermatitis Sleep Scale; BARI=baricitinib; DLQI=Dermatology Life Quality Index; EASI=Eczema Area and Severity Index; ITT=Intent-to-Treat; LSM=least squares mean; MMRM=mixed-effects model of repeated measures; NRS=numeric rating scale; PBO=placebo; PGI-S-AD=Patient Global Impression of Severity-AD; R=randomization; SD=standard deviation; SE=standard error; TCS=topical corticosteroid; vIGA-AD=validated Investigator Global Assessment for AD; W=Week

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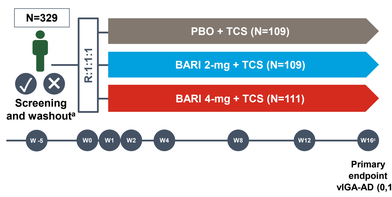
METHODS

Study Design, BREEZE-AD7

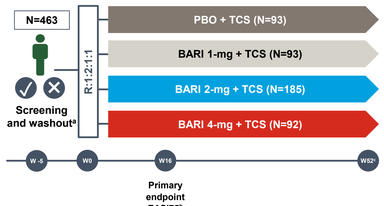


Key Inclusion Criteria

- ≥18 years old and diagnosis of AD for ≥12 months
- Moderate-to-severe AD at screening and randomization, defined as:
  - Validated Investigator Global Assessment for AD (vIGA-AD™) ≥3
  - Eczema Area and Severity Index (EASI) ≥16
  - Body surface area (BSA) ≥10%

[a] All patients washed out of AD treatments; [b] Proportion of patients achieving vIGA-AD (0,1) with a ≥2-point improvement; [c] Patients enter into long-term extension study BREEZE-AD3 or a post-treatment follow-up period (4 weeks)

Study Design, BREEZE-AD4

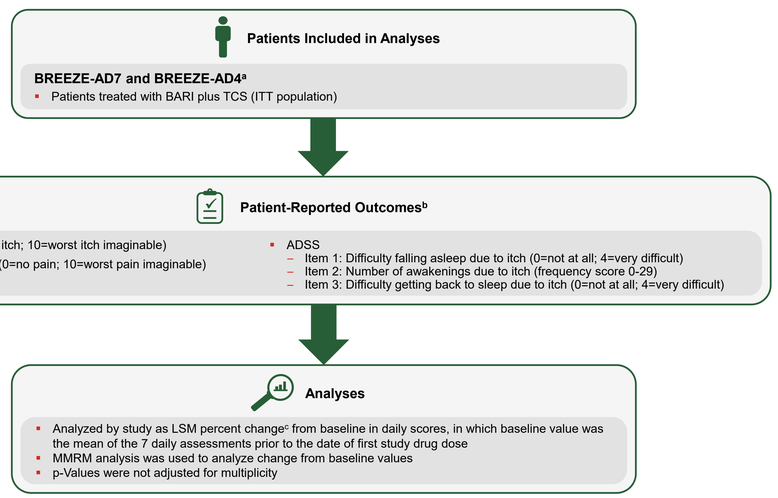


Key Inclusion Criteria

- ≥18 years old and diagnosis of AD for ≥12 months
- Moderate-to-severe AD at screening and randomization, defined as:
  - vIGA-AD ≥3
  - EASI ≥16
  - BSA ≥10%
- History of inadequate response, contraindication, or intolerance to cyclosporine

[a] All patients washed out of AD treatments; [b] Proportion of patients achieving 75% improvement from baseline in EASI score; [c] Patients completing W52 entered a double-blind, long-term extension through W104. Patients entering the long-term extension were evaluated for inclusion in a randomized down-titration substudy. Patients completing W104 will have the possibility to remain in the trial for up to 96 additional weeks

Analysis Populations, Assessment, and Statistical Analysis



[a] Patients in BREEZE-AD7 had inadequately responded to topical therapies, and patients in BREEZE-AD4 had inadequately responded to topical therapies and either experienced failure, were intolerant to, or had a contraindication to cyclosporine; [b] An electronic daily diary was used to assess symptoms in the past 24 hours; [c] LSM percent change from baseline = [LSM change from baseline / overall mean at baseline] × 100

RESULTS

Baseline Demographics and Disease Characteristics Were Similar Between Groups

	BREEZE-AD7			BREEZE-AD4			
	PBO + TCS (N=109)	BARI 2-mg + TCS (N=109)	BARI 4-mg + TCS (N=111)	PBO + TCS (N=93)	BARI 1-mg + TCS (N=93)	BARI 2-mg + TCS (N=185)	BARI 4-mg + TCS (N=92)
Age, years	33.7 (13.2)	33.8 (12.8)	33.9 (11.4)	38.7 (13.6)	38.9 (14.0)	37.3 (13.6)	38.7 (13.3)
Female, n (%)	38 (34.9)	39 (35.8)	36 (32.4)	44 (47.3)	35 (37.6)	52 (28.1)	35 (38.0)
Race, n (%)							
White	46 (42.2)	50 (45.9)	54 (48.6)	74 (79.6)	70 (75.3)	145 (78.4)	71 (77.2)
Asian	57 (52.3)	57 (52.3)	54 (48.6)	16 (17.2)	19 (20.4)	36 (19.5)	18 (19.6)
vIGA-AD of 4, n (%)	48 (44.4)	50 (45.9)	50 (45.0)	50 (53.8)	47 (50.5)	93 (50.5)	47 (51.1)
EASI	28.5 (12.3)	29.3 (11.9)	30.9 (12.6)	30.9 (11.6)	34.3 (13.5)	30.6 (12.4)	32.7 (13.7)
DLQI	15.0 (7.9)	15.0 (7.7)	14.7 (7.9)	14.5 (6.9)	14.3 (8.3)	13.6 (7.4)	14.0 (8.1)
PGI-S-AD	4.2 (0.8)	3.9 (0.8)	4.0 (0.8)	4.1 (0.7)	4.0 (0.8)	3.9 (0.7)	4.0 (0.9)
Itch NRS	7.4 (1.7)	7.0 (2.1)	7.0 (2.0)	7.1 (1.9)	6.7 (2.3)	6.7 (1.9)	6.7 (2.3)
ADSS							
Item 1	2.3 (1.1)	2.1 (1.1)	2.1 (1.0)	2.2 (1.1)	2.2 (1.1)	2.0 (1.1)	2.0 (1.2)
Item 2	1.8 (2.0)	1.9 (2.3)	1.8 (2.3)	1.6 (1.6)	2.2 (2.7)	1.9 (3.1)	2.1 (1.8)
Item 3	2.5 (0.9)	2.4 (1.0)	2.4 (0.8)	2.4 (1.0)	2.6 (0.9)	2.4 (0.9)	2.5 (1.0)
Skin Pain NRS	6.8 (2.3)	6.3 (2.5)	6.0 (2.5)	6.5 (2.3)	6.3 (2.7)	6.1 (2.4)	6.1 (2.6)

Data are mean (standard deviation) unless stated otherwise

DISCLOSURES

- **T. Buhl** has received honoraria as a consultant for: ALK-Abelló, AstraZeneca, Eli Lilly and Company, and Sanofi; has received research support from: Kiniksa, Philips, and Thermo Fisher Scientific; and has served as a paid speaker for: ALK-Abelló, Eli Lilly and Company, Janssen, Meda Pharmaceuticals, and Novartis; **D. Rosmarin** has received honoraria as a consultant for: AbbVie, Celgene, Dermavant Sciences, Eli Lilly and Company, Incyte, Janssen, Novartis, Pfizer, Regeneron, Sanofi, and Sun Pharmaceuticals; has received research support from: AbbVie, Bristol Myers Squibb, Celgene, Dermira, Eli Lilly and Company, Incyte, Janssen, Merck, Novartis, Pfizer, and Regeneron; and has served as a paid speaker for: AbbVie, Celgene, Eli Lilly and Company, Janssen, Novartis, Pfizer, Regeneron, and Sanofi; **E. Serra** has served on advisory boards or as a speaker for: AbbVie, Eli Lilly and Company, Galderma, Novartis, Pfizer, and Sanofi; **P. Fernandez-Peñas** has served on advisory boards for: AbbVie, Celgene, Eli Lilly and Company, Janssen, Meda Pharmaceuticals, Merck Sharp & Dohme, Novartis, and Roche; received grants/research support from: AbbVie, Amgen, Eli Lilly and Company, Janssen, Novartis, Pfizer, Regeneron, and Roche; and received honoraria or consultation fees from: AbbVie, Amgen, Eli Lilly and Company, Galderma, Janssen, La Roc, Merck Serono, Merck Sharp & Dohme, Novartis, Roche, and Schering Plough; **A. Igarashi** has received honoraria as a consultant or speaker for: AbbVie, Eli Lilly Japan, Japan Tobacco Inc, LEO Pharma, Maruho, Novartis, Sanofi, and Torii Pharmaceutical; and has received research support from: AbbVie, Amgen, Eli Lilly Japan, Japan Tobacco Inc, Novartis, Otsuka Pharmaceutical, and Sanofi; **M. P. Konstantinou** has served as a paid speaker for: AbbVie, Eli Lilly and Company, Janssen, and Novartis; **S. Chen** is an employee of: Syneos Health; **N. Lu** is an employee of: IQVIA; **E. Pierce** and **M. Casillas** are employees and shareholders of: Eli Lilly and Company
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