Rapid and Concurrent Improvements in Signs and Symptoms of Atopic Dermatitis with Baricitinib in Phase 3 Studies

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BACKGROUND

- Itch, skin pain, and sleep disturbance are highly burdensome symptoms in atopic dermatitis (AD)
- How quickly the signs and symptoms of AD improve after starting treatment is an important consideration
- Baricitinib is an oral selective and reversible inhibitor of Janus kinases (JAK)1 and JAK2
- The efficacy and safety of baricitinib were evaluated in adult patients with moderate-to-severe AD and a history of inadequate response or intolerance to existing topical therapies in 2 Phase 3 studies, BREEZE-AD1 (NCT03334396) and BREEZE-AD2 (NCT03334422)

OBJECTIVE

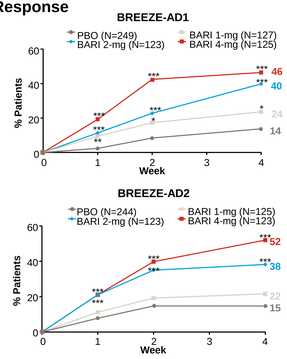
- To assess the onset and magnitude of changes across different severity scales and patient-reported outcomes for the first 4 weeks of treatment in BREEZE-AD1 and BREEZE-AD2

Abbreviations

AD=atopic dermatitis; ADSS=Atopic Dermatitis Sleep Scale; BARI=baricitinib; DLQI=Dermatology Life Quality Index; EASI=Eczema Area Severity Index; IGA=Investigator's Global Assessment; LSM=least squares mean; NRS=Numeric Rating Scale; PBO=placebo; POEM=Patient Oriented Eczema Measure; QD=once daily; SE=standard error; W=week

KEY RESULTS

Proportion of Patients Achieving EASI50 Response

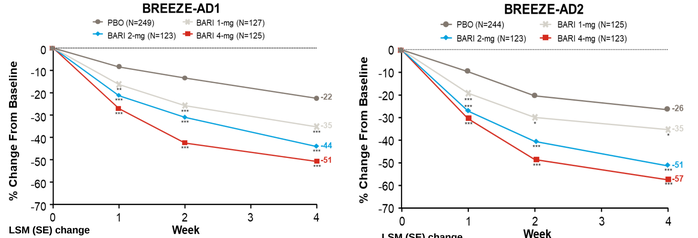


* p≤0.05 vs. PBO; ** p≤0.01 vs. PBO; *** p≤0.001 vs. PBO

Improvement From Baseline in Signs and Symptoms of Atopic Dermatitis[a]

[a] Percent change from baseline values were calculated as the change from baseline divided by the mean at baseline

Percent Change From Baseline in EASI[a]



LSM (SE) change	Week 1	Week 2	Week 4
PBO	-2.43 (0.48)	-3.96 (0.59)	-5.92 (0.71)
BARI 1-mg	-4.48 (0.64)	-6.92 (0.81)	-9.70 (0.96)
BARI 2-mg	-6.33 (0.64)	-8.74 (0.79)	-13.11 (0.90)
BARI 4-mg	-8.67 (0.65)	-13.14 (0.77)	-15.34 (0.86)

LSM (SE) change	Week 1	Week 2	Week 4
PBO	-3.28 (0.58)	-6.25 (0.78)	-7.95 (0.94)
BARI 1-mg	-6.34 (0.81)	-9.29 (1.03)	-10.71 (1.20)
BARI 2-mg	-8.36 (0.80)	-12.51 (1.01)	-15.17 (1.15)
BARI 4-mg	-9.68 (0.79)	-14.44 (0.99)	-16.78 (1.09)

* p≤0.05 vs. PBO; ** p≤0.01 vs. PBO; *** p≤0.001 vs. PBO; [a] Percent change from baseline values were calculated as the change from baseline divided by the mean at baseline

CONCLUSIONS

- Treatment with baricitinib resulted in rapid and concurrent improvements in skin measures, key symptoms, and quality of life
  - Spider plots revealed improvement of similar magnitude (from Week 1 onwards) during the 4 weeks in all major disease domains
- Statistically and clinically significant improvements were seen as early as Week 1
- Baricitinib represents a potential novel therapy for the treatment of patients suffering moderate-to-severe AD, with rapid improvement demonstrated across multiple, clinically important domains, including skin measures, symptoms, and quality of life

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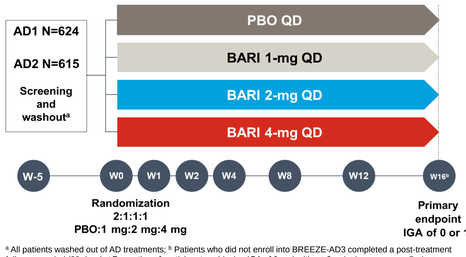
METHODS

Study Design, BREEZE-AD1 and BREEZE-AD2



[a] All patients washed out of AD treatments; [b] Patients who did not enroll into BREEZE-AD3 completed a post-treatment follow-up period (28 days); [c] Proportion of participants achieving IGA of 0 or 1 with a ≥2-point improvement; Patients experiencing unacceptable worsening of AD symptoms could receive rescue therapy at any time. Rescue therapy comprised triamcinolone 0.1% cream and/or hydrocortisone 2.5% ointment (or an equivalent topical corticosteroid cream/ointment if these formulations were not available)

Key Eligibility Criteria

- ≥18-years-old, and diagnosis of AD for ≥12 months
- Moderate-to-severe AD at screening and randomization, defined as:
  - Validated Investigator's Global Assessment of AD score of 3 or 4
  - Eczema Area Severity Index (EASI) ≥16
  - Body surface area involvement ≥10%
- Inadequate response or intolerance to ≥1 topical medication <6 months prior to screening
  - Patients who failed systemic therapies intended to treat AD within 6 months preceding screening will also be considered as a surrogate for having inadequate response to topical medication
- 2-week washout for topical corticosteroids and 4-week washout for systemic therapies
- No topical corticosteroid use allowed during treatment period, except as rescue

Assessments (up to Week 4)

- Proportion of patients achieving at least 50% improvement from baseline in EASI (EASI50)
- Percent changes from baseline in:
  - EASI
  - Itch Numeric Rating Scale (NRS: 0 = no itch; 10 = worst itch imaginable; past 24 hours)
  - Skin Pain NRS (0 = no pain; 10 = worst pain imaginable; past 24 hours)
  - Atopic Dermatitis Sleep Scale (ADSS)
    - Item 2: Number of nighttime awakenings (frequency score 0-29; past 24 hours)
  - Dermatology Life Quality Index
  - Patient-Oriented Eczema Measure

Statistical Analysis

- Intent-to-Treat population
  - Continuous data compared using mixed model repeated measure analysis
    - Model included change-from-baseline as the response variable, treatment, region, baseline disease severity, visit, and treatment-by-visit-interaction as fixed categorical effects and baseline, baseline-by-visit-interaction as fixed continuous effects
  - Categorical data compared using logistic regression analysis with non-responder imputation for missing data
    - Analysis included treatment, baseline value, region, and baseline disease severity as factors
- Data after any rescue therapy or treatment discontinuation were considered missing from the analysis

RESULTS

Baseline Characteristics and Disease Activity

	BREEZE-AD1				BREEZE-AD2			
	PBO (N=249)	BARI 1-mg (N=127)	BARI 2-mg (N=123)	BARI 4-mg (N=125)	PBO (N=244)	BARI 1-mg (N=125)	BARI 2-mg (N=123)	BARI 4-mg (N=123)
Age, years	35 (13)	36 (12)	35 (14)	37 (13)	35 (13)	33 (10)	36 (13)	34 (14)
Female, %	41%	39%	33%	34%	37%	36%	47%	33%
Race								
Caucasian, %	60%	58%	61%	56%	69%	68%	69%	67%
Asian, %	30%	31%	28%	33%	30%	29%	30%	31%
IGA of 4, %	42%	42%	42%	41%	50%	51%	50%	51%
EASI	32 (13)	29 (12)	31 (12)	32 (13)	33 (13)	33 (13)	35 (16)	33 (13)
Itch NRS	6.7 (2.0)	6.1 (2.1)	6.4 (2.2)	6.5 (2.0)	6.8 (2.2)	6.4 (2.2)	6.6 (2.2)	6.6 (2.2)
Skin Pain NRS	6.1 (2.5)	5.5 (2.4)	5.7 (2.6)	5.7 (2.4)	6.2 (2.5)	5.7 (2.7)	6.2 (2.5)	6.0 (2.6)
ADDS Item 2	3.4 (5.2)	2.5 (3.4)	2.3 (4.1)	3.3 (5.2)	1.8 (2.1)	1.6 (1.8)	2.1 (2.9)	1.9 (2.5)
DLQI	14 (7)	13 (7)	13 (8)	14 (7)	15 (8)	15 (8)	14 (8)	14 (8)
POEM	21 (6)	20 (6)	21 (6)	21 (6)	21 (6)	20 (7)	21 (6)	20 (6)

Data are mean (standard deviation) unless stated otherwise

Disclosures

- **E. L. Simpson** has received personal fees and/or has been an investigator for: Eli Lilly and Company, Galderma, Leo Pharma, Merck, Pfizer, Regeneron, and a consultant with honorarium for: AbbVie, Boehringer Ingelheim, Dermavant, Eli Lilly and Company, Incyte, Leo Pharma, Pfizer, Pierre Fabre Dermo Cosmetique, Regeneron, and Sanofi-Genzyme; **J. P. Thyssen** has been an advisory board member, and/or received speaker honoraria, and/or has participated in clinical studies for: Eli Lilly and Company, Pfizer, and Sanofi-Genzyme; **R. Bissonnette** has received grants/research support, honoraria, or consulting fees from: AbbVie, Amgen, ApoPharma, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly and Company, Galderma, GSK-Stiefel, Merck, Incyte, Janssen, Kineta, Leo Pharma, Novartis, Pfizer, Tribute, and Xenoport; **B. Jia**, **F. P. Nunes**, **M. Casillas**, **A. M. DeLozier**, **M. J. Rueda**, **J. M. Janes**, **X. Zhang**, and **M. Gamalo** and are current employees and shareholders of Eli Lilly and Company; **E. Guttman-Yassky** has received research funds (grants paid to the institution) from and/or been a consultant for: AbbVie, Almirall, Amgen, AnaptysBio, Asana Biosciences, Boehringer Ingelheim, Cara Therapeutics, Celgene, Concert, DBV, Dermavant, Dermira, DS Biopharma, Eli Lilly and Company, EMD Serono, Escalier, Glenmark, Galderma, Innovaderm, Janssen, Kiniska, Kyowa Kirin, Leo Pharma, Mitsubishi Tanabe, Novan, Pfizer, Ralexar, RAPT Therapeutics, Regeneron, Sanofi, Sienna Biopharma, UCB, and Union Therapeutics; **K. Reich** has been an advisory board member, and/or speaker, and/or consultant, and/or has participated in clinical studies for: AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celgene, Covagen, Forward Pharma, GlaxoSmithKline, Janssen-Cilag, Leo Pharma, Eli Lilly and Company, Medac, MSD, Novartis, Pfizer, Regeneron, Takeda, UCB, and Xenoport; **T. Bieber** has received grants as an investigator and honoraria for lecturing, or consulting fees from: AbbVie, Almirall, AnaptysBio, Arena, Asana Biosciences, Astellas, BioVersys, Boehringer Ingelheim, Celgene, Daichi-Sankyo, Dermavant/Roivant, DermTreat, DS Pharma, Eli Lilly and Company, Evaxion, FLX Bio, Galapagos/MorphoSys, Galderma, Glenmark, GlaxoSmithKline, Incyte, Kymab, Leo Pharma, L´Oréal, MenloTx, Novartis, Pfizer, Pierre Fabre, Sanofi-Regeneron, UCB, and Vectans
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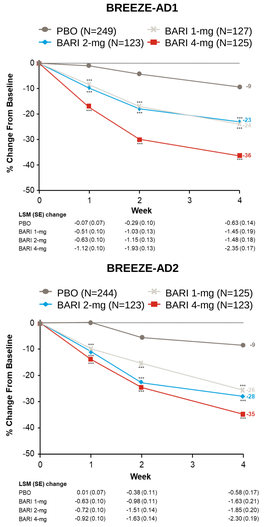
Percent Change From Baseline in Itch NRS[a]

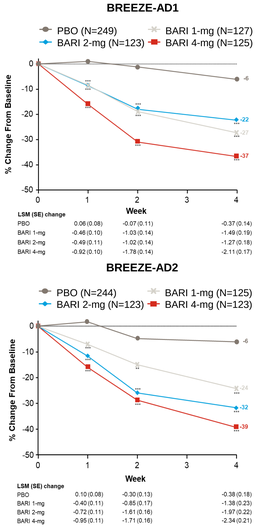


LSM (SE) change	Week 1	Week 2	Week 4
PBO	-0.07 (0.07)	-0.29 (0.10)	-0.63 (0.14)
BARI 1-mg	-0.51 (0.10)	-1.03 (0.13)	-1.45 (0.19)
BARI 2-mg	-0.63 (0.10)	-1.15 (0.13)	-1.48 (0.18)
BARI 4-mg	-1.12 (0.10)	-1.93 (0.13)	-2.35 (0.17)

LSM (SE) change	Week 1	Week 2	Week 4
PBO	0.01 (0.07)	-0.38 (0.11)	-0.58 (0.17)
BARI 1-mg	-0.53 (0.10)	-0.98 (0.11)	-1.63 (0.21)
BARI 2-mg	-0.72 (0.10)	-1.51 (0.14)	-1.85 (0.20)
BARI 4-mg	-0.92 (0.10)	-1.63 (0.14)	-2.30 (0.19)

*** p≤0.001 vs. PBO; [a] Percent change from baseline values were calculated as the change from baseline divided by the mean at baseline

Percent Change From Baseline in Skin Pain NRS[a]

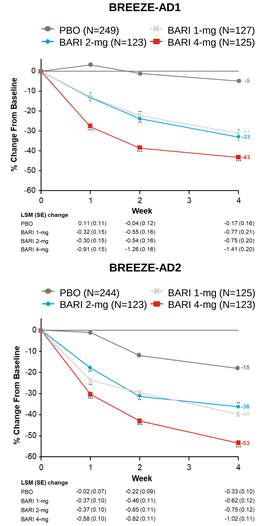


LSM (SE) change	Week 1	Week 2	Week 4
PBO	0.06 (0.08)	-0.07 (0.11)	-0.37 (0.14)
BARI 1-mg	-0.46 (0.10)	-1.03 (0.14)	-1.49 (0.19)
BARI 2-mg	-0.49 (0.11)	-1.02 (0.14)	-1.27 (0.18)
BARI 4-mg	-0.92 (0.10)	-1.78 (0.14)	-2.11 (0.17)

LSM (SE) change	Week 1	Week 2	Week 4
PBO	0.10 (0.08)	-0.30 (0.13)	-0.38 (0.18)
BARI 1-mg	-0.40 (0.11)	-0.85 (0.17)	-1.38 (0.23)
BARI 2-mg	-0.72 (0.11)	-1.61 (0.16)	-1.97 (0.22)
BARI 4-mg	-0.95 (0.11)	-1.71 (0.16)	-2.34 (0.21)

** p≤0.01 vs. PBO; *** p≤0.001 vs. PBO; [a] Percent change from baseline values were calculated as the change from baseline divided by the mean at baseline

Percent Change From Baseline in ADSS Item 2[a]



LSM (SE) change	Week 1	Week 2	Week 4
PBO	0.11 (0.11)	-0.04 (0.12)	-0.17 (0.16)
BARI 1-mg	-0.32 (0.15)	-0.55 (0.16)	-0.77 (0.21)
BARI 2-mg	-0.30 (0.15)	-0.54 (0.16)	-0.75 (0.20)
BARI 4-mg	-0.91 (0.15)	-1.26 (0.16)	-1.41 (0.20)

LSM (SE) change	Week 1	Week 2	Week 4
PBO	-0.02 (0.07)	-0.22 (0.09)	-0.33 (0.10)
BARI 1-mg	-0.37 (0.10)	-0.46 (0.11)	-0.62 (0.12)
BARI 2-mg	-0.37 (0.10)	-0.65 (0.11)	-0.75 (0.12)
BARI 4-mg	-0.58 (0.10)	-0.82 (0.11)	-1.02 (0.11)

* p≤0.05 vs. PBO; ** p≤0.01 vs. PBO; *** p≤0.001 vs. PBO; [a] Percent change from baseline values were calculated as the change from baseline divided by the mean at baseline

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