Efficacy of Baricitinib in Patients With Atopic Dermatitis and Atopic Comorbidities: Results of Pooled Data From 2 Phase 3 Monotherapy Randomized, Double-blind, Placebo-Controlled 16-Week Trials (BREEZE-AD1 and BREEZE-AD2)

610

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BACKGROUND

- Asthma and allergic rhinitis are frequent atopic comorbidities in atopic dermatitis (AD) and may influence the management of patients with AD[1]
- Baricitinib is an oral selective and reversible inhibitor of Janus kinase (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)[2]
  - BREEZE-AD1 and BREEZE-AD2 were conducted in multiple countries, excluding North America

OBJECTIVE

- To assess the efficacy and safety of baricitinib at Week 16 in patients with ≥1 atopic comorbidity at baseline in BREEZE-AD1 and BREEZE-AD2

REFERENCES

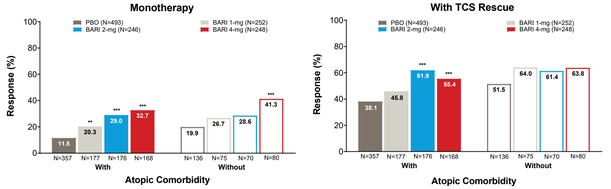
1. Silverberg JI. *Clin Dermatol*. 2017;35:360-366.
2. Simpson EL, et al. *Br J Dermatol*. 2020 Jan 29 [online ahead of print]. DOI: 10.1111/bjd.18898.

ABBREVIATIONS

AD=atopic dermatitis; ADSS=Atopic Dermatitis Sleep Scale; AE=adverse event; BAR=baricitinib; EASI=Eczema Area and Severity Index; EASI50=Eczema Area and Severity Index 50% improvement; HX=history; IGA=Investigator Global Assessment; MH=medical history; NRS=Numeric Rating Scale; PBO=placebo; QD=once daily; TEAE=treatment-emergent adverse event; TCS=topical corticosteroid; W=with; WO=without

KEY RESULTS

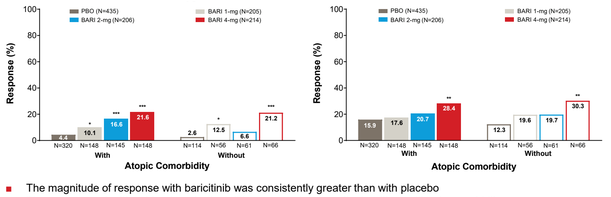
Proportion of Patients Achieving EASI50 Response at Week 16



- The magnitude of response with baricitinib was consistently greater than with placebo
- There were no significant treatment-effect differences between patients with or without comorbidity

** p≤0.01, *** p≤0.001 vs. PBO

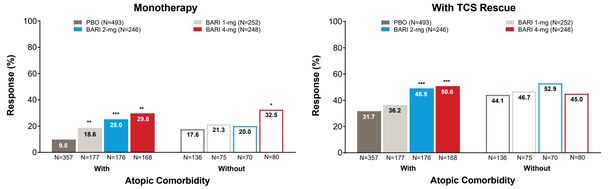
Proportion of Patients Achieving Itch NRS ≥4-Point Improvement Response at Week 16[a,b]



- The magnitude of response with baricitinib was consistently greater than with placebo
- There were no significant treatment-effect differences between patients with or without comorbidity

* p≤0.05, ** p≤0.01, *** p≤0.001 vs. PBO
[a] Analysis based on patients with Itch NRS ≥4 at baseline
[b] 0=no itch, 10=worst itch imaginable

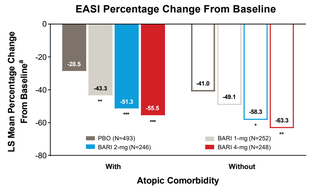
Proportion of Patients Achieving IGA (0, 1, 2) Response at Week 16[a]



- The magnitude of response with baricitinib was consistently greater than with placebo
- There were no significant treatment-effect differences between patients with or without comorbidity

* p≤0.05, ** p≤0.01, *** p≤0.001 vs. PBO
[a] 0=clear, 4=severe

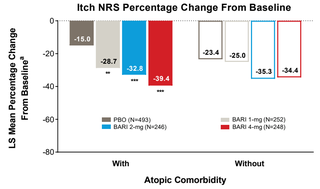
EASI Improvement at Week 16



- The change from baseline with baricitinib was consistently greater than with placebo
- There were no significant treatment-effect differences between patients with or without comorbidity

* p≤0.05, ** p≤0.01, *** p≤0.01 vs. PBO
[a] LS mean percentage change from baseline = (LS mean change from baseline / overall total mean at baseline) × 100

Itch Improvement at Week 16



- The change from baseline with baricitinib was consistently greater than with placebo
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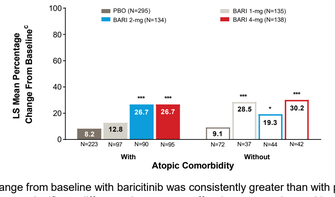
** p≤0.01, *** p≤0.001 vs. PBO
[a] LS mean percentage change from baseline = (LS mean change from baseline / overall total mean at baseline) × 100

Improvement in Sleep Disturbance Due to Itch at Week 16[a]



- The change from baseline with baricitinib was consistently greater than with placebo
- There was a significant difference in treatment effect between patients with or without comorbidity (p=0.0143)
  - The difference was based on the magnitude of the difference between baricitinib treatment and placebo; the direction of that difference was the same

* p≤0.05, ** p≤0.01, *** p≤0.01 vs. PBO
[a] ADSS Item 2 = How many times did your itch cause you to wake up last night?
[b] In patients with ADSS Item 2 score >1 at baseline
[c] LS mean percentage change from baseline = (LS mean change from baseline / overall total mean at baseline) × 100

Overview of Adverse Events

n (%)	BREEZE-AD1/AD2 PBO (N=493) W (N=357)	PBO (N=493) W/O (N=136)	BARI 1-mg (N=251) W (N=177)	BARI 1-mg (N=251) W/O (N=74)	BARI 2-mg (N=246) W (N=176)	BARI 2-mg (N=246) W/O (N=70)	BARI 4-mg (N=248) W (N=168)	BARI 4-mg (N=248) W/O (N=80)
Atopic comorbidity								
Any TEAE	213 (59.7)	59 (43.4)	107 (60.5)	28 (37.8)	107 (60.8)	35 (50.0)	107 (63.7)	32 (40.0)
Mild	123 (34.5)	35 (25.7)	53 (29.9)	20 (27.0)	63 (35.8)	25 (35.7)	70 (41.7)	22 (27.5)
Moderate	76 (21.3)	22 (16.2)	45 (25.4)	6 (8.1)	38 (21.6)	8 (11.4)	32 (19.0)	10 (12.5)
Severe	14 (3.9)	2 (1.5)	9 (5.1)	2 (2.7)	6 (3.4)	2 (2.9)	5 (3.0)	0
Serious AEs	13 (3.6)	2 (1.5)	9 (5.1)	1 (1.4)	2 (1.1)	1 (1.4)	3 (1.8)	0
Death	0	0	0	0	0	0	0	0
AEs leading to study discontinuation	2 (0.6)	0	3 (1.7)	0	3 (1.7)	0	2 (1.2)	0

- Most treatment-emergent adverse events were mild or moderate

Overview of Treatment-Emergent Infections

n (%)	BREEZE-AD1/AD2 PBO (N=493) W (N=357)	PBO (N=493) W/O (N=136)	BARI 1-mg (N=251) W (N=177)	BARI 1-mg (N=251) W/O (N=74)	BARI 2-mg (N=246) W (N=176)	BARI 2-mg (N=246) W/O (N=70)	BARI 4-mg (N=248) W (N=168)	BARI 4-mg (N=248) W/O (N=80)
Atopic comorbidity								
Patients with ≥1 infection	111 (31.1)	39 (28.7)	64 (36.2)	13 (17.6)	65 (36.9)	19 (27.1)	63 (37.5)	21 (26.3)
Opportunistic infection	0	0	0	0	0	0	0	0
Herpes zoster	1 (0.3)	0	0	0	0	2 (2.9)	0	0
Herpes simplex	10 (2.8)	4 (2.9)	11 (6.2)	2 (2.7)	11 (6.3)	0	8 (4.8)	6 (7.5)
Tuberculosis	0	0	0	0	0	0	0	0
Patients with ≥1 skin infection requiring antibiotic treatment	23 (6.4)	7 (5.1)	5 (2.8)	2 (2.7)	12 (6.8)	3 (4.3)	8 (4.8)	2 (2.5)

- Safety outcomes for patients with atopic comorbidities were similar to outcomes in the overall population[2]

CONCLUSIONS

- In adult patients with moderate-to-severe AD with comorbid atopic conditions, baricitinib treatment resulted in clinically meaningful improvements in skin symptoms, itch, and sleep disturbance
- In general, there were no treatment-effect differences between groups of patients with or without comorbidity
  - The only significant treatment-effect differences between patients with or without comorbidity were observed for ADSS Item 2, and the difference was based on magnitude, not on direction
- Overall safety outcomes for patients with atopic comorbidities were similar to outcomes in the overall trial population[2]

DISCLOSURES

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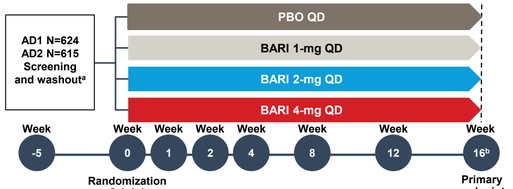
METHODS

Study Design, BREEZE-AD1 and BREEZE-AD2



[a] All patients washed out of AD treatments (2-week washout for TCS and 4-week washout for systemic therapies)
[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 TCS cream/ointment if these formulations were not available). TCS use was not allowed during the treatment period except as rescue

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 Global Assessment (IGA) of AD score of 3 or 4 (severe)
  - Eczema Area and 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 and intended to treat AD within 6 months preceding Screening were also considered as surrogates for having inadequate response to topical medication
- No topical corticosteroid (TCS) use allowed during treatment period, except as rescue

Assessments

Efficacy Assessments (at Week 16)

- Proportion of patients achieving ≥50% improvement in EASI (EASI50)
- Proportion of patients achieving IGA of 0, 1, or 2
- Proportion of patients achieving a 4-point improvement in itch Numeric Rating Scale (NRS)
- EASI percentage change from baseline through Week 16
- Itch NRS percentage change from baseline through Week 16
- Atopic Dermatitis Sleep Scale (ADSS) Item 2 percentage change from baseline at Week 16
  - ADSS Item 2 = How many times did your itch cause you to wake up last night?

Safety Assessments

- Frequency of adverse events and overview of infection in patients with and without atopic comorbidities[a]

Statistical Analysis

- Population: Pooled data from BREEZE-AD1 and BREEZE-AD2 clinical trials
- For discrete efficacy outcomes:
  - Data were analyzed using logistic regression[a]
  - Observations after TCS rescue were excluded and imputed in monotherapy analyses; observations after TCS rescue were included in TCS analyses
  - Non-responder imputation was used for missing data
- For continuous efficacy outcomes:
  - A mixed-model repeated measures (MMRM) analysis was used for EASI percentage change from baseline and Itch NRS percentage change from baseline as those assessments had multiple visits[b]
  - Analysis of covariance (ANCOVA) model was used for ADSS Item 2[c]
- Treatment-by-medical-history-comorbidity[d]-interaction was included in all models to test if treatment effects differ for patients with and without comorbidity
- There was no adjustment in p-values for multiplicity

[a] Terms in logistic regression: treatment, MH comorbidity, baseline disease severity (IGA), and treatment-by-MH-comorbidity and baseline
[b] Terms in MMRM: treatment, region, baseline disease severity (IGA), visit, MH comorbidity, treatment-by-visit-interaction, treatment-by-MH comorbidity-interaction, visit-by-MH comorbidity-interaction, and treatment-by-visit-by-MH-comorbidity-interaction, baseline, baseline-by-visit-interaction, and baseline-by-MH comorbidity
[c] Terms in ANCOVA: treatment, baseline value, region, baseline disease severity (IGA), MH comorbidity, and treatment-by-MH-comorbidity-interaction
[d] Prespecified MH comorbidity includes: adverse drug reaction, allergy to arthropod sting, allergy to chemicals, anaphylactic reaction, asthma, conjunctivitis allergic, dermatitis contact, food allergy, rhinitis allergic, seasonal allergy, and urticaria

[a] Prespecified medical history comorbidity (with) includes: adverse drug reaction, allergy to arthropod sting, allergy to chemicals, anaphylactic reaction, asthma, conjunctivitis allergic, dermatitis contact, food allergy, rhinitis allergic, seasonal allergy, and urticaria

RESULTS

Baseline Characteristics and Disease Activity

	BREEZE-AD1/AD2 PBO (N=493) W (N=357)	PBO (N=493) W/O (N=136)	BARI 1-mg (N=252) W (N=177)	BARI 1-mg (N=252) W/O (N=75)	BARI 2-mg (N=246) W (N=176)	BARI 2-mg (N=246) W/O (N=70)	BARI 4-mg (N=248) W (N=168)	BARI 4-mg (N=248) W/O (N=80)
Atopic comorbidity								
Age, years	34.9 (12.4)	36.7 (13.8)	34.6 (11.3)	33.8 (11.7)	34.0 (12.2)	38.3 (15.8)	35.2 (13.5)	36.0 (13.8)
Male, n (%)	226 (63.3)	76 (55.9)	108 (61.0)	50 (66.7)	107 (60.8)	40 (57.1)	114 (67.9)	51 (63.8)
Weight, kg	72.5 (15.1)	72.8 (16.8)	73.9 (17.2)	75.8 (16.0)	74.3 (16.7)	70.8 (14.9)	73.6 (17.3)	73.3 (13.3)
Duration since AD diagnosis, years	26.9 (14.1)	22.4 (16.0)	27.0 (13.5)	21.0 (14.1)	25.4 (13.1)	22.5 (16.5)	26.1 (14.4)	18.7 (14.6)
IGA, n (%)								
3	189 (52.9)	78 (57.4)	96 (54.2)	39 (52.0)	98 (55.7)	34 (48.6)	90 (53.6)	44 (55.0)
4	168 (47.1)	58 (42.6)	81 (45.8)	35 (46.7)	78 (44.3)	36 (51.4)	78 (46.4)	36 (45.0)
EASI	32.5 (12.8)	31.7 (13.2)	31.2 (12.3)	30.7 (12.6)	32.0 (13.3)	34.6 (16.0)	32.7 (12.5)	31.9 (13.1)
Itch NRS ≥4, n (%)	320 (89.6)	115 (84.6)	149 (84.2)	56 (74.7)	145 (82.4)	61 (87.1)	148 (88.1)	66 (82.5)

- Baseline demographics and disease activity were similar in patients with or without comorbidity

Data are mean (standard deviation) unless stated otherwise

Frequency of Medical History Comorbidity

n (%)	PBO (N=493)	BARI 1-mg (N=252)	BARI 2-mg (N=246)	BARI 4-mg (N=248)
Prespecified medical history of comorbidity	357 (72.4)	177 (70.2)	176 (71.5)	168 (67.7)
Comorbidity[a]				
Asthma	137 (38.4)	67 (37.9)	84 (47.7)	74 (44.0)
Allergic conjunctivitis	103 (28.9)	53 (29.9)	49 (27.8)	40 (23.8)
Allergic rhinitis	207 (58.0)	111 (62.7)	103 (58.5)	86 (51.2)
Contact dermatitis	37 (10.4)	27 (15.3)	22 (12.5)	17 (10.1)
Food allergy	149 (41.7)	72 (40.7)	73 (41.5)	63 (37.5)
Seasonal allergy	164 (45.9)	78 (44.1)	80 (45.5)	81 (48.2)
Urticaria	22 (6.2)	10 (5.6)	14 (8.0)	10 (6.0)

- The most common comorbidities were asthma, food allergy, allergic rhinitis, and seasonal allergy

[a] ≥5% occurrence, patients with multiple occurrences of the same event are counted under the highest severity