# Abrocitinib Induction, Randomized Withdrawal, and Response Recapture With Rescue Therapy in Patients With Moderate-to-Severe Atopic Dermatitis: Results From the JADE REGIMEN Phase 3 Trial

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**Disclosures**

**WG** has served as a scientific advisor and/or clinical study investigator for Pfizer Inc., Galderma, GSK, Eucerin, Johnson & Johnson, Janssen, Sanofi, BioNOOX, Beiersdorf/Eucerin. **ELS** reports grants from Pfizer Inc., Eli Lilly, Kyowa Kirin, LEO Pharma, Merck, and Regeneron and personal fees from Pfizer Inc., Bausch Health (Valeant), Dermira, Eli Lilly, Galderma, LEO Pharma, Menlo Therapeutics, Novartis, Regeneron, and Sanofi Genzyme. **AB** has served as a scientific advisor and/or clinical study investigator for Pfizer Inc., AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Evommune, Forte, Galderma, Incyte, Janssen, Landos, LEO Pharma, Novartis, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma. **RG** has served as an investigator for Pfizer, Amgen, Chugai, Regeneron, and UCB Pharma. **C-YC** is an investigator for Pfizer Inc., AbbVie, Dermira, Eli Lilly, Novartis, Oneness Biotech, Regeneron, Roche, and Sanofi; a consultant for Pfizer Inc., AbbVie, Eli Lilly, Novartis, Roche, and Sanofi; a speaker for Pfizer Inc., AbbVie, Eli Lilly, Mylan, Novartis, Roche, and Sanofi; and serves on advisory boards for Pfizer Inc., Mylan, Roche, and Sanofi. **MCC** is a former employee of Pfizer Inc. and may hold stock options. **MDB, HV, TK, PB, RR** are employees and shareholders of Pfizer Inc.

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# Background, Objective, and Methodology

**Background:** The chronic, relapsing-remitting nature of moderate-to-severe atopic dermatitis (AD) and population heterogeneity necessitates dosing flexibility. Abrocitinib is an oral Janus kinase 1 (JAK1) selective inhibitor under investigation for the treatment of moderate-to-severe AD

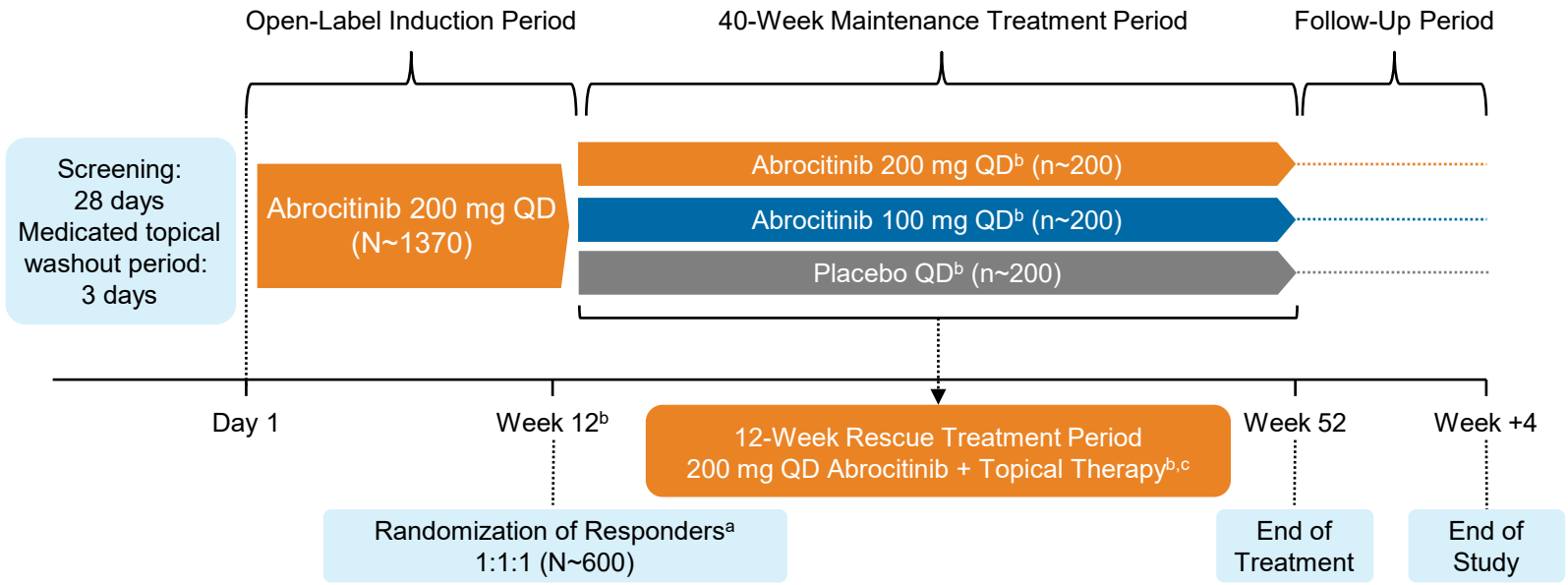
**Objective:** To evaluate response to treatment modification/interruption/reinitiation

## Study Design

Phase 3 multicenter, responder-enriched, double-blinded, placebo-controlled, randomized withdrawal study with rescue treatment in patients with protocol-defined flare (JADE REGIMEN, NCT03627767)

## Eligibility Criteria

- Adolescent and adult patients (≥12 years of age) with AD for ≥1 year
- Moderate-to-severe AD (IGA ≥3; EASI ≥16; %BSA ≥10; PP-NRS ≥4)
- Inadequate response or intolerance to topical medication or need for systemic therapy to control AD




### Primary Endpoint

Loss of response defined as ≥50% loss in initial EASI response with IGA score ≥2

### Other Secondary Endpoints

- IGA 0/1
- PP-NRS4
- EASI-75

### Safety

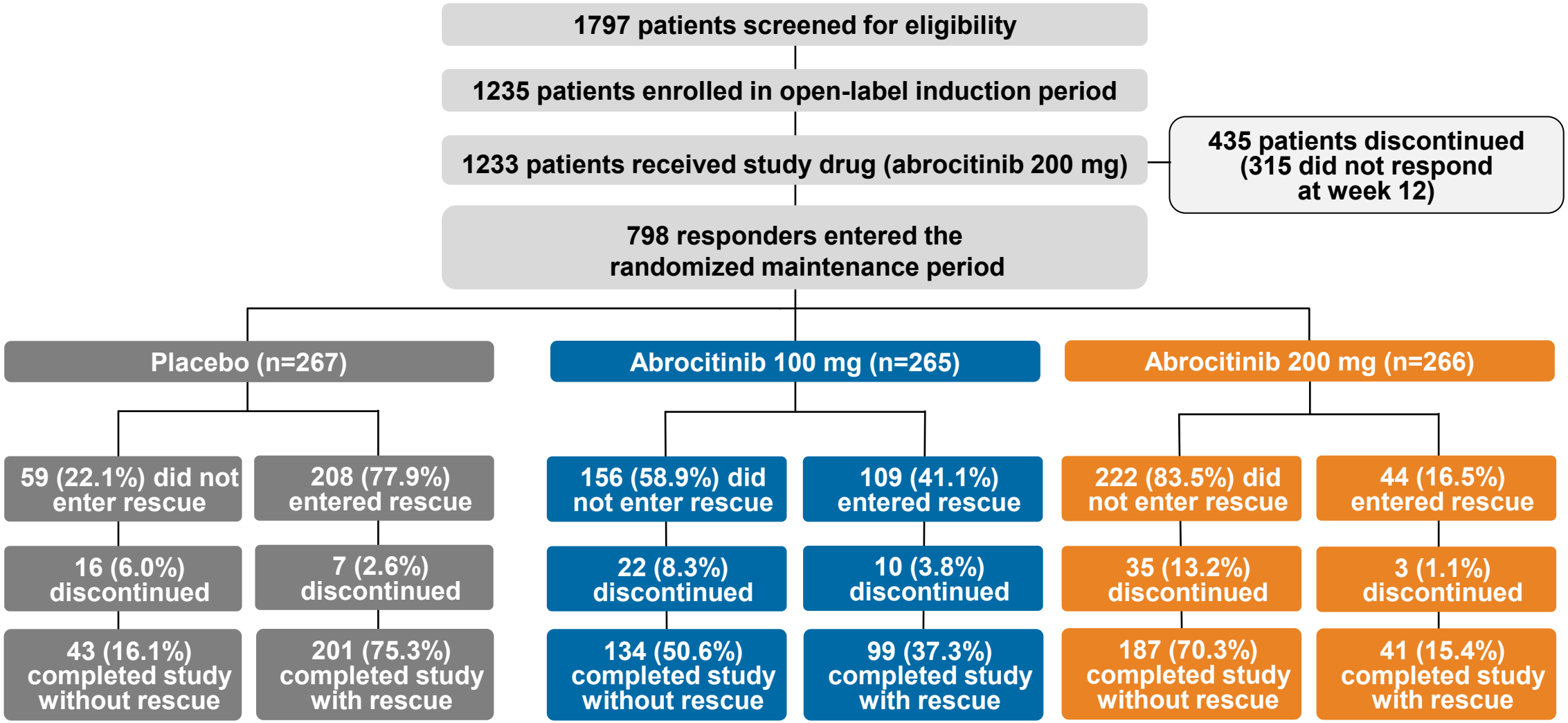
AE monitoring

### Randomization Stratification

Age (<18 years or ≥18 years)

AE, adverse event; %BSA, percentage of body surface area; EASI, Eczema Area and Severity Index; EASI-75, ≥75% improvement from baseline in EASI score; IGA, Investigator's Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale; PP-NRS4, ≥4-point improvement from baseline in PP-NRS score; QD once daily.The PP-NRS is used with permission of Regeneron Pharmaceuticals, Inc. and SAR&D. [a]Responder criteria at week 12 are defined as an IGA score of clear (0) or almost clear (1) with a ≥2 point reduction from baseline (IGA 0/1) and EASI-75; [b]Definition of flare: loss of ≥50% in EASI response and IGA score ≥2 at week 12; [c]Topical therapy included topical corticosteroids, calcineurin inhibitors, and crisaborole.

# Patient Disposition

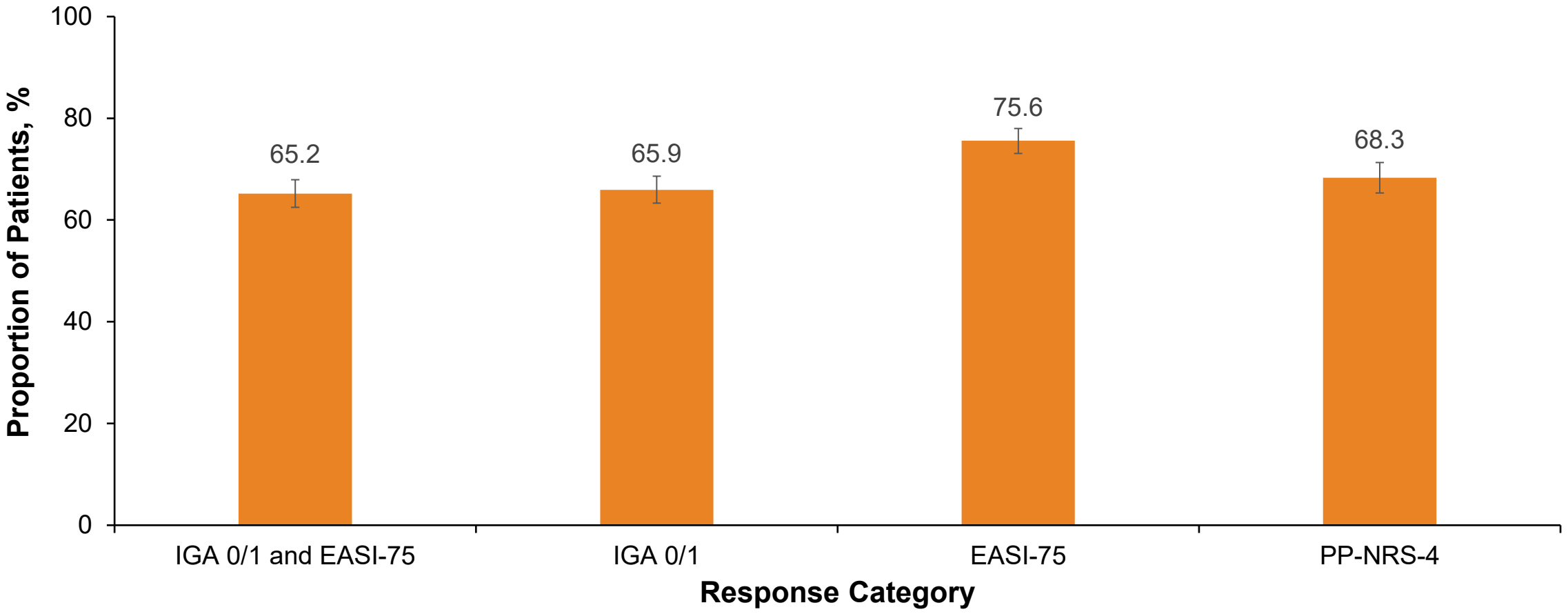


# Results 1: Demographics and Baseline Disease Characteristics

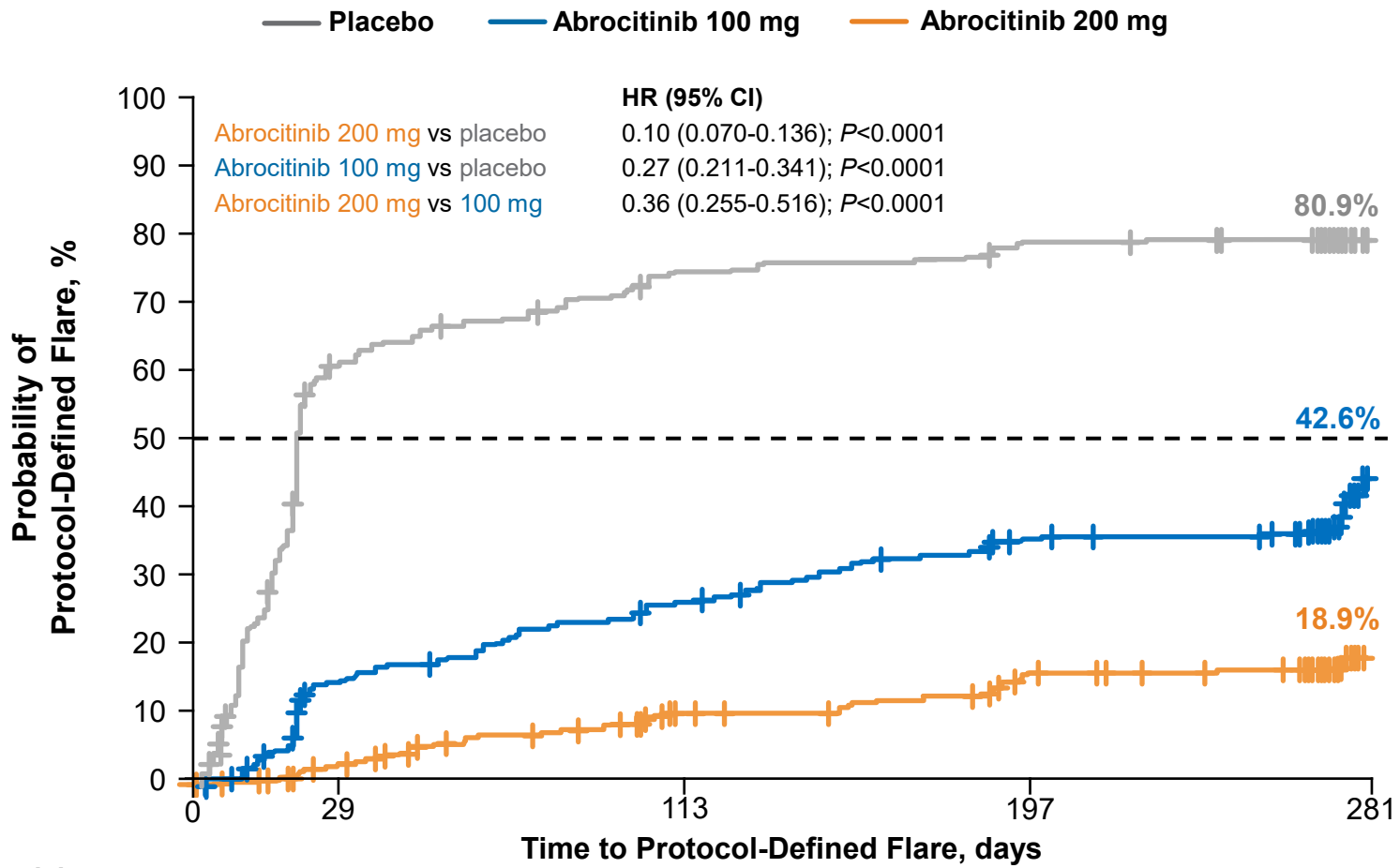
| | | Open-Label Period | | Randomized Maintenance Period | | |
|---|---|---|---|---|---|---|
| | | Total N=1233 | Total N=798 | Placebo n=267 | Abrocitinib 100 mg n=265 | Abrocitinib 200 mg n=266 |
| Age, mean (SD), y | | 31.6 (14.9) | 32.1 (14.8) | 31.8 (14.3) | 32.2 (14.9) | 32.3 (15.3) |
| Male, n (%) | | 684 (55.5) | 439 (55.0) | 141 (52.8) | 148 (55.8) | 150 (56.4) |
| Race, n (%) | White | 931 (75.5) | 621 (77.8) | 209 (78.3) | 208 (78.5) | 204 (76.7) |
| | Black/African American | 75 (6.1) | 33 (4.1) | 14 (5.2) | 9 (3.4) | 10 (3.8) |
| | Asian | 196 (15.9) | 124 (15.5) | 38 (14.2) | 41 (15.5) | 54 (16.9) |
| Disease duration, mean (SD), y | | 20.5 (14.6) | 20.9 (14.8) | 20.7 (14.9) | 20.5 (14.3) | 21.4 (15.1) |
| IGA, n (%) | Moderate (3) | 729 (59.1) | 508 (63.7) | 177 (66.3) | 161 (60.8) | 170 (63.9) |
| | Severe (4) | 504 (40.9) | 290 (36.3) | 90 (33.7) | 104 (39.2) | 96 (36.1) |
| EASI, mean (SD) | | 31.0 (12.3) | 30.3 (12.1) | 30.1 (12.2) | 30.5 (11.9) | 30.4 (12.3) |
| PP-NRS, mean (SD) | | 7.4 (1.7) | 7.3 (1.7) | 7.3 (1.7) | 7.2 (1.5) | 7.4 (1.8) |
| DLQI,[a] mean (SD) | | 16.0 (6.6) | 16.0 (6.5) | 15.9 (6.6) | 15.6 (6.3) | 16.5 (6.8) |
| CDLQI,[b] mean (SD) | | 12.3 (5.7) | 12.1 (5.5) | 13.4 (6.5) | 12.2 (5.0) | 10.7 (4.8) |

CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index.
[a]For patients aged ≥18 years; [b]For patients aged <18 years.

# Results 2: Week 12 Response to Abrocitinib 200 mg in Open-Label Induction Phase



# Results 3: Time to Protocol-Defined Flare During the Randomized Maintenance Period

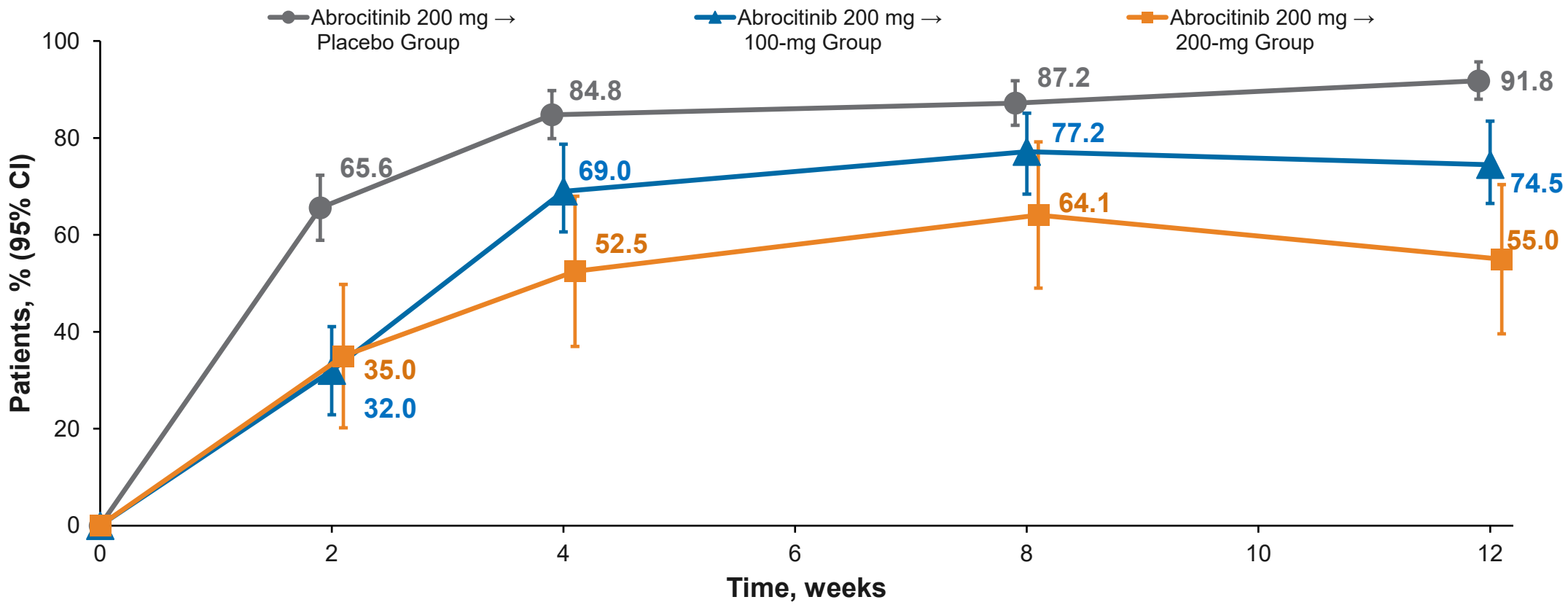



**Patients at risk,[a] n**

| | | | | | |
|---|---|---|---|---|---|
| Placebo | 267 | 112 | 63 | 48 | 20 |
| Abrocitinib 100 mg | 265 | 225 | 179 | 151 | 58 |
| Abrocitinib 200 mg | 266 | 255 | 220 | 201 | 69 |

HR, hazard ratio. [a]Patients who did not have flare and were continuing treatment. Flare: ≥50% loss of initial EASI response at week 12 with a new IGA score of ≥2.

# Results 4: Recovery of EASI-75 Response During the Rescue Period




| Evaluable patients, n | | | | |
|---|---|---|---|---|
| Placebo | 192 | 198 | 203 | 196 |
| Abrocitinib 100 mg | 100 | 100 | 101 | 102 |
| Abrocitinib 200 mg | 40 | 40 | 39 | 40 |

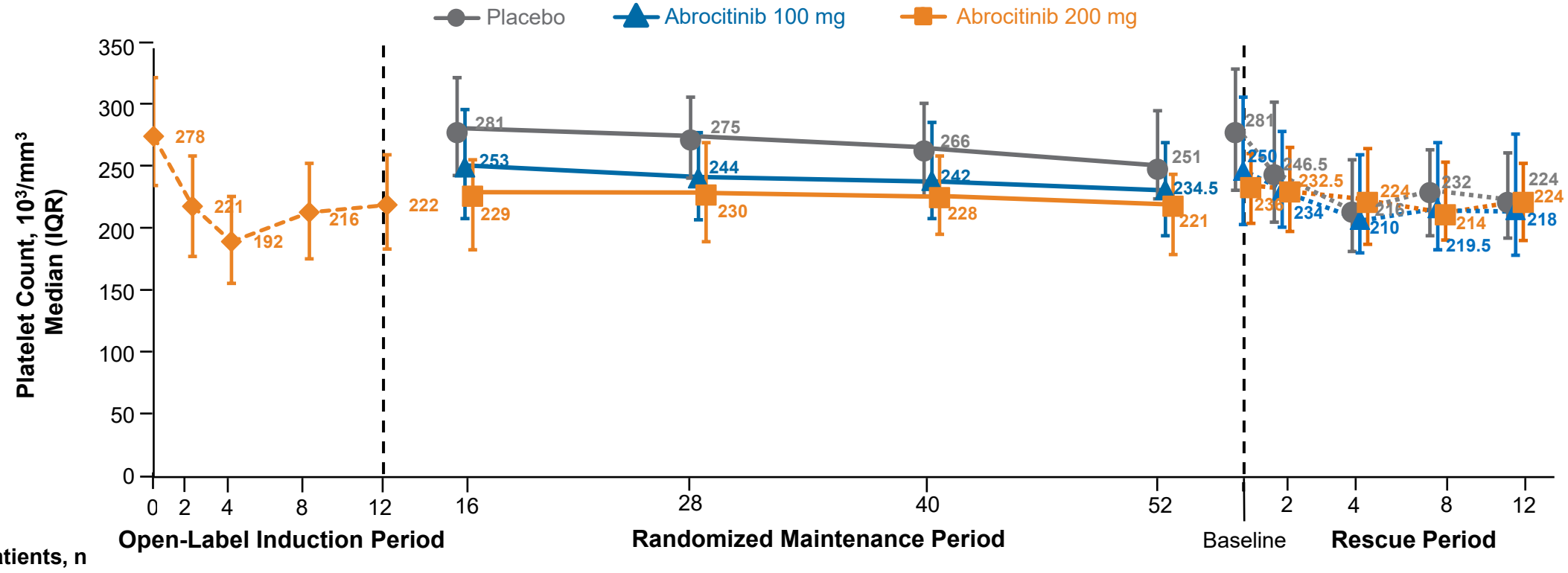
# Results 5: Summary of Adverse Events

| | Randomized Maintenance Period | | |
|---|---|---|---|
| **IR (95% CI)** | **Placebo N=267** | **Abrocitinib 100 mg n=265** | **Abrocitinib 200 mg n=266** |
| IRs for TEAEs occurring in ≥2% of patients (SAF-RA) | 163.18 (130.70-201.29) | 51.44 (39.86-65.32) | 63.10 (50.87-77.38) |
| Serious AEs, excluding events of AD | 3.18 (0.39-11.49) | 2.69 (0.73-6.88) | 7.77 (4.25-13.04) |
| Discontinuation because of AEs | 6.38 (1.74-16.34) | 3.36 (1.09-7.85) | 8.76 (5.01-14.23) |
| TEAEs with IR ≥4, excluding AD | | | |
| Nausea | 1.61 (0.04-8.95) | 1.35 (0.16-4.87) | 4.43 (1.91-8.72) |
| Bronchitis | 4.78 (0.99-13.97) | 2.03 (0.42-5.92) | 0.54 (0.01-3.03) |
| Conjunctivitis | 4.84 (1.00-14.14) | 2.02 (0.42-5.91) | 1.09 (0.13-3.92) |
| Herpes zoster | 1.59 (0.04-8.84) | 1.34 (0.16-4.85) | 4.40 (1.90-8.67) |
| Nasopharyngitis | 8.01 (2.60-18.70) | 6.98 (3.35-12.84) | 10.17 (6.03-16.07) |
| Upper respiratory tract infection | 9.80 (3.60-21.34) | 5.48 (2.37-10.80) | 4.42 (1.91-8.71) |
| Blood creatine phosphokinase increased | 1.59 (0.04-8.84) | 4.08 (1.50-8.89) | 7.85 (4.29-13.18) |
| Asthma | 4.77 (0.98-13.95) | 0.67 (0.02-3.74) | 2.19 (0.60-5.60) |
| Acne | 0.00 (0.00-5.85) | 3.42 (1.11-7.97) | 4.43 (1.91-8.73) |
| Pruritus | 6.44 (1.76-16.49) | 2.72 (0.74-6.97) | 1.64 (0.34-4.78) |

IR, incidence rate; SAF-RA, all subjects who were randomly assigned at week 12 and received ≥1 dose of study medication during the maintenance phase; TEAE, treatment-emergent adverse event.
IR = patients with events per 100 patient-years.

# Results 6: Summary of Clinical Laboratory Evaluations Throughout the Study

- No clinically significant changes were observed in hemoglobin level, neutrophil count, or lymphocyte count
- Platelet counts reached a nadir at week 4 of the induction period (decrease of 35%) and returned toward baseline thereafter, followed by stabilization throughout the maintenance and rescue periods




| Evaluable patients, n | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Placebo | | | | | | 127 | 59 | 45 | 36 | 195 | 192 | 199 | 198 | 192 |
| Abrocitinib 100 mg | | | | | | 223 | 178 | 152 | 120 | 99 | 97 | 99 | 100 | 91 |
| Abrocitinib 200 mg | 798 | 765 | 779 | 786 | 773 | 252 | 221 | 187 | 172 | 42 | 40 | 39 | 40 | 39 |

# Conclusions

- **12-week Induction With Abrocitinib 200 mg Monotherapy Was Highly Efficacious**
  - 65% of patients who received abrocitinib 200 mg achieved IGA 0/1 and EASI-75 responses
- **Most Responders Who Continued to Receive Abrocitinib During the Maintenance Period Did Not Experience Protocol-Defined Flare**
  - Most patients who continued with either the 200-mg or the 100-mg dose of abrocitinib maintained their response through 40 weeks of blinded follow-up
  - The probability of maintenance of response was higher for abrocitinib 200 mg than for 100 mg and for both abrocitinib doses compared with placebo
  - Time to flare was prolonged in the abrocitinib 200-mg and 100-mg arms compared with placebo
    - Decreasing the dose of abrocitinib improved the safety profile, indicating no carryover effect
- **Abrocitinib 200 mg in Combination With Topical Therapy Was Successful in Recapturing Response for Most Patients Who Experienced Flare**
  - 85% of patients who experienced a protocol-defined flare after discontinuation of abrocitinib treatment recaptured EASI-75 response by week 4 of rescue treatment

**The authors thank the patients and the JADE REGIMEN investigators for making this study possible**