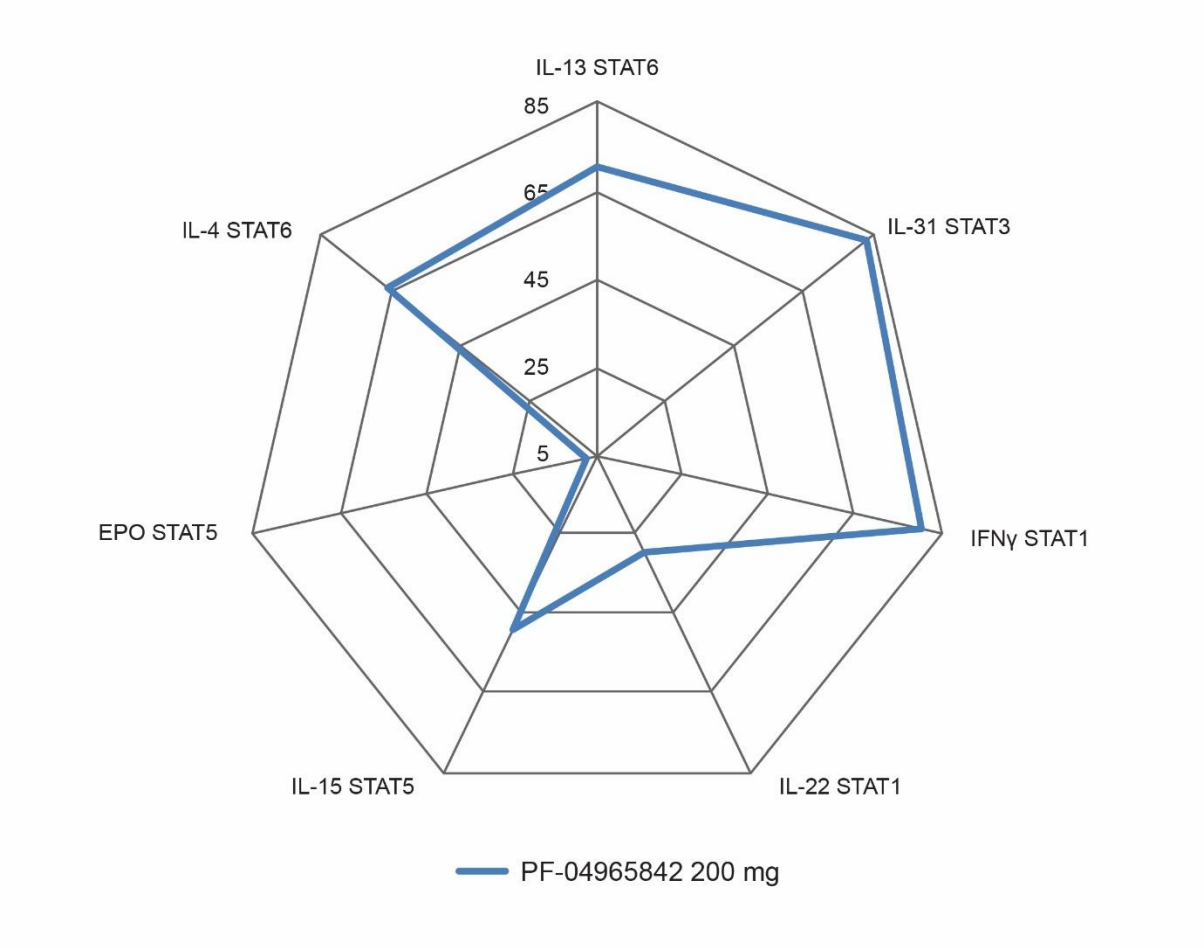
Supplementary Online Content

Gooderham MJ, Forman SB, Bissonnette R, et al. Efficacy and safety of oral Janus kinase 1 inhibitor abrocitinib for patients with atopic dermatitis: a phase 2 randomized clinical trial. Published online October 2, 2019. *JAMA Dermatol*. doi:10.1001/jamadermatol.2019.2855

eFigure 1. Average Daily Inhibiting Concentration for Specified Percentage Effect With Key Cytokines in Atopic Dermatitis



Numbers represent the specified percentage of effect (ie, IC_{85}). Percentages of cytokine inhibition ($IC_{XX=}100*C_{av}/[IC_{50} + C_{av}]$) were determined at clinically meaningful doses, converting to free concentrations for both IC_{50} and C_{av}. As an example, for the concentrations achieved with a 200-mg dose in humans, and using concentration response data from in vitro assays, we would predict approximately 65% inhibition of IL-4, 70% inhibition of IL-13, and 1% inhibition of EPO.
$C_{av,}$ average plasma concentration; EPO STAT5, erythropoietin; IC, inhibiting concentration; IFN, interferon; IL, interleukin; STAT, signal transducer and activator of transcription.

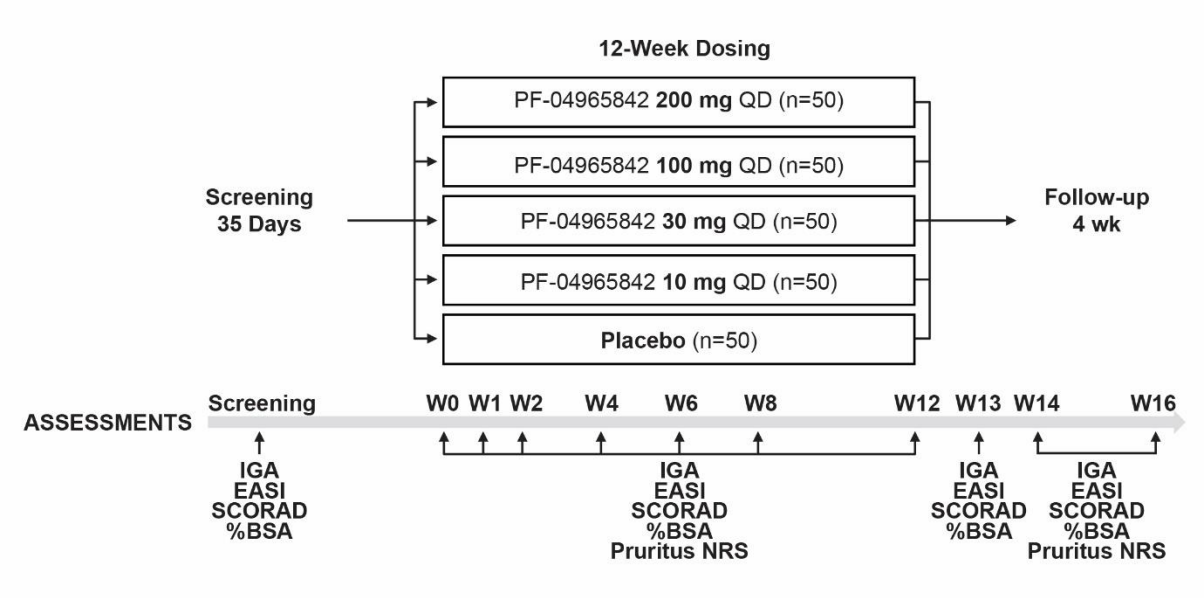
eTable 1. Investigators

Name	Institute	City, Country
Rodney Sinclair	Sinclair Dermatology	East Melbourne, Australia
George Varigos	Royal Melbourne Hospital	Parkville, Australia
Kurt Gebauer	Fremantle Dermatology	Fremantle, Australia
Lynda Spelman	Veracity Clinical Research	Woolloongabba, Australia
Michael Freeman	The Skin Centre	Benowa, Australia
Diana Rubel	Woden Dermatology	Philip, Australia
Ktut Arya	Australian Clinical Research Network	Sydney, Australia
Shireen Sidhu	North Eastern Health Specialists	Hectorville, Australia
Catherine Maari	Innovaderm Research Inc.	Montreal, Canada
Melinda Gooderham	SKiN Centre for Dermatology	Peterborough, Canada
Charles Lynde	Lynderm Research Inc.	Markham, Canada
Yves Poulin	Centre de Recherche Dermatologique du Quebec Metropolitain (CRDQ)	Quebec, Canada
Kim Papp	K Papp Clinical Research	Waterloo, Canada
Mani Raman	The Centre for Dermatology	Richmond Hill, Canada
Vincent Ho	University of British Columbia	Vancouver, Canada
Jerry Tan	Windsor Clinical Research Inc	Windsor, Canada
Sheetal Sapra	Research by ICLS	Oakville, Canada
Marni Wiseman	Wiseman Dermatology Research Inc.	Winnipeg, Canada
Ginette Girard	Diex Research Sherbrooke Inc.	Sherbrooke, Canada
Diamant Thaci	Universitaetsklinikum Schleswig-Holstein	Luebeck, Germany
Amir Yazdi	Universitaetsklinikum Tuebingen[a]	Tuebingen, Germany
Athanasios Tsianakas	Universitaetsklinikum Muenster Klinik fuer Hautkrankheiten	Muenster, Germany
Knut Schaekel	Universitaetsklinikum Heidelberg[a]	Heidelberg, Germany
Beatrice Gerlach	Hautarztpraxis Dr. Beatrice Gerlach[a]	Dresden, Germany
Margrit Simon	ISA GmbH	Berlin, Germany
Hans-Joachim Koenig	emovis GmbH[a]	Berlin, Germany
Michael Sticherling	Universitaetsklinikum Erlangen Hautklinik (Studienambulanz)[a]	Erlangen, Germany
Lajos Kemeny	Szegedi Tudomanyegyetem SzentGyorgyi Albert Klinikai Kozpont Borgyogyaszati es Allergologiai Klinika	Szeged, Hungary
Ivan Orojan	Bacs Kiskun Megyei Korhaz, Bor es Nemibeteggondozo	Kecskemet, Hungary
Noemi Bakos	ALLERGO-DERM BAKOS Kft.	Szolnok, Hungary
Gabriella Nagy	CRU Hungary Ltd.	Miskolc, Hungary
Ellen Frankel	Clinical Partners, LLC	Rhode Island, USA
James Solomon	Leavitt Medical Associates of Florida d/b/a Ameriderm Research	Florida, USA
Joseph Fowler	DS Research[a]	Kentucky, USA
Paul Yamauchi	Clinical Science Institute	California, USA
George Schmieder	Park Avenue Dermatology	Florida, USA

Name	Institute	City, Country
Matthew Zook	Olympian Clinical Research	Florida, USA
Peter Jenkin	Dermatology Associates[a]	Washington, USA
Jens Thiele	Dermatology Specialists, Inc.[a]	California, USA
Richard Beasley	Health Concepts	South Dakota, USA
Stacy Smith	California Dermatology & Clinical Research Institute	California, USA
Shondra Smith	Shondra L Smith, MD	Louisiana, USA
Emil Tanghetti	Center for Dermatology and Laser Surgery	California, USA
Stephen Schleicher	DermDox Centers for Dermatology	Pennsylvania, USA
Lawrence Sher	Peninsula Research Associates	California, USA
Jeffrey Weinberg	Forest Hills Dermatology Group	New York, USA
Jerry Bagel	Psoriasis Treatment Center of Central New Jersey	New Jersey, USA
Josep Genebriera-Delamo	North Florida Dermatology Associates, PA	Florida, USA
David Pariser	Virginia Clinical Research, Inc	Virginia, USA
Scott Fretzin	Dawes Fretzin Clinical Research Group, LLC	Indiana, USA
Melody Stone	MediSearch Clinical Trials	Missouri, USA
Seth Forman	Forward Clinical Trials	Florida, USA
George Murakawa	Somerset Skin Centre	Michigan, USA
Yvonne Knight	West End Dermatology Associates[a]	Virginia, USA
Emily Becker	Texas Dermatology and Laser Specialists	Texas, USA
Craig Teller	Bellaire Dermatology Associates	Texas, USA
Paul Getz	Dundee Dermatology	Illinois, USA
Scott Guenthner	The Indiana Clinical Trials Center	Indiana, USA
Iftikhar Hussain	Vital Prospects Clinical Research Institute, PC	Oklahoma, USA
Mark Ling	MedaPhase Inc.	Georgia, USA
Vincent Mirkil	Clinical Research Consortium[a]	Nevada, USA
Weily Soong	Clinical Research Center of Alabama	Alabama, USA
Bruce Strober	University of Connecticut Health Center (UConn Health)	Connecticut, USA
Laura Ferris	University of Pittsburgh Medical Center	Pennsylvania, USA
Brett King	Yale School of Medicine[a]	Connecticut, USA
Robert Nossa	The Dermatology Group, P.C.	New Jersey, USA
Chien Fang	Huntington Medical Foundation	California, USA
Neil Sadick	Sadick Research Group	New York, USA
Neal Bhatia	TCR Medical Corporation	California, USA

[a]Site received investigational products but did not randomize patients.

eFigure 2. Study design



%BSA, percentage of body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, numeric rating scale; QD, once-daily; SCORAD, Scoring Atopic Dermatitis; W, week.

eAppendix. Inclusion and Exclusion Criteria

Key Inclusion Criteria

1. Men or women between 18 and 75 years of age, inclusive, at time of informed consent
2. Patients willing and able to comply with scheduled visits, treatment plan, laboratory testing, and other study procedures
3. Men able to father children and women of childbearing potential and at risk for pregnancy had to agree to use a highly effective method of contraception throughout the study and for ≥28 days after the last dose of study treatment
4. Met the following atopic dermatitis criteria:
    a. Clinical diagnosis of chronic atopic dermatitis for ≥1 year before day 1 and confirmed atopic dermatitis (Hanifin and Rajka criteria[1] of atopic dermatitis) at the screening visit
    b. Inadequate response to treatment with topical medications (topical corticosteroids or topical calcineurin inhibitors) given for ≥4 weeks or unable to receive topical treatment within 12 months before the first dose of study drug because it was otherwise medically inadvisable (eg, application to a large %BSA which is associated with increased risk for systemic absorption and hypothalamic-pituitary-adrenal axis suppression, cutaneous side effects such as burning or stinging sensations with topical calcineurin inhibitors or skin atrophy, purpura, telangiectasia, and striae with chronic use of topical corticosteroids)
    c. Moderate-to-severe atopic dermatitis (percentage of affected body surface area ≥10, investigator's global assessment score ≥3, and Eczema Area and Severity Index score ≥12 at the screening and baseline visits)
5. Had to agree to avoid prolonged exposure to the sun and not to use tanning booths, sun lamps, or other ultraviolet light sources during the study
6. If receiving concomitant medications for any reason other than atopic dermatitis, had to be on a stable regimen, defined as not starting a new drug or changing dosage within 7 days or 5 half-lives (whichever was longer) before day 1. Patient had to be willing to stay on a stable regimen during the duration of the study

Exclusion Criteria

1. Severe acute or chronic medical or psychiatric condition or laboratory abnormality with the potential to interfere with the study
2. Active forms of other inflammatory skin diseases
3. Evidence of skin conditions (eg, psoriasis, seborrheic dermatitis, lupus) on day 1 that would interfere with evaluation of atopic dermatitis or response to treatment
4. Received any of the following treatments specified in the timeframes outlined as follows:
    a. Within 6 months before the first dose of study drug
        i. Any cell-depleting agents, including but not limited to rituximab: within 6 months before the first dose of study drug or 5 half-lives (if known), whichever was longer, or until lymphocyte count returned to normal, whichever was longer
    b. Within 12 weeks before the first dose of study drug
        i. Any studies with Janus kinase (JAK) inhibitors
        ii. Other biologics within 12 weeks before the first dose of study drug or 5 half-lives (if known), whichever was longer
    c. Within 8 weeks before the first dose of study drug
        i. Participation in other studies involving investigational drugs within 8 weeks before the first dose of study drug or within 5 half-lives (if known), whichever was longer
    d. Within 6 weeks before the first dose of study drug
        i. Had been vaccinated with live or attenuated live vaccine
    e. Within 4 weeks before the first dose of study drug
        i. Use of oral immune suppressants (eg, cyclosporine A, azathioprine, methotrexate, mycophenolate mofetil, systemic corticosteroids, interferon-γ) within 4 weeks before the first dose of study drug or within 5 half-lives (if known), whichever was longer
        ii. Phototherapy (narrow-band ultraviolet B) or broadband phototherapy
        iii. Regular use (more than 2 visits per week) of a tanning booth/parlor
    f. Within 1 week before the first dose of study drug

i. Topical treatments that could have affected atopic dermatitis (eg, corticosteroids, calcineurin inhibitors, tars, antibiotic creams, topical antihistamines)
Note: Corticosteroid inhalers and intranasal sprays were allowed for patients with stable asthma

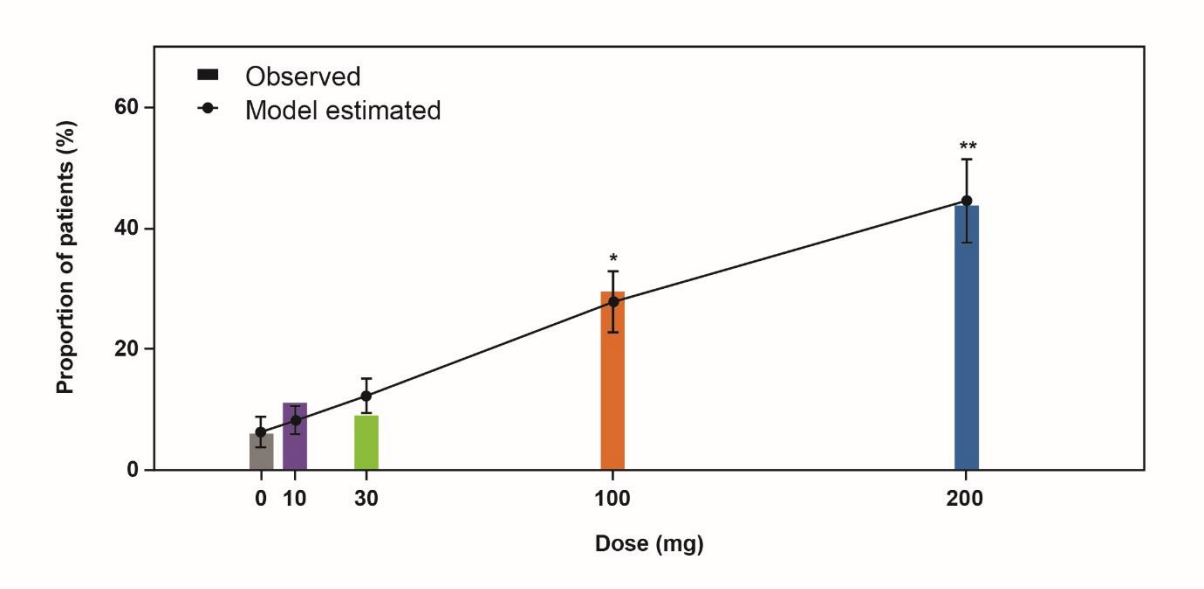
g. Herbal medications with unknown properties or known beneficial effects for atopic dermatitis

eTable 2. Investigator's Global Assessment (IGA)

Score	Category	Description[a]
0	Clear	Atopic dermatitis is cleared, except for any residual discoloration (postinflammatory hyperpigmentation and/or hypopigmentation)
1	Almost clear	Overall, atopic dermatitis is not entirely cleared, and remaining lesions are light pink (not including postinflammatory hyperpigmentation), and/or have barely palpable hard thickened skin and/or papules, and/or have barely perceptible lichenification; excoriation and oozing/crusting are absent
2	Mild	Overall, atopic dermatitis consists of lesions that are light red, with slight but definite hard thickened skin and/or papules; with slight but definite linear or picked scratch marks or penetrating surface injury; with slight but definite thickened skin, fine skin markings, and lichenoid scale; oozing/crusting is absent
3	Moderate	Overall, atopic dermatitis consists of lesions that are red, with easily palpable moderate hard thickened skin and/or papules; with moderate linear or picked scratch marks or penetrating surface injury; with moderate thickened skin, coarse skin markings, and coarse lichenoid scale; with slight oozing/crusting
4	Severe	Overall, atopic dermatitis consists of lesions that are deep, dark red, with severe hard thickened skin and/or papules; with severe linear or picked scratch marks or penetrating surface injury; with severe thickened skin with very coarse skin markings and lichenoid scale; with moderate to severe oozing/crusting

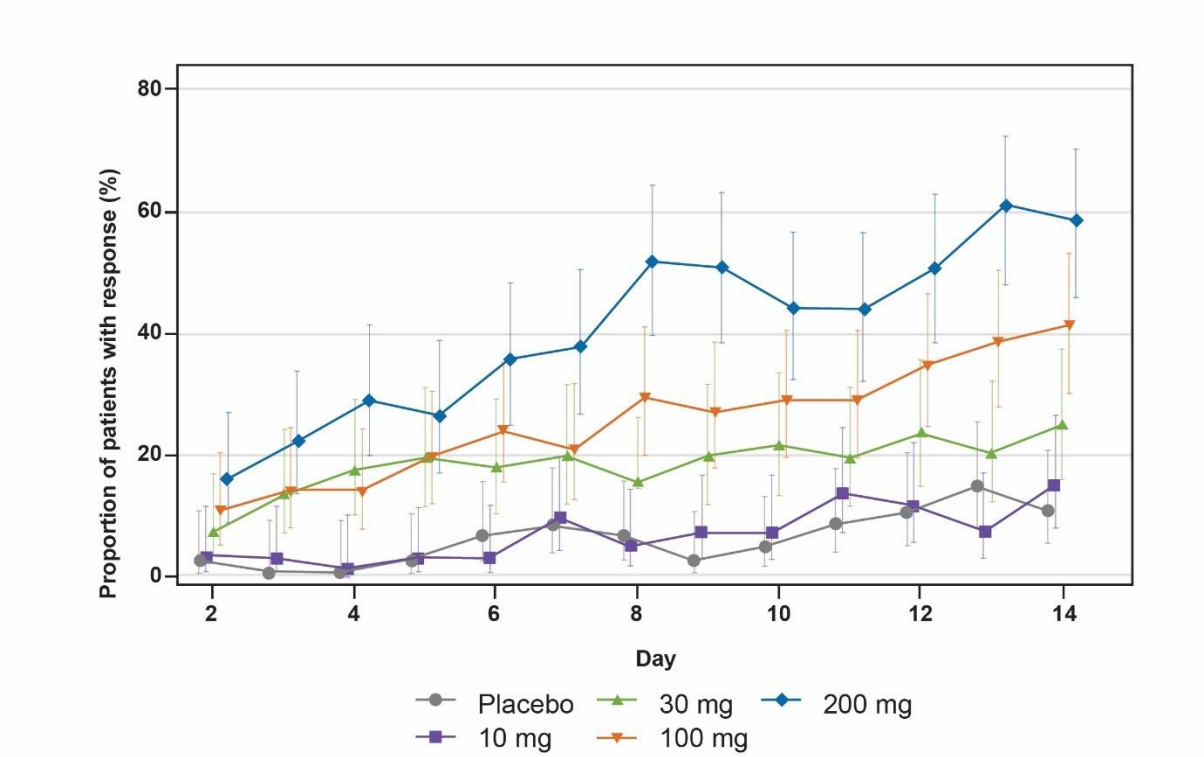
[a]The IGA will exclude scalp, palms, and soles from the assessment/scoring.

eFigure 3. Proportion of Patients Achieving Investigator's Global Assessment Clear or Almost Clear With ≥2-Grade Improvement from Baseline at Week 12 (E_{max} fitted curve with standard error)



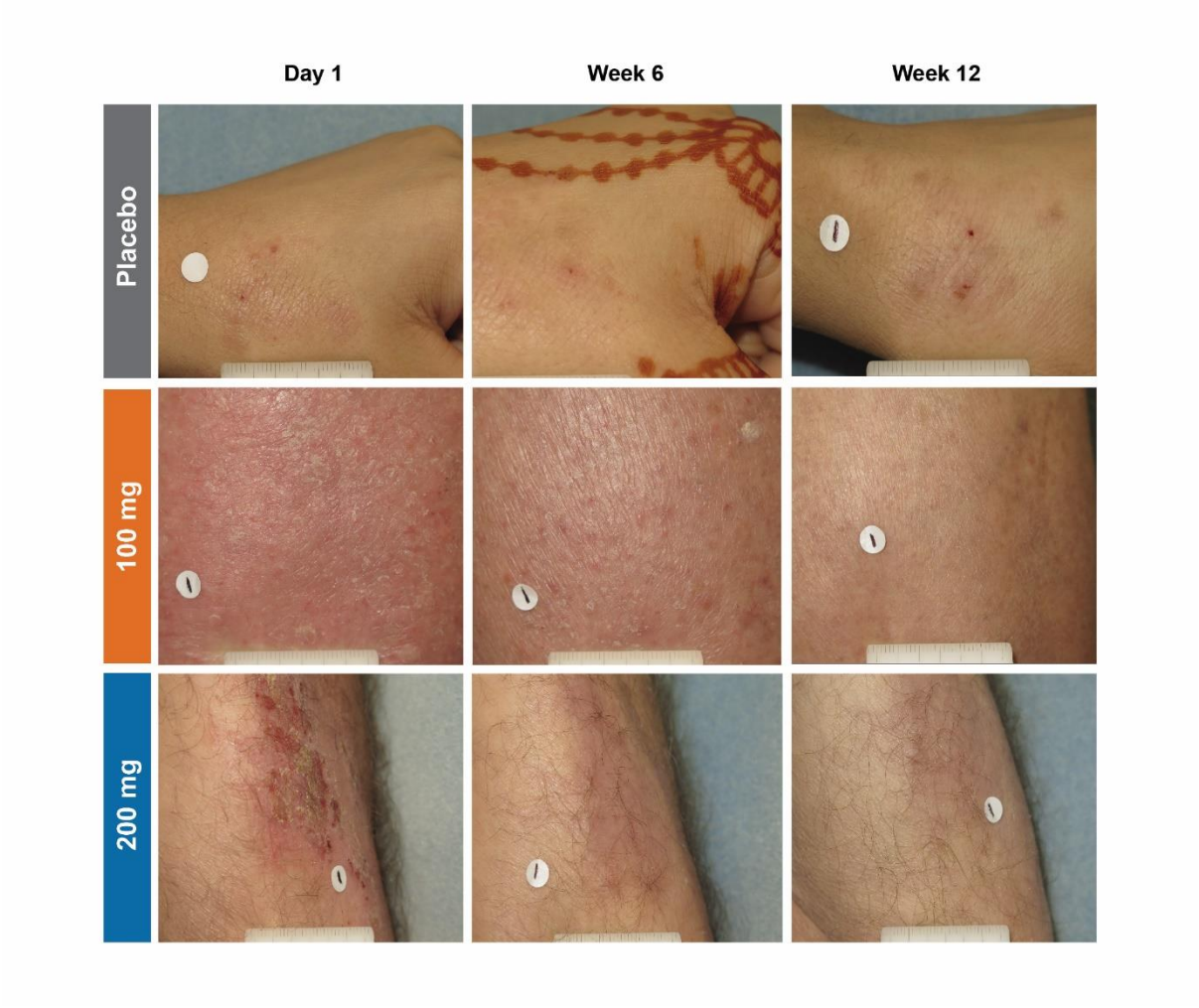
For discontinued patients, any missing value for all subsequent visits until week 12 was imputed using the nonresponder imputation approach. Baseline was defined as the last measurement before first dosing. E_{max} denotes the difference between maximum achievable response (at infinite dose) and baseline.

eFigure 4. Proportion of Patients With Baseline Pruritus NRS Score of ≥4 Achieving ≥4-Point Improvement From Baseline Over the First 2 Weeks



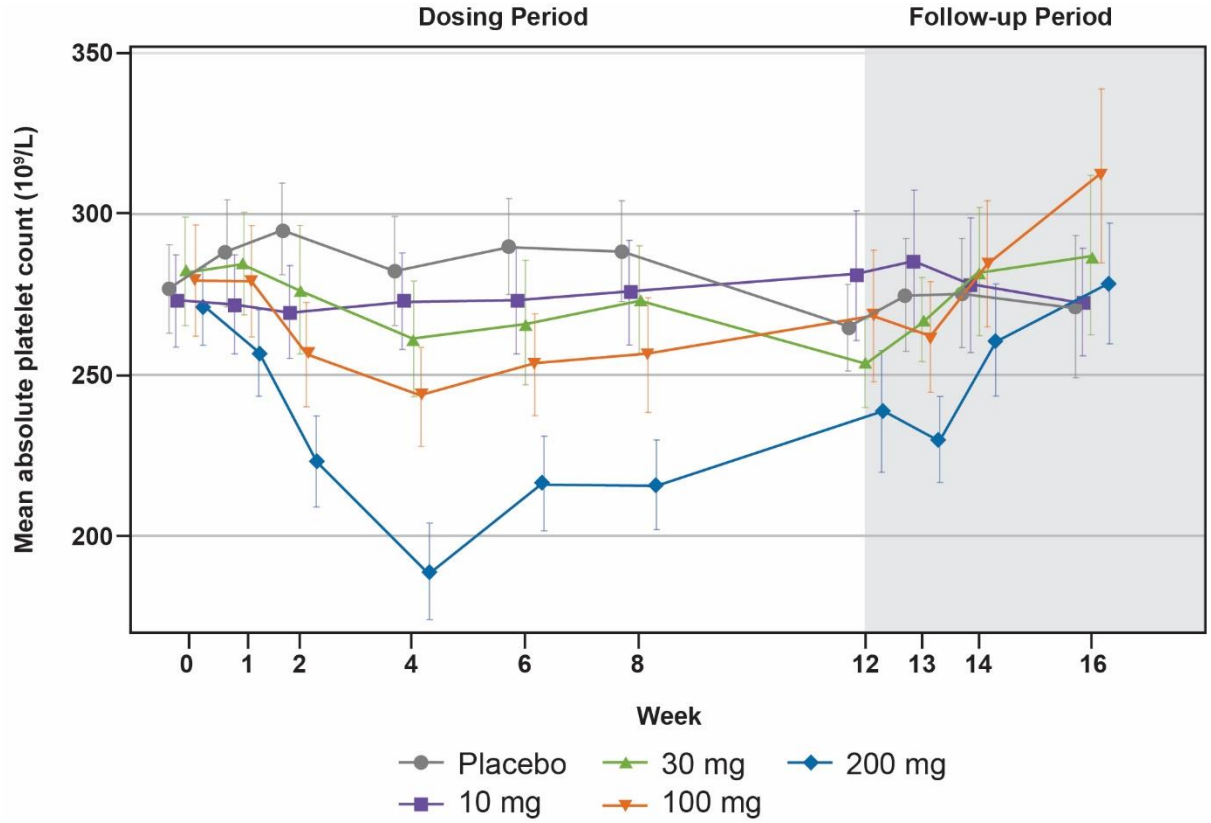
A logistic regression model was used including treatment as a main effect and baseline score as a covariate. Bars denote 90% CIs. For discontinued patients, any missing value for all subsequent visits until week 12 was imputed using the nonresponder imputation approach. Baseline was defined as the last measurement before first dosing. NRS, numeric rating scale.

eFigure 5. Photographic Evidence



Representative photographs at day 1, week 4, and week 12 are presented for patients treated with placebo, 100 mg abrocitinib, and 200 mg abrocitinib.

eFigure 6. Mean Absolute Value Versus Time for Platelets



Bars denote 90% CIs.

eTable 3. Summary of Serious Adverse Events

Preferred Term	Event Start/Stop, day	Causality
Placebo		
Dermatitis/condition aggravated	113/118	Unrelated
Dermatitis atopic	17/49	Unrelated
10 mg		
Malignant melanoma	135/205	Unrelated
Asthma/condition aggravated	20/23	Unrelated
100 mg		
Dermatitis atopic/condition aggravated	89/100	Unrelated
Eczema herpeticum[a]	21/30	Related
Asthma[a]	75/85	Unrelated
200 mg		
Pneumonia	102/110	Related
Pulmonary embolism[a]	80/155	Unrelated

[a]Treatment permanently discontinued because of a serious adverse event.

eReferences

1. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol.* 1980;60:44-47.