

Time-Interval Incidence Rates of Adverse Events in Patients With Moderate-to-Severe Atopic Dermatitis Treated With Abrocitinib

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Background, Objectives, Study Design, Assessments, and Statistical Analyses

Background

- Abrocitinib, an oral, once-daily, JAK1-selective inhibitor, is efficacious and well-tolerated in patients with moderate-to-severe AD¹
- Recent integrated safety analysis have identified headache, nausea, and acne as common AEs associated with abrocitinib treatment^{2,3}
 - AEs of special interest which may occur with JAK inhibitor treatment include herpes zoster, herpes simplex, serious infection, and NMSC^{2,3}
- Understanding the time scale on which AEs occur may be important for clinical decision making

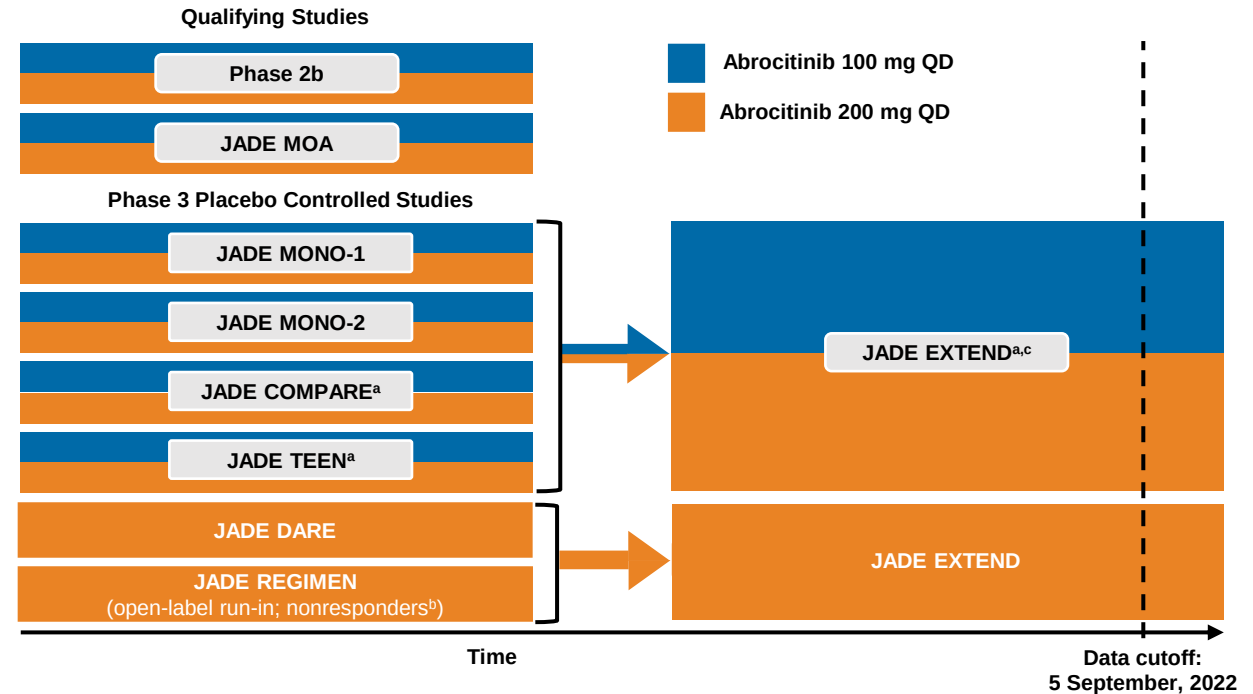
Objectives

- To evaluate the IR of AEs of special interest by time interval during long-term treatment with abrocitinib in the phase 3 JADE clinical program
- To evaluate the severity and duration of AEs of special interest

Study Design

- This post hoc analysis included a subset of patients aged ≥12 years with moderate-to-severe AD who received abrocitinib 200 mg and 100 mg from 8 phase 2/3 trials and 1 long-term extension trial (data cutoff: September 5, 2022)

Study Design



Assessments

- IRs were assessed at 3-month intervals for eczema herpeticum, herpes simplex, headache, nausea, and acne, and at 6-month intervals for serious infection, herpes zoster, and NMSC up to >48 months

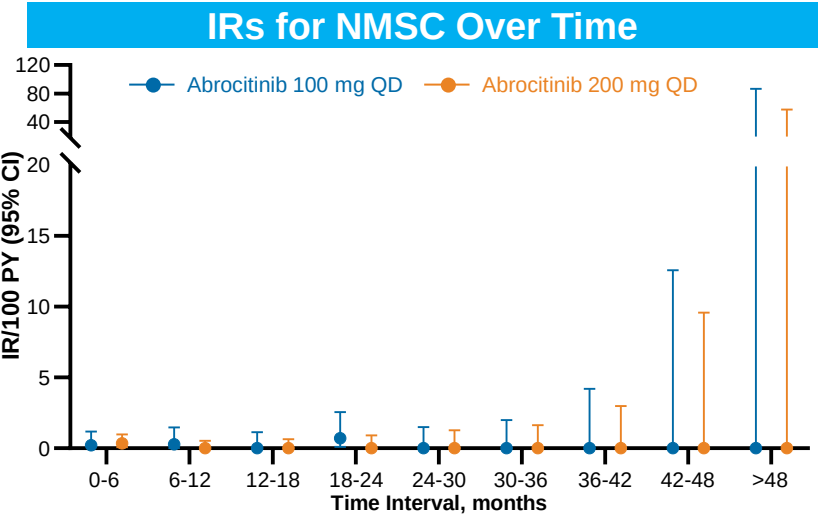
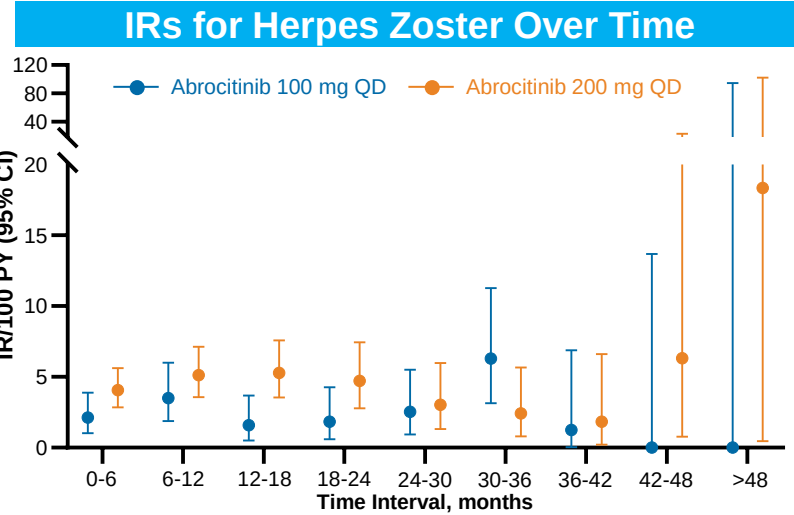
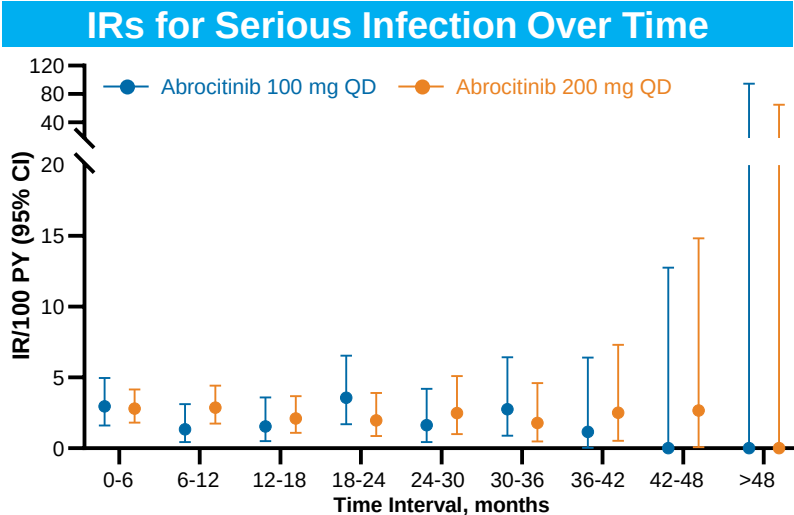
Statistical Analyses

- Data were included up to the end of the risk period (the shortest period of [last dose + 28 days], [death date], or [data cutoff date, JADE EXTEND only])

AD, atopic dermatitis; AE, adverse event; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IR, incidence rate; JAK1, Janus kinase 1; NMSC, nonmelanoma skin cancer; PY, patient-years; QD, once daily. IRs were defined as unique patients with events per 100 PY. ClinicalTrials.gov Identifiers: NCT02780167 (phase 2b); NCT03349060 (MONO-1); NCT03575871 (MONO-2); NCT03627767 (REGIMEN); NCT03720470 (COMPARE); NCT03796676 (TEEN); NCT03915496 (MOA); NCT04345367 (DARE); NCT03422822 (EXTEND). ^aPatients in JADE COMPARE, JADE TEEN, and the open-label rescue period of JADE REGIMEN received abrocitinib in combination with topical corticosteroids, and in JADE EXTEND, patients were permitted to use medicated or non-medicated topical treatments throughout the study. ^bNon-responders were patients who did not achieve an IGA score of clear/almost clear with a ≥ 2-grade improvement from baseline and a ≥ 75% improvement from baseline in EASI after 12 weeks of treatment with abrocitinib 200 mg. ^cIncludes patients who received their first dose of abrocitinib (100 mg or 200 mg) in JADE EXTEND after receiving placebo in a phase III placebo-controlled trial (MONO-1, MONO-2, COMPARE, TEEN) or dupilumab in JADE COMPARE or JADE DARE, as well as patients who first received abrocitinib in a qualifying phase III trial. 1. Reich K et al. *J Eur Acad Dermatol Venerol*. 2023;37(10):2056-2066. 2. Simpson EL et al. *Am J Clin Dermatol*. 2021;22(5):693-707. 3. Simpson EL et al. *Am J Clin Dermatol*. 2024;25(4):639-654.

Adverse Events per 6-Month Time Interval

- Time interval IRs/100 PYs with abrocitinib 200 mg and 100 mg ranged between 0-2.87 and 0-3.56 for serious infection and 1.83-18.34 and 0-6.30 for herpes zoster through >48 months and between 0-0.34 and 0-0.71 for NMSC through 24 months, with no additional events reported up to and beyond 48 months
 - Of all serious infection events, 55% and 41% were classified as severe with abrocitinib 200 mg and 100 mg, respectively; treatment was withdrawn for 41% and 53% of patients reporting serious infection events
 - Most events of herpes zoster and NMSC were mild or moderate in severity and did not result in treatment withdrawal with either abrocitinib dose



Summary of TE Events of Serious Infections		
		Abrocitinib 100 mg N=1053
		Abrocitinib 200 mg N=1997
Total, n (%)		44 (4.2)
Serious, n (%) ^a		80 (4.0)
Severity, n (%) ^a	Mild	3 (6.8)
	Moderate	23 (52.3)
	Severe	18 (40.9)
Treatment withdrawn, n (%) ^a		19 (52.8)

Summary of TE Events of Herpes Zoster		
		Abrocitinib 100 mg N=1053
		Abrocitinib 200 mg N=1997
Total, n (%)		51 (4.8)
Serious, n (%) ^a		136 (6.8)
Severity, n (%) ^a	Mild	4 (7.8)
	Moderate	11 (8.1)
	Severe	45 (33.1)
Severity, n (%) ^a	Moderate	28 (54.9)
	Severe	83 (61.0)
	Severe	4 (7.8)
Treatment withdrawn, n (%) ^a		8 (5.9)
Treatment withdrawn, n (%) ^a		3 (6.3)
Treatment withdrawn, n (%) ^a		6 (5.2)

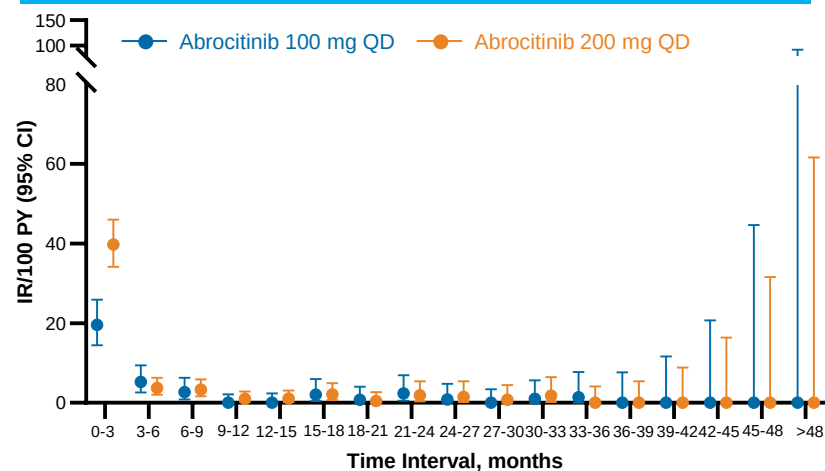
Summary of TE Events of NMSC		
		Abrocitinib 100 mg N=1053
		Abrocitinib 200 mg N=1997
Total, n (%)		4 (0.4)
Serious, n (%) ^a		3 (0.2)
Severity, n (%) ^a	Mild	0
	Moderate	2 (66.7)
	Severe	1 (33.3)
Severity, n (%) ^a	Moderate	1 (25.0)
	Severe	3 (75.0)
	Severe	1 (33.3)
Treatment withdrawn, n (%) ^a		0
Treatment withdrawn, n (%) ^a		1 (33.3)
Treatment withdrawn, n (%) ^a		0

AE, adverse event; IR, incidence rate; NMSC, nonmelanoma skin cancer; PY, patient-years; QD, once daily; TE, treatment-emergent. Serious AEs were defined as any event that resulted in death, was life-threatening or required inpatient hospitalization/prolongation of existing hospitalization, persistent/ significant disability/incapacity, or congenital anomaly/birth defect, or was considered an important medical event. AE severity was defined on the basis to which the event interfered with the patient's usual function. ^aProportion expressed relative to number of patients with events.

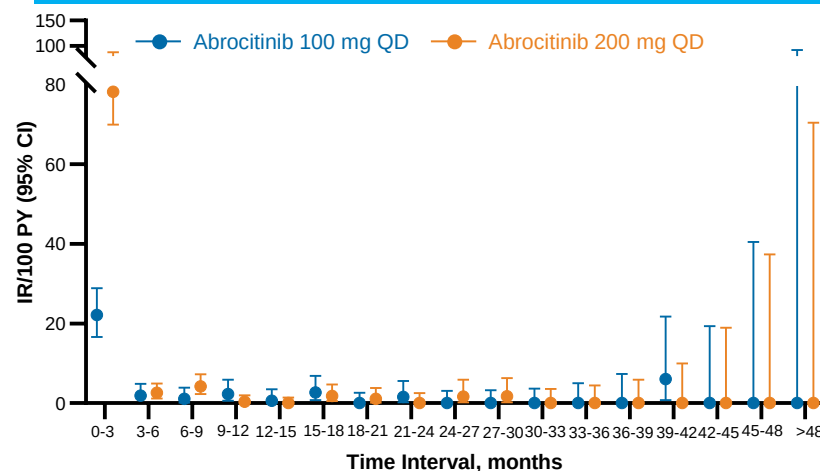
Adverse Events per 3-Month Time Interval

- Time interval IRs/100 PYs with abrocitinib 200 mg and abrocitinib 100 mg ranged between 0-39.77 and 0-19.56 for headache through 36 months, between 0-78.21 and 0-22.15 for nausea through 42 months, and between 0-31.35 and 0-8.72 for acne through >48 months, with no additional events of headache and nausea reported up to and beyond 48 months
 - No events of headache, nausea, or acne were considered serious, and most were mild or moderate in severity

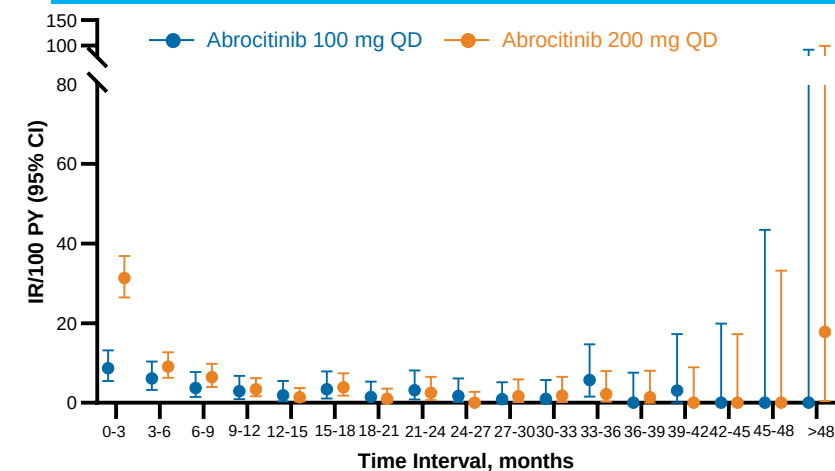
IRs for Headache Over Time



IRs for Nausea Over Time



IRs for Acne Over Time



Summary of TE Events of Headache

		Abrocitinib 100 mg N=1053	Abrocitinib 200 mg N=1997
Total, n (%)		74 (7.0)	224 (11.2)
Serious, n (%) ^a		0	0
Severity, n (%) ^a	Mild	57 (77.0)	166 (74.1)
	Moderate	17 (23.0)	53 (23.7)
	Severe	0	5 (2.2)
Treatment withdrawn, n (%) ^a		0	3 (2.9)

Summary of TE Events of Nausea

		Abrocitinib 100 mg N=1053	Abrocitinib 200 mg N=1997
Total, n (%)		73 (6.9)	358 (17.9)
Serious, n (%) ^a		0	0
Severity, n (%) ^a	Mild	68 (93.2)	283 (79.1)
	Moderate	5 (6.9)	67 (18.7)
	Severe	0	8 (2.2)
Treatment withdrawn, n (%) ^a		1 (2.8)	10 (6.0)

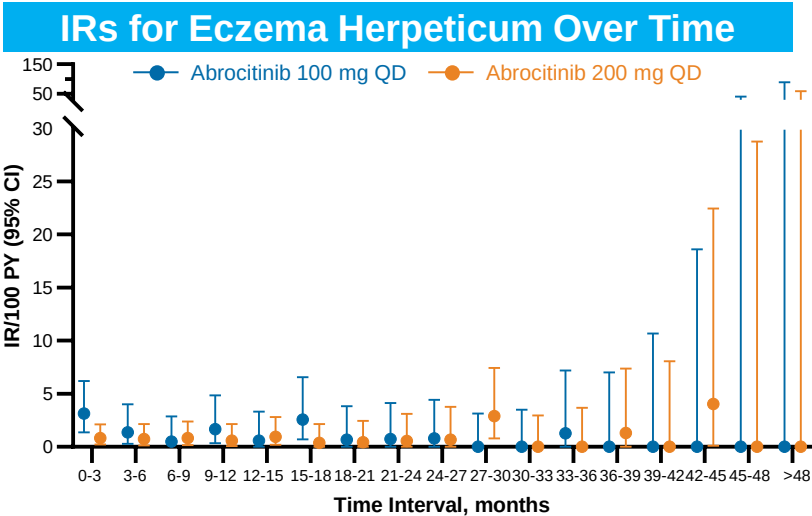
Summary of TE Events of Acne

		Abrocitinib 100 mg N=1053	Abrocitinib 200 mg N=1997
Total, n (%)		70 (6.6)	237 (11.9)
Serious, n (%) ^a		0	0
Severity, n (%) ^a	Mild	57 (81.4)	183 (77.2)
	Moderate	12 (17.1)	53 (22.4)
	Severe	1 (1.4)	1 (0.4)
Treatment withdrawn, n (%) ^a		0	1 (0.6)

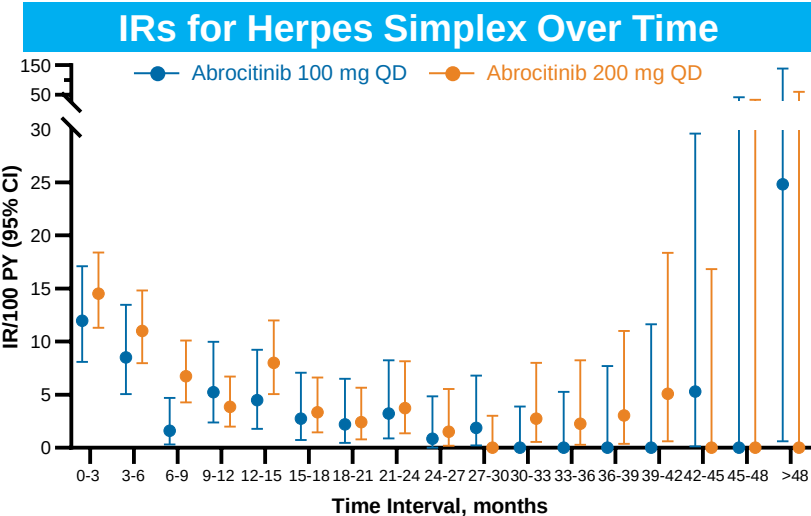
AE, adverse event; IR, incidence rate; PY, patient-years; QD, once daily; TE, treatment-emergent. Serious AEs were defined as any event that resulted in death, was life-threatening or required inpatient hospitalization/prolongation of existing hospitalization, persistent/significant disability/incapacity, or congenital anomaly/birth defect, or was considered an important medical event. AE severity was defined on the basis to which the event interfered with the patient's usual function. ^aProportion expressed relative to number of patients with events.

Adverse Events per 3-Month Time Interval

- Time interval IRs/100 PYs with abrocitinib 200 mg and abrocitinib 100 mg ranged between 0-4.03 and 0-3.15 for eczema herpeticum and between 0-14.52 and 0-24.81 for herpes simplex through >48 months
 - Most events of eczema herpeticum and herpes simplex were considered mild or moderate in severity and did not result in treatment withdrawal



Summary of TE Events of Eczema Herpeticum		
	Abrocitinib 100 mg N=1053	Abrocitinib 200 mg N=1997
Total, n (%)	24 (2.3)	25 (1.3)
Serious, n (%) ^a	6 (25.0)	4 (16.0)
Severity, n (%) ^a	Mild	8 (32.0)
	Moderate	13 (52.0)
	Severe	4 (16.0)
Treatment withdrawn, n (%) ^a	3 (17.7)	2 (10.0)



Summary of TE Events of Herpes Simplex		
	Abrocitinib 100 mg N=1053	Abrocitinib 200 mg N=1997
Total, n (%)	83 (7.9)	200 (10.0)
Serious, n (%) ^a	3 (3.6)	4 (2.0)
Severity, n (%) ^a	Mild	134 (67.0)
	Moderate	62 (31.0)
	Severe	4 (2.0)
Treatment withdrawn, n (%) ^a	4 (6.2)	4 (2.7)

AE, adverse event; IR, incidence rate; PY, patient-years; QD, once daily; TE, treatment-emergent.
Serious AEs were defined as any event that resulted in death, was life-threatening or required inpatient hospitalization/prolongation of existing hospitalization, persistent/significant disability/incapacity, or congenital anomaly/birth defect, or was considered an important medical event.
AE severity was defined on the basis to which the event interfered with the patient's usual function.
^aProportion expressed relative to number of patients with events.

Conclusions

- Acne, herpes simplex, eczema herpeticum, headache, and nausea had numerically higher IRs than other evaluated endpoints in this analysis in patients with moderate-to-severe AD, with fluctuations across time intervals, albeit with low PYs in some intervals
- IRs for headache, nausea, acne, and herpes simplex were higher early in treatment than later time intervals
- IRs for herpes zoster were generally higher with abrocitinib 200 mg than 100 mg, indicating a possible dose-dependent risk
- Together, these results highlight the importance of monitoring patients with moderate-to-severe AD throughout the abrocitinib treatment period

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