Integrated Safety Analysis of Abrocitinib in 3848 Patients With Moderate-to-Severe Atopic Dermatitis: Data From More Than 7000 Patient-Years With Up to ~4.5 Years of Exposure

Long-Term Safety Analysis of Abrocitinib for Moderate-to-Severe Atopic Dermatitis

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Gary Chan, **Herwig Koppensteiner**, **Haiyun Fan**, and **Justine Alderfer** are employees and shareholders of Pfizer Inc.

Shefali Vyas and Kanti Chittuluru were employees and shareholders of Pfizer Inc. at the time the study was conducted.

Table of Content

AD, atopic dermatitis; AESI, adverse event of special interest; ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; IR, incidence rate.

1 Introduction and Objective

Introduction

- Abrocitinib is an oral, once-daily, JAK1-selective inhibitor approved for the treatment of adults and adolescents with moderate-to-severe AD[1-3]
- In phase 3 clinical trials, abrocitinib was efficacious and well-tolerated as monotherapy or in combination with medicated topical therapies in patients with moderate-to-severe AD[4-9]
- A previous comprehensive analysis of long-term abrocitinib safety using integrated data from 3802 patients with abrocitinib exposure of more than 5200 PY showed that abrocitinib has a manageable long-term safety profile[10]

Objective

- To provide updated long-term integrated safety data of more than 7000 PY, with some patients having abrocitinib exposure of up to ~4.5 years[a], and to evaluate safety events stratified by risk factors

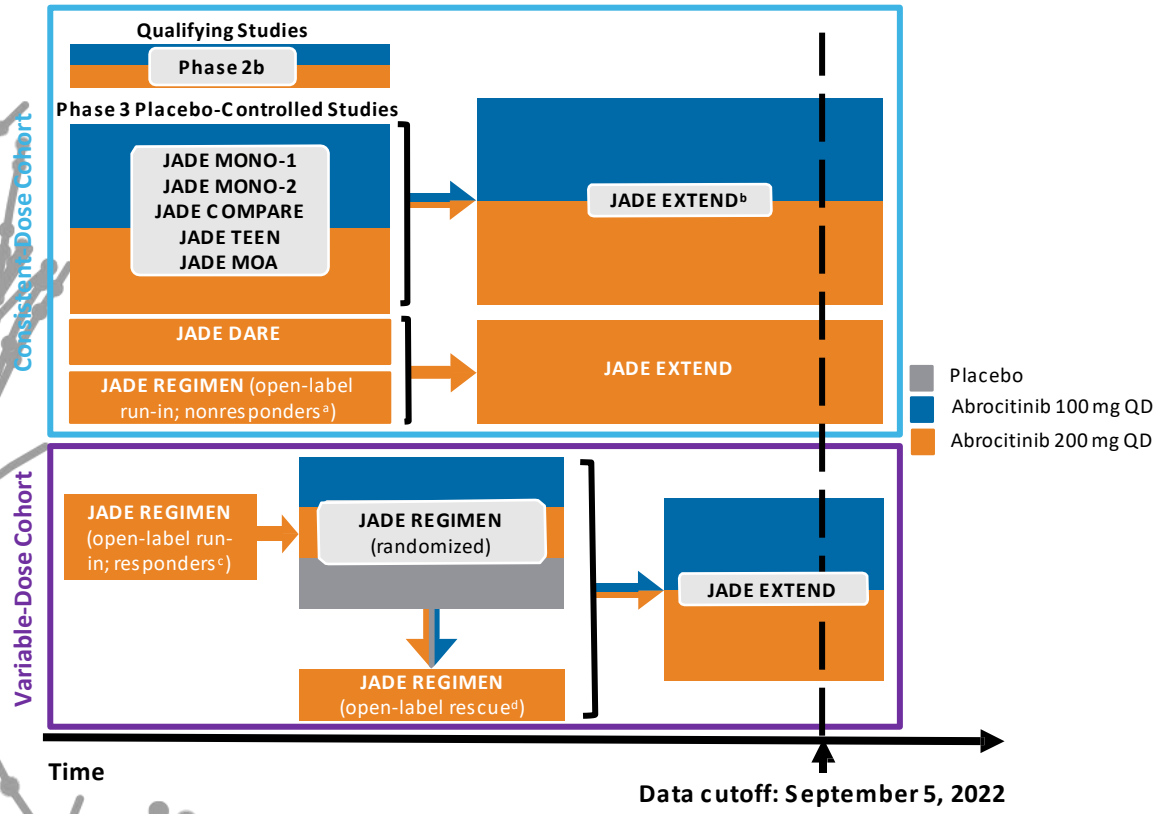
JAK, Janus kinase; PY, patient-years. [a]Based on the range of abrocitinib exposure, 1-1714 days in the consistent-dose cohort and 89-1537 days in the variable-dose cohort.

1. Cibinqo (abrocitinib) tablets, for oral use. Prescribing information. Pfizer Inc.; 2023. 2. Cibinqo 100 mg film-coated tablets. Summary of product characteristics. Pfizer, Limited; 2021. 3. European Medicines Agency. Cibinqo® (abrocitinib). Summary of product characteristics. Belgium: Pfizer Europe MA EEIG; 2024. 4. Gooderham MJ et al. *JAMA Dermatol*. 2019;155(12):1371-1379. 5. Silverberg JI et al. *JAMA Dermatol*. 2020;156(8):863-873. 6. Simpson EL et al. *Lancet*. 2020;396(10246):255-266. 7. Blauvelt A et al. *J Am Acad Dermatol*. 2022;86:104-112. 8. Bieber T et al. *N Engl J Med*. 2021;384(12):1101-1112. 9. Eichenfield LF et al. *JAMA Dermatol*. 2021;157(10):1165-1173. 10. Simpson EL et al. *Am J Clin Dermatol*. 2024;10.1007/s40257-024-00869-w.

2 Methods

Patients, Assessments, and Study Design

- Data from patients enrolled in eight phase 2 and phase 3 qualifying parent trials and 1 long-term extension trial were pooled into 2 cohorts:
  - The consistent-dose cohort comprised patients who received the same abrocitinib dose (200 mg or 100 mg) during the entire exposure time in the qualifying JADE trials, and/or in JADE EXTEND
  - The variable-dose cohort included patients who were randomly assigned to the maintenance period of JADE REGIMEN after induction and, therefore, could have received different abrocitinib doses throughout exposure time in JADE REGIMEN and who subsequently entered JADE EXTEND to receive a consistent dose
- IRs (95% CI; number of patients with events per 100 PY) for AESIs were assessed in patients stratified by baseline age categories, by baseline age and number of CV risk factors, and by baseline ASCVD risk scores

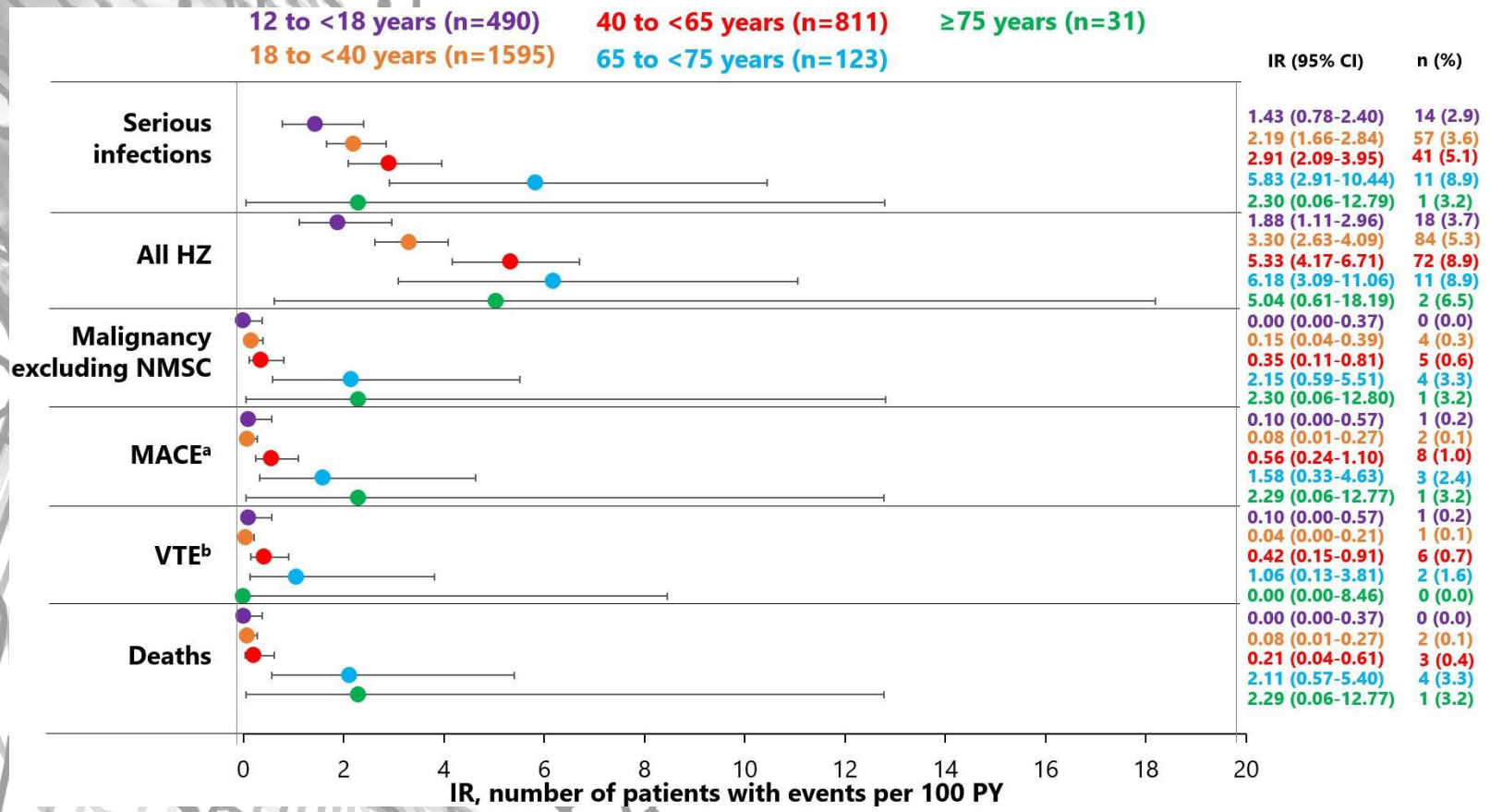


EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; QD, once daily. ASCVD risk scores are categorized as low (<5%), borderline (≥5 to <7.5%), intermediate (≥7.5 to <20%), or high (≥20%). JADE EXTEND (NCT03422822) is an ongoing trial. Qualifying parent trials included the phase 2b study (NCT02780167) trial, and phase 3 JADE MONO-1 (NCT03349060), JADE MONO-2 (NCT03575871), JADE REGIMEN (NCT036277678), JADE TEEN (NCT03796676), JADE COMPARE (NCT03720470), JADE MOA (NCT03915496), and JADE DARE (NCT04345367) trials. [a]Patients who did not achieve an IGA score of 0 (clear) or 1 (almost clear) with a ≥2-grade improvement from baseline and ≥75% improvement from baseline in EASI after 12 weeks of treatment with abrocitinib 200 mg. [b]Includes patients who received their first dose of abrocitinib (200 mg or 100 mg) in JADE EXTEND after receiving placebo in a phase 3 placebo-controlled trial (MONO-1, MONO-2, COMPARE, TEEN, MOA) or dupilumab in JADE COMPARE or JADE DARE, as well as patients who first received abrocitinib in a qualifying phase 3 trial. [c]Patients in the open-label run-in period who were considered responders (IGA score of 0 [clear] or 1 [almost clear] with a ≥2-grade improvement from baseline and ≥75% improvement from baseline in EASI) after 12 weeks of treatment with abrocitinib 200 mg were randomly assigned to treatment with abrocitinib 200 mg, abrocitinib 100 mg, or placebo. [d]Patients who experienced a flare (≥50% loss of Week 12 EASI response and new IGA score ≥2) during the maintenance period of JADE REGIMEN entered a 12-week open-label rescue period (abrocitinib 200 mg + topical medicated treatment).

3 IRs for AESIs Stratified by Baseline Age Categories

- In the consistent-dose cohort, IRs (95% CI) for AESIs per 100 PY were numerically higher in older versus younger patients
- The sample size was very small for the ≥75 years of age category, resulting in large CIs

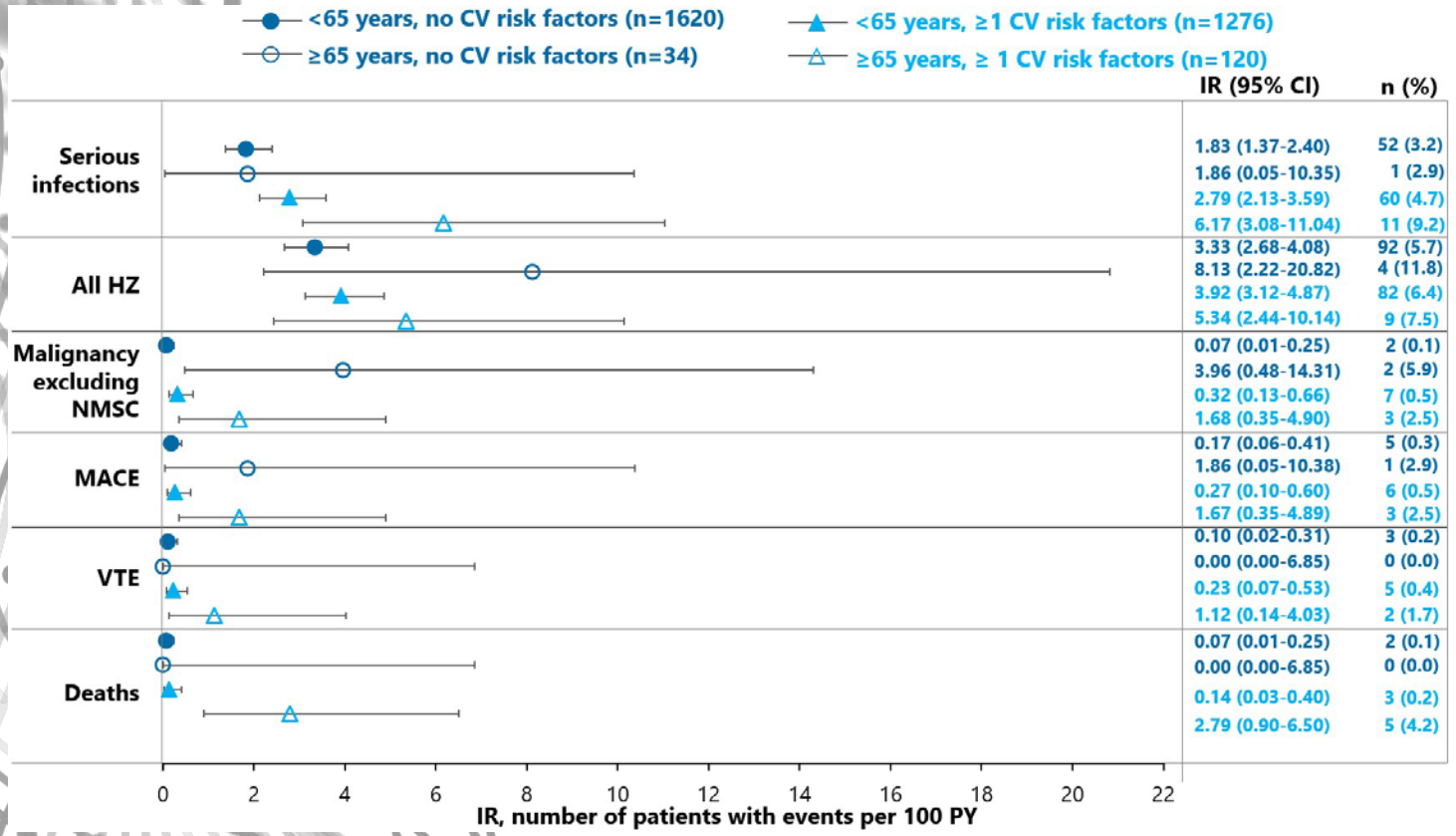
Data for IRs for serious and severe AEs, AEs leading to study discontinuation, and deaths for both the consistent- and variable-dose cohorts are shown in the supplementary material (via the QR code at the end of the presentation)



AE, adverse events; HZ, herpes zoster; MACE, major cardiovascular events; NMSC, nonmelanoma skin cancer; VTE, venous thromboembolism. [a]1 event of MACE was reported in a 16-year-old Asian male patient with ongoing AD, gout, and hyperuricaemia (treated with febuxostat) in the abrocitinib 100 mg group; an incidental finding of slight lacunar white matter degeneration on the right ventricle was adjudicated as an ischaemic stroke based on the magnetic resonance imaging report despite no report of clinical syndrome concerning stroke; there was no suspicion of stroke, and the event was not considered serious. [b]1 nonfatal pulmonary embolism occurred in a 16-year-old Black/African American male patient with morbid obesity in the abrocitinib 200 mg group; the patient had an extensive family history of pulmonary embolism, including an 18-year-old brother with pulmonary embolism.[1] 1. Simpson JI et al. *Am J Clin Dermatol.* 2021;22:693-707.

4 IRs for AESIs Stratified by Baseline Age Categories and CV Risk Factors

- In the consistent-dose cohort, IRs for AESIs tended to be higher in older patients aged ≥65 years and with CV risk factors than those aged <65 years and without CV risk factors
- Risk factors included smoking, diabetes mellitus, hypertension, baseline HDL cholesterol <40 mg/dL, baseline LDL cholesterol ≥130 mg/dL, rheumatoid arthritis, and CAD
  - History of CAD included a history of revascularization procedure, coronary artery bypass grafting, myocardial infarction, cardiac arrest, unstable angina, or acute coronary syndrome



Additional data for IRs for AESIs stratified by baseline age (including patients aged <50 or ≥50 years), and by 0, ≥1, or ≥2 CV risk factors are shown in the supplementary material (via the QR code at the end of the presentation)

CAD, coronary artery disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

5 IRs for AESIs by ASCVD Risk Scores at Baseline

- In the consistent-dose cohort, IRs for AESIs were generally higher in patients with intermediate or high ASCVD risk scores than those with low or borderline scores

Events		ASCVD Risk Score			
		Low (n=2448)	Borderline (n=129)	Intermediate (n=224)	High (n=93)
Serious infections	n (%) IR (95% CI)	92 (3.8) 2.18 (1.76-2.68)	7 (5.4) 3.12 (1.25-6.43)	14 (6.3) 3.90 (2.13-6.54)	5 (5.4) 3.09 (1.00-7.22)
All HZ	n (%) IR (95% CI)	143 (5.8) 3.49 (2.94-4.11)	8 (6.2) 3.64 (1.57-7.16)	18 (8.0) 5.26 (3.12-8.32)	8 (8.6) 5.30 (2.29-10.44)
Malignancies (excluding NMSC)	n (%) IR (95% CI)	6 (0.2) 0.14 (0.05-0.31)	0 0.00 (0.00-1.62)	5 (2.2) 1.39 (0.45-3.23)	3 (3.2) 1.85 (0.38-5.42)
MACE	n (%) IR (95% CI)	4 (0.2) 0.09 (0.03-0.24)	1 (0.8) 0.44 (0.01-2.44)	4 (1.8) 1.10 (0.30-2.82)	3 (3.2) 1.85 (0.38-5.42)
VTE	n (%) IR (95% CI)	6 (0.2) 0.14 (0.05-0.31)	1 (0.8) 0.44 (0.01-2.44)	2 (0.9) 0.55 (0.07-1.98)	1 (1.1) 0.62 (0.02-3.44)
Deaths	n (%) IR (95% CI)	3 (0.1) 0.07 (0.01-0.21)	1 (0.8) 0.44 (0.01-2.44)	2 (0.9) 0.55 (0.07-1.98)	4 (4.3) 2.47 (0.67-6.32)

ASCVD risk scores
Low: <5%
Borderline: ≥5 to <7.5%
Intermediate: ≥7.5 to <20%
High: ≥20%

ASCVD risk scores were calculated based on sex, age, race, SBP, DBP, total cholesterol, HDL cholesterol, LDL cholesterol, medication use, diabetes mellitus (yes/no), smoking history (yes/no), hypertension history (yes/no)

DBP, diastolic blood pressure; SBP, systolic blood pressure. All IRs are per 100 PYs.

6 IRs for AESIs in Patients With AD in Population-Based Cohort Studies

- In the consistent-dose cohort, IRs for MACE, VTE, and malignancies (excluding NMSC) generally reflected the rates of these events in real-world studies of patients with AD

Patients With Events/100 PY	Abrocitinib 100 mg N=1053	Abrocitinib 200 mg N=1997	All Abrocitinib N=3050
MACE n (%) IR (95% CI)	6 (0.6) 0.30 (0.11-0.65)	9 (0.5) 0.28 (0.13-0.52)	15 (0.5) 0.28 (0.16-0.47)
Nonfatal VTE n (%) IR (95% CI)	1 (0.1) 0.05 (0.00-0.28)	9 (0.5) 0.28 (0.13-0.52)	10 (0.3) 0.19 (0.09-0.35)
Malignancies (excluding NMSC) n (%) IR (95% CI)	3 (0.3) 0.15 (0.03-0.43)	11 (0.6) 0.34 (0.17-0.60)[a]	14 (0.5) 0.26 (0.14-0.44)

[a]In addition, there was 1 event in the abrocitinib 200 mg group, gastric adenocarcinoma, which occurred early in the treatment period and symptoms were present prior to taking study treatment. The IR in the 200 mg group, excluding that subject, was 0.31/100 PY (95% CI, 0.15-0.56). [b]In adult patients with overall risk factors for malignancy: 11.41 (95% CI, 9.83-13.25) per 100 PY for adult patients with a history of malignancy (excluding NMSC/cervical cancer); IR for adult patients without a history of malignancy: 0.44 (95% CI, 0.40-0.48).[2] [c]Excludes NMSC and cervical carcinoma *in situ*. IR, 0.51 (95% CI, 0.44-0.60) per 100 PY for adult patients with a history of malignancy (excluding NMSC/cervical cancer).1. Egeberg A et al. Presented at Revolutionizing Atopic Dermatitis (RAD) Virtual Conference; December 10, 2023. Poster 534. 2. Data on File. Pfizer Inc.; New York, NY, USA. 3. Hedderson MM et al. *PLoS One*. 2022;17(11):e0277469. 4. Hedderson MM, et al. *BMJ Open*. 2023;13:e071172. 5. Wan J et al. *Br J Dermatol*. 2023;189(1):53-61. 6. Wan J et al. *J Allergy Clin Immunol Pract*. 2023;11(10):3123-3132.e3.

Patients With Events/100 PY	Danish Cohort[1,2] (n=17,341)	Kaiser Cohort[2-4] (n=8197)	THIN Cohort[2,5,6] (n=625,083)
MACE n (%) IR (95% CI)	367 (2.1) 0.26 (0.24-0.29)	92 (1.1) 0.26 (0.21-0.32)	22,810 (3.6) 0.64 (0.63-0.64)
Nonfatal VTE n (%) IR (95% CI)	NA 0.14 (0.12-0.16)[1]	70 (0.9) 0.2 (0.15-0.25)	15,872 (2.5) 0.44 (0.43-0.45)
Malignancies (excluding NMSC) n (%) IR (95% CI)	NA 0.59 (0.54-0.64)[b]	156 (1.9) 0.44 (0.38-0.51)[c]	29,585 (4.6) 0.83 (0.82-0.83)

Danish Cohort (2000-2018)[1,2]	A population-based cohort study of Danish individuals aged ≥12 years with ≥1 diagnosis of AD (all severities)
Kaiser Cohort (2007-2018)[3,4]	A retrospective US cohort study of the Kaiser Permanente Northern California health plan members aged ≥12 years diagnosed with moderate-to-severe AD. Eligibility criteria of this study were selected to mirror the population of patients with moderate-to-severe AD from recent AD clinical trial programs
THIN Cohort (1994-2015)[5,6]	A retrospective UK cohort study of individuals (all ages) with mild-to-severe AD. Data shown are for individuals aged ≥18 years

Additional details on the Danish, Kaiser, and THIN cohorts are shown in the supplementary material (via QR code at the end of the presentation)

7 Conclusions

- In this updated integrated abrocitinib safety analysis using data with more than 7000 PY of exposure in patients with moderate-to-severe AD, abrocitinib had a manageable long-term safety profile, consistent with the previously reported risk profile
- There were no new safety signals reported
- Rates of AESIs, including serious infections, malignancies, cardiovascular events, such as MACE and VTE, and deaths, tended to be higher in older patients with ≥1 CV risk factors and in patients with intermediate and high ASCVD risk scores
- Rates of AESIs in patients treated with abrocitinib generally reflected those observed in real-world studies of patients with AD