

**Rates of Cardiovascular Events Among Patients With Moderate-to-Severe Atopic  
Dermatitis: A Retrospective Cohort Study**

Monique M. Hedderson,<sup>1</sup> Fei Xu,<sup>1</sup> Charles P. Quesenberry,<sup>1</sup> Sneha Sridhar,<sup>1</sup> Jamie Geier,<sup>2</sup> Adina  
R. Lemeshow<sup>2</sup>

<sup>1</sup>Kaiser Permanente Northern California, Oakland, CA; <sup>2</sup>Pfizer, Inc., New York, NY

**Background:** Evidence suggests a relationship between atopic dermatitis (AD) and cardiovascular (CV) disease, including increased risk for myocardial infarction, angina, heart failure, and major adverse cardiovascular events (MACEs). However, the incidence rate (IR) of CV events among patients with moderate-to-severe AD is unknown. This retrospective cohort study was conducted to identify IRs of CV events in patients with moderate-to-severe AD in a population representative of patients with access to healthcare.

**Objectives:** To evaluate IRs for CV events in a cohort of Kaiser Permanente Northern California (KPNC) members diagnosed with moderate-to-severe AD

**Methods:** This retrospective cohort study (2007-2018, inclusive) was conducted within the KPNC healthcare delivery system. The cohort comprised patients who were  $\geq 12$  years of age, given a diagnosis of AD between 2007 and 2018, and enrolled in a health plan for  $\geq 12$  months before the study index date. The study index date was defined as the first date at which an eligible patient filled a prescription for a topical or systemic agent or the first date at which a patient received phototherapy. Moderate-to-severe disease was defined as disease necessitating topical therapy or phototherapy (moderate) or systemic treatment (severe) for a diagnosis of AD. A sample of 100 patients was adjudicated to determine the reliability of the criteria used to accurately identify cases of moderate-to-severe AD. Adjudication was conducted by a board-certified dermatologist, and an agreement of  $\geq 80\%$  between the cases identified by study parameters and dermatologist medical record review was deemed acceptable. CV events included MACE, venous thrombotic event (VTE), deep vein thrombosis (DVT), and pulmonary embolism (PE). CV events were analyzed regardless of presumed causality, graded in terms of severity and relationship to study treatment, and coded using the Medical Dictionary for Regulatory Activities (MedDRA). IRs were reported overall and by year of study index date and

were analyzed separately in 2 age groups ( $\geq 12$  to  $< 18$  vs  $\geq 18$  years [adults vs minors]; and  $< 65$  vs  $\geq 65$  years [seniors vs nonseniors]), sex, race, ethnicity, and selected additional risk factors.

**Results:** Among 34,405 health plan members with an AD diagnosis between 2007 and 2018, 8197 patients had moderate-to-severe AD. Most (7158 [87.3%]) had moderate AD. Adjudication of AD severity indicated that the definitions used to classify moderate and severe AD were acceptable (agreement for confirmed cases  $\geq 80\%$ ). The highest IR (95% CIs) per 1000 person-years (PYs) was MACE (2.6 [2.1-3.2]), followed by VTE (2.0 [1.5-2.5]), DVT (1.6 [1.2-2.1]), and PE (0.7 [0.5-1.0]). IRs were lower for patients aged 12-17 years than for patients  $\geq 18$  years for all CV events (MACE, 0.0 [0.0-0.0] vs 3.1 [2.6-3.8]; VTE, 0.5 [0.2-1.6] vs 2.2 [1.8-2.8]; DVT, 0.5 [0.2-1.6] vs 1.8 [1.4-2.3]; and PE, 0.2 [0.0-1.2] vs 0.8 [0.5-1.2], respectively). DVT and PE IRs were higher among patients aged  $\geq 65$  years than those  $< 65$  years (DVT, 5.5 [3.6-8.5] vs 1.1 [0.8-1.6], respectively; and PE, 1.8 [0.9-3.8] vs 0.6 [0.4-0.9], respectively). MACE IRs (95% CI) were higher among men (4.5 [3.4-5.8]) than women (1.6 [1.1-2.2]) and among former smokers (4.3 [2.7-6.9]) than never smokers (1.8 [1.3-2.5]). IRs of MACE, VTE, and DVT were higher among AD patients with diabetes than those without (MACE, 9.3 [6.0-14.6] vs 2.2 [1.7-2.8]; VTE, 5.1 [2.8-9.1] vs 1.8 [1.4-2.3]; DVT, 4.1 [2.2-7.9] vs 1.4 [1.1-1.9], respectively).

**Conclusion:** In patients with moderate-to-severe AD, representative of patients with access to healthcare in the United States, CV events with the highest IR was MACE, followed by VTE, DVT, and PE. The IRs per 1000 PYs of MACE were higher among men, and IRs of all CV events except PE were higher among patients with diabetes. This study is one of the first to report CV event IRs among patients with moderate-to-severe AD, and it provides valuable information for ongoing clinical trials in this patient population.