Risk of non-melanoma skin cancer in patients with moderate-to-severe atopic dermatitis: a United States population-based study using claims data

Mark Lebwohl¹, Emma Yue², Whitney Krueger², Brian Berman³, Christopher G Bunick⁵, Todd Schlesinger⁷, Ayman Grada²

¹Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York City, New York, United States; ²AbbVie Inc., North Chicago, Illinois, United States; ³Skin and Cancer Associates, Aventura, Florida, United States; ⁴Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, Florida, United States; ⁵Department of Dermatology, Yale School of Medicine, New Haven, Connecticut, United States; ⁶Program in Translational Biomedicine, Yale University School of Medicine, New Haven, Connecticut, United States; ⁷Clinical Research Center of the Carolinas, Charleston, South Carolina, United States

Introduction/Background: Non-melanoma skin cancer (NMSC), including basal and squamous cell carcinoma, are associated with prolonged intermittent sun exposure (specifically ultraviolet radiation). Atopic dermatitis (AD) is a chronic inflammatory skin disease associated with multiple comorbidities.¹ ² While AD is associated with an increased risk of skin cancers,³ data on the underlying risk of NMSC in patients with AD are inconsistent.¹

Objective: To evaluate NMSC incidence and risk in patients with AD compared with a non-AD matched control cohort and patients with rheumatoid arthritis (RA). To evaluate the effect of disease activity, analyses were repeated in patient subgroups with moderate-to-severe disease.

Methods: This retrospective observational study used US claims data from the Optum Clinformatics Data Mart. Eligible patients were aged ≥ 18 years with diagnosed AD (≥ 2 claims for AD or ≥ 1 claim for AD or eczema with asthma and/or hay fever, food allergies, or allergic
rhinitis) between March 2017–March 2023. The cohort entry date was the date of the first qualifying disease diagnosis. Patients were classified as having moderate-to-severe disease if they received dupilumab for AD or advanced systemic therapy for RA during follow-up. Comparator groups included non-AD control cohorts (matched 1:1 to the AD and moderate-to-severe AD cohorts, respectively, by age [± 1 year], sex, and cohort entry date), patients diagnosed with RA (≥ 2 claims ≥ 7 days apart filed by a rheumatologist), and patients with moderate-to-severe RA. Crude NMSC incidence rates were reported. Relative risk was calculated using multivariable Cox proportional hazard models adjusted for baseline demographics, comorbidities, and medications.

**Results:** This analysis included data from 391,753 patients with AD (7136 with moderate-to-severe AD) and 97,445 patients with RA (35,846 with moderate-to-severe RA). The matched AD and non-AD cohorts each included 381,221 patients. The matched moderate-to-severe AD and non-AD cohorts each included 7134 patients. The mean (SD) age in years was 58.1 (18.8) for AD and non-AD cohorts after matching and 67.0 (13.6) for RA. The median (IQR) follow-up time in days was 1087 (487–1485) for AD, 1218 (548–1782) for RA, and 1013 (376–1562) for non-AD controls. The NMSC incidence per 100 patient-years (95% CI) was 2.12 (2.10, 2.15) for AD and 1.74 (1.72, 1.77) for matched non-AD controls, 2.11 (1.87, 2.35) for moderate-to-severe AD and 1.28 (1.10, 1.47) for matched non-AD controls, 2.33 (2.28, 2.38) for RA, and 2.03 (1.94, 2.12) for moderate-to-severe RA. The relative NMSC risk (adjusted hazard ratio [95% CI]) was greater in patients with AD vs matched non-AD controls (1.32 [1.30, 1.35]) and moderate-to-severe AD vs matched non-AD controls (1.36 [1.12, 1.65]; **Figure 1A**). There was no significant difference in NMSC risk in patients with AD compared with RA (1.03 [1.00, 1.06]) or moderate-to-severe AD compared with moderate-to-severe RA (0.97 [0.87, 1.08]). On average, NMSC risk was > 6 times higher in patients with AD with a history of NMSC vs those without; history of other malignancies and organ transplantation were also associated with
increased NMSC risk (Figure 1B). NMSC risk was ≥ 35% lower in patients who were female vs male, and patients who were Asian, Hispanic, or Black vs White (Figure 1B).

Conclusions: Patients with AD demonstrated a higher NMSC risk compared with non-AD matched controls, and a similar NMSC risk compared with patients with RA; patterns were consistent for patients with moderate-to-severe disease. NMSC risk was higher in patients with AD with a history of NMSC or other malignancies. As a limitation, patients with AD were commonly examined by dermatologists who were likely to look for and find NMSC. Characterizing the underlying NMSC risk among patients with AD may inform treatment benefit-risk assessments.

Key Words: Atopic dermatitis, moderate-to-severe, nonmelanoma skin cancer, real-world study
REFERENCES

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Whitney Krueger – AbbVie – Employee – may hold stock and/or stock options in the company

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Figure 1. Risk of NMSC in patients with AD. (A) Relative risk of NMSC in patients with AD, non-AD controls, and RA and (B) Predictors of NMSC risk in patients with AD based on baseline demographic and clinical characteristics.

AD, atopic dermatitis; HR, hazard ratio; NMSC, nonmelanoma skin cancer; RA, rheumatoid arthritis; ref, reference.

**a**Evaluated as a continuous variable; hazard ratio reflects a 1-year change in age.

**b**Within the 365 days before the index date.

**c**Excluding NMSC.

*P < .05; **P < .01; ***P < .001.