Risk of malignancy excluding nonmelanoma skin cancer in patients with moderate-to-severe atopic dermatitis in the United States: a population-based study using claims data

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Introduction/Background: Patients with atopic dermatitis (AD) may be at an increased risk for a range of malignancies, including lymphoma.¹ However, real-world data characterizing malignancy risk among US patients with AD remain limited.

Objective: To evaluate the risk of malignancy excluding non-melanoma skin cancer (NMSC) in patients with AD compared to individuals without AD and to those with rheumatoid arthritis (RA). Additionally, these analyses were repeated in a subgroup of patients with moderate-to-severe disease to evaluate the effect of disease activity on cancer risk.

Methods: This retrospective observational claims-based study utilized the Optum Clinformatics Data Mart. Eligible patients were aged ≥18 years with a diagnosis of AD or RA during the study period (March 2017–December 2019). Diagnosis was determined using International Classification of Diseases (ICD)-9 or ICD-10 codes for AD (≥2 claims for AD or ≥1 claim for AD with asthma and/or hay fever, food allergies, allergic rhinitis, or eczema) and RA (≥2 claims ≥ 7 days apart and filled by a rheumatologist). Receipt of advanced systemic therapy during the follow-up period was used as a proxy for disease severity in patients with AD (dupilumab only) and RA. Patients with AD were matched 1:1 with non-AD controls based on age (±1 year), sex,
and cohort entry date. Follow-up occurred until study end, disenrollment, death, or occurrence of an adverse event of interest. Malignancies excluding NMSC were identified based on 2 separate ICD diagnosis codes ≥30 days apart in an inpatient or outpatient setting. For each comparative analysis, the risk of malignancy excluding NMSC was calculated using a multivariable-adjusted Cox proportional hazards model with results reported as an adjusted hazard ratio (aHR).

**Results:** This analysis included 391,753 patients with AD (7136 with moderate-to-severe AD) and 97,455 patients with RA (35,846 with moderate-to-severe RA). The matched non-AD cohort included 381,221 patients and the matched non-AD cohort for moderate-to-severe disease included 7134 patients. The mean (SD) age at cohort entry date was lower for patients in the AD and matched non-AD controls than those in the RA cohort (58.0 [18.8] years for AD, 58.1 [18.8] years for non-AD controls, and 67.0 [13.6] years for RA). Median (IQR) follow-up was 1093 (490–1492) days for AD, 995 (357–1552) days for non-AD controls, and 1190 (484–1773) days for RA. The incidence of malignancies excluding NMSC per 100 patient-years (95% CI) was 2.18 (2.15, 2.21) for AD, 2.38 (2.35, 2.41) for non-AD controls, 3.32 (3.25, 3.38) for RA, 2.43 (2.18, 2.69) for moderate-to-severe AD, and 2.57 (2.47, 2.67) for moderate-to-severe RA. The risk of malignancies excluding NMSC (aHR [95% CI]) was lower for AD vs matched non-AD controls (0.92 [0.90, 0.93]; P<.001) and for moderate-to-severe AD vs their matched non-AD controls (0.76 [0.63, 0.91]; P<.01) (Figure). Although the risk of malignancies excluding NMSC (aHR [95% CI]) was lower in patients with AD vs RA (0.97 [0.94, 0.99]; P=.03), there was no significant difference in risk for patients with moderate-to-severe AD vs moderate-to-severe RA (1.06 [0.95, 1.18]; P=.28). Among patients with AD, the risk of malignancies excluding NMSC (aHR [95% CI]) was greater among patients who were older (1.04 [1.04, 1.04]; P<.001) and those with a history of any type of malignancy excluding NMSC and including recurrence (12.76 [12.32, 13.22]; P<.001), cardiovascular disease (1.12 [1.07, 1.17]; P<.01), smoking (1.15 [1.11,
1.19; \( P < .01 \), asthma (1.05 [1.01, 1.08]; \( P < .01 \)), or chronic liver disease (1.16 [1.10, 1.22]); \( P < .01 \)).

**Conclusions:** Patients with AD demonstrated a lower risk of malignancy excluding NSMC vs matched controls without AD. This lower risk was also observed in patients with moderate-to-severe AD vs their matched non-AD controls and in patients with AD vs RA.

**References:**


**Keywords:** atopic dermatitis, claims analysis, malignancy, real-world
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Figure. Risk of Malignancy (Excluding NMSC) in Patients With AD. (A) Relative Risk of Malignancy (Excluding NMSC) in Patients With AD, RA, and Non-AD Controls and (B) Risk of Malignancy (Excluding NMSC) in Patients With AD Based on Baseline Demographic and Clinical Characteristics

A

B

AD, atopic dermatitis; COPD, chronic obstructive pulmonary disease; CV, cardiovascular; NMSC, nonmelanoma skin cancer; RA, rheumatoid arthritis

*P<.01

a365 days prior to index date.

bExcluding NMSC.