Non-Melanoma Skin Cancer Risk Among Patients in the Psoriasis Longitudinal Assessment and Registry (PSOLAR)

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To the Editor: Patients with psoriasis are at increased risk of developing non melanoma skin cancer (NMSC), including squamous cell carcinoma (SCC) and basal cell carcinoma (BCC).[1,2] The risk is especially elevated among those who previously received systemic treatment or phototherapy.[2] Systemic treatments, including biologic therapies and methotrexate (MTX), are effective in managing immune-mediated diseases; however, they may increase susceptibility to NMSC due to immunosuppression or other factors.[3]

This observational study from PSOLAR (PSOriasis Longitudinal Assessment and Registry) followed the effect of biologic and MTX exposure on the incidence and risk of NMSC among approximately 12,000 patients with psoriasis who were candidates for systemic therapy or phototherapy and had follow-up examinations every 6 months up to 8 years.[4] Our study population included patients without a prior history of BCC or SCC. Exposures included biologics (tumor necrosis factor inhibitors [TNFi] and ustekinumab [UST], considered together [combined] or separately by class) and MTX.The exposure interval extended from the first dose on registry until 91 days after last dose, discontinuation from registry, data extraction, therapy switch, or death. Outcomes were occurrence of first BCC or first SCC. The comparator cohort included patients without biologic or MTX exposure (non biologic/non-MTX [NB/NM]). Crude incidence rates (IRs) were calculated, and Cox regression modeling was used to compare risk between each treatment cohort and the NB/NM comparator, after adjusting for potential confounders.

While patient characteristics were generally similar across treatment cohorts at enrollment, the modeled analysis adjusted for significant differences in covariates noted in Table 1. Crude IRs were notable for a high rate of BCC in the MTX cohort. In the overall population, modeled analyses showed that exposure to biologics (combined) did not significantly change the risk of BCC (hazard ratio [HR]: 2.09 [95% confidence interval (CI): 0.90–4.85], P=0.0843) (Table 1). Considering classes separately, exposure to TNFi increased the risk of BCC (HR: 2.54 [95% CI: 1.08–5.98], P=0.0324), but exposure to UST did not. Exposure to MTX also increased the risk of BCC (HR: 8.58 [95% CI: 3.29–22.4], P<0.0001). In contrast, none of the exposures changed the risk of SCC, except for UST, which significantly decreased SCC risk. We obtained similar point estimates of risk for patients who began treatment after enrollment (incident population) compared with the overall population, although no estimates reached statistical significance.

In summary, we found that BCC risk increased with exposure to TNFi or MTX but not with exposure to UST. In contrast, exposure to either class of biologics or MTX did not increase SCC risk. Limitations include an observational design with associated biases, such as treatment selection bias, and imbalances across cohorts that might not be adequately adjusted for in the analysis. Patients in this analysis also had no prior history of NMSC; therefore, results may not be generalizable. Finally, the incident population analysis lacked power to confirm observations in the overall population. In conclusion, these findings will offer guidance to clinicians in assessing skin cancer risk and surveillance approaches in patients with psoriasis.

Disclosure:

Richard G. Langley has been a Principal Investigator, an Advisory Board member, and/or Speaker for AbbVie, Amgen, Boehringer Ingleheim, Celgene, Leo-Pharma, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Sun Pharma, and UCB. Sunil Kalia is a member of the PSOLAR steering committee and is also an Advisory Board member, Consultant, and Principal Investigator for Janssen, AbbVie, Novartis, Amgen, Eli Lilly, Celgene, and Leo-Pharma. Mona Ståhle has received honoraria and served as an Advisory Board member for Leo-Pharma, UCB,

TABLE 1.

Adjusted Hazard Ratios for Risk of Non-Melanoma Skin Cancer Subtypes (Overall and Incident Populations)

	Overall Population (N=7955)		Incident Population (N=3491)[1]	
First NMSC Subtype	NB/NM Reference HR (95% CI)	*P* Value[2]	NB/NM Reference HR (95% CI)	*P* Value[2]
BCC[3]				
Biologics (combined)	2.09 (0.90–4.85)	0.0843	2.20 (0.80–6.03)	0.1262
TNFi	2.54 (1.08–5.98)	0.0324	2.45 (0.79–7.63)	0.1217
UST	1.35 (0.49–3.67)	0.5619	1.94 (0.58–6.53)	0.2850
MTX[4]	8.58 (3.29–22.4)	<0.0001	--	--
SCC[5]				
Biologics (combined)	0.67 (0.32–1.41)	0.2905	0.78 (0.31–1.97)	0.5966
TNFi	0.91 (0.43–1.95)	0.8113	1.12 (0.40–3.14)	0.8296
UST	0.30 (0.10–0.90)	0.0319	0.47 (0.13–1.78)	0.2677
MTX[4]	1.34 (0.42–4.21)	0.6191	--	--

The overall population included all patients enrolled in PSOLAR who were treatment users at entry (current users) and all patients who began treatment after entry into the registry (ie, incident treatment users). The incident patient population is a subset of the overall population and included all patients enrolled in PSOLAR who began treatment after entry into the registry (ie, incident treatment users).
Abbreviations: --, not applicable; ADA, adalimumab; BCC, basal cell carcinoma; CI, confidence interval; ETN, etanercept; HR, hazard ratio; IFX, infliximab; MTX, methotrexate; NB/NM, non-biologic/non-methotrexate; NMSC, non-melanoma skin cancer: PSOLAR, Psoriasis Longitudinal Assessment and Registry; PUVA, psoralens + ultraviolet A; SCC, squamous cell carcinoma; TNFi, tumor necrosis factor inhibitor; UST, ustekinumab.
[1]Includes 2318 patients in the biologics (combined) cohort and 1173 patients in the NB/NM cohort; 432 MTX users were not included.
[2]Multivariate model included the following covariates: age, race, duration of psoriasis, number of biologics (UST, ADA, ETN, IFX), history of malignancy (other than NMSC), history of cyclosporine, history of oral retinoids (etretinate and acitretin), and PUVA.
[3]SCC was not censored at the first event reported time.
[4]There were no incident MTX users.
[5]BCC was not censored at the first event reported time.

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This observational study was registered with ClinicalTrials.gov: NCT00508547. An institutional review board or ethics committee approved the PSOLAR protocol at each site, and the study was conducted in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use guidelines on Good Clinical Practices and principles of the Declaration of Helsinki as well as other national and local laws and regulations, as appropriate.

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