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Acitretin for Secondary Prevention of Keratinocyte Cancers in a Veteran Population: A Retrospective Cohort Study

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Acitretin, a vitamin A derivative used for psoriasis, can prevent keratinocyte carcinoma (KC). It induced regression of keratoacanthomas (KA) in animal models, presumably by activating retinoic acid and retinoid X receptors that regulate gene expression for growth and proliferation.[1,2] In clinical trials, incident squamous cell carcinoma (SCC) was reduced by 88% in transplant recipients receiving acitretin. Reduction in incidence of basal cell carcinoma (BCC) and SCC was not statistically significant in non-transplant patients, though trends supported acitretin use.[3,4] We describe acitretin use for KC prevention in a clinical setting, with particular focus on elderly patients who are non-transplant recipients.

Patients prescribed acitretin between January 1, 2010 and August 31, 2020 at the Providence VA Medical Center were identified using pharmacy records. Records were subsequently screened for diagnoses of KCs, including SCC, BCC, SCC in situ, KA, and basosquamous carcinoma.

A total of 55 patients were identified; 15 with KCs were included for data extraction (see Table). Acitretin dosage ranged from 10mg weekly to 25mg twice daily. The mean age and BMI were 84 ± 8 years and 25 ± 4 kg/m^2, respectively, 90% were white, all were male, 60% were deceased at time of review, and the mean follow-up period was 2.2 years. Five patients developed a keratinocyte carcinoma within the first year of acitretin use. Of these five patients, three developed a keratinocyte carcinoma within 3 months of acitretin prescription which may suggest that these cancers developed before the full benefit of acitretin was realized. No patient took nicotinamide and three used imiquimod cream, one of whom also used 5-fluorouracil cream. Comparing the overall mean number of new KCs per year before and after acitretin among included patients, we observed a non-significant decrease of 9.9% (P>0.10).

Here, we highlight obstacles to acitretin use in dermatology clinics outside of randomized trial settings. The elderly

TABLE 1.

Annual Rate of New Keratinocyte Carcinomas

Patient ID	Follow-up (years)	Mean Number of New Keratinocyte Cancers Per Year		Acitretin for Other Dermatologic Condition	Excluded, Reason[2]
		Pre-acitretin[1]	Post-acitretin		
3	2	Missing	3.5	--	Yes, 1
5	4	2.6	3.5	--	Yes, 1
9	2	4.5	2	--	Yes, 1
21	2	Missing	1	--	--
27	2	Missing	0	--	--
29	3	3	3.33	--	Yes, 2
33	1	1.5	1	--	--
35	1	0.75	0	Pityriasis rubra pilaris	--
43	2	Missing	0.5	Psoriasis	--
44	1	1	0	Hailey-Hailey	--
46	6	Missing	1.33	--	--
50	4	1	1	Psoriasis	--
51	3	6	16	--	Yes, 2
53	2	2.83	7	--	--
54	1	Missing	1	Psoriasis	--

[1]Missing values for new keratinocyte cancers per year before acitretin treatment indicate no dermatological visits recorded between 2010¬–2020 prior to acitretin prescription.
[2]Reasons for exclusion: 1 = termination of acitretin due to side effects, 2 = transplant recipient

population included in our study may be more representative of patients who seek KC prevention to avoid surgical procedures. Study limitations include small sample size and incomplete patient records. Notably, acitretin doses observed in this study were highly variable. Side effects of acitretin are dose-dependent,[5] but there is no standard for chemoprevention. Further studies may determine whether doses low enough to be tolerated by elderly patients would be effective as chemoprevention, especially compared or in combination with possible alternative proposed interventions. Guidelines for chemoprevention for this high-risk elderly population, which demographic trends show will be enlarging in the coming decades, should be developed.

DISCLOSURES

Rachel K. Lim has no conflicts of interest to disclose. Martin A. Weinstock, MD, PhD has no conflicts of interest to disclose. Shoshana M. Landow, MD, MPH has no conflicts of interest to disclose. The statements in this article are those of the authors and not of the VA.

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