Table I. Background clinical parameters and treatment outcomes (N = 53)

Characteristics	Value
Sex, n (%)	
Male	2 (3.77)
Female	51 (96.22)
Skin phototype	
II	2 (3.77)
III	22 (41.50)
IV	24 (45.28)
V	5 (9.43)
Age at onset, y	
Mean ± SD	33.5 ± 8.2
Minimum, maximum	17, 50
Years of melasma before starting oral TA	
Mean ± SD	11.03 ± 8.4
Minimum, maximum	1, 36
Clinical parameters	
Main affection, n (%)	
Centrofacial	28 (52.83)
Malar	19 (35.84)
Mandibular	6 (11.32)
Melasma Severity Score, n (%)	
Mild (mMASI of 2.7-4.9)	5 (9.43)
Moderate (mMASI of 5-7.2)	20 (37.73)
Severe (mMASI of 7.3 or more)	28 (52.83)

Treatment outcomes	mMASI	Sp-MELASQOL
Group: 650 mg TA daily		
Baseline	8.25	36.88
Week 8	6.51	—
Week 20	4.4	26.2
Group: 650 mg TA + HQ 4% daily		
Baseline	8.20	32.80
Week 8	5.57	—
Week 20	3.12	16.69
Adverse effects to TA (n = 7), n		
Breast pain	4	
Abdominal pain/inflammation	1	
Arthralgias	1	
Hypo-oligomenorrhea	1	

HQ, Hydroquinone; *mMASI*, Modified Melasma Area and Severity Index; *Sp-MELASQOL*, Spanish-language Melasma Quality of life; *TA*, tranexamic acid.

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Characterizing index keratinocytic carcinomas in commercially insured adults younger than age 50 years in the United States

To the Editor: More than 3 million people are affected by keratinocyte carcinomas (KCs) in the United States, an often-cited estimate from Medicare claims and population survey data for patients 65 years old and older.[1] However, less is known about KCs in younger populations. In this retrospective cohort study, we used health administrative claims data to characterize index KC in commercially insured adults aged 18 to 50 years.

We interrogated the IBM MarketScan Commercial Database, a claims database containing 20 to 40 million US employees (2011-2017), using a previously validated algorithm[2] pairing International Classification of Diseases diagnosis codes with Current Procedural Terminology procedural codes to identify index KC. Enrollees (aged 18-50 inclusive) with 12-months continuous enrollment prior to their index service date were captured. Enrollees with any prior malignancy history of the lip or skin;

Table I. Demographic data of patients with an index keratinocyte carcinoma

Characteristics	Female (n = 63,811)	Male (n = 50,399)	Total (N = 114,210)
Age, mean (SD), y	43.42 (5.9)	44.16 (5.5)	43.8 (5.7)
Age at diagnosis, y, n (%)			
18-20	123	99	222 (0.2)
21-30	2377	1230	3607 (3.2)
31-40	14,118	9366	23,484 (20.6)
41-50	47,193	39,704	86,897 (76)
Region, n (%)			
Northeast	10,053	7837	17,890 (15.7)
North Central	12,367	8740	21,107 (18.5)
South	29,385	23,286	52,671 (46.1)
West	11,022	9764	20,786 (18.2)
Unspecified	984	772	1756 (1.5)
Index keratinocyte carcinoma, n (%)			
BCC	54,421	41,566	95,987 (84)
SCC	9031	8461	1492 (15.3)
BCC and SCC	359	372	731 (0.6)

Table II. Association between female sex and type of index keratinocyte carcinoma

	All KCs		BCC		SCC	
Age group, y	Female:male ratio	*P* value	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
All ages (18-50)	1.27	<.0001	1.227 (1.188-1.267)	<.0001	0.815 (0.789-0.842)	<.0001
18-30	1.88		1.597 (1.275-2.000)		0.626 (0.500-0.785)	
31-40	1.51		1.366 (1.255-1.486)		0.732 (0.673-0.797)	
41-50	1.12		1.161 (1.121-1.203)		0.861 (0.831-0.892)	

predisposing conditions of skin cancer; and/or an immunosuppressed state were excluded. Specific International Classification of Diseases/Current Procedural Terminology inclusion and exclusion codes are available in Supplemental Tables I and II, respectively (available via Mendeley at https://doi.org/10.17632/mrzgyyzt5n.1).

Collected data included age, sex, geographic region, and procedure type for index KCs. Chi-square tests were used for between-group comparisons. Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

A total of 114,210 unique patients met inclusion/exclusion criteria (Table I). The overall mean age was 43.8 years, with 76% in their fifth decade. The majority (55.9%) were women; 84% had an index basal cell carcinoma (BCC), 15.3% with squamous cell carcinoma (SCC), and 0.6% with both BCC and SCC.

Across all age groups, women were more likely than men to have an index BCC (OR, 1.227; 95% CI, 1.188-1.267; $P < .0001$), with the greatest difference in the 18- to 30-year-old age group (OR, 1.597; 95% CI, 1.275-2.000, $P < .0001$). In contrast, women were less likely than men to have an index SCC (OR, 0.815; 95% CI, 0.789-0.842; $P < .0001$) (Table II).

Procedures to treat KC include destruction, standard excision, and Mohs micrographic surgery (MMS). Subgroup analysis showed that a significantly greater proportion of women aged 18 to 30 years received MMS for their index BCC compared with women aged 41 to 50 years ($P < .0001$). Additionally, these BCCs were likelier to occur on high- and medium-risk areas as defined by appropriate use criteria for MMS utilization[3] (OR, 1.2; 95% CI, 1.184-1.401; $P < .0001$).

Our results corroborate well-known trends (ie, age-related increases[4] and BCC predominance in younger women[5]) in a large cohort of commercially insured adults. We also show that index BCCs in women aged 18 to 30 years are more likely to occur on areas appropriate for MMS, indicating involvement of cosmetically or functionally sensitive sites, such as the face. Younger women also utilize MMS to a significantly

greater degree, suggesting the presence of other aggressive features in their tumors. Because little is known about the impact of KC, these findings suggest that health-related outcomes and quality-of-life measures may warrant further investigation.

Limitations include not capturing uninsured, publicly insured, or privately insured individuals who did not seek medical services. The true number of index KCs is likely underestimated due to our continuous enrollment restriction. Detailed demographic data, clinical information, or behavioral practices are also not available. Nevertheless, we report results and trends from a population for which there is a paucity of data.

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Proton pump inhibitors are associated with increased risk of alopecia areata: A nationwide nested case-control study

To the Editor: Alopecia areata (AA) is a common autoimmune disease.[1] Although the exact pathogenesis remains obscure, growing evidence has suggested a link between AA and the gastrointestinal microbiome, described as the skin-gut axis.[2] Moreno-Arrones et al[3] found bacterial biomarkers associated with the disease status of AA, which stressed the skin-gut axis. Meanwhile, prolonged use of proton pump inhibitors (PPIs) has been associated with gut dysbiosis.[4] This nationwide nested case-control study examined the association between PPI use and the risk of AA.

We identified all individuals exposed to any PPI between January 1998 and December 2013 from the National Health Insurance Research Database in Taiwan. The AA cases are defined as individuals without a history of hair and hair follicles diseases (International Classification of Diseases-Ninth Clinical Modification code 704) at the enrollment time and subsequently diagnosed with AA (code 704.01). The diagnosis of AA was made by board-certified dermatologists or rheumatologists. The time of the first PPI exposure and the time of AA diagnosis were defined as the enrollment time and the study end time, respectively.

For each AA patient, one control individual without AA was selected after matching for age, sex, residence, monthly premium, enrollment time, study end time, and comorbidity. The cumulative defined daily dose was used to quantify the PPI use. The standardized mean difference was used to compare baseline characteristics between study groups. Logistic regression analysis was used to evaluate the association between PPI use and AA risk.

We identified 35,552 patients with prior exposure to PPI (Table I). A dose-response relationship was found between PPI use and the risk of AA after