

Biologic Therapy for Psoriasis and Risk of Malignancies in a Hispanic Population: A Single Center Retrospective Cohort

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Objectives: Psoriasis is a chronic inflammatory autoimmune disease with an increasing burden. Biologic agents are considered a key treatment modality in improving quality of life for psoriasis patients. However, the potential carcinogenic effect of these agents has become a concerning factor due to their immunomodulatory effects. The purpose of this study is to evaluate differences in the incidence of skin and systemic malignancies in biologic-naïve patients vs biologic-treated patients.

Methods: This retrospective study evaluated chart data from the University of Puerto Rico dermatology clinics, from August 2020 through January 2023. The inclusion criteria for biologic-naïve patients were to be 18 years or older, diagnosed with psoriasis, unexposed to previous systemic therapy, and with available baseline clinical characteristics. The biologic-exposed had to meet the same criteria and must have received at least 6 months of biologic therapy. Patients who had a previous history of phototherapy were excluded from the study.

Results: A total of 402 patients were evaluated; 172 from the biologic naïve group and 230 from the biologic exposed group. The incidences of NMSC and systemic malignancy for the biologic-naïve group (2.32% and 1.74%) and the biologic-exposed group (2.17% and 2.60%) showed no significant difference (p -value = 0.47). In the biologic-exposed group, patients exposed to adalimumab had the highest incidence of both NMSC and systemic malignancy. However, this difference was not statistically significant. The most common systemic malignancies were colorectal and prostate carcinomas.

Conclusions: There was no significant difference in cancer incidence in patients treated with topical versus biologic therapy for psoriasis.

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Key words: Psoriasis, Hispanics, Biologic therapy, Non-melanoma skin cancer, Malignancy

Psoriasis is a chronic inflammatory autoimmune disease with increased disease burden. Biologic agents have become an effective and safe therapeutic alternative compared to previous conventional therapy for this condition, significantly improving quality of life for patients. They target molecules such as tumor necrosis factor alpha (TNF- α), interleukins (IL), and Janus Kinase (JAK), among others, that have complex roles in the immune system involving inflammatory, oncogenic, and oncolytic pathways, for which cancer immunosurveillance mechanisms may be negatively impacted (1-2). In solid-organ transplant patients receiving immunosuppressive therapy, it has been observed that immunosuppression increases the risk of a variety of skin cancers, which include squamous cell carcinoma (SCC), Kaposi sarcoma, Merkel cell carcinoma, basal cell carcinoma, and melanoma (2-3). However, the data on the malignant effects associated with the biologic agents used in psoriasis is inconsistent because of both, the underlying inflammation that these patients tend to have and the other treatment modalities, such as phototherapy, to which they are exposed. Several studies have shown that psoriasis patients have an overall increased risk of lymphoproliferative disease and non-melanoma skin cancer (NMSC), most likely secondary to the immunologic mechanisms driving the condition and the UV light exposure associated with phototherapy (1,4).

Associations between SCC and TNF- α inhibitors have been suggested in patients with rheumatologic conditions, although they have been more frequently observed in psoriasis patients, implying both treatment-related and underlying disease risks (1-2, 5).

There is limited and unclear data concerning the carcinogenic potential of biologic therapies in a Hispanic population. Puerto Rican and other Hispanics in the United States may have a disproportionate burden of malignancies influenced by access to healthcare, cultural beliefs, genetic predisposition, and underlying modifiable risk factors (6-7). While overall cancer incidence in Hispanics is comparable to non-hispanics, morbidity and mortality is increased (6). For this reason, further long-term

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research in this population is warranted. Furthermore, there are insufficient studies adjusting for confounding factors such as phototherapy. Thus, the aim of this study was to evaluate differences in the incidence of skin and systemic malignancies in patients treated with topical therapy only versus biologic therapy in a Hispanic population.

Methods

This study was an IRB approved single-center retrospective chart review conducted from August 2021 to January 2023 at the University of Puerto Rico Dermatology Clinics. The cohort was divided into two groups, biologic-naïve and biologic-exposed group. Biologic agents evaluated included adalimumab, ixekizumab, ustekinumab, etanercept, secukinumab, risankizumab, and guselkumab. We evaluated sociodemographic and clinical variables such as age, gender, and disease duration. Additional variables that were measured during the study were disease severity, current and previous use of topical and/or systemic therapy, history of previous systemic therapies, and history of NMSC, melanoma, or any other malignancies.

The inclusion criteria considered were patients with a diagnosis of psoriasis, who were 18 years or older with baseline clinical characteristics available on record. Patients in the biologic-naïve group had been exposed to topical therapy only. Patients in the biologic-exposed group had to be treated with a biologic agent for at least six months to be included. They were not excluded if they had previous exposure to systemic medication used to treat psoriasis. Patients in the biologic-exposed group were excluded if there was a discontinuation of treatment prior to 6 months, if there was a previous exposure to phototherapy, or if they were lost to follow-up. Patients in the biologic-naïve group were excluded if there was a previous exposure to systemic therapy (methotrexate, acitretin, etc.), if there was a previous exposure to phototherapy, or if they were lost to follow-up. Patients with previous exposure to phototherapy were excluded in order to adjust for confounding variables that may contribute to development of skin malignancies.

The data in this study were analyzed using descriptive statistics for categorical variables and a t-test to establish differences among groups.

Results

A total of 402 patients were evaluated; 172 belonged to the biologic-naïve group and 230 to the biologic-exposed group. In the biologic-naïve group, the mean age was

46 years, 67% of the patients were female, and 33% were male (Table 1). On the other hand, in the biologic-treated group, the average age was 52 years, 48% of the subjects were female, and 52% were male (Table 1). The average disease durations were 4 and 7 years for the biologic-naïve and biologic-exposed groups, respectively (Table 1). Overall, the two groups had no significant differences in the baseline age and disease duration (p -value = 0.62).

The incidences of NMSC and systemic malignancy for the biologic-naïve group (2.32% and 1.74%, respectively) and the biologic-exposed group (2.17% and 2.60%, respectively) showed no significant difference (P -value = 0.47) (Table 2). In the biologic-exposed group, patients exposed to adalimumab had the highest incidence of NMSC and systemic malignancy (1.63%) when compared to those exposed to other biologic agents (Table 3). However, this difference was not statistically significant. Of the patients exposed to Adalimumab, 5.4% developed malignancies (NMSC and/or a solid tumor), with 33.3% of the solid tumors

Table 1. Baseline demographic and clinical characteristics for biologic naïve and biologic exposed groups

	N	Mean age	Male	Female	Disease duration	Initial TBSA involvement	TBSA involvement during therapy
Biologic naïve	172	46 y/o	33%	67%	4 years	Not available	Not available
Biologic exposed	230	52 y/o	52%	48%	7 years	70%	10%

Table 2. Incidence of malignancy and NMSC in the biologic naïve and biologic exposed group

	NMSC	Systemic cancer
Biologic naïve group	5/172 (2.32%)	3/172 (1.74%)
Biologic exposed group	5/230 (2.17%)	6/230 (2.60%)

Table 3. Incidence of malignancy and NMSC on topical therapy vs those exposed to different available biologic agents

	Number of patients with active exposure	Number of patients with prior exposure	NMSC	Systemic cancer
Topical therapy only	172	-	2.32%	1.74%
Adalimumab (Humira)	54	131	1.63%	1.63%
Ustekinumab (Stelara)	18	57	1.35%	1.35%
Ixekizumab (Taltz)	104	53	0.64%	1.27%
Etanercept (Enbrel)	8	7	0	0
Secukinumab (Cosentyx)	3	8	0	0
Risankizumab (Skyrizi)	33	5	0	0
Guselkumab (Tremfya)	10	7	0	0

being colorectal, prostate, or Warthin's tumors. Of the patients exposed to Ixekizumab, 2.5% developed malignancies, with 50% percent of the solid tumors being hepatocellular carcinoma or colorectal cancer. Overall, the most common solid-tumor malignancies observed were colorectal and prostate cancer. Furthermore, the average ages for patients in the exposed and non-exposed groups who developed malignancies were 69 and 74 years, respectively (p -value = 0.43), regardless of their exposure to biologic agents.

Discussion

Given the limited data regarding the risk of malignancy in Hispanic patients with psoriasis treated with biologics, our study aimed to evaluate the difference in the incidence of malignancy in biologic-naïve versus biologic-exposed patients. No significant difference was established between the two groups in our study, mimicking outcomes observed in the literature.

Our study assessed the incidence in individuals with psoriasis across all available biologic therapies and found no association between the length of exposure to therapy or the development of malignancies. Furthermore, no significant differences were found when comparing the incidence of malignancy (NMSC and systemic malignancies) associated with adalimumab, ixekizumab, and ustekinumab, to that of topical therapy. Similarly, studies focusing on TNF alpha inhibitors have not found an association with increase in overall cancer risk (8). Studies on other biologic agents have also failed to show an increased risk for malignancy in general. However, of the different biologic agents available for treating psoriasis, TNF-alpha inhibitors, have been implicated as increasing the risk of NMSCs, most commonly SCC (5,9). There is mixed evidence regarding the risk of malignancy associated with biologic therapies, given the short-term nature of the studies that have been conducted and the confounding factors that might have been present.

Previous studies compared the differences in cancer incidence between patients with psoriasis and the members of a healthy control population. Comparing these two patient populations could lead to bias, given that patients with psoriasis tend to have an increased baseline risk for malignancy, regardless of the use of biologic therapy. Studies comparing malignancy risk in rheumatoid arthritis and psoriasis patients on tumor necrosis factor (TNF) alpha inhibitors, have found that psoriasis patients are more likely to develop NMSC, further suggesting that these patients tend to have a greater risk of developing that form of cancer (1-2, 5).

Consistent with what is described in the literature, in which no clear association between melanoma and biologic or systemic therapy has been established, no patient in either group of our study developed melanoma (10). Furthermore, studies excluding patients with exposure to phototherapy, as ours, have not found an increased risk of melanoma in patients with psoriasis (11).

The two most common systemic malignancies observed in our study were colorectal cancer and prostate cancer. Colorectal cancer is the third most common cancer in the USA and PR, while prostate cancer is the most common cancer in men in the USA

and PR (12). The average ages for patients with psoriasis who developed malignancies were above 65 years of age, regardless of their exposure, for which age can be a contributing factor for malignancy, given that cancer is considered the main cause of death in the 65 to 75 age group.

Some important limitations to point out include the retrospective nature of the study, the fact that it was conducted at a single tertiary healthcare institution, the small sample size that was evaluated, and the possible selection bias resulting from less representation of exposure to newer biologics. However, we excluded the use of phototherapy to adjust for confounding factors that could increase the risk of skin cancer in psoriasis patients, which could be considered one of the strengths of our study.

Our results, along with previously published literature, highlight the low indexes of both skin cancer and internal malignancies in psoriasis patients managed with biological agents. These results are reassuring to both physicians and patients. Nevertheless, dermatologists should continue vigilance for possible skin cancers and patients should comply with age-appropriate cancer screening tests. Further long-term data on the malignancy risk associated with biologic therapy is needed.

Resumen

Objetivos: La psoriasis es una enfermedad inflamatoria crónica que afecta la calidad de vida de los pacientes, por lo que el uso de biológicos se ha vuelto fundamental en el manejo de la condición para aliviar la carga de la condición. Sin embargo, el potencial carcinogénico de estos agentes se ha identificado como una preocupación dada sus efectos inmunomoduladores. El objetivo de este estudio es valorar las diferencias en incidencia de malignidades de la piel y sistémicas en pacientes con y sin tratamiento con agentes biológicos. **Métodos:** Se llevó a cabo un estudio retrospectivo evaluando datos de récord electrónico en las clínicas de Dermatología de la Universidad de Puerto Rico, desde agosto de 2020 hasta enero de 2023. Los criterios de inclusión para pacientes sin uso previo de biológicos fueron ser mayor de 18 años, tener un diagnóstico de psoriasis, sin exposición previa a tratamiento sistémico y con características clínicas de base reportadas. Los pacientes con tratamiento de biológicos debían cumplir con los mismos criterios en adición a haber utilizado agentes biológicos por más de 6 meses. Pacientes con uso previo de fototerapia fueron excluidos del estudio. **Resultados:** Se evaluaron un total de 402 pacientes; 172 en el grupo sin uso de biológicos y 230 en el grupo de exposición a biológicos. No hubo diferencia significativa ($p=0.47$) en la incidencia de cáncer de piel (no melanoma) y malignidad sistémica entre el grupo sin biológicos (2.32% and 1.74%) y el grupo expuesto a biológicos (2.17% and 2.60%). En el grupo expuesto a biológicos, los pacientes con exposición a adalimumab tuvieron mayor incidencia de ambas malignidades de piel (no-melanoma) y sistémicas. Sin embargo, no fue una diferencia estadísticamente significativa. Las malignidades sistémicas más comunes que se identificaron fueron carcinoma colorrectal y de próstata. **Conclusión:** No hubo diferencia significativa en malignidades entre los pacientes de psoriasis con y sin exposición a biológicos.

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References

- Geller S, Xu H, Lebwohl M, Nardone B, Lacouture ME, Kheterpal M. Malignancy Risk and Recurrence with Psoriasis and its Treatments: A Concise Update. *Am J Clin Dermatol*. 2018;19(3):363-375. doi:10.1007/s40257-017-0337-2
- Kreher MA, Konda S, Noland MMB, Longo MI, Valdes-Rodriguez R. Risk of melanoma and nonmelanoma skin cancer with immunosuppressants, part II: Methotrexate, alkylating agents, biologics, and small molecule inhibitors. *J Am Acad Dermatol*. 2023;88(3):534-542. doi:10.1016/j.jaad.2022.11.043
- Scott FI, Mamtani R, Brensinger CM, et al. Risk of Nonmelanoma Skin Cancer Associated With the Use of Immunosuppressant and Biologic Agents in Patients With a History of Autoimmune Disease and Nonmelanoma Skin Cancer. *JAMA Dermatol*. 2016;152(2):164-172. doi:10.1001/jamadermatol.2015.3029
- Vaengebjerg S, Skov L, Egeberg A, Loft ND. Prevalence, Incidence, and Risk of Cancer in Patients With Psoriasis and Psoriatic Arthritis: A Systematic Review and Meta-analysis. *JAMA Dermatol*. 2020;156(4):421-429. doi:10.1001/jamadermatol.2020.0024
- Asgari MM, Ray GT, Geier JL, Quesenberry CP. Malignancy rates in a large cohort of patients with systemically treated psoriasis in a managed care population. *J Am Acad Dermatol*. 2017;76(4):632-638. doi:10.1016/j.jaad.2016.10.006
- Miller KD, Ortiz AP, Pinheiro PS, et al. Cancer statistics for the US Hispanic/Latino population, 2021. *CA Cancer J Clin*. 2021;71(6):466-487. doi:10.3322/caac.21695
- Niu Z, Rivera YM, Baskar J, et al. Barriers and facilitators to skin cancer prevention among Hispanics: a qualitative study. *BMC Public Health*. 2024;24(1):2690. Published 2024 Oct 2. doi:10.1186/s12889-024-20000-2
- Bonovas S, Minozzi S, Lytras T, et al. Risk of malignancies using anti-TNF agents in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: a systematic review and meta-analysis. *Expert Opin Drug Saf*. 2016;15(sup1):35-54. doi:10.1080/14740338.2016.1238458
- Peleva E, Exton LS, Kelley K, Kleyn CE, Mason KJ, Smith CH. Risk of cancer in patients with psoriasis on biological therapies: a systematic review. *Br J Dermatol*. 2018;178(1):103-113. doi:10.1111/bjd.15830
- Esse S, Mason KJ, Green AC, Warren RB. Melanoma Risk in Patients Treated With Biologic Therapy for Common Inflammatory Diseases: A Systematic Review and Meta-analysis. *JAMA Dermatol*. 2020;156(7):787-794. doi:10.1001/jamadermatol.2020.1300
- Semaka A, Salopek TG. Risk of Developing Melanoma With Systemic Agents Used to Treat Psoriasis: A Review of the Literature. *J Cutan Med Surg*. 2022;26(1):87-92. doi:10.1177/12034754211038509
- Xia C, Dong X, Li H, et al. Cancer statistics in China and United States, 2022: profiles, trends, and determinants. *Chin Med J (Engl)*. 2022;135(5):584-590. Published 2022 Feb 9. doi:10.1097/CM9.0000000000002108