

ABOUT THE AUTHOR



Ron Vender, MD, FRCPC

Dr. Ron Vender is a Dermatologist practicing in Hamilton, Ontario, where he is the founder and director of Dermatrials Research Incorporated and Venderm Consulting Inc. He has served as principal investigator in more than 120 clinical trials, enrolling over 1,000 participants. He is an Associate Clinical Professor in the Department of Medicine, Division of Dermatology, at McMaster University, and serves on the editorial boards of several high-impact journals. Dr. Vender is one of a small number of Canadians elected to the International Psoriasis Council and is a member of the Canadian Professors of Dermatology and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis. Dr. Vender represents Canada on multiple global educational steering committees and international advisory boards. He has authored over 180 peer-reviewed publications, including work published in leading journals such as *The Lancet* and *The New England Journal of Medicine*, and his posters, abstracts, and lectures have been presented internationally across five continents and in more than 50 countries.

Affiliations: Associate Clinical Professor, Department of Medicine, Division of Dermatology, McMaster University, Hamilton, ON

KEY TAKEAWAYS:

- Psoriasis confers a modest overall increase in malignancy risk, concentrated in NMSC and selected lymphoid cancers, and amplified by disease severity and cumulative PUVA/systemic exposure.
- Chronic systemic inflammation and, in some contexts, therapy-related immunomodulation jointly shape cancer risk in psoriasis, rather than biologic treatment being uniformly carcinogenic.
- Modern biologic and targeted therapies—including IL-17 and IL-23 inhibitors, as well as PDE4 and TYK2 inhibitors—generally show no clear increase in overall malignancy or recurrence risk, though ongoing pharmacovigilance and individualized oncology input remain crucial.
- Management should be multidisciplinary and risk-adapted, combining effective psoriasis control with tailored cancer surveillance and aggressive modification of lifestyle risk factors (smoking, alcohol, obesity, UV exposure).

Psoriasis and Malignancy

Ron Vender, MD, FRCPC

Introduction

Psoriasis is a chronic systemic inflammatory disease that confers a modest, but reproducible, increase in malignancy risk, particularly for non-melanoma skin cancer (NMSC) and

lymphohematologic malignancies such as cutaneous T-cell lymphoma and Hodgkin lymphoma. This risk rises alongside disease severity and cumulative inflammatory burden.¹⁻⁴ Evidence from meta-analyses and large registries

show that once confounding factors are accounted for, the incidence of most solid tumours approximates that of the general population, while excess risk remains concentrated in NMSC and lymphoma.²⁻⁶ Additionally, the high rates of smoking, alcohol use, obesity, and metabolic syndrome among individuals with psoriasis further amplifies the risk of lung, bladder, liver, breast, endometrial, and colorectal cancers, highlighting the synergistic impact of lifestyle factors and chronic inflammation.^{1,2,7}

Inflammatory Pathways Linking Psoriasis and Cancer

Mechanistically, psoriasis exemplifies inflammation-driven carcinogenesis, with genome-wide and transcriptomic studies demonstrating overlap between psoriasis susceptibility loci and oncogenic pathways.^{1,7} Persistent activation of innate and adaptive immunity sustains a cytokine-rich microenvironment characterized by reactive oxygen species, angiogenic factors, and impaired DNA repair, promoting tumour initiation and progression while undermining immunosurveillance.^{1,7,8} The central tumour necrosis factor (TNF)–interleukin (IL)–23–IL-17 axis not only drives keratinocyte hyperproliferation and dermal inflammation but also recapitulates hallmarks of tumour-promoting inflammation, including nuclear factor kappa B (NF- κ B) and signal transducer and activator of transcription 3 (STAT3) activation, vascular endothelial growth factor overexpression, recruitment of myeloid-derived suppressor cells, and alternatively activated macrophages.^{1,7-9} Within this network, IL-12 predominantly supports antitumour immunity through Th1 polarization, interferon- γ production, and enhancement of cytotoxic lymphocyte and NK-cell function, whereas IL-23 and IL-17 sustain Th17 responses, angiogenesis, STAT3 activation, and immune evasion, and may contribute to resistance to immune checkpoint inhibitors.⁸⁻¹⁰

Context-Dependent Malignancy Risk in Psoriasis

Epidemiologic evidence from the past two decades consistently characterizes psoriasis as a condition with a moderate, context-dependent

increase in cancer risk rather than a generalized carcinogenic state.¹⁻⁴ Systematic reviews and meta-analyses report overall cancer relative risks at approximately 1.14–1.21, with higher values observed for NMSC and lymphoma, and stronger signals among patients with moderate-to-severe disease or those receiving systemic or biologic therapies.²⁻⁴ A large Danish study involving a cohort of over 60,000 patients demonstrated increased standardized incidence ratios for NMSC, lymphoma, and lung cancer, while UK and Australasian datasets corroborate elevated rates of cutaneous T-cell lymphoma and keratinocyte cancers, particularly in the setting of ultraviolet exposure, smoking, and historical immunosuppression.^{2-4,6,11,12} Importantly, when these factors are rigorously controlled, the incidence of most solid tumours approximates that of the general population, underscoring that excess cancer risk in psoriasis is selective and heavily modulated by comorbidities and prior therapies.^{2-4,6}

Historical Therapies and Malignancy Burden

Historical treatments account for much of the cutaneous and lymphoid malignancy burden observed in older cohorts.^{2,3,11,13-15} Psoralen and ultraviolet A (PUVA) phototherapy is clearly carcinogenic, showing a dose-dependent increase in squamous-cell carcinoma and a probable increase in melanoma, especially after 200–250 sessions; this elevated risk persists for over a decade after exposure.^{11,13,14} Cyclosporine, introduced before modern pharmacovigilance, suppresses T-cell-mediated tumour surveillance and facilitates oncogenic viral reactivation, leading to higher rates of NMSC and lymphoma, particularly with prolonged use or when administered sequentially with PUVA.^{11,14,15} Methotrexate, while a long-standing systemic mainstay, has been associated with increased NMSC in observational cohorts and randomized cardiovascular trials, whereas acitretin appears chemopreventive for keratinocyte carcinoma by normalizing keratinocyte differentiation and promoting apoptosis in dysplastic clones.^{11,13-16}

Malignancy Risk with Biologic and Targeted Therapies: Reassuring Long-Term Evidence

The introduction of biologics and newer targeted small molecules has substantially reshaped the malignancy risk-benefit calculus.^{1,7,8,15} TNF inhibitors initially raised concern because TNF plays dual roles in tumour biology—chronic low-grade signalling can drive proliferation and angiogenesis, while TNF is also central for cytotoxic immune defence. However, contemporary meta-analyses and registry data show no significant increase in overall invasive malignancy in psoriasis or across other immune-mediated diseases, aside from a small but consistent excess of NMSC, particularly among patients with substantial prior phototherapy or actinic damage.^{15,17-19} IL-12/23 and IL-23 inhibitors (e.g., ustekinumab, guselkumab, risankizumab, tildrakizumab) represent a more selective immunologic paradigm; long-term extension studies and pooled pharmacovigilance data have not demonstrated an increased rate of invasive malignancy or NMSC and meta-analyses in patients with prior cancer show no elevated risk of new or recurrent malignancy under these agents.^{1,7,8,10,18,19}

Malignancy Considerations with IL-17 and IL-23-Targeted Therapy

IL-17 and IL-23 inhibitors are of particular interest given mechanistic evidence that IL-23/Th17 signalling is pro-tumorigenic.^{1,7-9,20} Population-based and clinical data indicate that blocking IL-17 and IL-23 does not increase overall or site-specific malignancy rates and may, by dampening STAT3/NF- κ B-driven inflammation while sparing cytotoxic T-cell function, theoretically reduce inflammation-driven carcinogenic potential, though this remains to be proven in prospective trials.^{1,7-9,20,21} Large international datasets and focused series in patients with prior solid tumours report no signal of increased recurrence or new malignancy under IL-17A inhibitors, supporting their use in carefully selected patients with a history of cancer.^{20,21} Apremilast, a phosphodiesterase 4 inhibitor, offers a non-immunosuppressive option that reduces pro-inflammatory cytokines and has not been associated with increased malignancy, even in

patients with prior cancer or significant comorbid burdens.^{8,15,22,23} Deucravacitinib, a highly selective tyrosine kinase 2 (TYK2) inhibitor, modulates IL-12, IL-23, and type I interferon signalling without broad Janus kinase inhibition and has shown malignancy rates comparable to placebo and background population levels; however, isolated cases of lymphoma highlight the need for ongoing pharmacovigilance as real-world data accumulate.^{8,16,24,25}

Individualized Treatment Strategies in Psoriasis and Malignancy

Contemporary management of psoriasis in patients with current or previous malignancy emphasizes individualized, multidisciplinary decision-making rather than categorical avoidance of systemic therapy.^{1-3,7,15,18,19,22,23,26} Initial assessment should document tumour type, stage, treatment course, prognosis, time since remission, and recurrence potential, recognizing that the traditional five-year “cancer-free” rule is increasingly challenged by emerging data showing that modern biologics—particularly IL-17 and IL-23 inhibitors—do not appear to increase new or recurrent malignancy compared with background rates in appropriately selected patients.^{14,21,22,26} In the setting of active cancer, clinicians generally prioritize topical therapies, limited/targeted phototherapy (avoiding high cumulative ultraviolet exposure in those predisposed to skin cancer), and apremilast for mild to moderate disease, reserving biologics for severe or refractory psoriasis only after oncology consultation, especially when quality-of-life impairment is substantial.^{8,14,15,22,23} For patients in remission, decisions to re-introduce or initiate systemic therapy should be guided by tumour biology, disease stability, and patient preferences. IL-17 and IL-23 inhibitors are often favoured over broadly immunosuppressive agents, while methotrexate and cyclosporine are reserved for exceptional indications, and acitretin remains suitable for those at high risk of NMSC.^{11,14,21,22,23,26}

Risk-Adapted Surveillance and Prevention

Risk-adapted surveillance and lifestyle modification are crucial components for mitigating malignancy risk in psoriasis.^{1-3,7,11,13,14,17,27} Before starting systemic or biologic therapy, a

comprehensive baseline evaluation—including full-skin examination, dermatoscopy of suspicious lesions, lymph-node palpation, and review of prior phototherapy and immunosuppressant exposure—should be combined with age-appropriate screening (e.g., breast, colorectal, cervical, prostate) according to national guidelines, with earlier or intensified screening for patients with long-standing severe disease or significant carcinogenic exposures.^{1-3,7,9,11,13-15,22} During treatment, registry data do not justify uniformly intensified cancer screening solely because of biologic use; rather, clinicians should maintain standard guideline-based screening, complemented by annual skin examinations for most patients and six-monthly skin checks for those with prior PUVA exposure, NMSC, or extensive immunosuppression, with synchronization of dermatologic and oncologic follow-up in patients with a cancer history.^{2,3,11,13,14,17,22,23} Lifestyle counselling should focus on smoking cessation, alcohol moderation, weight management, and photoprotective behaviours, which collectively reduce independent cancer risks, decrease systemic inflammatory burden, and help reframe malignancy prevention as a shared, modifiable target in psoriasis care.^{1,2,7,11,13,14,27}

Conclusion

Psoriasis is best understood as a chronic inflammatory disease that confers a modest, selective increase in malignancy risk—principally for NMSC and lymphoid cancers—driven by systemic inflammation, lifestyle factors, and historical exposures such as PUVA, methotrexate, and cyclosporine, and that when these confounders are addressed, the incidence of most solid tumours approaches that of the general population.^{1-4,6,7,11,13-15,25,27} The TNF–IL-23–IL-17 axis mechanistically links psoriatic inflammation to carcinogenesis while providing a rationale for pathway-specific targeting. Current evidence indicates that IL-17 and IL-23 inhibitors, apremilast, and selective TYK2 inhibitors do not significantly increase overall invasive malignancy or cancer recurrence, apart from a persistent NMSC signal associated with

TNF inhibitors.^{1,5,7-9,10,14,15,17,19-26,28} Consequently, management should shift from categorical avoidance of systemic therapy in patients with current or prior malignancy to an individualized, multidisciplinary decision-making approach that integrates tumour biology, prior carcinogenic exposures, and patient values, within a framework of guideline-based screening and proactive lifestyle modification, as growing registry and biomarker data increasingly allow malignancy risk in psoriasis to be quantified and actively managed as part of personalized care.^{1-3,7,11,13-15,18,19,22,23,25,27}

The author would like to acknowledge the assistance of Dr Tiago Torres, MD, PhD Oporto PT

Correspondence

Ron Vender, MD, FRCPC
Email: ron.vender@me.com

Financial Disclosures

R.V.: Grants/Research Support, Speakers Bureau/Honoraria: AbbVie, Alumis, Amgen, Arcutis, Bausch Health, Bristol Myers Squibb, Celltrion, JAMP, Janssen, Leo, Lilly, Meiji, Novartis, Organon, Orka, Sandoz, Sun, Takeda, UCB

References

1. Bruni M, Lobefaro F, Pellegrini C, Mastrangelo M, Gualdi G, Esposito M, et al. Psoriasis and cancer: the role of inflammation, immunosuppression, and cancer treatment. *Expert Opin Biol Ther.* 2025;25(4):395-411. doi:10.1080/14712598.2025.2471093
2. Loft ND, Vaengebjerger S, Skov L. Cancer risk in patients with psoriasis: should we be paying more attention? *Expert Rev Clin Immunol.* 2020;16(7):479-492. doi:10.1080/1744666X.2020.1754194
3. Vaengebjerger 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
4. Trafford AM, Parisi R, Kontopantelis E, Griffiths CEM, Ashcroft DM. Association of psoriasis with the risk of developing or dying of cancer: a systematic review and meta-analysis. *JAMA Dermatol.* 2019;155(12):1390-1403. doi:10.1001/jamadermatol.2019.3056
5. Krzysztófik M, Brzewski P, Cuber P, Kacprzyk A, Kulbat A, Richter K, et al. Risk of melanoma and non-melanoma skin cancer in patients with psoriasis and psoriatic arthritis treated with targeted

- therapies: a systematic review and meta-analysis. *Pharmaceuticals (Basel)*. 2023;17(1):14. Published 2023 Dec 21. doi:10.3390/ph17010014
6. Bellinato F, Gisondi P, Girolomoni G. Risk of lymphohematologic malignancies in patients with chronic plaque psoriasis: a systematic review with meta-analysis. *J Am Acad Dermatol*. 2022;86(1):86-96. doi:10.1016/j.jaad.2021.07.050
 7. Mateescu LA, Savu AP, Mutu CC, Vaida CD, Serban ED, Bucur S, et al. The intersection of psoriasis and neoplasia: risk factors, therapeutic approaches, and management strategies. *Cancers (Basel)*. 2024;16(22):4224. Published 2024 Dec 18. doi:10.3390/cancers16244224
 8. Mansilla-Polo M, Morgado-Carrasco D. Biologics versus JAK inhibitors. Part I: cancer risk. A narrative review. *Dermatol Ther (Heidelb)*. 2024;14(6):1389-1442. doi:10.1007/s13555-024-01166-4
 9. Vangilbergen M, Stockman A, Van De Velde A, Garmyn M, Punie K, Hillary T. The role of interleukin-17 and interleukin-23 inhibitors in the development, progression, and recurrence of cancer: a systematic review. *JAAD Int*. 2024;17:71-79. Published 2024 Aug 16. doi:10.1016/j.jdin.2024.06.006
 10. Ergen EN, Yusuf N. Inhibition of interleukin-12 and/or interleukin-23 for the treatment of psoriasis: what is the evidence for an effect on malignancy? *Exp*
 11. Rademaker M, Rubel DM, Agnew K, Andrews M, Armour KS, Baker C, et al. Psoriasis and cancer. An Australian/New Zealand narrative. *Australas J Dermatol*. 2019;60(1):12-18. doi:10.1111/ajd.12889
 12. Davis MS, Spencer RK, Johnson CE, Elhage KG, Jin JQ, Hakimi M, et al. Risk of cutaneous T-cell lymphoma with psoriasis biologic therapies. *Dermatol Ther (Heidelb)*. 2024;14(1):15-30. doi:10.1007/s13555-023-01074-z
 13. Thatiparthi A, Martin A, Liu J, Wu JJ. Risk of skin cancer with phototherapy in moderate-to-severe psoriasis: an updated systematic review. *J Clin Aesthet Dermatol*. 2022;15(6):68-75. *Dermatol*. 2018;27(7):737-747. doi:10.1111/exd.13676
 14. Potestio L, Tommasino N, Lauletta G, Salsano An, Lucagnano G, Menna L, et al. The impact of psoriasis treatments on the risk of skin cancer: a narrative review. *Adv Ther*. 2024;41(10):3778-3791. doi:10.1007/s12325-024-02968-w
 15. 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
 16. Vanni KMM, Berliner N, Paynter NP, Glynn RJ, MacFadyen J, Colls J, et al. Adverse effects of low-dose methotrexate in a randomized double-blind placebo-controlled trial: adjudicated hematologic and skin cancer outcomes in the Cardiovascular Inflammation Reduction Trial. *ACR Open Rheumatol*. 2020;2(12):697-704. doi:10.1002/acr2.11187
 17. Wu WT, Chiang MC, Huang YC. The risk of malignancy in patients with psoriasis treated with long-term tumor necrosis factor-alpha inhibitors: a systematic review and meta-analysis. *Clin Exp Dermatol*. 2025;50(5):968-980. doi:10.1093/ced/llae503
 18. Isufi D, Schwarz CW, Jensen MB, Seidelin J, Skov L, Loft N. Risk of new or recurrent cancer during treatment with biologics in patients with immune-mediated inflammatory diseases and previous cancer: a meta-analysis. *Clin Exp Med*. 2025;25(1):219. Published 2025 Jun 25. doi:10.1007/s10238-025-01738-4
 19. 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
 20. Kridin K, Abdelghaffar M, Mruwat N, Ludwig RJ, Thaçi D. Are interleukin-17 and interleukin-23 inhibitors associated with malignancies? Insights from an international population-based study. *J Eur Acad Dermatol Venereol*. 2024;38(2):315-324. doi:10.1111/jdv.19520
 21. Bellinato F, Gisondi P, Maurelli M, Girolomoni G. IL-17A inhibitors in patients with chronic plaque psoriasis and history of malignancy: a case series with systematic literature review. *Dermatol Ther*. 2021;34(2):e14889. doi:10.1111/dth.14889
 22. Denaro N, Nazzaro G, Murgia G, Scarfi F, Cauchi C, Carrera CG, et al. A multidisciplinary approach to patients with psoriasis and a history of malignancies or on-treatment for solid tumors: a narrative literature review. *Int J Mol Sci*. 2023;24(24):17540. Published 2023 Dec 16. doi:10.3390/ijms242417540
 23. Puig L, Notario J, López-Ferrer A, et al. [Translated article] Recommendations from the Spanish Academy of Dermatology and Venereology Psoriasis Working Group on the management of patients with cancer and psoriasis. *Actas Dermosifiliogr*. 2024;115(7):T702-T711. doi:10.1016/j.ad.2024.05.011
 24. Mödl B, Zwolanek D, Schwertner K, Krauß D, Moritsch S, Scharf I, et al. TYK2 promotes immunosurveillance of colorectal cancer liver metastasis. *Cancer Res*. 2026;86(1):80-98. doi:10.1158/0008-5472.CAN-24-4224
 25. Mastorino L, Dapavo P, Avallone G, Merli M, Cariti C, Rubatto M, et al. Biologic treatment for psoriasis in cancer patients: should they still be considered forbidden? *J Dermatolog Treat*. 2022;33(5):2495-2502. doi:10.1080/09546634.2021.1970706
 26. Ro C, Ormaza Vera A, Adawi W, Yap A, Enos CW. Assessment of primary malignancy risk following initiation of biologic therapy in psoriasis patients. *JID Innov*. 2025;5(6):100397. Published 2025 Jul 4. doi:10.1016/j.xjidi.2025.100397
 27. Yang Y, Zhang Q, Huang A, Zhao J, Yang J, Wang L, Xu G. All-cause and cause-specific mortality in psoriasis patients: a systematic review and meta-analysis. *Front Immunol*. 2025;16:1610499. Published 2025 Jul 24. doi:10.3389/fimmu.2025.1610499
 28. Chen AY, Wolchok JD, Bass AR. TNF in the era of immune checkpoint inhibitors: friend or foe? *Nat Rev Rheumatol*. 2021;17(4):213-223. doi:10.1038/s41584-021-00584-4