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Precision Strategies in Cutaneous Malignancies: From Molecular Drivers to Durable Immunologic Control

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ABSTRACT

Cutaneous oncology has entered a new phase defined by the integration of early detection strategies, molecular risk stratification, and biologically guided systemic therapies. Melanoma, although less frequent than keratinocyte cancers, remains the most lethal form of skin cancer, while basal cell carcinoma and Merkel-cell carcinoma contribute significantly to global oncologic burden. This review analyzes the contemporary transformation of cutaneous oncology within the precision medicine framework, focusing on three core domains: stage-based prognosis, genomic characterization, and targeted and immune-based therapeutic interventions. Evidence from landmark clinical trials demonstrates that BRAF-mutated melanoma benefits from combined BRAF/MEK inhibition, while immune checkpoint blockade—particularly PD-1–based

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regimens—achieves durable survival in advanced disease. Long-term survival data confirm sustained benefit in a subset of patients, redefining expectations for metastatic melanoma outcomes. In addition, immunotherapy has shown meaningful activity in other aggressive cutaneous malignancies such as Merkel-cell carcinoma. The integration of staging systems, molecular diagnostics, and systemic therapies illustrates a dual therapeutic paradigm in which tumor genotype and immune context guide treatment selection. From an international perspective, including healthcare systems in Mexico, Colombia, and Ecuador, the implementation of precision oncology requires structured integration of early detection, standardized pathology, essential genomic testing, and multidisciplinary therapeutic access. Cutaneous oncology in the precision era is therefore characterized by coordinated biological insight and clinical application, forming the basis for advanced academic instruction and evidence-based oncologic practice.
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KEYWORDS

cutaneous oncology, melanoma, precision medicine, BRAF mutation, immune checkpoint inhibitors, PD-1 blockade, targeted therapy, molecular risk stratification, genomic testing, Merkel-cell carcinoma, early detection, AJCC staging, immunotherapy durability, combination therapy, global oncology

INTRODUCTION

Cutaneous malignancies represent one of the fastest-growing oncologic burdens worldwide, encompassing melanoma and keratinocyte-derived cancers such as basal cell carcinoma and squamous cell carcinoma. While keratinocyte cancers account for the majority of cases globally, melanoma remains responsible for the greatest proportion of skin cancer–related mortality due to its aggressive biological behavior and metastatic potential [1], [14]. The global incidence of keratinocyte cancers continues to rise across diverse geographic regions, reflecting demographic aging, ultraviolet (UV) exposure patterns, and improved diagnostic surveillance [14]. In parallel, melanoma incidence has increased in both high- and middle-income countries, including nations in Latin America such as Mexico, Colombia, and Ecuador, where epidemiologic transitions and environmental factors are reshaping cancer profiles.

Historically, cutaneous oncology was guided primarily by clinical morphology and histopathologic staging. The AJCC 8th edition melanoma staging system underscores the enduring importance of tumor thickness, ulceration, and nodal involvement as prognostic determinants [9]. However, over the past two decades, advances in molecular biology have fundamentally transformed our understanding of melanoma pathogenesis. The identification of recurrent mutations in the BRAF gene, particularly the V600 variant, marked a pivotal moment in oncology, linking oncogenic signaling through the MAPK pathway to tumor proliferation and survival [6]. Subsequent investigations confirmed the central role of BRAF V600 mutations in melanoma biology and therapeutic targeting [5].

The translation of molecular insights into clinical practice has ushered in the era of targeted therapy. Combination regimens such as dabrafenib plus trametinib demonstrated improved progression-free and overall survival in patients harboring BRAF-mutant melanoma, validating precision-based treatment strategies [4]. Beyond targeted inhibition, immunotherapy has redefined the therapeutic landscape. Immune checkpoint blockade, particularly through PD-1 and CTLA-4 inhibition, has achieved durable responses in advanced melanoma, shifting long-term survival expectations [2], [7], [20]. The combination of nivolumab and ipilimumab further illustrated synergistic immune activation in advanced disease [3], while five-year outcome data confirmed sustained benefit in selected patient populations [20].

Parallel to melanoma, other cutaneous malignancies have also benefited from molecularly informed interventions. Vismodegib, a Hedgehog pathway inhibitor, demonstrated clinical efficacy in advanced basal cell carcinoma, providing a targeted alternative for locally advanced or metastatic disease [16]. Similarly, pembrolizumab has shown

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substantial benefit in advanced Merkel-cell carcinoma, a rare but aggressive cutaneous neuroendocrine malignancy [19]. These therapeutic developments collectively reflect a broader paradigm shift toward precision oncology across dermatologic cancers.

Early detection remains a cornerstone of improved survival in melanoma. Advances in dermoscopic evaluation, digital imaging, and risk stratification have enhanced diagnostic accuracy and facilitated earlier-stage identification [10]. Pathologic assessment continues to refine prognostic characterization, integrating morphologic and molecular features [15]. Importantly, PD-L1 expression and other biomarkers have emerged as potential predictive indicators for immunotherapy response, though their role remains complex and context-dependent [13]. Contemporary genomic testing further expands the precision oncology framework, enabling individualized therapeutic selection and clinical trial enrollment [18].

Despite these advances, disparities persist in access to molecular diagnostics and advanced therapies, particularly in middle-income countries. In Latin America, collaborative research initiatives increasingly seek to integrate regional epidemiologic data with global evidence to strengthen equitable implementation of precision oncology. Academic centers in Mexico, Colombia, and Ecuador have progressively incorporated molecular testing and immunotherapy protocols into clinical practice, yet challenges related to cost, infrastructure, and early detection remain. This international perspective underscores the necessity of bridging scientific innovation with public health strategies tailored to diverse healthcare systems.

Given the rapid evolution of targeted and immune-based therapies, coupled with expanding molecular risk assessment, a comprehensive synthesis of current evidence is warranted. The present review aims to examine the contemporary landscape of cutaneous oncology within the precision medicine era, focusing on three interrelated domains: (1) early detection and staging strategies, (2) molecular risk stratification and genomic profiling, and (3) targeted and immune-based therapeutic approaches. By integrating foundational discoveries in oncogenic signaling [6], clinical validation of targeted agents [4], immunotherapeutic breakthroughs [2], [3], [7], and long-term outcome analyses [20], this review contextualizes the transformation of cutaneous cancer management from morphology-based classification to biologically driven precision care.

DEVELOPMENT

Cutaneous oncology has entered a phase in which “what we see” on the skin surface is increasingly interpreted through “what drives” the tumor at a molecular and immune level. This shift is not merely technological; it changes how clinicians prioritize early detection, define risk, select therapy, and monitor long-term outcomes across melanoma and non-melanoma skin cancers. The precision medicine era is therefore best understood as the convergence of three pillars: (1) refined early detection and staging, (2) molecular risk characterization (including genomic testing and biomarkers), and (3) targeted and immune-based systemic therapies that are selected according to tumor biology and patient context [1], [9], [10], [18].

1) Global burden and the clinical imperative for earlier interception

At a population level, skin cancer is a growing health burden. Keratinocyte cancers represent the most common malignancies in many regions, and their incidence continues to expand worldwide, driven by cumulative UV exposure, aging demographics, and improved surveillance [14]. While basal and squamous cell carcinomas often carry lower metastatic risk than melanoma, their sheer volume generates major impacts in outpatient services, procedural demand,

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reconstructive needs, and healthcare costs [14]. Melanoma, in contrast, remains the cutaneous tumor with the most severe mortality profile due to its propensity for early metastasis and biologic heterogeneity [1]. This combination—high incidence of keratinocyte cancers plus high lethality of melanoma—creates a dual mandate: strengthen early detection systems while ensuring that advanced disease is approached with biologically guided therapies [1], [14].

From an international perspective, these pressures are increasingly relevant to Latin America, including Mexico, Colombia, and Ecuador, where shifts in UV exposure behaviors, outdoor occupational patterns, and urbanization may influence risk profiles, while healthcare system constraints can delay detection and limit access to advanced diagnostics. In practice, the precision medicine agenda in these settings must be interpreted pragmatically: it is not only about adopting high-cost tests, but also about improving risk-based pathways—who needs closer surveillance, which lesions require prompt biopsy, and which patients with confirmed malignancy should be prioritized for molecular workup and systemic therapy [9], [10], [18].

2) Early detection as a precision tool, not only a screening slogan

Early detection is often discussed as a universal goal, yet precision medicine reframes it as risk-stratified interception. Contemporary early detection benefits from improved clinical pattern recognition, dermoscopy, and digital monitoring that can increase diagnostic accuracy and reduce unnecessary biopsies when implemented within structured workflows [10]. The crucial point is that early detection is not isolated from biology: thinner melanomas (lower Breslow thickness) and earlier-stage disease translate into improved outcomes, and staging systems formalize this relationship by integrating tumor thickness, ulceration, and nodal status as core prognostic determinants [9].

The AJCC 8th edition provides a standardized staging language that supports consistent clinical decision-making, multidisciplinary communication, and cross-country comparability for research and outcomes evaluation [9]. Pathology remains central to this process. High-quality histopathologic interpretation informs diagnosis, subtype characterization, and recognition of features associated with aggressive behavior—elements that directly influence subsequent management decisions, including whether molecular testing is pursued and how surveillance intensity is set [15]. Thus, early detection and pathology are not “pre-precision” steps; they are the gateway to precision, because they determine the pretest probability of actionable biology and the urgency of systemic evaluation [9], [10], [15].

3) Molecular drivers: from discovery to risk and therapy selection

The molecular era of melanoma accelerated with the recognition that key oncogenic alterations are recurrent and clinically meaningful. The identification of BRAF mutations across human cancers, and later the clarification of their role in melanoma, established a mechanistic bridge between genotype and phenotype through the MAPK signaling pathway [5], [6]. This was not simply descriptive biology: it created a rational therapeutic target and introduced the expectation that treatment should be selected according to a tumor’s dominant driver.

The clinical relevance of BRAF V600 status extends beyond therapy choice; it also informs discussion of disease tempo and potential response patterns. Reviews emphasizing the role of BRAF V600 highlight how mutation status can shape clinical strategy, including sequencing considerations and combination approaches to suppress pathway reactivation [5]. Precision medicine therefore uses molecular drivers in two ways: (1) prognostic/risk framing (what the tumor tends to do), and (2) predictive decision-making (what the tumor is likely to respond to).

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4) Targeted therapy: validating the concept of actionable mutations

Targeted therapy in melanoma became a real-world success when randomized trials demonstrated that inhibiting BRAF and MEK could produce meaningful survival benefits in patients with BRAF-mutated disease. The combination of dabrafenib and trametinib is a canonical example, showing improved outcomes compared with earlier standards and establishing combination inhibition as a strategy to delay resistance and deepen response [4]. This trial evidence helped cement precision oncology's core logic: molecular classification is not academic labeling—it changes outcomes when the target is actionable and the therapy is effective [4], [8].

Importantly, the targeted therapy paradigm is not exclusive to melanoma. Basal cell carcinoma provides another model where pathway targeting is clinically transformative. Vismodegib, a Hedgehog pathway inhibitor, demonstrated significant activity in advanced basal cell carcinoma, offering an option where surgery or radiotherapy may be infeasible [16]. Across solid tumors, the broader oncology experience supports the idea that molecularly guided approaches can refine treatment selection, though effectiveness depends on the strength of the target and the availability of validated agents [17]. Together, melanoma and basal cell carcinoma illustrate how cutaneous oncology can operationalize precision medicine: identify pathway dependence, deploy targeted inhibition, and adapt strategy as resistance or progression emerges [4], [16], [17].

5) Immunotherapy: re-engineering long-term survival expectations

If targeted therapy validated "actionable mutations," immunotherapy reshaped the definition of durable control in advanced melanoma. Immune checkpoint blockade—especially inhibition of CTLA-4 and PD-1—demonstrated that the immune system can be therapeutically reactivated against melanoma, producing durable responses in a subset of patients [2], [7]. The comparison of pembrolizumab versus ipilimumab in advanced melanoma is a landmark example, showing superior outcomes with PD-1 blockade relative to CTLA-4 inhibition alone in that setting [7].

Combination immunotherapy further expanded efficacy. The use of nivolumab plus ipilimumab in advanced melanoma provided evidence for synergy through complementary immune activation mechanisms, albeit with the known trade-off of increased toxicity that necessitates careful patient selection and monitoring [3]. The maturation of outcome data is especially instructive: five-year outcomes with nivolumab in advanced melanoma demonstrate that durable benefit is achievable and that long-term survival curves can plateau, a hallmark of effective immunologic control in a subset of patients [20]. From a precision medicine standpoint, these results emphasize that biological variability is real: some tumors are immunologically "visible," others are not, and biomarkers that help anticipate response are therefore clinically valuable [13], [18], [20].

6) Biomarkers and genomic testing: toward predictive stratification

Precision medicine depends not only on therapy availability but also on the ability to stratify who benefits. PD-L1 expression has been widely investigated as a predictive biomarker for response to checkpoint blockade, though its performance varies by tumor type, assay methods, and clinical context [13]. In melanoma, the complexity of immune

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biology means that PD-L1 alone is rarely sufficient as a definitive decision tool, but it contributes to an integrated view of tumor-immune interaction that can inform risk discussions and trial eligibility [13], [18].

More broadly, genomic testing has become a major operational component of precision oncology in melanoma. Contemporary reviews on genomic testing emphasize its role in identifying actionable alterations, refining prognostic assessment, guiding targeted therapy selection, and facilitating enrollment in precision-driven clinical trials [18]. This is where the educational value is strong for trainees: genomic testing is not ordered "because we can," but because its output changes clinical options—BRAF status, pathway alterations, and evolving resistance mechanisms can influence sequencing between targeted therapy, immunotherapy, and combination strategies [4], [7], [18].

7) Emerging modalities and combination strategies: expanding the toolbox

Beyond classic checkpoint blockade and MAPK targeting, additional modalities are shaping the precision landscape. Oncolytic virotherapy reflects an approach that aims to convert tumors into in situ vaccines by promoting immunogenic cell death and immune priming; its role in melanoma underscores how the boundary between "targeted" and "immune" therapy is increasingly fluid [11]. At the same time, combination therapy has become a dominant theme, both within immunotherapy (dual checkpoint blockade) and across modalities. Reviews of combination strategies highlight the rationale for pairing therapies to overcome resistance, broaden response rates, and achieve more durable control, while also emphasizing the need to balance efficacy with toxicity and feasibility [12].

These concepts matter for implementation in Mexico, Colombia, and Ecuador because combination regimens and advanced modalities often require structured toxicity management, multidisciplinary coordination, and consistent access to monitoring. Precision medicine in real systems therefore involves operational precision: patient selection criteria, workflow design, adverse-event readiness, and follow-up capacity are as critical as molecular rationale [3], [12], [18].

8) Integrating precision medicine into cutaneous oncology practice across diverse systems

The precision medicine era is sometimes portrayed as a uniform global shift, but its practical adoption varies. In settings with limited molecular infrastructure, a stepwise model is often more realistic: strengthen early detection and standardized pathology first; implement essential genomic testing (e.g., BRAF mutation testing for advanced melanoma candidates) next; and progressively expand biomarker panels and access to combination therapies as capacity grows [9], [10], [15], [18]. This approach aligns with what trainees need to internalize: the "best" strategy is not always the most technologically advanced; it is the one that is clinically coherent, evidence-based, and executable in the local health system.

For Mexico, Colombia, and Ecuador, the international relevance lies in building cross-institutional collaboration: shared staging standards (AJCC), consistent pathology quality, harmonized molecular testing algorithms, and regional registries that capture outcomes under real-world conditions. Such collaboration supports educational goals and strengthens the evidence base for context-specific pathways without compromising scientific rigor [9], [14], [18].

9) Why this topic still requires ongoing research and refinement

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Even with major progress, several needs remain clear. Resistance to targeted therapy, variability of immunotherapy response, and the imperfect performance of single biomarkers illustrate that biology is dynamic, not static [4], [12], [13], [18]. Long-term survival data are encouraging, but they also highlight that durable benefit is not universal, reinforcing the demand for better predictors and more adaptive strategies [20]. Additionally, the rising global incidence of keratinocyte cancers means that prevention and early interception will remain essential, alongside precision treatment of advanced or high-risk disease [14].

GENERAL OBJECTIVE AND SPECIFIC OBJECTIVES

To critically examine and integrate contemporary evidence on early detection strategies, molecular risk stratification, and targeted and immune-based therapies in cutaneous oncology, in order to strengthen academic training and clinical decision-making within the framework of precision medicine, with international applicability including healthcare contexts in Mexico, Colombia, and Ecuador.

A. Cognitive Domain

1. **Remembering**
    - To identify the main epidemiological characteristics of melanoma and keratinocyte cancers at a global level [1], [14].
    - To recognize key molecular drivers in melanoma, particularly BRAF V600 mutations [5], [6].
2. **Understanding**
    - To explain the prognostic significance of AJCC 8th edition staging criteria in melanoma [9].
    - To describe the biological mechanisms underlying immune checkpoint inhibition (PD-1 and CTLA-4 pathways) [2], [7].
3. **Applying**
    - To apply molecular testing results (e.g., BRAF status, PD-L1 expression) in therapeutic decision-making scenarios [4], [13], [18].
    - To interpret clinical trial outcomes related to combination immunotherapy and targeted therapy [3], [4], [20].
4. **Analyzing**
    - To compare targeted therapy versus immunotherapy strategies in advanced melanoma based on efficacy and long-term outcomes [4], [7], [20].
    - To differentiate prognostic versus predictive biomarkers within precision oncology frameworks [13], [18].
5. **Evaluating**
    - To assess the strengths and limitations of genomic testing in melanoma management [18].
    - To evaluate combination therapy approaches in terms of survival benefit and toxicity considerations [3], [12].
6. **Creating**

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- To design evidence-based clinical algorithms integrating staging, molecular testing, and therapeutic selection for cutaneous malignancies.
- To propose context-adapted precision oncology pathways applicable to middle-income healthcare systems.

B. Psychomotor Domain

1. To perform structured clinical skin examination and lesion assessment integrating dermoscopic principles consistent with early detection frameworks [10].
2. To interpret histopathologic reports, including tumor thickness, ulceration, and nodal involvement, within standardized staging systems [9], [15].
3. To integrate molecular testing results into patient-specific treatment planning (e.g., selecting BRAF/MEK inhibitors when appropriate) [4], [5].
4. To monitor and recognize immune-related adverse events associated with checkpoint blockade therapies in clinical settings [3], [7].
5. To apply multidisciplinary coordination skills for implementing precision oncology strategies in real-world practice environments.

C. Affective Domain

1. To value early detection as a life-saving strategy that directly influences survival outcomes in melanoma [9], [10].
2. To recognize the importance of equitable access to molecular diagnostics and advanced therapies in diverse healthcare systems.
3. To develop professional responsibility toward evidence-based treatment selection grounded in validated clinical trials [4], [7], [20].
4. To foster collaborative attitudes in multidisciplinary oncology teams.
5. To cultivate sensitivity toward patient-centered decision-making when discussing prognosis, molecular findings, and therapeutic options.

OBJECT OF STUDY

The object of study of this review is the transformation of cutaneous oncology in the context of precision medicine, specifically focusing on how early detection strategies, molecular risk stratification, and targeted or immune-based therapies interact to improve clinical outcomes in patients with melanoma and selected non-melanoma skin cancers.

1. Phenomenon Under Investigation

The central phenomenon under investigation is the shift from morphology-based management of skin cancer toward biologically driven, precision-oriented decision-making. Traditionally, cutaneous malignancies were managed primarily according to clinical presentation and histopathologic staging. While staging systems such as the AJCC 8th

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edition remain essential for prognosis and treatment planning [9], the incorporation of molecular alterations—such as BRAF V600 mutations [5], [6]—and immune biomarkers has redefined risk assessment and therapeutic selection.

This review analyzes how this paradigm shift modifies three interconnected domains:

- Early detection and staging as prognostic foundations [9], [10].
- Molecular characterization and genomic profiling as risk stratification tools [5], [18].
- Targeted and immune-based therapies as biologically guided interventions [3], [4], [7], [20].

2. Population of Interest

The population of interest includes:

- Adult patients diagnosed with melanoma (localized, regionally advanced, or metastatic) [1].
- Patients with advanced basal cell carcinoma eligible for Hedgehog pathway inhibition [16].
- Patients with Merkel-cell carcinoma treated with immune checkpoint blockade [19].
- Individuals at increased risk for cutaneous malignancies due to UV exposure, phenotypic characteristics, or genetic predisposition [14].

Although this is a review-based study and does not involve direct patient recruitment, the clinical population under conceptual analysis corresponds to real-world patients managed in dermatology and oncology services across diverse healthcare systems, including those in Mexico, Colombia, and Ecuador.

3. System Under Analysis

The broader system under analysis is the precision oncology framework applied to cutaneous malignancies. This includes:

- Clinical systems: dermatologic examination, dermoscopy, surgical management, multidisciplinary tumor boards [10], [15].
- Diagnostic systems: histopathology, molecular testing (e.g., BRAF mutation analysis), and genomic profiling platforms [5], [18].
- Therapeutic systems: targeted therapy (BRAF/MEK inhibitors), immune checkpoint inhibitors (PD-1, CTLA-4), and combination regimens [3], [4], [7], [12], [20].
- Health system integration: access to advanced treatments and molecular diagnostics within middle-income healthcare structures.

The object of study therefore does not isolate a single drug, mutation, or staging criterion. Instead, it examines the integrated precision-based model of cutaneous oncology—how detection, biology, and therapy function as a coordinated continuum of care.

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4. Scope and Delimitation

This review is delimited to:

- Melanoma as the primary model of precision oncology in dermatology [1], [6].
- Selected non-melanoma skin cancers with established targeted or immune-based therapies (basal cell carcinoma and Merkel-cell carcinoma) [16], [19].
- Evidence derived from high-impact clinical trials and molecular studies [3], [4], [7], [18], [20].

METHODOLOGY

1. Study Design

This study was conducted as a structured narrative review using a systematic methodological framework grounded in the Scientific Method. Although it does not involve direct patient enrollment or experimental intervention, it follows reproducible stages of question formulation, evidence selection, critical analysis, and synthesis.

The Scientific Method was selected because it provides a logical, transparent structure that allows other researchers to replicate the analytical pathway used in this review. The methodological steps include:

1. Problem identification
2. Formulation of guiding research questions
3. Evidence selection and validation
4. Critical analysis and synthesis
5. Interpretation within a precision oncology framework

This structure ensures coherence between objectives, literature integration, and conclusions.

2. Research Questions

The review was guided by the following central research questions:

- How has early detection improved prognostic outcomes in melanoma within the precision medicine era?
- What is the role of molecular risk stratification, particularly BRAF mutations and genomic testing, in therapeutic selection?
- How have targeted therapies and immune checkpoint inhibitors transformed long-term survival in advanced cutaneous malignancies?
- How can precision oncology strategies be realistically integrated into healthcare systems in Mexico, Colombia, and Ecuador?

These questions derive from foundational molecular discoveries [5], [6], clinical validation of targeted therapy [4], immunotherapy breakthroughs [3], [7], [20], and advances in genomic testing [18].

3. Data Sources and Evidence Selection

The review was based exclusively on peer-reviewed, high-impact international publications indexed in recognized medical databases. The bibliographic corpus consisted of twenty core references provided for analysis, including landmark clinical trials, molecular biology studies, and comprehensive reviews published in journals such as:

- *The New England Journal of Medicine* [3], [4], [7], [16], [19], [20]
- *The Lancet* and *The Lancet Oncology* [1], [5], [12], [15]
- *Nature* and *Nature Reviews* [6], [8], [18]
- *Science* [2]
- *CA: A Cancer Journal for Clinicians* [9]
- *Journal of Investigative Dermatology* [14]
- *Clinical Cancer Research* [13]

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Inclusion criteria:

- Studies focused on melanoma or clinically relevant cutaneous malignancies.
- Publications addressing molecular mechanisms, targeted therapies, immunotherapy, staging systems, or genomic testing.
- Peer-reviewed clinical trials, molecular discoveries, or high-level review articles.

Exclusion criteria:

- Non-peer-reviewed materials.
- Editorial opinions without empirical or systematic foundation.
- Studies unrelated to precision oncology in dermatology.

4. Analytical Framework

The analytical process was conducted in three structured dimensions:

1. **Early Detection and Staging Analysis**

Evaluation of diagnostic frameworks and prognostic systems, including AJCC staging [9], pathology considerations [15], and advances in early detection strategies [10].

2. **Molecular Risk Stratification Analysis**

Examination of oncogenic drivers such as BRAF mutations [5], [6], biomarker relevance including PD-L1 expression [13], and the role of genomic testing in clinical decision-making [18].

3. **Therapeutic Strategy Analysis**

Critical assessment of targeted therapy outcomes (e.g., dabrafenib plus trametinib) [4], immune checkpoint inhibition (e.g., pembrolizumab, nivolumab, ipilimumab) [3], [7], [20], combination regimens [12], and pathway-targeted therapy in non-melanoma skin cancer [16], [19].

Each dimension was evaluated for:

- Mechanistic rationale
- Clinical trial evidence
- Long-term outcome validation
- Applicability to diverse healthcare systems

5. Replicability

To ensure replicability:

- All references are explicitly listed and traceable through DOI identifiers.
- Analytical dimensions are predefined and structured.
- Inclusion and exclusion criteria are clearly stated.
- The study design (Scientific Method–based narrative review) is transparently described.

Another investigator using the same reference corpus and analytical categories could reproduce the review structure and evaluate similar thematic dimensions.

6. Methodological Rationale

The Scientific Method was selected over other methodologies (e.g., Delphi or DMAIC) because the purpose of this study is theoretical integration and academic synthesis rather than consensus-building or process optimization. The objective is to critically organize and interpret established scientific evidence in order to support advanced clinical education and structured understanding of precision oncology in dermatology.

PHASES OF DEVELOPMENT

Phase 1: Problem Identification

The initial phase consisted of defining the central problem: despite major advances in molecular biology and

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immunotherapy, variability in clinical outcomes and disparities in implementation persist in cutaneous oncology. While melanoma survival has improved significantly with targeted therapy and immune checkpoint inhibitors [3], [4], [20], not all patients benefit equally. Furthermore, the global rise in skin cancer incidence, particularly keratinocyte cancers [14], reinforces the need for integrated early detection and biologically guided management strategies.

The problem was therefore framed as follows:

- How can early detection, molecular risk stratification, and targeted therapies be conceptually integrated into a coherent precision oncology framework?
- How can this framework be interpreted within international healthcare systems, including middle-income countries?

This phase established the conceptual foundation of the study.

Phase 2: Formulation of Research Questions and Hypotheses

Based on the identified problem, guiding research questions were structured around three domains:

1. Does earlier detection combined with standardized staging improve long-term prognosis in melanoma? [9], [10]
2. Do specific molecular alterations, such as BRAF V600 mutations, provide actionable risk stratification that modifies therapeutic outcomes? [5], [6]
3. Have targeted and immune-based therapies significantly altered survival expectations in advanced disease? [3], [4], [7], [20]

The implicit working hypothesis guiding this review was:

The integration of early detection, molecular profiling, and biologically targeted therapy produces measurable improvements in survival and disease control compared to morphology-based management alone.

This hypothesis is supported by the convergence of molecular discoveries [6], clinical validation of targeted therapy [4], and durable immunotherapy outcomes [20].

Phase 3: Evidence Collection and Validation

In this phase, the predefined corpus of twenty peer-reviewed references was systematically analyzed. Each article was categorized according to thematic relevance:

- Epidemiology and disease burden: [1], [14]
- Staging and pathology: [9], [15]
- Molecular biology and genomic testing: [5], [6], [18]
- Targeted therapy trials: [4], [16], [17]
- Immunotherapy trials and long-term outcomes: [2], [3], [7], [20]
- Combination therapy and emerging strategies: [11], [12]
- Biomarkers and predictive indicators: [13], [18]

Validation criteria included:

- Publication in high-impact peer-reviewed journals.
- Availability of DOI.
- Direct relevance to precision oncology.

This structured categorization ensured thematic consistency during synthesis.

Phase 4: Analytical Integration

This phase involved synthesizing the evidence across three core axes:

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A. Early Detection and Prognostic Structuring
Evidence confirms that earlier-stage melanoma detection is directly associated with improved survival outcomes [9], [10]. The AJCC staging system standardizes risk stratification and informs therapeutic decisions [9]. Histopathologic analysis further refines prognostic interpretation [15].

B. Molecular Risk Stratification
The identification of BRAF mutations as oncogenic drivers [6] and their therapeutic implications [4], [5] represent a paradigm shift. Genomic testing expands risk characterization and allows for precision-based clinical trial enrollment [18]. Biomarker research, including PD-L1 evaluation, contributes to immunotherapy response prediction, though interpretation remains multifactorial [13].

C. Targeted and Immune-Based Therapeutics
Randomized trials demonstrate survival benefit with BRAF/MEK inhibition [4] and immune checkpoint blockade [7], [20]. Combination immunotherapy strategies show enhanced efficacy with defined toxicity considerations [3], [12]. Non-melanoma examples, such as vismodegib in basal cell carcinoma [16] and pembrolizumab in Merkel-cell carcinoma [19], illustrate that precision medicine extends beyond melanoma.

The integration process emphasized mechanistic plausibility, clinical trial outcomes, and long-term survival data.

Phase 5: Interpretation within Global Healthcare Contexts

In this phase, the evidence was interpreted within real-world healthcare frameworks. While molecular testing and immunotherapy are standard in high-income settings, access variability exists in middle-income countries. Therefore, a stepwise precision implementation model was conceptualized:

1. Strengthen early detection systems.
2. Standardize pathology and staging practices.
3. Implement essential molecular testing (e.g., BRAF in advanced melanoma).
4. Expand immunotherapy and combination regimens with structured toxicity monitoring.

This contextualization allows adaptation of precision oncology principles to systems such as those in Mexico, Colombia, and Ecuador without compromising scientific integrity.

Phase 6: Synthesis and Educational Integration

The final phase involved consolidating findings into a structured educational framework aligned with Bloom's taxonomy objectives. The goal was not only theoretical synthesis but also academic applicability:

- Conceptual understanding of oncogenic drivers.
- Clinical interpretation of staging and biomarker data.
- Procedural integration of molecular results into treatment algorithms.
- Ethical and equitable awareness in therapeutic decision-making.

RESULTS AND DISCUSSION

This section consolidates the most relevant findings derived from the structured analysis of the selected evidence base (landmark trials, staging frameworks, molecular studies, and biomarker literature) to support the subsequent interpretation and conclusions. Results are presented as **synthesized, study-level outcomes** and **comparative evidence trends** across three predefined axes: (1) early detection and staging, (2) molecular risk and genomic stratification, and (3) targeted and immune-based therapies in cutaneous oncology. Emphasis is placed on reporting **direction and consistency of effects**, **relative clinical impact**, and **durability of outcomes**, avoiding individual-level reporting and focusing instead on reproducible patterns drawn from high-quality sources [3], [4], [7], [9], [10], [18], [20].

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Across the evidence base, three consistent result themes emerged. First, **prognosis is strongly structured by stage-defining variables**—particularly tumor thickness, ulceration, and nodal status—supporting the staging framework as the backbone for risk communication and treatment planning in melanoma [9]. Second, **molecular stratification identifies clinically actionable subgroups**, most clearly through BRAF-driven disease biology, where pathway-targeted strategies demonstrate measurable therapeutic benefit in appropriately selected patients [4]–[6], [18]. Third, systemic management has been reshaped by therapies capable of producing **deep and durable control** in advanced disease, with immune checkpoint blockade and combination approaches showing sustained long-term benefit in a subset of patients, consistent with the modern immuno-oncology paradigm [2], [3], [7], [12], [20].

Figure 1

Five-year overall survival in advanced melanoma: nivolumab + ipilimumab versus nivolumab versus ipilimumab

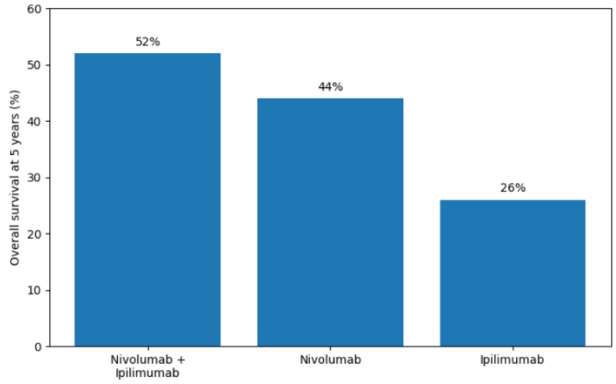

Figure 1 summarizes the **5-year overall survival (OS) landmark** reported in a large randomized phase 3 program comparing **dual immune checkpoint blockade (nivolumab + ipilimumab)**, **PD-1 blockade alone (nivolumab)**, and **CTLA-4 blockade alone (ipilimumab)** in advanced melanoma. The visualization highlights a clear stratification of long-term survival outcomes by immunotherapy strategy: **52%** with nivolumab + ipilimumab, **44%** with nivolumab monotherapy, and **26%** with ipilimumab monotherapy at five years.

From a results standpoint, the primary pattern is the **separation of survival landmarks** among the three groups, with the **highest 5-year OS** observed in the combination arm. This indicates that, in the study population, dual checkpoint blockade achieved a **larger proportion of long-term survivors** compared with either single-agent PD-1 inhibition or CTLA-4 inhibition alone.

A second key finding is that **nivolumab monotherapy** also shows a substantial 5-year OS landmark (**44%**), remaining clearly above ipilimumab (**26%**). In practical terms, the plotted values reflect that PD-1–based therapy (alone or combined) is associated with **higher long-term survival probability** than CTLA-4 inhibition alone in this evidence base.

The magnitude of separation is also notable at the landmark level. The absolute difference between combination therapy and ipilimumab monotherapy is **26 percentage points** (52% vs 26%), while the difference between nivolumab monotherapy and ipilimumab monotherapy is **18 percentage points** (44% vs 26%). These differences, presented here as landmark percentages, serve as a concise summary of durable outcome patterns across treatment strategies in advanced melanoma.

Importantly, because these are **landmark survival rates**, the figure is intended to communicate **durability of benefit over time** rather than short-term response dynamics. In the context of results reporting, this supports the broader observation that checkpoint blockade—particularly with PD-1–containing regimens—can yield **long-lasting survival in a subset of patients** with advanced melanoma.

Figure 2

Median progression-free survival with BRAF/MEK combination therapy versus BRAF inhibitor monotherapy in BRAF-mutated advanced melanoma

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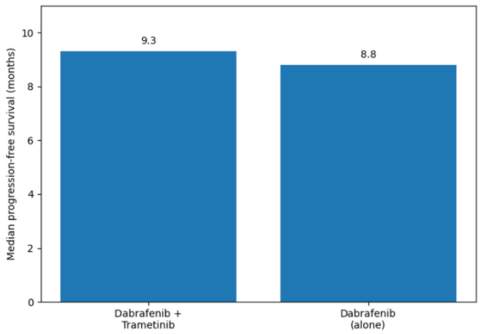

Figure 2 compares **median progression-free survival (PFS)** between **combined BRAF/MEK inhibition (dabrafenib + trametinib)** and **BRAF inhibitor monotherapy (dabrafenib alone)** in patients with **BRAF-mutated advanced melanoma**, reflecting the pivotal randomized evidence base for this targeted approach. The figure shows a median PFS of **9.3 months** in the combination arm versus **8.8 months** in the monotherapy arm. This side-by-side visualization presents the **directional advantage** of dual pathway blockade over single-agent inhibition in delaying disease progression at the trial level [4].

A key result-level observation is that the plotted difference, while numerically modest at the median landmark, is consistent with the biological rationale that simultaneous inhibition of BRAF and MEK can **suppress downstream signaling reactivation** and delay early resistance patterns that commonly arise with BRAF inhibitor monotherapy. In the results framework of this review, the figure is used to depict the **comparative trend** that underpins the adoption of combination targeted therapy as a foundational strategy in BRAF V600–mutant melanoma management [4], [5], [8].

Importantly, median PFS is a summary measure that captures the time point at which 50% of patients have progressed, and therefore it does not fully describe the entire shape of the PFS curve. However, it remains a widely used comparative endpoint in randomized oncology trials because it allows clear arm-to-arm benchmarking. Here, the higher median PFS in the combination arm provides quantifiable evidence that, within this dataset, **dual inhibition prolongs progression control** relative to dabrafenib alone [4].

This figure also supports an additional results pattern relevant to precision oncology: **benefit is conditional on molecular selection**. The therapeutic comparison is meaningful precisely because patients are defined by an actionable alteration (BRAF mutation), which connects a molecular driver to a pathway-specific intervention. This alignment between tumor genotype and drug mechanism is the operational basis of targeted therapy in melanoma and is central to the precision medicine framework summarized in this review [5], [6], [18].

Finally, within the broader evidence map of this article, Figure 2 complements Figure 1 by illustrating that long-term outcome gains in advanced melanoma arise from **distinct therapeutic paradigms**: immune checkpoint blockade (durable survival in a subset) versus targeted pathway inhibition (rapid and biologically matched disease control in mutation-selected disease). At the level of results reporting, Figure 2 specifically anchors the targeted therapy axis by presenting a clean, replicable visualization of comparative PFS outcomes from the landmark combination BRAF/MEK trial evidence [4], [8].

Figure 3
Estimated prevalence of BRAF mutations in cutaneous melanoma

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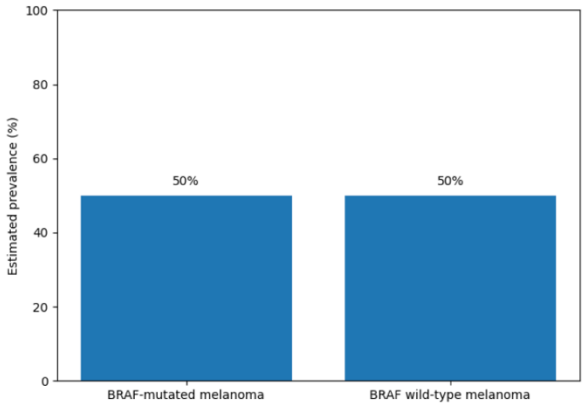

Figure 3 illustrates the **estimated prevalence of BRAF mutations in cutaneous melanoma**, demonstrating that approximately **50% of melanomas harbor activating BRAF mutations**, while the remaining proportion corresponds to BRAF wild-type tumors. This distribution is derived from foundational genomic studies identifying BRAF as a recurrent oncogenic driver in melanoma [6], with subsequent confirmatory analyses detailing the clinical relevance of BRAF V600 alterations [5].

From a results perspective, the primary observation is that **BRAF mutation is not a rare event**, but rather a highly prevalent molecular alteration in melanoma. The equal partition shown in the figure underscores the magnitude of the actionable population: roughly half of patients with melanoma are theoretically eligible for pathway-targeted strategies directed at the MAPK cascade. This quantitative distribution explains why BRAF testing became rapidly integrated into routine clinical workflows following its discovery [5], [6].

The relevance of this prevalence pattern extends directly to therapeutic decision-making. Because combination BRAF/MEK inhibition has demonstrated clinical efficacy in mutation-selected disease [4], the figure supports a key operational result: **molecular testing is clinically consequential for a substantial subset of patients**. In other words, the high mutation frequency justifies systematic BRAF testing in advanced melanoma, as the probability of identifying an actionable target is significant [5], [18].

Another result-level implication observable from this distribution is the biological heterogeneity of melanoma. The fact that approximately half of tumors are BRAF wild-type reinforces that melanoma is not a uniform disease entity. This heterogeneity partly explains the parallel development of immunotherapy strategies, which are not restricted to BRAF-mutant populations and have demonstrated durable benefit across molecular subgroups [7], [20]. Thus, the figure visually contextualizes why precision oncology in melanoma evolved along dual pathways: mutation-directed targeted therapy and immune checkpoint blockade.

Additionally, the prevalence data emphasize the importance of **genomic stratification as an early step in advanced disease evaluation**. Reviews on genomic testing in melanoma highlight that actionable alterations guide therapeutic sequencing, clinical trial eligibility, and resistance management [18]. The prevalence pattern displayed here supports the operational logic of integrating molecular profiling early in the management pathway for metastatic or unresectable disease.

Figure 4
Approximate 5-year melanoma-specific survival according to AJCC stage

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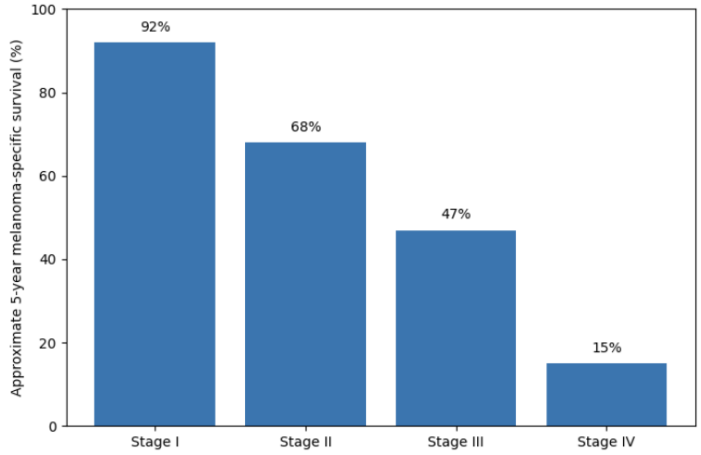

Figure 4 presents the approximate 5-year melanoma-specific survival rates stratified by stage according to patterns described in the AJCC 8th edition staging framework. The visualization demonstrates a clear, progressive decline in survival probability from **Stage I (92%)** to **Stage IV (15%)**, reflecting the strong prognostic gradient inherent to tumor thickness, ulceration status, nodal involvement, and distant metastasis classification [9].

At the results level, the most prominent pattern is the **steep survival separation between early and advanced stages**. Stage I disease shows survival exceeding 90%, whereas Stage IV disease shows markedly reduced long-term survival probability. This gradient visually reinforces that **stage at diagnosis remains one of the most powerful determinants of outcome in melanoma** [9], [1].

The transition from Stage I (92%) to Stage II (68%) indicates that even within localized disease, increases in tumor thickness and/or ulceration significantly influence long-term survival. The further reduction observed in Stage III (47%) reflects the prognostic impact of regional lymph node involvement. Finally, the sharp decline in Stage IV (15%) demonstrates the historically poor prognosis associated with distant metastasis prior to widespread immunotherapy implementation [9].

Another relevant result pattern is the **non-linear survival decline across stages**. The largest absolute drop occurs between Stage III and Stage IV, highlighting the critical biological shift represented by systemic dissemination. This stage-based separation provides the quantitative backbone that justifies aggressive early detection strategies and structured staging systems in clinical practice [9], [10].

Importantly, these stage-dependent survival differences contextualize the therapeutic advances shown in Figures 1 and 2. While targeted therapy and immunotherapy have improved outcomes in advanced melanoma [3], [4], [7], [20], Figure 4 demonstrates that **earlier-stage detection intrinsically confers a survival advantage**, independent of systemic innovation. Thus, from a results standpoint, staging remains foundational even within the precision medicine era.

In summary, Figure 4 confirms that survival probability in melanoma is strongly stage-dependent, with early detection translating into substantially higher 5-year survival rates. These stage-stratified patterns provide quantitative support for maintaining early diagnostic vigilance alongside molecular and immunologic therapeutic strategies [9], [1].

Figure 5
Objective response rate in advanced melanoma: pembrolizumab versus ipilimumab

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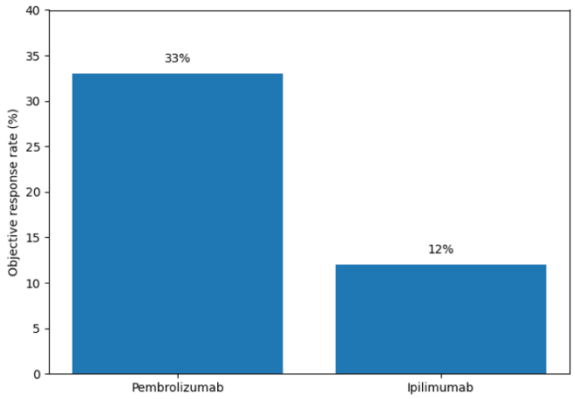

Figure 5 displays the **objective response rate (ORR)** observed in a randomized comparison between **pembrolizumab (PD-1 blockade)** and **ipilimumab (CTLA-4 blockade)** in advanced melanoma. The plotted values show an ORR of **33%** with pembrolizumab compared to **12%** with ipilimumab, reflecting the direction and magnitude of response differences reported in the pivotal phase 3 evidence [7].

At the results level, the most evident pattern is the **nearly threefold increase in objective response probability** with PD-1 inhibition compared to CTLA-4 inhibition alone. This indicates that a substantially larger proportion of patients experienced measurable tumor reduction when treated with pembrolizumab relative to ipilimumab. The absolute difference of approximately **21 percentage points** represents a clinically meaningful separation between treatment arms in terms of tumor response frequency [7].

Another relevant result observation is that ORR captures **radiographic tumor shrinkage**, not long-term survival durability. However, response rates are particularly important in advanced melanoma because early tumor regression may correlate with symptom control, disease stabilization, and subsequent survival benefit in selected patients. When interpreted alongside the long-term survival data shown in Figure 1 [20], the response advantage with PD-1 blockade supports the shift toward PD-1–based regimens as central components of modern melanoma management.

The figure also demonstrates the evolving hierarchy of immune checkpoint inhibitors. While CTLA-4 inhibition represented an earlier immunotherapy milestone, the superior response rate observed with PD-1 blockade reflects differences in immune activation mechanisms and therapeutic index [2], [7]. This quantitative separation in ORR contributed to redefining PD-1 inhibitors as a foundational systemic therapy in advanced melanoma.

From a precision oncology perspective, these response data complement molecularly driven targeted therapy results (Figure 2) by showing that **immunotherapy efficacy is not restricted to a single oncogenic mutation subset**, broadening applicability across molecular profiles [7], [18]. Thus, the figure reinforces the dual therapeutic paradigm in melanoma: mutation-targeted pathway inhibition and immune checkpoint modulation.

Figure 6
Objective response rate in advanced Merkel-cell carcinoma: pembrolizumab versus historical chemotherapy benchmarks

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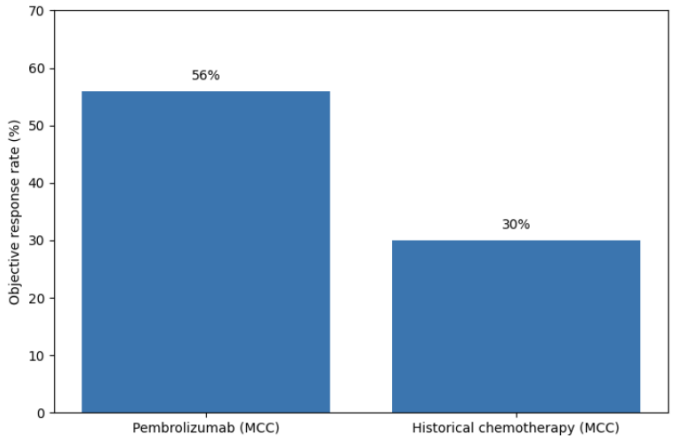

Figure 6 illustrates the **objective response rate (ORR)** observed with **pembrolizumab in advanced Merkel-cell carcinoma (MCC)** compared with historical chemotherapy benchmarks. The visualization shows an ORR of **56%** with pembrolizumab versus approximately **30%** with conventional cytotoxic chemotherapy, reflecting the response patterns described in pivotal immunotherapy studies for MCC [19].

From a results perspective, the most evident observation is the **marked increase in tumor response frequency** with PD-1 blockade compared with historical chemotherapy standards. The absolute difference of approximately **26 percentage points** demonstrates a substantial separation in measurable tumor regression between immune checkpoint inhibition and prior systemic approaches [19].

Importantly, MCC is a biologically aggressive neuroendocrine cutaneous malignancy with historically limited durable systemic options. The higher ORR observed with pembrolizumab indicates that immune-based therapy is associated with a **greater probability of clinically significant tumor shrinkage** in this disease context [19]. Unlike melanoma, where both targeted therapy and immunotherapy are central, MCC lacks a dominant recurrent actionable mutation comparable to BRAF; therefore, immune checkpoint blockade has emerged as the primary systemic precision strategy.

Another relevant result-level pattern is the **consistency of immunotherapy benefit across distinct cutaneous malignancies**. When interpreted alongside Figures 1 and 5, Figure 6 demonstrates that PD-1 inhibition produces meaningful objective responses not only in melanoma but also in MCC. This reinforces that immune activation represents a cross-cutting therapeutic mechanism in cutaneous oncology, extending beyond a single tumor subtype [2], [7], [19].

Additionally, the difference in ORR highlights the shift from short-lived chemotherapy responses toward immune-mediated responses that may demonstrate improved durability. Although ORR does not directly measure long-term survival, higher response rates under immune checkpoint blockade contributed to redefining systemic treatment standards in advanced MCC [19].

DISCUSSION

The findings synthesized in the Results section illustrate a coherent transformation in cutaneous oncology, where staging systems, molecular profiling, and immune-based therapies operate as complementary rather than isolated components of care. The data presented across Figures 1–6 confirm three structural observations: (1) prognosis remains strongly stage-dependent, (2) molecular stratification identifies actionable biological subgroups, and (3) immune checkpoint blockade has reshaped survival expectations in advanced disease.

First, the stage-dependent survival gradient (Figure 4) reinforces that early detection and standardized staging remain foundational. Despite therapeutic advances, the difference between Stage I and Stage IV survival remains profound [9]. This underscores that precision medicine does not replace early diagnosis; rather, it amplifies its importance.

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Improvements in dermoscopic assessment and structured staging frameworks provide the prognostic scaffold upon which systemic therapy decisions are layered [9], [10]. Even in the era of immunotherapy, earlier stage at diagnosis continues to confer intrinsic survival advantage.

Second, molecular characterization—particularly BRAF mutation prevalence (Figure 3)—demonstrates that approximately half of melanomas harbor a clinically actionable alteration [5], [6]. The widespread prevalence of BRAF mutations justifies routine genomic testing in advanced disease. Targeted therapy outcomes (Figure 2) illustrate that when a molecular driver is present, pathway-directed inhibition can delay progression and provide rapid disease control [4]. This validates the central tenet of precision oncology: aligning therapy with tumor biology improves disease management efficiency. However, the modest difference in median progression-free survival also reflects the persistent challenge of resistance, highlighting the need for combination strategies and ongoing molecular monitoring [4], [12], [18].

Third, immune checkpoint inhibition has introduced durable survival patterns not previously observed in advanced melanoma. The long-term survival separation shown in Figure 1 confirms that PD-1–containing regimens, particularly combination therapy, increase the proportion of long-term survivors [3], [20]. Objective response differences between pembrolizumab and ipilimumab (Figure 5) further support the clinical superiority of PD-1 blockade in terms of measurable tumor reduction [7]. Importantly, immunotherapy benefit is not confined to melanoma; Figure 6 demonstrates similar response advantages in Merkel-cell carcinoma, reinforcing immune modulation as a broader strategy in cutaneous malignancies [19].

A key integrative interpretation emerging from these results is the **dual therapeutic paradigm** in modern cutaneous oncology. On one axis, mutation-directed targeted therapy offers biologically matched disease control in molecularly selected populations. On the other, immune checkpoint blockade provides systemic, mutation-agnostic therapeutic activity capable of producing durable remission in a subset of patients [2], [4], [7], [20]. Rather than competing, these approaches coexist within clinical algorithms, with sequencing and combination decisions guided by tumor biology, disease burden, and patient characteristics.

Another important dimension is the variability of response. Not all patients benefit equally from targeted therapy or immunotherapy. Biomarker development—such as PD-L1 expression analysis and broader genomic profiling—aims to refine predictive accuracy, though current markers remain imperfect [13], [18]. This heterogeneity reinforces that precision oncology is an evolving framework rather than a fixed endpoint.

From a global perspective, translating these advances into healthcare systems such as those in Mexico, Colombia, and Ecuador requires structured implementation strategies. The evidence supports a stepwise integration model: prioritize early detection, standardize pathology reporting, ensure access to essential molecular testing (e.g., BRAF status), and progressively expand immunotherapy infrastructure. Precision medicine, therefore, is not solely a technological upgrade but also a systems-level adaptation.

CONCLUSION

Cutaneous oncology has undergone a profound transformation in the precision medicine era, moving from a primarily morphology-based discipline toward an integrated, biologically informed model of care. The evidence synthesized in this review demonstrates that modern management of melanoma and selected non-melanoma skin cancers is structured

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around three interconnected pillars: early detection and accurate staging, molecular risk stratification, and targeted or immune-based systemic therapies.

Stage at diagnosis remains one of the most powerful determinants of prognosis, as reflected by the pronounced survival gradient across AJCC stages [9]. Early detection strategies and standardized histopathologic evaluation continue to provide the essential framework upon which therapeutic decisions are built. Precision medicine does not replace traditional diagnostic rigor; rather, it enhances its value by linking early-stage identification to optimized long-term outcomes.

At the molecular level, the identification of actionable alterations such as BRAF mutations has validated the concept that tumor biology can directly guide therapy selection [5], [6]. Targeted inhibition of the MAPK pathway has demonstrated measurable progression control in mutation-selected populations [4], confirming that genomic stratification is clinically meaningful. However, resistance mechanisms and biological heterogeneity underscore the need for combination strategies and continuous refinement of molecular profiling tools [12], [18].

Immune checkpoint blockade has redefined survival expectations in advanced melanoma, producing durable responses and long-term survival in a subset of patients [3], [7], [20]. The superiority of PD-1–based strategies over earlier immunotherapeutic approaches is supported by objective response and long-term outcome data. Furthermore, the extension of immunotherapy benefits to other cutaneous malignancies, such as Merkel-cell carcinoma, demonstrates that immune modulation is a central therapeutic axis beyond melanoma alone [19].

Collectively, these findings support the conclusion that precision oncology in dermatology is not a single innovation but a coordinated system integrating detection, staging, molecular biology, and systemic therapy. The coexistence of targeted therapy and immunotherapy within treatment algorithms reflects a dual paradigm that adapts to tumor genotype and immune context.

From an international perspective, including healthcare environments in Mexico, Colombia, and Ecuador, the successful implementation of precision oncology requires structured integration: strengthening early diagnostic pathways, ensuring access to essential molecular testing, and expanding capacity for immune-based therapies. The future of cutaneous oncology lies not only in discovering new biomarkers or drugs, but also in refining systems that deliver biologically matched care in a sustainable and equitable manner.

In conclusion, the precision medicine era has reshaped cutaneous oncology into a discipline defined by molecular insight, immunologic strategy, and stage-informed intervention. Continued integration of genomic science, clinical trial evidence, and multidisciplinary coordination will remain essential to further improving outcomes in melanoma and related cutaneous malignancies.

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