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Clinical Effectiveness of Programmed Cell Death Protein-1 (PD-1) Inhibitors in Advanced Cutaneous Squamous Cell Carcinoma: A Systematic Review

[1] Wita Zahara*, [2] Subagio, [3] Naomi Winny Tioline, [4] Iman Agus Lisanto
[1] RSUD H. Abdul Manap Kota Jambi, Indonesia *; email: Witazaharadr@gmail.com
[2] RSUD H. Abdul Manap Kota Jambi, Indonesia; email: 1973subagio@gmail.com
[3] RSUD H. Abdul Manap Kota Jambi, Indonesia; email: dr.naomitioline@gmail.com
[4] RS Bhayangkara Lodewijk Mandacan, Papua Barat, Indonesia; email: Imanaguslisanto17@gmail.com
*Correspondence

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Abstract
Introduction: *Advanced cutaneous squamous cell carcinoma (cSCC) is associated with a poor prognosis, particularly in patients with unresectable locally advanced or metastatic disease, while conventional systemic therapies generally achieve objective response rates below 30%.* ***Objective:*** *This study aimed to systematically evaluate the clinical efficacy and safety of Programmed Cell Death Protein-1 (PD-1) inhibitors in patients with advanced cSCC.* ***Method:*** *A PRISMA 2020-based systematic review searched PubMed, ScienceDirect, and Wiley Online Library for studies published from January 2020 to March 2026. Twenty eligible studies involving cemiplimab, pembrolizumab, or nivolumab were included.* ***Result and Discussion:*** *Clinical trials reported objective response rates of 44.0–45.2% for cemiplimab, 35.2–50.0% for pembrolizumab, and 61.3% for nivolumab, while real-world studies reported 35.1–80.6%. Comparative studies showed improved overall survival and durable responses. Common adverse events included fatigue, rash, and immune-related toxicities.* ***Conclusion:*** *PD-1 inhibitors provide effective and well-tolerated first-line systemic therapy for advanced cSCC.*

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Introduction

Cutaneous squamous cell carcinoma (cSCC) is the second most common form of non-melanoma skin cancer and represents a growing global health burden because of its increasing incidence and potential for aggressive clinical behavior. Recent estimates show that more than one million new cases of cSCC occur annually in the United States, with incidence continuing to rise as a result of cumulative ultraviolet (UV) radiation exposure, population aging, increasing rates of immunosuppression, and expanded skin cancer screening programs. These advanced forms of cSCC are associated with substantially poorer clinical outcomes, increased disease-related morbidity, and reduced overall survival. Historically, systemic treatment options for advanced cSCC have been limited, with conventional chemotherapy and epidermal growth factor receptor (EGFR)-targeted therapy providing only modest clinical benefit and relatively low objective response rates. Consequently, there has been a pressing need to develop more effective systemic therapies capable of producing durable tumor responses while maintaining acceptable safety profiles. The emergence of immune checkpoint inhibition has fundamentally transformed the therapeutic landscape for advanced cSCC by targeting immune escape mechanisms exploited by tumor cells (Migden *et al*., 2020; Rischin *et al*., 2020; Baggi *et al*., 2021; Jiang *et al*., 2024).

The increasing incidence of cSCC is closely associated with several well-established environmental and host-related risk factors. Chronic cumulative exposure to ultraviolet radiation is considered the principal etiological factor because it induces DNA damage and promotes cutaneous carcinogenesis. Other important risk factors include advanced age, systemic immunosuppression, fair skin phenotype, and chronic sun exposure, all of which contribute to the rising burden of cSCC worldwide. Patients with immunocompromised conditions are particularly susceptible to developing aggressive disease and are at increased risk of recurrence, nodal metastasis, and disease-related mortality. Approximately 3% of patients with cSCC develop regional lymph node metastases, showing the clinical importance of early diagnosis and effective systemic treatment for advanced disease. These epidemiological characteristics emphasize the growing need for effective therapies capable of achieving durable disease control in patients with advanced cSCC (Jiang *et al*., 2024).

The programmed cell death protein-1 (PD-1) pathway plays a pivotal role in suppressing antitumor immune responses by inhibiting T-cell activation after binding to its ligands expressed on tumor cells and cells within the tumor microenvironment. Pharmacological inhibition of PD-1 restores cytotoxic T-cell activity, thereby enhancing immune-mediated tumor destruction and generating more durable clinical responses than conventional systemic therapies. Among currently available PD-1 inhibitors, cemiplimab has become the first agent specifically approved for advanced cSCC based on favorable efficacy showed in prospective clinical trials. Subsequently, pembrolizumab and nivolumab have also shown encouraging antitumor activity in patients with unresectable, recurrent, and metastatic cSCC across different clinical settings. These findings collectively support the growing role of PD-1 blockade as the cornerstone of systemic therapy for advanced cSCC (Migden *et al*., 2020; Rischin *et al*., 2020; Hughes *et al*., 2021; Lang *et al*., 2023).

Evidence supporting PD-1 inhibitors continues to expand through both prospective clinical trials and real-world observational studies. Clinical trials have consistently showed meaningful objective response rates, prolonged progression-free survival, and durable responses following treatment with cemiplimab and pembrolizumab in patients

with advanced disease. In parallel, real-world studies have confirmed that these favorable outcomes can also be achieved in more heterogeneous patient populations, including elderly individuals, patients with significant comorbidities, and those with immunocompromised conditions who are often underrepresented in clinical trials. Furthermore, phase II evidence evaluating nivolumab has shown promising therapeutic activity, suggesting that the clinical benefits of PD-1 inhibition are not restricted to a single agent. Nevertheless, differences in study design, patient characteristics, treatment regimens, and reported clinical outcomes have resulted in considerable heterogeneity across the currently available literature, making direct comparisons between studies challenging (Baggi *et al*., 2021; Hughes *et al*., 2021; Lang *et al*., 2023; Verkerk *et al*., 2024).

Despite the growing body of evidence on immunotherapy for advanced cSCC, the available studies differ considerably in design, patient characteristics, and reported outcomes, making the whole clinical evidence difficult to interpret. Combining findings from prospective clinical trials and real-world studies allows a broader evaluation of treatment response, survival outcomes, and treatment-related toxicity across routine clinical settings. This approach also helps identify areas where the evidence is consistent as well as aspects that remain uncertain. Therefore, this systematic review evaluates the clinical effectiveness and safety of PD-1 inhibitors, including cemiplimab, pembrolizumab, and nivolumab, in patients with advanced cutaneous squamous cell carcinoma. By summarizing the currently available evidence, this review aims to support treatment selection in clinical practice and show priorities for future research on PD-1 inhibitor therapy in advanced cSCC (Migden *et al*., 2020; Rischin *et al*., 2020; Baggi *et al*., 2021; Hughes *et al*., 2021; Lang *et al*., 2023; Verkerk *et al*., 2024).

Method

This study was conducted as a systematic literature review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure methodological transparency and reproducibility. A comprehensive literature search was performed using three electronic databases, namely PubMed, ScienceDirect, and Wiley Online Library, to identify studies published between January 2020 and March 2026. The search strategy combined controlled vocabulary and free-text keywords related to *cutaneous squamous cell carcinoma*, *advanced cSCC*, *PD-1 inhibitors*, *cemiplimab*, *pembrolizumab*, *nivolumab*, and *immunotherapy*. After duplicate records were removed, titles and abstracts were screened to identify potentially relevant studies. Full-text articles that met the predefined eligibility criteria were subsequently assessed for inclusion in the review. The study selection process was documented using a PRISMA 2020 flow diagram to ensure a transparent description of the identification, screening, eligibility assessment, and inclusion of studies.

Eligible studies included original human research involving adult patients (≥ 18 years) with locally advanced, recurrent, or metastatic cutaneous squamous cell carcinoma who received treatment with cemiplimab, pembrolizumab, or nivolumab. Both prospective clinical trials and real-world observational studies were eligible if they reported at least one clinical outcome, including overall survival (OS), progression-free survival (PFS), objective response rate (ORR), recurrence-free survival (RFS), or adverse events (AE). Narrative reviews, systematic reviews, meta-analyses, editorials, conference abstracts without sufficient data, case reports, preclinical studies, and articles with non-extractable outcome data were excluded. Relevant information extracted from each

eligible study included study design, patient characteristics, intervention, sample size, follow-up duration, efficacy outcomes, and safety outcomes. Because substantial heterogeneity existed across the included studies in terms of design, patient population, and reported endpoints, the findings were synthesized descriptively rather than through quantitative meta-analysis. Table 1, show eligibility study.

Table 1
Eligibility Criteria and Study Characteristics Based on the PICOS

Item	Description
Study design	Systematic literature review conducted according to the PRISMA 2020 guidelines.
Databases	PubMed, ScienceDirect, and Wiley Online Library.
Search period	January 2020 - March 2026.
Population (P)	Adult patients (≥ 18 years) with advanced cutaneous squamous cell carcinoma (locally advanced, recurrent, or metastatic).
Intervention (I)	PD-1 inhibitors, including cemiplimab, pembrolizumab, and nivolumab.
Comparator (C)	Any comparator or single-arm studies without a control group.
Outcomes (O)	Overall survival (OS), progression-free survival (PFS), objective response rate (ORR), recurrence-free survival (RFS), and adverse events (AE).
Eligible study (S)	Phase II clinical trials, prospective studies, retrospective cohort studies, comparative studies, and real-world observational studies.
Inclusion criteria	Original human studies involving adult patients receiving PD-1 inhibitor therapy for advanced cSCC and reporting at least one predefined clinical outcome.
Exclusion criteria	Narrative reviews, systematic reviews, meta-analyses, editorials, conference abstracts with insufficient data, case reports, preclinical studies, animal studies, and studies with non-extractable outcome data.
Data synthesis	Narrative qualitative synthesis due to heterogeneity in study design, patient characteristics, and reported outcomes.

Result and Discussion

1. Result

A total of 20 studies met the predefined eligibility criteria and were included in the final qualitative synthesis, as shown in Figure 1. The literature selection process followed the PRISMA 2020 framework, beginning with database identification, duplicate removal, title and abstract screening, full-text eligibility assessment, and final study inclusion. The detailed selection process is illustrated in the PRISMA flow diagram to provide transparency regarding study identification and exclusion at each stage. The included studies represented a broad spectrum of evidence, including prospective phase II clinical trials, long-term follow-up analyses, retrospective cohort studies, real-world observational studies, and nationwide comparative cohort studies.

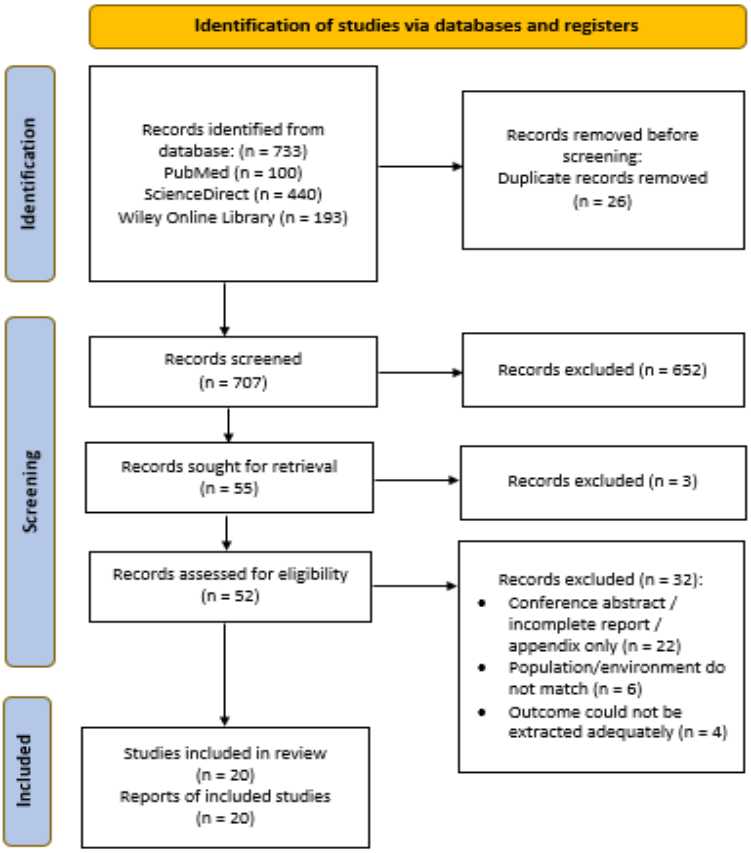

Figure 1. PRISMA 2020 Flow Diagram

Following the study selection process, detailed characteristics of each eligible study were extracted, including study design, patient population, intervention, treatment outcomes, and safety findings. Among the 20 included studies, four were phase II clinical trials or long-term analyses of clinical trials, while the remaining studies consisted primarily of retrospective real-world cohorts and two large comparative cohort studies. Cemiplimab was the most extensively investigated PD-1 inhibitor, whereas pembrolizumab and nivolumab were evaluated in fewer studies but consistently showed clinically meaningful antitumor activity (Migden *et al*., 2020; Rischin *et al*., 2020; Lang *et al*., 2023; Hughes *et al*., 2021; Hughes *et al*., 2025). Several real-world studies additionally explored treatment effectiveness in elderly patients, immunocompromised populations, and patients with diverse clinical characteristics, thereby complementing evidence generated from prospective clinical trials (Baggi *et al*., 2021; Ríos-Viñuela *et al*., 2022; Averbuch *et al*., 2023; Rohaan *et al*., 2023; McLean *et al*., 2024; Ksienski *et al*., 2024; Nardone *et al*., 2024; Faoro *et al*., 2025; Haigh *et al*., 2025; Yakobson *et al*., 2023). A comprehensive of the characteristics and principal outcomes of the included studies is showed in Table 2.

Table 2
Characteristics of the Included Studies

Author	Intervention	Outcomes
Migden *et al.*, 2020	Cemiplimab 3 mg/kg	ORR 44%; CR 13%, PR 31%. Grade 3-4 AE 44%; TEAE 29%; 1 therapy-related death.

Rischin *et al.*, 2020	Cemiplimab *fixed dose* or 3 mg/kg	ORR per pooled ICR 45.2%. AE: fatigue 27.0%, diarrhea 23.5%.
Hughes *et al.*, 2021	Pembrolizumab 200 mg	ORR 50.0% la-cSCC and 35.2% r/m-cSCC. Grade 3-5 TRAE 11.9%.
Lang *et al.*, 2023	Nivolumab	ORR 61.3%. Hematologic subgroup: ORR 45.5%, TRAE 58.1%; Grade 3 AE 19.4%.
Hughes *et al.*, 2025	Cemiplimab	Group 1-3: ORR 47.2%. Group 6: ORR 44.8%. TEAE Grade ≥ 3 = 31.1% (group 1-3) and 34.5% (group 6).
Baggi *et al.*, 2021	Cemiplimab	ORR 58.0%, TRAE 42.7%; Grade 3-4 AE 9.2% and 2 fatal events.
Rios-Viñuela *et al.*, 2022	Cemiplimab	62% responded to therapy; CR 23%, PR 38%. AE 46% (mostly grade 1).
Averbuch *et al.*, 2023	PD-1 inhibitor	93 patients: ORR 80.6%. Toxicity 55%; Grade ≥ 3 AE in 25 patients, and 5 deaths.
Yakobson *et al.*, 2023	Cemiplimab or pembrolizumab	Median PFS 8.94 months, DCR 91.4. TRAE 85.6% (mostly grade 1-2).
Verkerk *et al.*, 2024	Cemiplimab	ORR 35.1%. Median PFS 12.2 months; median OS 24.2 months. Grade ≥ 3 TRAE 29.8%.
Faoro *et al.*, 2025	Cemiplimab	ORR 47.8%, 12-month OS 56.6%; 12-month PFS 47.9%. TRAE 51.1%; no grade 4-5.
Nardone *et al.*, 2024	Cemiplimab	Median PFS and OS not reached; mean PFS 21.3 months, mean OS 25.3 months.
Ksienski *et al.*, 2024	Cemiplimab	Grade ≥ 3 irAE 27.4%; discontinuation of therapy due to irAE 31.1%; hospitalization due to irAE 11.3%. ORR by age: 50.0%, 60.4%, 54.5%.
Haigh *et al.*, 2025	Cemiplimab	ORR 60.8%; CBR 74.3%. Median PFS and OS not reached; 38% showed durable response.
Robert *et al.*, 2026	Cemiplimab vs conventional systemic therapy	Median OS 21.2 vs 9.8 months. Median PFS 13.7 vs 5.3 months. ORR 56.6% vs 32%. AE 27% on cemiplimab vs 33% on conventional therapy.
Samaran *et al.*, 2026	Anti-PD-1	Median OS 26 vs 14 months. Median SFS 22 vs 8 months.
Bennett *et al.*, 2026	Cemiplimab	ORR 72%; CR 22%, PR 50%. Median PFS 56.4 months; median OS not reached; 5-year OS 60%.
Ciobotariu *et al.*, 2026	Cemiplimab	ORR 72%, DCR 74.4%, median PFS 6.4 months. Discontinuation of therapy due to AE 7%.
Rohaan *et al.*, 2023	Cemiplimab	ORR 52%; median PFS 10.9 months; median OS 26.1 months; Grade 3-4 AE 22%.

McLean *et al.*, 2024	Cemiplimab + Pembrolizumab	ORR 60% (278 evaluable patients). 12-month OS 78%; 12-month PFS 65%. irAE grade ≥ 2 19%; no deaths.

The efficacy analysis showed consistently favorable clinical outcomes following PD-1 inhibitor therapy across both prospective clinical trials and real-world studies. In phase II clinical trials, the objective response rate (ORR) ranged from 44.0-45.2% for cemiplimab, 35.2-50.0% for pembrolizumab, and 61.3% for nivolumab (Migden *et al*., 2020; Rischin *et al*., 2020; Hughes *et al*., 2021; Lang *et al*., 2023). Across real-world cohorts, ORR varied between 35.1% and 80.6%, while median progression-free survival (PFS) ranged from 5.9 to 29.5 months, reflecting differences in patient characteristics and clinical practice settings (Baggi *et al*., 2021; Verkerk *et al*., 2024; Ríos-Viñuela *et al*., 2022; Averbuch *et al*., 2023; Rohaan *et al*., 2023; McLean *et al*., 2024; Ksienski *et al*., 2024; Nardone *et al*., 2024; Ciobotariu *et al*., 2026; Faoro *et al*., 2025; Haigh *et al*., 2025; Yakobson *et al*., 2023). Comparative cohort studies further showed a significant survival advantage associated with PD-1 inhibitors, with median overall survival reaching 21.2 versus 9.8 months in the French TOSCA study and 26 versus 14 months in the nationwide French cohort comparing anti-PD-1 therapy with conventional systemic treatment (Robert *et al*., 2026; Samaran *et al*., 2026). Long-term follow-up of the EMPOWER-CSCC-1 cohort showed sustained clinical benefit, with a median PFS of 56.4 months and a 5-year overall survival of 60%, indicating durable responses among treatment responders (Hughes *et al*., 2025; Bennett *et al*., 2025). Additionally, median time to response was approximately 1.9-2.1 months for cemiplimab and 2.6 months for pembrolizumab, while disease control rates consistently exceeded 50% across multiple studies and complete responses were reported in a proportion of patients. PD-1 inhibitors showed an acceptable safety profile, with fatigue, rash, and immune-related adverse events representing the most frequently reported toxicities; however, grade 3-4 adverse events remained clinically relevant in a subset of patients receiving treatment (Rischin *et al*., 2020; Lang *et al*., 2023; Hughes *et al*., 2021; Baggi *et al*., 2021; Verkerk *et al*., 2024; McLean *et al*., 2024).

2. Discussion

PD-1 inhibitors have fundamentally changed the management of advanced cutaneous squamous cell carcinoma (cSCC) by shifting systemic treatment from conventional cytotoxic approaches toward immune-based therapy. Rather than providing only temporary tumor control, PD-1 blockade restores antitumor immune surveillance through reactivation of cytotoxic T lymphocytes, thereby producing more durable and clinically meaningful responses. The consistently favorable outcomes observed across different study designs support the biological rationale for targeting the PD-1 pathway in cSCC, a malignancy characterized by high tumor mutational burden and strong immunogenicity resulting from chronic ultraviolet-induced DNA damage. Among the available agents, cemiplimab remains the most extensively investigated because evidence is available from prospective trials, long-term follow-up analyses, real-world cohorts, and comparative studies. Nevertheless, the available evidence also suggests that pembrolizumab and nivolumab share the same therapeutic mechanism and provide meaningful clinical benefit in appropriately selected patients. Collectively, these findings reinforce the current role of PD-1 inhibitors as the preferred first-line systemic therapy

for patients with advanced cSCC who are not candidates for curative surgery or radiotherapy (Migden *et al*., 2020; Rischin *et al*., 2020; Baggi *et al*., 2021; Lang *et al*., 2023; Hughes *et al*., 2021; Hughes *et al*., 2025).

Although real-world studies generally include patients with more heterogeneous clinical characteristics than those enrolled in clinical trials, the overall direction of treatment benefit remained consistent across different healthcare settings. This consistency suggests that the effectiveness of PD-1 inhibitors is maintained even in populations that are traditionally underrepresented in prospective studies, including elderly patients and individuals with immunocompromised conditions. Variability among observational studies is therefore more likely to reflect differences in baseline patient characteristics and clinical practice rather than differences in the intrinsic activity of PD-1 inhibitors. These observations improve the external validity of the available evidence and increase confidence that the reported benefits are applicable to routine oncology practice. Consequently, real-world evidence serves as an important complement to prospective trials when evaluating the overall effectiveness of PD-1 inhibitors in advanced cSCC (Baggi *et al*., 2021; Verkerk *et al*., 2024; Ríos-Viñuela *et al*., 2022; Averbuch *et al*., 2023; Rohaan *et al*., 2023; McLean *et al*., 2024; Ksienski *et al*., 2024; Nardone *et al*., 2024; Ciobotariu *et al*., 2026; Faoro *et al*., 2025; Haigh *et al*., 2025; Yakobson *et al*., 2023).

Comparative cohort studies further strengthen the clinical significance of PD-1 inhibition because they directly compare immunotherapy with historical systemic treatment strategies. Unlike conventional chemotherapy, which is often limited by short-lived responses and cumulative toxicity, immune checkpoint inhibition appears capable of producing durable immune control that may persist even after treatment discontinuation in selected patients. The long-term follow-up findings included in this review support the concept that immunotherapy can modify the natural history of advanced cSCC rather than simply delaying disease progression. These observations are consistent with current treatment recommendations that prioritize PD-1 inhibitors whenever curative local treatment is no longer feasible. Therefore, the available comparative evidence supports the integration of PD-1 inhibitors as the foundation of systemic therapy for advanced cSCC while highlighting the need to optimize treatment sequencing in future studies (Robert *et al*., 2026; Samaran *et al*., 2026; Bennett *et al*., 2025; Hughes *et al*., 2025).

The safety profile identified in this review shows that PD-1 inhibitors are generally manageable when appropriate monitoring and supportive care are implemented. Most adverse events are characteristic of immune checkpoint inhibition and require timely recognition because delayed management may result in treatment interruption or severe immune-related complications. These findings show that successful immunotherapy depends not only on drug efficacy but also on multidisciplinary management and adherence to established guidelines for immune-related adverse events. In addition, several studies suggested that baseline clinical characteristics and inflammatory biomarkers may influence treatment outcomes, indicating the potential value of individualized risk stratification in future clinical practice. However, current evidence remains insufficient to recommend these factors as routine predictive biomarkers because prospective validation is still limited. Further biomarker-driven research is therefore required to improve patient selection while maintaining the favorable benefit-risk profile of PD-1 inhibitors (Baggi *et al*., 2021; Verkerk *et al*., 2024; McLean *et al*., 2024; Ksienski *et al*., 2024; Nardone *et al*., 2024; Ciobotariu *et al*., 2026; Haigh *et al*., 2025).

Most included studies were single-arm clinical trials or retrospective observational cohorts, limiting the ability to directly compare the relative efficacy of individual PD-1 inhibitors. Methodological heterogeneity across studies, including differences in patient selection, disease stage, follow-up duration, and outcome definitions, also restricted quantitative comparisons and precluded meta-analysis. Despite these limitations, the consistency of evidence across multiple study designs strengthens the overall conclusion that PD-1 inhibitors provide meaningful clinical benefit in advanced cSCC. Future research should prioritize randomized comparative trials, standardized real-world registries, and biomarker-guided treatment strategies to optimize therapeutic sequencing and identify patients who derive the greatest benefit from immunotherapy. The evidence synthesized in this review supports PD-1 inhibitors as the cornerstone of systemic treatment for advanced cSCC while highlighting important directions for future clinical investigation (Migden *et al*., 2020; Rischin *et al*., 2020; Lang *et al*., 2023; Hughes *et al*., 2021; Hughes *et al*., 2025; Robert *et al*., 2026; Samaran *et al*., 2026).

Conclusion

PD-1 inhibitors show consistent clinical effectiveness in the treatment of advanced cutaneous squamous cell carcinoma (cSCC), providing significant improvements in objective response rate, progression-free survival, and overall survival across a wide range of clinical settings. Among the available agents, cemiplimab is supported by the most robust body of evidence, while pembrolizumab and nivolumab also show meaningful and durable antitumor activity. Comparative observational studies suggest that PD-1 inhibitor therapy is associated with improved survival outcomes compared with conventional non-PD-1 systemic treatments. Although the safety profile of PD-1 inhibitors is generally acceptable and manageable, optimal clinical outcomes depend on appropriate patient selection, close monitoring, and prompt recognition and management of immune-related adverse events (irAEs). Based on the current evidence, PD-1 inhibitors should be considered the preferred first-line systemic therapy for patients with unresectable, locally advanced, recurrent, or metastatic cutaneous squamous cell carcinoma.

Reference

Averbuch, I., Salman, S., Shtamper, N., Doweck, I., Popovtzer, A., Markel, G., ... & Billan, S. (2023). First-line programmed death-1 inhibitor treatment for locoregionally advanced or metastatic cutaneous squamous cell carcinoma–A real-world experience from Israel. *Frontiers in Oncology*, *13*, 1117804. doi.org/10.3389/fonc.2023.1117804

Baggi, A., Quaglino, P., Rubatto, M., Depenni, R., Guida, M., Ascierto, P. A., ... & Bossi, P. (2021). Real world data of cemiplimab in locally advanced and metastatic cutaneous squamous cell carcinoma. *European journal of cancer*, *157*, 250-258. doi.org/10.1016/j.ejca.2021.08.018

Bennett, C., McLean, L. S., Lim, A. M., Bressel, M., Guminski, A., Hughes, B. G., ... & Rischin, D. (2025). Extended follow-up outcomes of patients with advanced cutaneous squamous cell carcinoma treated with cemiplimab on EMPOWER-CSCC-1: A retrospective cohort study. *Journal of the American Academy of Dermatology*. doi.org/10.1016/j.jaad.2025.11.080

Ciobotariu, I., Nardo, L. D., Stefani, A. D., Paradisi, A., Mannino, M., Brunetti, F., & Peris, K. (2026). Neutrophil-to-Lymphocyte Ratio Dynamics and Progression-Free Survival in Advanced Cutaneous Squamous Cell Carcinoma Treated With Cemiplimab. *Dermatologic Therapy*, *2026*(1), 8309058. doi.org/10.1155/dth/8309058

Faoro, L., Salizzato, V., Coppola, M., Carpanese, D., Fabozzi, A., Tondulli, L., Marconcini, R., Spagnolo, F., Del Bianco, P., Chiarion-Sileni, V., & Piccin, L. (2025). Real-world multicentre observational study of effectiveness and toxicity in patients with advanced cutaneous squamous cell carcinoma treated with cemiplimab. *Journal of the European Academy of Dermatology and Venereology, 39*, e50–e53. doi.org/10.1111/jdv.20066

Haigh, J. E., Rack, S., Yan, R., Babu, S., Donnelly, O., Walter, H., Faust, G., Bhagani, S., Isola, P., & Metcalf, R. (2025). Evaluation of clinical parameters associated with response and resistance to cemiplimab in locally advanced and metastatic cutaneous squamous cell carcinoma: A multi-institutional retrospective cohort study. *Current Oncology, 32*(3), Article 168. doi.org/10.3390/curroncol32030168

Hughes, B. G., Guminski, A., Bowyer, S., Migden, M. R., Schmults, C. D., Khushalani, N. I., ... & Rischin, D. (2025). A phase 2 open-label study of cemiplimab in patients with advanced cutaneous squamous cell carcinoma (EMPOWER-CSCC-1): Final long-term analysis of groups 1, 2, and 3, and primary analysis of fixed-dose treatment group 6. *Journal of the American Academy of Dermatology*, *92*(1), 68-77. doi.org/10.1016/j.jaad.2024.06.108

Hughes, B. G. M., Munoz-Couselo, E., Mortier, L., Bratland, Å., Gutzmer, R., Roshdy, O., ... & Grob, J. J. (2021). Pembrolizumab for locally advanced and recurrent/metastatic cutaneous squamous cell carcinoma (KEYNOTE-629 study): an open-label, nonrandomized, multicenter, phase II trial. *Annals of Oncology*, *32*(10), 1276-1285. doi.org/10.1016/j.annonc.2021.07.008

Jiang, R., Fritz, M., & Que, S. K. T. (2024). Cutaneous squamous cell carcinoma: an updated review. *Cancers*, *16*(10), 1800. doi.org/10.3390/cancers16101800

Ksienski, D., Truong, P. T., Bone, J. N., Egli, S., Clarkson, M., Patterson, T., ... & Lakkunarajah, S. (2024). Advanced cutaneous squamous cell carcinoma: Impact of age on the safety and efficacy of cemiplimab and the prognostic significance of blood biomarkers. *Journal of Geriatric Oncology*, *15*(5), 101789. doi.org/10.1016/j.jgo.2024.101789

Lang, R., Welponer, T., Richtig, E., Wolf, I., Hoeller, C., Hafner, C., ... & Laimer, M. (2023). Nivolumab for locally advanced and metastatic cutaneous squamous cell carcinoma (NIVOSQUACS study)—Phase II data covering impact of concomitant haematological malignancies. *Journal of the European Academy of Dermatology and Venereology*, *37*(9), 1799-1810. doi.org/10.1111/jdv.19218

McLean, L.S., Lim, A.M., Bressel, M., Lee, J., Ladwa, R., Guminski, A.D., Hughes, B., Bowyer, S., Briscoe, K., Harris, S., Kukard, C., Zielinski, R., Alamgeer, M., Carlino, M., Mo, J., Park, J.J., Khattak, M.A., Day, F. and Rischin, D. (2024), Immune checkpoint inhibitor therapy for advanced cutaneous squamous cell carcinoma in Australia: a retrospective real world cohort study. *Med J Aust,* 220: 80-90. https://doi.org/10.5694/mja2.52199

Migden, M. R., Khushalani, N. I., Chang, A. L. S., Lewis, K. D., Schmults, C. D., Hernandez-Aya, L., ... & Rischin, D. (2020). Cemiplimab in locally advanced cutaneous squamous cell carcinoma: results from an open-label, phase 2, single-arm trial. *The Lancet Oncology*, *21*(2), 294-305. doi.org/10.1016/S1470-2045(19)30728-4

Nardone, V., Napolitano, S., Gagliardi, F., Esposito, A., Caraglia, F., Briatico, G., ... & Troiani, T. (2024). Previous radiotherapy increases the efficacy of cemiplimab in the treatment of locally advanced and metastatic cutaneous squamous cell carcinoma: A retrospective analysis. *Journal of the American Academy of Dermatology*, *91*(4), 678-683. doi.org/10.1016/j.jaad.2024.06.023

Ríos-Viñuela, E., Álvarez, P., Lavernia, J., Serra-Guillén, C., Requena, C., Bernia, E., Diago, A., Llombart, B., & Sanmartín, O. (2022). Cemiplimab in advanced cutaneous squamous cell carcinoma: Real-world experience in a monographic oncology center. *Actas Dermo-Sifiliográficas, 113*(6), 610–615. doi.org/10.1016/j.ad.2021.04.011

Rischin, D., Migden, M. R., Lim, A. M., Schmults, C. D., Khushalani, N. I., Hughes, B. G., ... & Guminski, A. (2020). Phase 2 study of cemiplimab in patients with metastatic cutaneous squamous cell carcinoma: primary analysis of fixed-dosing, long-term outcome of weight-based dosing. *Journal for immunotherapy of cancer*, *8*(1), e000775. doi.org/10.1136/jitc-2020-000775

Robert, C., Gérard, G., Lanoy, E., Quéreux, Q., Bernard, P., Viguier, M., ... & Mortier, L. (2026). Cemiplimab versus historical systemic treatments for locally advanced or metastatic cutaneous squamous cell carcinomas: Results from the French study TOSCA. *European Journal of Cancer*, 116596. doi.org/10.1016/j.ejca.2026.116596

Rohaan, M. W., Duizer, M. L., Devriese, L. A., Meerveld-Eggink, A., Brandts, W. F., van Thienen, J. V., ... & Haanen, J. B. (2023). Real-world data on tolerability and clinical response of cemiplimab in patients with advanced cutaneous squamous cell carcinoma: a retrospective, multicentre cohort study from The Netherlands. *EJC Skin Cancer*, *1*, 100007. doi.org/10.1016/j.ejcskn.2023.100007

Samaran, Q., Bettuzzi, T., & Sbidian, E. (2026). Comparative effectiveness of first-line anti-PD-1 versus cetuximab in advanced cutaneous squamous cell carcinoma: A nationwide population-based study using the French national health data system. *European Journal of Cancer, 237*, Article 116585. doi.org/10.1016/j.ejca.2026.116585

Verkerk, K., Geurts, B. S., Zeverijn, L. J., van der Noort, V., Verheul, H. M., Haanen, J. B., ... & Bloemendal, H. J. (2024). Cemiplimab in locally advanced or metastatic cutaneous squamous cell carcinoma: prospective real-world data from the DRUG Access Protocol. *The Lancet Regional Health–Europe*, *39*. doi.org/10.1016/j.lanepe.2024.100875

Yakobson, A., Abu Jama, A., Abu Saleh, O., Michlin, R., & Shalata, W. (2023). PD-1 inhibitors in elderly and immunocompromised patients with advanced or metastatic cutaneous squamous cell carcinoma. *Cancers, 15*(16), Article 4041. doi.org/10.3390/cancers15164041