



Review Article

AI-Driven Checkpoint Inhibitor Response in Precision Oncology

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Artificial intelligence (AI) is transforming precision oncology by helping predict responses to immune checkpoint inhibitors (ICIs) into cancers such as non-small cell lung cancer. Biomarkers like tumor mutational burden (TMB) and PD-L1 expression guide treatment decisions, but their predictive value can vary across tumor types and patient populations. AI-driven models that integrate genomic, imaging, and clinical data improve precision, yet high costs, data complexity, and limited implementation restrict widespread adoption. Emerging models using more accessible variables such as cancer type, age, prior therapy, albumin levels, and neutrophil-to-lymphocyte ratio offer practical alternatives that complement TMB-based prediction. In Africa, challenges are heightened by limited biomarker testing, underrepresentation in global genomic datasets, and the risk of algorithmic bias. However, Africa's substantial genetic diversity offers opportunities to advance understanding of tumor-immune interactions. Building robust local data ecosystems, strengthening computational capacity, and supporting African-led AI innovation will be essential for equitable integration of AI in cancer immunotherapy. These efforts directly align with the Sustainable Development Goals, particularly SDG 3 (Good Health and Well-Being) and SDG 9 (Industry, Innovation, and Infrastructure), ensuring that emerging technologies benefit all populations, including those across Africa.

Keywords: AI, Immune Checkpoint Inhibitors, Precision Oncology, Machine Learning, Predictive Biomarkers, Tumor Mutational Burden, Algorithmic Bias, African Genomic Diversity, Immuno-oncology, Clinical Decision Support.

INTRODUCTION

Artificial intelligence (AI) and machine learning (ML) are increasingly applied in precision oncology to integrate molecular, clinical, and imaging data, facilitating the discovery of new biomarkers and supporting individualized treatment strategies. In cancer immunotherapy with immune checkpoint inhibitors (ICIs), AI is particularly valuable for analyzing complex datasets to predict patient responses and uncover mechanisms of resistance (Fountzilias et al. 2025). Immuno-oncology aims to modulate the host immune system to recognize and eliminate tumor cells through approaches such as ICIs, chimeric antigen receptor T (CAR-T) cell therapy, cytokines, and therapeutic vaccines. Among these, ICIs targeting programmed cell death protein 1

(PD-1)/programmed death-ligand 1 (PD-L1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) have transformed cancer care by producing durable responses across several malignancies (Hargadon et al. 2018; Obeagu 2025). However, therapeutic outcomes remain variable, reflecting tumor heterogeneity, complexity of the immune microenvironment, and the absence of universally reliable biomarkers (Nagasaki et al. 2022). Biomarkers such as tumor mutational burden (TMB), microsatellite instability (MSI), and tumor-infiltrating lymphocytes (TILs) are widely used to guide patient selection for ICIs. However, their predictive accuracy differs across cancer types and populations (Presti et al. 2022; Vega et al. 2021). AI-driven approaches,

including ML-based TIL quantification from routine histology, have improved the prediction of ICI response compared with traditional biomarkers (Rakae et al. 2023). Similarly, deep-learning (DL) models applied to transcriptomic and imaging data have identified immune signatures associated with treatment outcomes (Zhang et al. 2023; Shamaï et al. 2022). So far, advancements in AI have produced tools such as IBM Watson for Health, PathAI, Owkin, Deep Genomics, and Immunai (**Figure 1**), which support patient stratification, biomarker discovery,

target identification, and pathology analysis (Griffin et al. 2022; Philippidis 2020; Svrcek et al. 2022; Unger et al. 2024; Zhou et al. 2019). However, these advances are limited by data availability, algorithmic bias, and the underrepresentation of African genomic diversity restricts model generalizability (Cau et al., 2025, Olatunji et al., 2023). Addressing these disparities through inclusive data generation, federated learning, and African-led AI development will be essential to ensure equitable integration of AI-driven immuno-oncology.

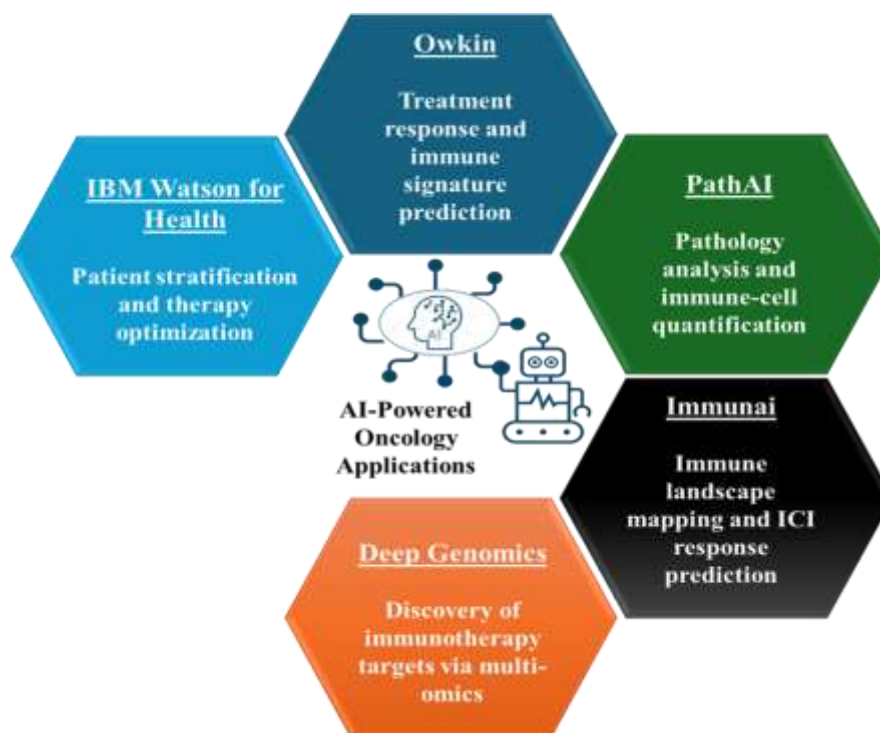


Figure 1. AI platforms drive immune oncology. These tools, IBM Watson for Health, PathAI, Owkin, Deep Genomics, and Immunai, analyze multi-omic, imaging, and clinical data to enable patient stratification, identify predictive biomarkers, and support immunotherapy target discovery in precision oncology.

2. Tumor Immunology and AI-Driven Immuno-Oncology

Immune checkpoint pathways regulate T-cell activation through receptor-ligand interactions. Key inhibitory receptors include PD-1, CTLA-4, lymphocyte-activation gene 3 (LAG3), T-cell immunoglobulin and mucin-domain containing-3 (TIM3), T cell immunoreceptor with Ig and ITIM domains (TIGIT), primarily on T lymphocytes

(Kamali et al. 2023). PD-1 binding to PD-L1/PD-L2 on tumor or antigen-presenting cells inhibits T-cell activation, proliferation, and cytokine production (Gutic et al. 2023). ICIs, such as anti-PD-1 (nivolumab, pembrolizumab), anti-PD-L1 (atezolizumab, durvalumab), and anti-CTLA-4 (ipilimumab), restore antitumor immunity and improve clinical outcomes across malignancies (Hargadon et al. 2018; Obeagu 2025). Resistance arises mainly from impaired antigen recognition, T-cell infiltration, or effector dysfunction (Nagasaki et al. 2022). Tumor mutational burden reflects neoantigen load (Sun et al. 2025), and convolutional neural networks (CNNs) on H&E slides can predict high-TMB tumors using TIL counts (Shimada et al. 2021). MSI from DNA mismatch repair deficiencies enhances ICI sensitivity, with AI/ML models improving predictive accuracy from histopathology

(Hildebrand et al. 2021; Yamaguchi et al. 2024; Johannet et al. 2025). The tumor microenvironment (TME) also modulates ICI response, where higher TIL density correlates with better survival (Presti et al. 2022). ML-based quantification enables automated assessment integrated into routine pathology workflows, sometimes outperforming TMB alone (Rakaee et al. 2023). Integrated predictive models combining transcriptomic and clinical data can stratify patients by immune-evasion signatures, outperforming conventional pathologic factors (Xue et al. 2025). To address these challenges and leverage tumor biomarkers effectively, AI and ML approaches can integrate histopathology, genomic, imaging, and clinical data, enhancing predictive power and supporting patient stratification. AI enhances immuno-oncology by integrating complex multi-omic, imaging, and clinical datasets (Krishnan et al. 2023; Swanson et al. 2023). Key AI models include deep learning (DL), natural language processing (NLP), radiomics, radiogenomics, and predictive modeling (Evangelou et al. 2025). Deep learning identifies non-linear relationships among genomic alterations, immune gene expression, and clinical outcomes, enabling accurate response predictions across cancer types (Baiao et al. 2025; Shamai et al.

2022; Hu et al. 2021; Wang et al. 2024). In resource-limited settings, AI can overcome limitations of scarce or low-quality data, such as MRI imaging for brain tumors (Parida et al. 2024). Ensemble and autoencoder models integrate single-cell and bulk RNA-seq or transcriptomic/genomic data to stratify likely responders and non-responders to ICIs (Bourlard et al. 2022; Xu et al. 2023; Shamai et al. 2022; Zhang et al. 2023). AI approaches span ML classifiers, DL models, NLP, multi-omics frameworks, and federated/transfer learning (**Table 1**). CNNs on digitized H&E slides identify TIL clusters, stromal patterns, and PD-L1 expression (Hu et al. 2021; Rauf et al. 2023). Radiomics captures spatial heterogeneity and immune phenotypes from CT scans, MRI, and PET scans, while integrative genomics compresses high-dimensional molecular and clinical data to stratify patients (Banchereau et al. 2016; Wu et al. 2025). Spatial transcriptomics and AI-driven clustering map immune niches predictive of therapy response (Aung et al. 2025). Multi-omics AI identifies novel biomarkers, maps immune cell distributions, and connects imaging phenotypes to molecular alterations (Ge et al. 2025; Hu et al. 2021; Park et al. 2025; Wu et al. 2025; Reel et al. 2021).

Table 1. Key AI Approaches in Immuno-Oncology, Data Types, Predictive Features, and Clinical Utility.

Artificial intelligence approach/model	Data types integrated	Key predictive features	Cancer types studied	Clinical or research utility	References
Machine-learning classifiers (random forest, support vector machine, gradient-boosted trees)	Somatic mutation panels, gene expression, clinical, and laboratory data	Tumor mutational burden, PDL-1 expression, neoantigen load, composite gene signatures	Melanoma, non-small-cell lung cancer	Stratification of responders and improved survival prediction	(Samstein et al. 2019; Yang et al. 2024)
Deep-learning models (convolutional neural networks, autoencoders)	Digital histopathology images, computed tomography, and positron emission tomography	Spatial maps of tumor-infiltrating immune cells; tumor microenvironment phenotypes; digital surrogates of immune biomarkers	Multiple solid tumors, including non-small-cell lung cancer, melanoma, colorectal cancer	Automated immune phenotyping and imaging-based prediction of response	(Abousamra et al. 2021; Liu et al. 2025; Saltz et al. 2018)
Natural-language processing on clinical text	Electronic health records, clinical notes, pathology reports	Contextual and temporal clinical features	Breast, lung, & colorectal cancers	Extraction of outcomes, trial matching, and adverse-event monitoring	(Munzone et al. 2024; Zeng et al. 2021)

Multi-omics integration frameworks	Genomic, transcriptomic, proteomic, T-cell receptor sequencing	T-cell exhaustion and immune resistance features	Melanoma, non-small-cell lung cancer	Identification of resistance mechanisms and multi-omic prediction	(Anagnostou et al. 2020; Riaz et al. 2017; Xu et al. 2024)
Federated learning and transfer-learning approaches	Multi-site imaging and clinical datasets	Site-independent imaging and immune-related features	Breast, lung, & prostate cancers	Privacy-preserving cross-site model training and inclusion of underrepresented populations	(Pati et al. 2022; Teo et al. 2024)

Real-time AI monitoring of immune activation and toxicity is emerging. Blood, cytokine, and imaging data analyzed through ML detect early immune-related adverse events, while NLP on electronic health records identifies early symptoms (Cajander et al. 2024; Guo et al. 2023; Chalasani et al. 2023). Wearable biosensors allow continuous patient monitoring for subclinical immune responses (Chitnis et al. 2023; Schneider et al. 2021). Clinically validated

AI models outperform manual scoring for PD-L1 and TIL quantification, estimate TMB computationally, and integrate multi-omic immune signatures such as interferon-gamma and cytolytic activity to guide ICI therapy (Prelaj et al. 2024; Michaels et al. 2024; Vega et al. 2024). These diverse AI approaches form a comprehensive ecosystem supporting immuno-oncology, from biomarker discovery to patient stratification, which is illustrated in **Figure 2**.

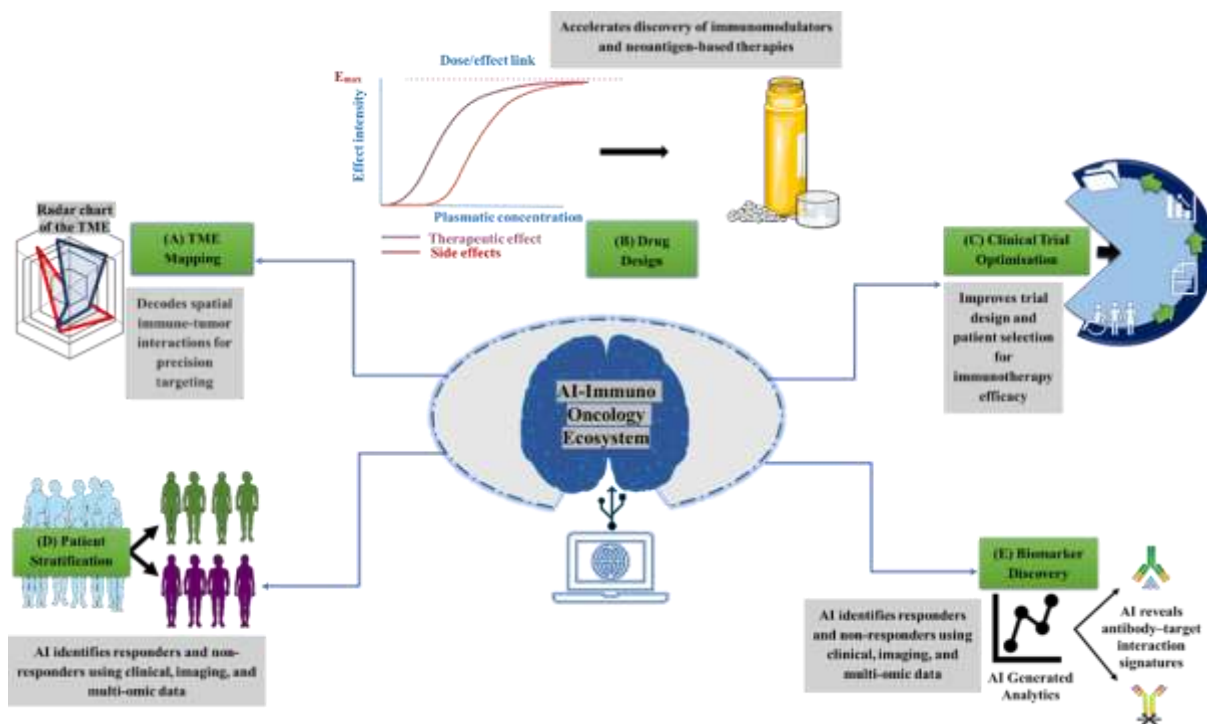


Figure 2. Integrated AI-Immuno-Oncology Ecosystem. This figure illustrates how (A) tumor microenvironment mapping, (B) drug design, (C) clinical trial optimization, (D) patient stratification, and (E) biomarker discovery interact to enhance precision targeting and accelerate immunotherapy development

3. Precision Oncology and Clinical Translation in the African Context

Precision oncology aims to tailor cancer treatment based on molecular and genomic profiling, improving efficacy, reducing toxicity, and promoting equitable

outcomes (Horgan et al. 2025). In Africa, implementation is constrained by limited infrastructure, workforce shortages, and underrepresentation of African genomes in global datasets, which reduces the relevance of many diagnostic tools and therapies (Ashinze et al. 2025; Gueye et al. 2024). Strengthening regional collaboration, sustainable funding, and policy frameworks is critical to ensure research and clinical applications reflect Africa's genetic diversity and healthcare realities (Rulten et al. 2023; Wang et al. 2023). These efforts directly support SDG 3 by aiming to reduce cancer-related morbidity and mortality and improve equitable access to precision therapies. High-throughput sequencing enables identification of driver mutations, gene fusions, and pathway alterations that shape treatment response. However, adoption of ICIs and other precision therapies is limited by costs, scarce biomarker testing, and inadequate diagnostic infrastructure (Olatunji et al. 2023). AI can enhance the prediction of immune responses, integrate genomic and imaging data, and identify novel biomarkers, supporting personalized decision-making. Precision approaches can improve cost-effectiveness by reducing ineffective treatments and hospitalizations and by informing pharmacogenomic-guided dosing to enhance safety biomarkers, and integrating genomic with imaging data to guide clinical decision-making (Olagunju 2023; Steijger et al. 2022; Weth et al. 2024; Saleem et al. 2025). Less than 2% of global genomic data is derived from African populations, leading to variant misclassification and limited biomarker accuracy (Adebamowo et al. 2023; Bentley et al. 2020; Zhang et al. 2022). Distinct mutational landscapes in triple-negative breast cancer, prostate cancer, and hepatocellular carcinoma demonstrate the need for locally relevant predictive tools (Ansari-Pour et al. 2021; Yao et al. 2025). AI models trained on homogeneous datasets risk bias and underperformance in African cohorts, emphasizing inclusion of African genomic and clinical data for equitable precision medicine (Cau et al. 2025). Robust data infrastructure and governance are essential for multi-site AI development, harmonized standards, and federated learning (Jiang et al. 2025; Mboowa et al. 2024). Investments in genomic hubs, bioinformatics training, and secure computing enable large-scale local model development. Initiatives such

as H3ABioNet and African Centres of Excellence in Bioinformatics expand capacity, though digital divides between urban and rural institutions persist (Akingbola et al. 2024; Kabukye et al. 2022; Rotimi et al. 2020). Biological and environmental factors, including infection burden, diet, and exposure, influence TME, creating context-specific immune and stromal profiles that affect treatment response (Simba et al. 2022; Yao et al. 2025). Ethical and governance frameworks, including informed consent, benefit sharing, and data sovereignty, are central to African-led AI and precision oncology initiatives (de Vries et al. 2015; Kabata et al. 2023; Tindana et al. 2019). In clinical translation, AI and ML enhance cancer care by supporting screening, diagnosis, prognosis, imaging, therapeutic planning, and integration of multi-omics data (Absalan et al. 2025). Accurate predictive biomarkers are essential due to heterogeneity in patient responses to ICIs, influenced by tumor-intrinsic, microenvironmental, and host immune factors (Sankar et al. 2022). AI applications have progressed from experimental models to clinically evaluated tools, improving biomarker prediction, patient stratification, and identification of novel immune-related biomarkers (Oisakede et al. 2025; Olawade et al. 2025). AI supports clinical trial optimization, including patient recruitment and cohort selection. Decision-tree and random-forest algorithms, NLP models, and transformer-based DL methods analyze electronic health records, genetic data, and demographic information to match patients to suitable trials and improve trial efficiency, particularly for rare cancers (Lotter et al. 2024). Transition to clinical practice requires careful external and multi-site validation to ensure generalizability across diverse populations (Fountzilias et al. 2025; Oisakede et al. 2025). Adaptive learning approaches, where AI systems update continuously with new patient data, can enhance model robustness and clinical applicability (Bobowicz et al. 2025).

4. Challenges and Ethical Implications

Africa generates vast amounts of health data, yet much remains inaccessible or poorly curated, limiting its integration into AI systems. High data costs and limited connectivity exclude large populations from contributing to digital datasets, reinforcing dependence on Global North data sources (Pasipamire

et al. 2024). As a result, African demographics and clinical patterns remain underrepresented, and economic value rarely returns to local communities (Grancia 2025; Pham 2025; Hassan 2023). Weak institutional capacity, fragmented data systems, and uneven regulatory structures further hinder safe AI deployment, while only 28% of sub-Saharan Africans have internet access, restricting participation in global genomic and clinical modelling initiatives (Pasipamire et al. 2024; Victor 2025). Equity remains central but difficult to achieve; SDG 3 and SDG 9 highlight the need for stronger health systems and digital infrastructure (Pasipamire et al. 2024; United Nations 2025). Africa's historical exclusion from therapeutic development contributes to poorer outcomes (Chin et al. 2023; Grancia 2025). AI models trained predominantly on non-African datasets inherit these inequities, producing misclassification, misdiagnosis, and biased resource allocation, especially in low-resource environments (Akingbola et al. 2024; Chin et al. 2023; Joseph 2025). Addressing these gaps requires fairness audits, diverse development teams, multilingual or synthetic datasets, and community engagement throughout the AI lifecycle (Batoool et al. 2025; Ajibade et al. 2025; Chin et al. 2023). While high-income countries adopted oncology AI earlier, African implementation largely accelerated after 2018, reflecting persistent gaps in investment and infrastructure (Akingbola et al. 2024). Kenya, Ghana, South Africa, and Egypt are expanding AI use in health and social services, but regulatory preparedness varies widely (Grancia 2025; Pasipamire et al. 2024). Ethical governance, including informed consent, data privacy, and human oversight, is essential for trustworthy oncology applications (Ajibade et al. 2025; Mennella et al. 2024). Rapid expansion raises concerns about unconsented data extraction from the Global South; frameworks such as UNESCO's AI Ethics Recommendations aim to safeguard equity, sustainability, and responsible deployment (Nina M. Waals 2025).

5. Future Directions and Conclusion

Precision oncology is rapidly evolving, with ICIs and targeted therapies improving outcomes (Lin et al. 2025). AI, including ML and DL, has emerged as a key tool for analysing complex datasets, enhancing diagnostics, guiding treatment decisions, and

monitoring therapy responses (Rehan 2024). Effective integration requires representative datasets and robust technological infrastructure to ensure equitable impact across populations (Lin et al. 2025). Many AI models function as "black boxes," limiting transparency and clinician oversight, which can perpetuate bias (Mohamed et al. 2025). Explainable AI methods are essential for interpretability, ethical integration, and patient-centered decision-making (Garg 2025; Rehan 2024). AI systems must be adaptable to both high- and low-resource settings, supporting mobile screening, tele-oncology, and point-of-care diagnostics. South-South partnerships among Africa, Asia, and Latin America can improve representation in clinical and genomic datasets, reducing bias and enhancing generalizability (Manson et al. 2023; Waljee et al. 2022). Capacity building in AI research, oncology informatics, and data governance, alongside investment in secure data-sharing and scalable computing solutions, will strengthen local implementation (Manson et al. 2023; Sebastian et al. 2022). African-led AI initiatives can reshape global oncology by integrating population-specific biology and locally driven research agendas (Dako et al. 2025). Ethical frameworks and regulatory guidelines are essential to ensure transparency, accountability, and patient benefit (Far 2023). AI offers transformative potential in oncology, particularly in underrepresented and resource-limited settings. Realizing this potential requires addressing data bias, infrastructure gaps, and transparency challenges, while fostering collaboration, inclusivity, and ethical governance. Prioritizing patient-centred strategies and equitable implementation can advance precision oncology globally and help bridge disparities in cancer care.

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