

## Review Article

# Personalised Cancer Treatment: The Era of Precision Oncology - A Comprehensive Review

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## ABSTRACT

Personalised cancer treatment, also known as precision oncology, represents a paradigm shift from conventional “one-size-fits-all” cancer therapy towards an approach guided by the unique genetic, molecular, and environmental characteristics of each patient and tumour. Advances in genomics, molecular diagnostics, and bioinformatics have enabled targeted and immune-based therapies that significantly improve outcomes and reduce toxicity. This study was therefore set up to provide a comprehensive review of the principles, clinical applications, current challenges, and future directions of personalized cancer treatment in the era of precision oncology.

Relevant peer-reviewed literature published in the past decade (2015–2025) was reviewed from databases including PubMed, Scopus, and Google Scholar. Emphasis was placed on studies exploring molecular biomarkers, targeted therapy, immunotherapy, and pharmacogenomics across various cancer types. The study found that the integration of molecular profiling and targeted therapeutics has transformed cancer management, with substantial clinical benefits in malignancies such as breast, lung, colorectal, and melanoma. Emerging technologies—including next-generation sequencing, liquid biopsy, and artificial intelligence enhance diagnosis, treatment selection, and real-time disease monitoring. However, challenges persist in accessibility, cost, ethical regulation, and tumour heterogeneity, particularly in low- and middle-income countries. Precision oncology has indeed shown to redefine cancer care, enabling therapies tailored to individual molecular and clinical profiles. Broader implementation requires equitable access to molecular diagnostics, multidisciplinary collaboration, and integration of AI-driven decision tools to realise the full promise of personalised medicine globally.

**Keywords:** Biomarkers, Cancer treatment, Genomics, Immunotherapy, Personalised medicine, Pharmacogenomics, Precision oncology, Targeted therapy

## INTRODUCTION

Personalised cancer treatment, also known as precision oncology, represents a transformative approach that tailors therapeutic interventions to the unique molecular and genetic characteristics of an individual's tumour rather than applying uniform treatment protocols<sup>1</sup>. The evolution of this concept

has been driven by rapid advances in genomics, molecular diagnostics, and targeted therapeutics, which have enabled identification of actionable mutations and specific biomarkers that guide therapy selection<sup>2,3</sup>.

Conventional cancer management relied largely on histopathological classification and empirical

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chemotherapy. However, with the advent of next-generation sequencing (NGS) and liquid biopsy technologies, clinicians can now perform real-time molecular profiling, detect minimal residual disease (MRD), and monitor tumour evolution non-invasively<sup>4,5</sup>. This has paved the way for highly specific treatment strategies such as tyrosine kinase inhibitors (TKIs) for EGFR-mutated lung cancer, HER2-targeted monoclonal antibodies for breast cancer, and immune checkpoint inhibitors for malignancies expressing PD-L1 or microsatellite instability-high (MSI-H) phenotypes<sup>6,7</sup>. (Table 1)

Despite the remarkable clinical benefits,

implementation of precision oncology remains limited by tumour heterogeneity, emergent drug resistance, high cost, and restricted access to molecular testing in low- and middle-income regions<sup>8,9</sup>. Moreover, ethical and regulatory issues surrounding genomic data use continue to pose challenges to global adoption<sup>10</sup>.

This review critically examines the evolution, molecular basis, diagnostic innovations, and clinical applications of personalised cancer treatment, highlighting key therapeutic advances, ongoing challenges, and emerging opportunities for global integration of precision oncology. (Table 1)

Table 1: Evolution of Cancer Treatment Paradigms

Era	Key Therapeutic Approach	Guiding Principle	Examples
Pre-2000s	Conventional chemotherapy	Non-specific cytotoxic drugs	Cisplatin, Doxorubicin
2000–2010	Targeted therapy	Molecular targets identified	Imatinib (BCR-ABL), Trastuzumab (HER2)
2010–2020	Precision oncology	Genomic profiling and biomarkers	EGFR-TKIs, ALK inhibitors
2020–Present	Data-driven personalised medicine	Multi-omics and AI integration	ctDNA, AI-guided therapy, neoantigen vaccines

The evolution of cancer treatment from traditional cytotoxic chemotherapy to precision oncology has been driven by advances in molecular biology, genomics, and targeted therapy development. The Human Genome Project and subsequent breakthroughs in next-generation sequencing (NGS) paved the way for precision-guided therapeutics and biomarker-based treatment strategies (Table 1). This paradigm shift is summarized through major milestones, including molecular subtyping, immunotherapy, and integration of multi-omics approaches<sup>1–6,12,21,25</sup>.

**Molecular Basis of Personalised Cancer Therapy.** The foundation of personalised cancer treatment lies in understanding the molecular alterations that drive tumour initiation, progression, and therapeutic response<sup>11</sup>. Advances in cancer genomics have revealed that malignancies once classified by organ or histology are, in fact, molecularly heterogeneous, defined by specific driver mutations, epigenetic modifications, and signalling pathway aberrations<sup>12,13</sup>. These insights have enabled the development of therapies targeting distinct molecular lesions, fundamentally reshaping oncology practice<sup>14</sup>.

**Genomic and Epigenetic Alterations:** High-throughput next-generation sequencing (NGS) has

allowed comprehensive characterisation of somatic mutations, copy number variations, and chromosomal rearrangements across tumour genomes<sup>15</sup>. Oncogenic drivers such as EGFR, KRAS, BRAF, PIK3CA, and ALK have become actionable biomarkers with corresponding targeted therapies<sup>16</sup>. Similarly, HER2 amplification in breast and gastric cancers predicts response to trastuzumab and other HER2-directed agents<sup>17</sup>.

Epigenetic mechanisms, including DNA methylation, histone modification, and non-coding RNA regulation, also influence tumour behaviour and drug response<sup>18</sup>. Aberrant promoter methylation can silence tumour suppressor genes such as MLH1 and BRCA1, leading to genomic instability<sup>19</sup>. Understanding these alterations has spurred the development of epigenetic therapies such as histone deacetylase (HDAC) inhibitors and DNA methyltransferase (DNMT) inhibitors, which are now under clinical evaluation<sup>20</sup>.

**Tumour Microenvironment and Molecular Crosstalk:** The tumour microenvironment (TME) comprising immune cells, stromal components, and extracellular matrix plays a pivotal role in tumour progression and therapeutic resistance<sup>21</sup>. Crosstalk between cancer cells and the TME via cytokines,

growth factors, and exosomes influences tumour growth and metastatic potential <sup>22</sup>. Molecular profiling of the TME has identified immune checkpoints (PD-1, PD-L1, CTLA-4) as therapeutic targets, leading to the success of immune checkpoint inhibitors across multiple cancers <sup>23,24</sup>. (Table 2)

**Multi-Omics Integration:** Recent advances integrate genomics, transcriptomics, proteomics, and metabolomics to provide a systems-level understanding of cancer biology <sup>25</sup>. Multi-omics approaches improve biomarker discovery, predict

drug response, and elucidate resistance mechanisms <sup>26</sup>. Integration of these datasets through artificial intelligence (AI) and machine learning algorithms is enhancing precision in patient stratification and therapeutic decision-making <sup>27,28</sup>. (Table 2)

Overall, the molecular understanding of cancer has transformed therapeutic paradigms from conventional cytotoxic regimens to biomarker-guided precision medicine, marking a cornerstone in modern oncology <sup>29</sup>.

Table 2: Major Molecular Biomarkers and Associated Targeted Therapies

Cancer Type	Key Biomarker	Targeted Agent(s)	Clinical Application
Breast	HER2 amplification	Trastuzumab, Pertuzumab	HER2-positive breast cancer
Lung	EGFR mutation, ALK fusion	Osimertinib, Alectinib	NSCLC targeted therapy
Colorectal	KRAS/NRAS, BRAF V600E	Cetuximab, Encorafenib	Predicts anti-EGFR therapy response
Melanoma	BRAF V600E	Dabrafenib, Vemurafenib	Targeted therapy for metastatic disease
Prostate	BRCA1/2, ATM	Olaparib	PARP inhibition in DNA repair-deficient tumours
Haematologic	FLT3, IDH1/2	Midostaurin, Ivosidenib	Targeted acute myeloid leukemia therapy

Recent multicenter analyses have highlighted regional disparities in receptor expression patterns, with variable proportions of ER-PR-and HER2-negative tumors across African and global cohorts (Table 2)<sup>4-17</sup>

### Therapeutic Modalities in Precision Oncology

The molecular characterisation of tumours has revolutionised therapeutic strategies, enabling clinicians to tailor treatments to specific molecular aberrations rather than relying on broad cytotoxic chemotherapy <sup>30</sup>. The main modalities that define precision oncology include targeted therapies, immunotherapy, gene- and cell-based therapies, and pharmacogenomics-driven interventions, each contributing to improved outcomes and reduced treatment-related toxicity <sup>31</sup>.

**Targeted Therapies:** Targeted therapy exploits specific genetic mutations and dysregulated signalling pathways driving tumour growth <sup>32</sup>. Small-molecule inhibitors and monoclonal antibodies act on targets such as EGFR, BRAF, HER2, ALK, and PI3K, showing significant benefits in selected patient subsets <sup>33</sup>.

For instance, EGFR-mutated non-small cell lung cancer (NSCLC) responds to osimertinib, while BRAF V600E-mutated melanoma demonstrates a durable response to dabrafenib and trametinib <sup>34</sup>. Similarly, HER2-positive breast cancer patients benefit from trastuzumab, pertuzumab, and trastuzumab deruxtecan, which have markedly

improved survival outcomes <sup>35</sup>.

Resistance to targeted therapy, however, remains a challenge. Secondary mutations, pathway reactivation, and tumour heterogeneity often lead to relapse <sup>36</sup>. Combination regimens and sequential targeting strategies are being explored to overcome resistance mechanisms <sup>37</sup>.

**Immunotherapy:** This represents a major leap in personalised cancer care by harnessing the patient's immune system to recognise and eradicate tumour cells <sup>38</sup>. Immune checkpoint inhibitors (ICIs), including anti-PD-1, anti-PD-L1, and anti-CTLA-4 antibodies, have achieved unprecedented responses in melanoma, lung, and renal cancers <sup>39</sup>. Predictive biomarkers such as PD-L1 expression, tumour mutational burden (TMB), and microsatellite instability-high (MSI-H) status are used to identify responsive patients <sup>40</sup>. Tumour-agnostic approvals—such as pembrolizumab for MSI-H or TMB-high tumours—highlight the transition toward molecularly defined treatment across cancer types <sup>41</sup>.

However, immune-related adverse events, non-responsiveness in some patients, and the cost of therapy remain significant barriers <sup>42</sup>. Ongoing research aims to develop personalised cancer

vaccines, oncolytic viruses, and adoptive cell transfer (ACT) strategies to enhance specificity and reduce toxicity<sup>43</sup>.

**Gene and Cell-Based Therapies:** Gene- and cell-based interventions target the genetic root of malignancy through genomic modification or immune reprogramming. Chimeric antigen receptor (CAR) T-cell therapy has shown remarkable efficacy in refractory haematologic malignancies by redirecting T-cell cytotoxicity against tumour-associated antigens<sup>44</sup>.

Emerging gene editing tools, such as CRISPR-Cas9, allow correction of pathogenic mutations and engineering of resistant immune cells, paving the way for durable remission<sup>45</sup>. While currently limited by manufacturing costs and safety considerations, these approaches represent the future frontier of precision oncology<sup>46</sup>.

**Pharmacogenomics:** This studies the influence of genetic variation on drug metabolism, efficacy, and toxicity, allowing dose individualisation and avoidance of adverse reactions<sup>47</sup>. Variants in genes such as TPMT, DPYD, and UGT1A1 affect response to thiopurines, fluoropyrimidines, and irinotecan, respectively<sup>48</sup>. Incorporating pharmacogenomic testing into clinical decision-making enhances treatment safety and optimises therapeutic outcomes<sup>49</sup>.

#### Integration of Therapeutic Modalities:

Modern precision oncology increasingly integrates targeted, immune, and pharmacogenomic approaches, informed by molecular diagnostics and computational analytics. The convergence of these modalities—often in combination therapies—aims to achieve durable remission, delay resistance, and personalise treatment sequencing<sup>50,51</sup>. (Table 3)

Table 3: Clinical and Technological Components of Precision Oncology

Component	Function	Examples/Tools
Genomic Profiling	Detects actionable mutations	NGS panels, Whole exome sequencing
Liquid Biopsy	Non-invasive tumour monitoring	ctDNA, CTCs, exosomes
Companion Diagnostics	Matches drugs to biomarkers	FoundationOne CDx, Guardant360
Immunotherapy	Immune checkpoint blockade	Anti-PD-1/PD-L1, CTLA-4 inhibitors
Data Integration	Multi-omics data synthesis	Bioinformatics, AI, cloud-based platforms

#### Diagnostic and Technological Innovations in Precision Oncology:

The success of personalised cancer treatment relies on the precision and sensitivity of diagnostic technologies that detect actionable mutations, guide therapy selection, and monitor therapeutic response. Over the past decade, innovations in molecular diagnostics, imaging, and bioinformatics have revolutionised cancer care by enabling earlier detection, accurate molecular classification, and dynamic disease monitoring<sup>52,53</sup>.

**Next-Generation Sequencing (NGS):** NGS remains the backbone of precision oncology, allowing high-throughput analysis of multiple oncogenic mutations, copy number variations, and gene fusions<sup>54</sup>. It supports tumour profiling at the genomic, transcriptomic, and epigenetic levels, facilitating the identification of therapeutic targets in cancers such as EGFR-mutated lung adenocarcinoma, BRAF-mutant melanoma, and

ALK translocations<sup>55,56</sup>. The emergence of whole-exome and whole-genome sequencing has further expanded molecular understanding of tumour biology and resistance mechanisms<sup>57</sup>.

**Liquid Biopsy and Circulating Biomarkers:** Liquid biopsy, which detects circulating tumour DNA (ctDNA), circulating tumour cells (CTCs), and exosomes in blood or body fluids, represents a non-invasive alternative to tissue biopsy<sup>58,59</sup>. It enables longitudinal monitoring of tumour evolution, early detection of minimal residual disease (MRD), and assessment of therapeutic resistance<sup>60,61</sup>. ctDNA-based assays such as Guardant360 and FoundationOne Liquid CDx have gained clinical validation for guiding targeted therapy<sup>62,63</sup>.

**Artificial Intelligence and Bioinformatics:** The integration of artificial intelligence (AI) and machine learning (ML) tools has enhanced diagnostic precision by automating pattern recognition, genomic data interpretation, and

predictive modelling<sup>64</sup>. AI-assisted image analysis supports histopathologic classification, while ML algorithms correlate multi-omic data with treatment outcomes, enabling adaptive therapy design<sup>65,66</sup>.

#### **Radiogenomics and Functional Imaging:**

Radiogenomics integrates imaging phenotypes with genomic data to non-invasively infer tumour biology and treatment response<sup>67</sup>. Techniques such as positron emission tomography (PET), multiparametric MRI, and radiomics are increasingly used to correlate molecular features with radiological patterns<sup>68,69</sup>. These advances enable early prediction of response to immunotherapy and detection of metastatic potential.

#### **Digital Pathology and Multi-Omic Integration:**

Digital pathology platforms and multi-omic integration (genomic, proteomic, metabolomic, and epigenomic data) offer a comprehensive landscape of tumour heterogeneity<sup>70,71</sup>. This integrated approach improves precision in diagnosis and guides personalised treatment planning, forming the cornerstone of systems oncology.

#### **Clinical Applications of Personalised Cancer Therapy:**

The translation of molecular and genomic discoveries into clinical oncology has redefined cancer management. Precision oncology enables the selection of therapies based on specific genetic aberrations, molecular pathways, and tumour microenvironment profiles, rather than tumour origin alone<sup>72</sup>. This section outlines the most impactful applications across major cancer types.

**Breast Cancer:** Breast cancer remains a prototype for personalised oncology through the integration of hormone receptor testing and HER2-targeted therapy<sup>73</sup>. Determination of estrogen receptor (ER), progesterone receptor (PR), and HER2/neu status guides hormonal therapy and targeted drug use<sup>74</sup>. HER2-positive tumours benefit from trastuzumab, Pertuzumab, and ado-trastuzumab emtansine (T-DM1), which have significantly improved survival<sup>75</sup>. Moreover, PIK3CA and BRCA1/2 mutation testing allows the use of PI3K inhibitors (alpelisib) and PARP inhibitors (olaparib, talazoparib) respectively<sup>76,77</sup>.

Molecular subtyping and genomic assays such as

Oncotype DX and MammaPrint further personalise adjuvant therapy by predicting recurrence risk<sup>78,79</sup>.

**Lung Cancer:** Non-small-cell lung cancer (NSCLC) has witnessed dramatic improvements through genotype-directed therapy. Identification of actionable mutations such as EGFR, ALK, ROS1, BRAF, RET, and MET allows targeted treatment using tyrosine kinase inhibitors (TKIs)<sup>80,81</sup>. For instance, osimertinib demonstrates superior progression-free survival in EGFR-mutated NSCLC<sup>82</sup>, while crizotinib, alectinib, and lorlatinib are effective for ALK-rearranged tumours<sup>83</sup>. Immune checkpoint inhibitors such as pembrolizumab and nivolumab are used in tumours expressing PD-L1 or showing high tumour mutational burden (TMB)<sup>84</sup>.

**Colorectal Cancer:** Personalised treatment in colorectal cancer (CRC) is driven by RAS, BRAF, and MSI testing. Patients with KRAS or NRAS wild-type tumours benefit from anti-EGFR monoclonal antibodies (Cetuximab, panitumumab), while BRAF V600E-mutant tumours respond to BRAF/MEK inhibitor combinations<sup>85,86</sup>. Microsatellite instability-high (MSI-H) or mismatch repair-deficient (dMMR) cancers exhibit remarkable sensitivity to immune checkpoint blockade, particularly pembrolizumab<sup>87</sup>. Furthermore, circulating tumour DNA (ctDNA) monitoring assists in minimal residual disease (MRD) detection and early recurrence prediction<sup>88</sup>.

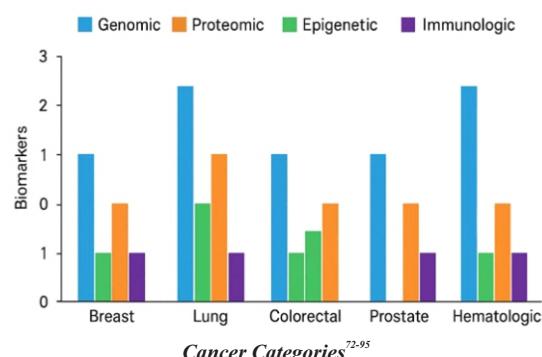
**Melanoma:** Melanoma was among the earliest cancers to benefit from targeted and immune-based therapies. BRAF V600E/K mutations, present in ~50% of cases, are treated with BRAF inhibitors (vemurafenib, dabrafenib) combined with MEK inhibitors (trametinib, cobimetinib), achieving durable responses<sup>89</sup>. Additionally, immunotherapies targeting CTLA-4 (ipilimumab) and PD-1 (nivolumab, pembrolizumab) have revolutionised survival outcomes<sup>90,91</sup>. Integration of genomic profiling has enabled adaptive therapy strategies based on resistance mechanisms and tumour evolution<sup>92</sup>.

**Haematologic Malignancies:** In leukemias and lymphomas, genomic and proteomic profiling drives precise therapeutic targeting. BCR-ABL fusion in chronic myeloid leukemia (CML) is

effectively targeted by imatinib and next-generation TKIs (dasatinib, nilotinib)<sup>9,3</sup>. Similarly, FLT3 and IDH1/2 mutations in acute myeloid leukemia (AML) guide the use of targeted inhibitors (midostaurin, ivosidenib, and enasidenib)<sup>94</sup>. Precision approaches in haematologic cancers have also leveraged CAR T-cell therapy, which reprograms immune cells to recognise specific antigens such as CD19<sup>95</sup>. (Figure 1)

### Emerging Trends

Recent advances include tumour-agnostic therapies, such as larotrectinib and entrectinib for NTRK fusions, and pembrolizumab for MSI-H or TMB-high tumours<sup>96</sup>. These approvals signify a shift toward biomarker-based, rather than site-specific, treatment paradigms. Precision oncology is thus expanding into a molecularly driven, pan-cancer framework.



Clustered bar chart showing the number of genomic, proteomic, epigenetic, and immunologic biomarkers identified across different cancer types. Genomic biomarkers are consistently the most prevalent, highlighting their central role in precision oncology.<sup>72-95</sup>

Figure 1: Distribution of Biomarker Types Across Major Cancer Categories

### Challenges and Limitations of Personalised Cancer Therapy

Despite its transformative promise, personalised cancer treatment faces numerous clinical, technical, ethical, and socioeconomic challenges that hinder its universal implementation, particularly in low- and middle-income countries (LMICs)<sup>97,98</sup>.

**Tumour Heterogeneity and Evolution:** A major biological limitation of precision oncology lies in intra-tumour and inter-tumour heterogeneity, which cause variable therapeutic responses and resistance

<sup>99</sup>. Clonal evolution allows subpopulations of tumour cells to acquire new mutations under therapeutic pressure, leading to treatment escape and disease relapse<sup>100,101</sup>. For example, secondary EGFR T790M or ALK G1202R mutations can confer resistance to TKIs in lung cancer<sup>102,103</sup>. This dynamic evolution necessitates longitudinal molecular monitoring using liquid biopsy or sequential re-biopsy.

### Limited Access to Genomic Testing:

Comprehensive genomic profiling remains largely restricted to high-income settings due to infrastructure deficits, cost, and limited laboratory capacity in LMICs<sup>104</sup>. In Sub-Saharan Africa, fewer than 10% of tertiary hospitals have access to NGS or validated molecular diagnostic platforms<sup>105</sup>. The lack of local biorepositories, bioinformatics infrastructure, and trained molecular pathologists further compounds diagnostic inequality<sup>106</sup>.

**Economic and Logistical Barriers:** The cost of NGS testing, targeted therapy, and immunotherapy is prohibitive for many health systems. For instance, a single round of targeted therapy may cost several thousand USD monthly, rendering long-term access unsustainable<sup>107</sup>. Additionally, cold-chain logistics, patent restrictions, and import delays limit the timely availability of precision drugs in many regions<sup>108,109</sup>.

**Ethical, Legal, and Data Governance Concerns:** Genomic sequencing generates vast amounts of sensitive genetic data, raising privacy and consent challenges. Concerns about genomic data ownership, cross-border sharing, and potential discrimination persist in countries with weak data protection frameworks<sup>110</sup>. International ethical guidelines advocate for transparent governance, secure data storage, and equitable benefit sharing in genomics research<sup>111</sup>.

**Health System Inequities:** Implementation of precision oncology requires multidisciplinary tumour boards, molecular tumour registries, and bioinformatics support, which are often absent in resource-limited environments<sup>112,113</sup>. Furthermore, inequitable inclusion of African and underrepresented populations in global genomic databases limits the clinical relevance of existing biomarkers<sup>114,115</sup>.

### Drug Resistance and Limited Predictive

**Biomarkers:** Even in advanced centres, drug resistance remains a formidable obstacle. Both primary resistance (absence of initial response) and acquired resistance (progression after response) occur frequently across tumour types<sup>116</sup>. Predictive biomarkers for immunotherapy (e.g., PD-L1, TMB, MSI) are imperfect and do not always correlate with clinical benefit<sup>117,118</sup>. Thus, combination strategies and new biomarker discovery are ongoing research priorities. (Table 4)

Table 4: Key Barriers to Global Precision Oncology Implementation

Barrier Category	Specific Limitation	Impact on Care	Possible Solution
Economic	High cost of sequencing and drugs	Limited access to testing and therapy	Subsidised regional hubs
Infrastructure	Lack of molecular labs & databases	Incomplete patient stratification	Regional genomics centres
Human Capacity	Shortage of trained personnel	Delays in interpretation and reporting	Workforce training programs
Ethical/Legal	Data privacy and ownership issues	Restricts data sharing	Stronger genomic governance
Population Diversity	Underrepresentation in datasets	Biased therapeutic outcomes	Inclusion of African/Asian cohorts

Adapted from recent global and regional analyses highlighting socioeconomic, infrastructural, and ethical challenges limiting the implementation of precision oncology in diverse healthcare systems<sup>115, 119-124</sup>.

### Implementation Gaps in LMICs

Precision oncology in Africa faces fragmented health systems, inconsistent funding, and low cancer registry coverage<sup>119,120</sup>. Collaborative initiatives such as the African Cancer Genomics Consortium (ACGC) and H3Africa aim to improve genomic research infrastructure and data harmonisation<sup>121</sup>. Nonetheless, large-scale integration into national cancer control programmes remains limited by political, economic, and human resource constraints<sup>122</sup>.

### Challenges and Limitations in the Implementation of Precision Oncology

Despite the remarkable advances achieved through precision oncology, widespread implementation faces several clinical, infrastructural, socioeconomic, and ethical barriers, especially in low- and middle-income countries (LMICs). These challenges span from technological limitations and cost constraints to data governance and equity issues, ultimately restricting the realisation of personalised care on a global scale<sup>123-127</sup>.

**Economic and Infrastructural Constraints:** High-throughput genomic testing, next-generation sequencing (NGS), and companion diagnostic assays are expensive, limiting their accessibility in

resource-constrained settings. The cost of sequencing and targeted therapies remains prohibitive, while the lack of molecular pathology laboratories and bioinformatics infrastructure exacerbate inequality in access<sup>128,129</sup>. In Africa, only a small fraction of cancer centres possess molecular diagnostic capacity, impeding biomarker-driven therapy<sup>130,131</sup>.

**Limited Genomic Data Diversity:** Current cancer genomic databases are predominantly based on European and North American populations, resulting in underrepresentation of African, Asian, and other ethnic groups<sup>132,133</sup>. This lack of diversity can lead to biased therapeutic insights, inaccurate biomarker interpretation, and limited efficacy of gene-targeted drugs in non-Western populations<sup>134</sup>.

**Tumour Heterogeneity and Drug Resistance:** Intertumoural and intratumoural heterogeneity complicate treatment design and response prediction. Tumours evolve dynamically under therapeutic pressure, leading to the emergence of resistant clones and secondary mutations<sup>135,136</sup>. Mechanisms such as EGFR T790M mutation or ALK fusion variants exemplify adaptive resistance that necessitate continuous molecular monitoring<sup>137</sup>.

**Data Management, Privacy, and Ethical Issues:** Precision oncology relies heavily on massive

genomic datasets, which raise critical concerns regarding data privacy, informed consent, and ethical governance. Issues of data ownership and cross-border sharing hinder collaborative genomic research<sup>138,139</sup>. Moreover, inadequate legal frameworks for genetic data protection in many LMICs amplify these risks<sup>140</sup>.

**Shortage of Trained Personnel:** A successful precision oncology program requires a multidisciplinary team comprising oncologists, pathologists, molecular biologists, bioinformaticians, and genetic counsellors. Unfortunately, a shortage of trained experts in these fields remains a significant obstacle in most developing countries<sup>141,142</sup>.

**Regulatory and Policy Barriers:** The absence of clear national frameworks for molecular testing, approval of targeted therapies, and reimbursement policies limits clinical integration. Regulatory heterogeneity and delayed drug approval timelines further delay access to lifesaving therapies<sup>143,144</sup>.

### Future Directions and Emerging Frontiers in Precision Oncology

The future of cancer therapy is rapidly evolving beyond traditional precision oncology into a multi-dimensional, data-driven era that integrates genomics, proteomics, metabolomics, digital pathology, and artificial intelligence (AI) to refine diagnosis, prognosis, and therapeutic decision-making<sup>145-147</sup>. These emerging frontiers hold the potential to democratise personalised medicine, improve predictive accuracy, and enhance global access to cancer precision care.

**Integration of Artificial Intelligence and Machine Learning:** Artificial intelligence (AI) and machine learning (ML) are transforming oncology by enabling pattern recognition, predictive modelling, and decision support across diagnostic and therapeutic domains<sup>148, 149</sup>. AI-driven algorithms enhance radiomics, pathomics, and genomic data interpretation, improving tumour classification and drug response prediction<sup>150</sup>. For instance, deep learning models can identify subtle histopathological and radiological features that correlate with molecular subtypes and treatment outcomes<sup>151</sup>. Moreover, AI platforms are being

incorporated into clinical workflows to guide biomarker selection, predict immunotherapy response, and detect minimal residual disease (MRD) in real time<sup>152</sup>.

**Multi-Omics and Systems Biology:** The integration of multi-omics technologies—including genomics, transcriptomics, proteomics, metabolomics, and epigenomics—offers a holistic understanding of tumour biology<sup>153,154</sup>. Multi-omic profiling enables identification of novel therapeutic targets and pathway-level vulnerabilities, leading to more effective combination therapies<sup>155</sup>. For example, proteogenomic mapping projects, such as the Clinical Proteomic Tumor Analysis Consortium (CPTAC), are revealing dynamic interactions between genomic alterations and protein-level effects, improving translational relevance<sup>156</sup>.

**Expansion of Liquid Biopsy and Real-Time Monitoring:** Advancements in circulating tumour DNA (ctDNA), circulating tumour cells (CTCs), and exosomal RNA technologies have made liquid biopsy an indispensable tool for non-invasive, longitudinal cancer monitoring<sup>157,158</sup>. These tools facilitate early detection of relapse, therapeutic resistance tracking, and MRD surveillance<sup>159</sup>. As sensitivity and specificity improve, liquid biopsy is anticipated to complement, and in some cases replace, invasive tissue biopsies in clinical oncology<sup>160</sup>.

**Personalized Immunotherapy and Neoantigen Targeting:** Next-generation immunotherapies, such as neoantigen-based vaccines and personalised T-cell receptor (TCR) therapies, are revolutionising the immuno-oncology landscape<sup>161,162</sup>. Advances in bioinformatics now allow patient-specific identification of tumour neoantigen that can elicit robust cytotoxic T-cell responses. These strategies, combined with checkpoint inhibitors, show promise for durable remissions in refractory cancers<sup>163,164</sup>.

**Global Equity and Implementation Science:** A major frontier lies in bridging the equity gap in precision oncology between high-income and low- and middle-income countries (LMICs). Expanding genomic databases to include African and other underrepresented populations will improve therapeutic equity and global relevance<sup>165, 166</sup>.

Implementation science must guide the integration of affordable diagnostic technologies, public-private partnerships, and telemedicine-based molecular tumour boards to build capacity in LMICs<sup>167,168</sup>.

#### Future Outlook:

The convergence of AI, multi-omics, digital pathology, and real-world evidence will define the next generation of precision oncology. Success will depend on cross-disciplinary collaboration, equitable access, transparent data governance, and adaptive clinical trial designs. A patient-centred, globally inclusive model of precision cancer care will be essential to realise the full promise of personalised oncology in the coming decades<sup>169,170</sup>.

#### CONCLUSION

Precision oncology has revolutionised cancer care by aligning therapy with individual molecular and genetic profiles, leading to improved outcomes and reduced toxicity. However, its global impact remains uneven due to economic, infrastructural, and ethical disparities, particularly in low-resource settings. Expanding access to molecular diagnostics, strengthening collaborative research, and integrating AI-driven tools are essential to achieving equitable, personalised cancer treatment worldwide.

#### RECOMMENDATIONS

Enhance access to affordable molecular diagnostics, including NGS and biomarker testing, particularly in regional cancer centres of low- and middle-income countries. Promote inclusion of diverse populations in global genomic databases to improve equity and treatment relevance. Strengthen workforce capacity through international training collaborations in oncology, pathology, molecular biology, and bioinformatics. Integrate AI, telemedicine, and digital pathology to advance precision diagnostics. Establish strong policy and ethical frameworks for genomic data governance and equitable therapy access. Encourage public-private partnerships to drive innovation, research translation, and sustainable precision oncology infrastructure.

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