ISSN: 2347-6567

International Journal of Allied Medical Sciences and Clinical Research (IJAMSCR)

IJAMSCR |Vol.14 | Issue 1 | Jan - Mar -2026

www.ijamscr.com

DOI : https://doi.org/10.61096/ijpar.v14.iss1.2026.199-208

Review

Targeted Therapy in Oncology: Pharmacological Advances and Clinical Challenges

Sayanolla Archana[1], Nandini Penchala[2*], A. Dhanush Kumar[3], HB. Allankritha Sri[4], Akhila Ajith[5], Thota Lakshmi[6]

[1 2 3 4 5 6] *Doctor of Pharmacy, Department of Pharmacy Practice, Malla Reddy College of Pharmacy, Hyderabad, Telangana, India*

*Author for correspondence- Nandini Penchala
Email: drnandinipenchala@gmail.com

Published on:
24.02.2026

Published by:
Futuristic Publications

2026| All rights reserved.

Creative Commons Attribution 4.0 International License.

Abstract

Targeted therapy has fundamentally transformed contemporary oncology by shifting cancer management from empiric cytotoxic chemotherapy toward mechanism-based precision medicine guided by molecular tumor profiling. Unlike conventional chemotherapy, which non-selectively damages rapidly proliferating cells, targeted therapies interact with specific molecular abnormalities that drive malignant transformation and progression. These agents inhibit critical oncogenic pathways involved in cell proliferation, apoptosis evasion, angiogenesis, metastasis, and DNA repair. Major pharmacological classes include monoclonal antibodies directed against extracellular receptors or ligands, small-molecule tyrosine kinase inhibitors (TKIs) targeting intracellular signaling cascades, antibody–drug conjugates (ADCs) enabling selective cytotoxic delivery, and synthetic lethality-based agents such as poly(ADP-ribose) polymerase (PARP) inhibitors designed for tumors with defective homologous recombination repair mechanisms.

Clinical application of targeted therapies has significantly improved response rates, progression-free survival, and overall survival across a wide range of malignancies including breast cancer, non-small cell lung cancer, colorectal cancer, melanoma, and hematological cancers. In several settings, these therapies have converted previously fatal cancers into chronic manageable diseases. However, long-term therapeutic efficacy remains limited by multiple factors, including intrinsic and acquired resistance, clonal tumor heterogeneity, activation of compensatory signaling pathways, biomarker limitations, treatment-related toxicities, and substantial financial burden.

Recent pharmacological advances aim to overcome these challenges through development of next-generation inhibitors active against resistance mutations, rational combination regimens targeting parallel pathways, nanotechnology-based drug delivery systems to enhance tumor selectivity, and real-time molecular monitoring using liquid biopsy. Furthermore, artificial intelligence-

assisted predictive modeling is emerging as a promising tool for individualized therapy selection and early detection of therapeutic resistance. This review provides a comprehensive overview of the pharmacological foundations of targeted anticancer therapy, classification of major drug classes, molecular mechanisms of resistance, and key clinical challenges. It also discusses evolving therapeutic strategies and future directions toward adaptive, data-driven, and fully personalized oncology.

Keywords: Targeted therapy; Precision oncology; Tyrosine kinase inhibitors; Monoclonal antibodies; PARP inhibitors; Antibody–drug conjugates; Drug resistance; Biomarkers; Personalized medicine; Cancer pharmacology.

1. Introduction

Cancer remains one of the leading causes of morbidity and mortality worldwide and represents a major public health burden across both developed and developing countries. According to global cancer statistics, the incidence of malignancies continues to rise due to aging populations, environmental exposures, lifestyle changes, and improved detection methods. Traditional anticancer treatment has historically relied on surgery, radiotherapy, and cytotoxic chemotherapy. Among these, chemotherapy became the cornerstone of systemic cancer treatment because of its ability to eliminate rapidly dividing cells (1). However, cytotoxic agents lack biological specificity and damage both malignant and normal proliferating tissues such as bone marrow, gastrointestinal mucosa, and hair follicles. Consequently, treatment is frequently associated with severe adverse effects including myelosuppression, mucositis, alopecia, organ toxicity, and immunosuppression, which limit dose intensity and compromise therapeutic outcomes. These limitations highlighted the need for more selective and biologically rational anticancer approaches.

Targeted therapy represents a major paradigm shift in oncology by focusing on molecular abnormalities that drive tumorigenesis rather than general cellular proliferation (1). The transition from empirical cytotoxic therapy to mechanism-based treatment was made possible by advances in molecular biology and cancer genomics. Malignant transformation is now understood as a multistep process involving genetic mutations, epigenetic alterations, and dysregulated cellular signaling networks. Cancer cells acquire hallmark capabilities such as sustained proliferative signaling, resistance to apoptosis, angiogenesis, invasion, metastasis, and immune evasion. Unlike chemotherapy, targeted agents are designed to interfere with specific proteins essential for these processes, thereby providing tumor-selective cytotoxicity with relatively lower systemic toxicity.

Advances in cancer genomics revealed that malignancies are driven by specific oncogenic mutations involving receptor tyrosine kinases, intracellular signaling cascades, angiogenesis pathways, and DNA repair mechanisms (2). Examples include epidermal growth factor receptor (EGFR) mutations in lung cancer, human epidermal growth factor receptor-2 (HER2) amplification in breast cancer, anaplastic lymphoma kinase (ALK) rearrangements in lung adenocarcinoma, and BRAF mutations in melanoma. These genetic alterations result in constitutive activation of signaling pathways such as PI3K/AKT/mTOR and RAS/RAF/MEK/ERK that promote uncontrolled cell growth and survival. Targeted therapies inhibit these oncogenic drivers and thereby suppress tumor proliferation, induce apoptosis, and reduce metastatic potential while minimizing damage to normal tissues (3). This selective mechanism significantly improves the therapeutic index compared with conventional chemotherapy.

Unlike chemotherapy, targeted therapy is based on the principles of precision medicine, in which treatment selection depends on tumor molecular profiling such as EGFR mutation, HER2 amplification, ALK rearrangement, or BRCA mutation (4). Molecular diagnostic techniques including next-generation sequencing, fluorescence in situ hybridization, polymerase chain reaction assays, and liquid biopsy enable identification of actionable mutations in clinical practice. Patients are therefore treated according to tumor genotype rather than tumor location alone, representing a fundamental change in oncology treatment strategy. These therapies have significantly improved response rates, progression-free survival, and overall survival in several malignancies including non-small cell lung cancer (NSCLC), breast cancer, melanoma, colorectal cancer, and certain hematologic

cancers (5). In many settings, targeted agents have transformed previously fatal cancers into chronic manageable diseases, emphasizing their growing importance in modern cancer therapeutics.

2. Molecular Basis of Targeted Therapy

Cancer development is a multistep biological process driven by deregulation of cellular signaling pathways that normally regulate proliferation, apoptosis, angiogenesis, and DNA repair. Genetic mutations, chromosomal rearrangements, and epigenetic modifications lead to constitutive activation of growth-promoting pathways and inactivation of tumor suppressor mechanisms. As a result, malignant cells acquire uncontrolled proliferative capacity, resistance to programmed cell death, metabolic adaptation, and the ability to invade surrounding tissues and metastasize to distant organs (3).

One of the most extensively studied oncogenic mechanisms involves the epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor (HER/ErbB) family signaling pathway. Activation of EGFR triggers receptor dimerization and autophosphorylation of intracellular tyrosine kinase domains, initiating downstream signaling cascades including RAS/RAF/MEK/ERK and PI3K/AKT/mTOR pathways. Mutations or overexpression of these receptors result in continuous proliferative signaling independent of ligand binding, a phenomenon commonly observed in non-small cell lung cancer and breast cancer. Targeted inhibition of EGFR and HER2 receptors interrupts this signaling cascade and suppresses tumor growth.

Angiogenesis represents another essential hallmark of cancer. Tumors require continuous blood supply to sustain growth beyond a few millimeters in size. This process is primarily mediated by vascular endothelial growth factor (VEGF), which stimulates endothelial cell proliferation and formation of abnormal tumor vasculature. Overexpression of VEGF is associated with aggressive tumor behavior, increased metastatic potential, and poor prognosis. Anti-angiogenic therapies therefore aim to deprive tumors of oxygen and nutrients by inhibiting VEGF signaling (4).

Intracellular signaling pathways also play a crucial role in oncogenesis. The PI3K/AKT/mTOR pathway regulates cellular metabolism, survival, and proliferation. Aberrant activation due to PI3K mutations, PTEN loss, or receptor activation promotes resistance to apoptosis and enhances tumor cell survival. Similarly, activation of the RAS/RAF/MEK pathway drives continuous cellular proliferation and is commonly implicated in melanoma, colorectal cancer, and lung cancer. Pharmacological inhibition of these pathways results in cell cycle arrest and apoptosis in tumor cells.

Defects in DNA repair mechanisms constitute another major driver of cancer progression. Mutations in BRCA1 and BRCA2 genes impair homologous recombination repair, forcing cancer cells to rely on alternative repair mechanisms mediated by poly-ADP ribose polymerase (PARP). Targeted inhibition of PARP leads to accumulation of DNA damage and selective cancer cell death through synthetic lethality. This concept has become a cornerstone of precision oncology.

Overall, targeted therapy blocks these oncogenic drivers and prevents tumor progression by interfering with specific molecular pathways essential for cancer survival (3). Among these molecular targets, receptor tyrosine kinases (RTKs) play a central role in tumor growth, invasion, and metastasis; inhibition of these receptors produces significant therapeutic benefit across multiple malignancies (6). The development of small-molecule kinase inhibitors has revolutionized cancer therapy by selectively targeting intracellular signaling networks, resulting in improved response rates and survival outcomes compared with conventional cytotoxic chemotherapy (7).

3. Classification of Targeted Therapies

Targeted anticancer therapies are broadly classified according to their molecular structure and mechanism of action. The major pharmacological categories include monoclonal antibodies, small-molecule tyrosine kinase inhibitors, angiogenesis inhibitors, synthetic lethality-based drugs, and antibody-drug conjugates. Each class interacts with distinct molecular components involved in tumor growth and survival.

3.1 Monoclonal Antibodies

Monoclonal antibodies (mAbs) are large biologic molecules designed to bind extracellular ligands or cell-surface receptors and inhibit activation of oncogenic signaling pathways. Because of their high specificity, they selectively target tumor cells expressing the antigen while sparing normal tissues.

These antibodies exert anticancer activity through multiple mechanisms. They block receptor activation by preventing ligand binding and receptor

dimerization, thereby inhibiting downstream signaling pathways responsible for cellular proliferation. In addition, monoclonal antibodies stimulate antibody-dependent cellular cytotoxicity and complement-mediated cytotoxicity, allowing immune cells to recognize and destroy malignant cells (8). Some antibodies also serve as targeted delivery systems for cytotoxic agents in the form of antibody-drug conjugates.

HER2-targeted antibodies such as trastuzumab inhibit receptor dimerization and downstream signaling cascades, resulting in growth arrest and apoptosis in HER2-positive tumors (8). Over the past two decades, antibody-based therapies have become standard treatment in several malignancies including breast cancer, colorectal cancer, lymphoma, and lung cancer (9).

3.2 Tyrosine Kinase Inhibitors (TKIs)

Tyrosine kinase inhibitors are small-molecule drugs capable of entering cells and binding intracellular kinase domains of activated receptors. Unlike monoclonal antibodies, TKIs act within the cytoplasm and block phosphorylation-dependent signaling pathways essential for tumor growth.

Important examples include EGFR inhibitors such as gefitinib, erlotinib, and osimertinib; BCR-ABL inhibitors such as imatinib used in chronic myeloid leukemia; and ALK inhibitors such as crizotinib and lorlatinib used in lung cancer. These agents suppress tumor proliferation, survival signaling, and angiogenesis by preventing activation of downstream pathways (10).

More than 50 receptor tyrosine kinases have been identified as regulators of malignant cell behavior, and pharmacological inhibition of these enzymes has become a fundamental component of modern precision oncology (11). The oral bioavailability and intracellular activity of TKIs make them particularly suitable for long-term cancer management.

3.3 Angiogenesis Inhibitors

Tumor progression depends on the development of new blood vessels that supply oxygen and nutrients to proliferating cancer cells. This process, known as angiogenesis, is primarily mediated by vascular endothelial growth factor (VEGF) signaling.

Anti-angiogenic therapies inhibit VEGF or its receptor and thereby prevent formation of tumor vasculature. Reduction of blood supply leads to tumor starvation, decreased metastatic spread, and improved response to other anticancer treatments (12). These drugs are widely used in colorectal cancer, renal cell carcinoma, and lung cancer.

3.4 PARP Inhibitors and Synthetic Lethality

Certain cancers harbor defects in homologous recombination DNA repair pathways, particularly due to mutations in BRCA1 or BRCA2 genes. These tumor cells depend heavily on PARP-mediated repair mechanisms for survival.

PARP inhibitors such as olaparib and talazoparib block this alternative repair pathway, resulting in accumulation of DNA damage and selective tumor cell death through the concept of synthetic lethality (12). These agents have demonstrated significant clinical efficacy in BRCA-mutated breast and ovarian cancers and represent a major advancement in genotype-guided therapy (13).

3.5 Antibody-Drug Conjugates (ADCs)

Antibody-drug conjugates combine the targeting ability of monoclonal antibodies with the cytotoxic potency of chemotherapy. The antibody component binds tumor-specific antigens, and after internalization releases a highly potent cytotoxic payload within the cancer cell.

This targeted delivery enhances therapeutic efficacy while minimizing systemic toxicity compared with conventional chemotherapy (14). New-generation ADCs utilize improved linker technology and more potent payloads, leading to enhanced tumor response rates and prolonged survival outcomes in several cancers (15).

4. Pharmacological Advances

Rapid progress in molecular biology, drug design, and computational sciences has led to significant advancements in targeted oncology. Modern therapeutic strategies are increasingly aimed not only at inhibiting oncogenic drivers but also at overcoming resistance, improving drug delivery, and individualizing treatment selection. These advances have substantially enhanced clinical outcomes and transformed several cancers into manageable chronic diseases.

4.1 Next-Generation Targeted Agents

One of the major limitations of early targeted therapies was the rapid development of acquired resistance due to secondary mutations in the drug target. To address this challenge, next-generation inhibitors have been designed to selectively bind mutated receptor conformations that are resistant to first-generation drugs.

For example, in non-small cell lung cancer, resistance to early EGFR inhibitors frequently occurs due to the T790M mutation within the kinase domain. Third-generation EGFR inhibitors were specifically developed to inhibit this resistant mutation while sparing wild-type receptors, thereby improving therapeutic selectivity and reducing toxicity (5). Similarly, second-site mutations in anaplastic lymphoma kinase (ALK) lead to resistance against early ALK inhibitors, and newer agents with improved binding affinity and central nervous system penetration demonstrate superior efficacy (16).

These next-generation agents prolong progression-free survival, enhance response rates, and delay disease relapse, highlighting the importance of structure-guided drug development in precision oncology.

4.2 Combination Therapy

Monotherapy with targeted agents often leads to compensatory activation of alternative signaling pathways, resulting in treatment resistance. Combination therapy aims to overcome this limitation by simultaneously inhibiting multiple oncogenic pathways or integrating different treatment modalities.

Combining targeted therapy with chemotherapy can increase tumor cell kill, while combination with immunotherapy enhances immune-mediated tumor destruction. Dual blockade strategies targeting parallel pathways have demonstrated improved survival outcomes and delayed resistance compared with single-agent therapy (17). Such approaches are increasingly used in metastatic cancers and represent a cornerstone of modern oncologic treatment planning.

4.3 Biomarker-Driven Therapy

Precision oncology relies on identification of predictive biomarkers to match patients with the most effective treatment. Advances in molecular diagnostics, including next-generation sequencing and liquid biopsy, allow detection of actionable mutations using circulating tumor DNA.

This biomarker-guided approach enables real-time monitoring of tumor evolution and early identification of resistance mutations, allowing clinicians to modify therapy before clinical progression occurs (4). Consequently, treatment selection is increasingly determined by molecular characteristics rather than tumor histology alone, improving response rates and reducing unnecessary toxicity.

4.4 Nanotechnology-Based Drug Delivery

Nanotechnology has emerged as an innovative strategy to enhance targeted drug delivery. Nanoparticles can encapsulate anticancer drugs and preferentially accumulate within tumor tissue through enhanced permeability and retention effects.

This targeted accumulation increases local drug concentration while minimizing systemic exposure and toxicity. Nanocarriers also improve drug stability, prolong circulation time, and enable controlled drug release, thereby enhancing therapeutic efficacy (18). Such delivery systems are particularly promising for highly potent agents with narrow therapeutic indices.

4.5 Artificial Intelligence in Targeted Therapy

Artificial intelligence is increasingly integrated into oncology to optimize treatment selection and predict clinical outcomes. Machine learning algorithms can analyze genomic data, clinical parameters, and treatment responses to identify patterns that predict drug sensitivity and resistance.

AI-based predictive models are capable of forecasting adverse drug reactions and therapeutic response with high sensitivity and specificity, thereby enabling personalized treatment planning (19). This approach represents an important step toward fully individualized cancer therapy and may significantly improve long-term outcomes.

5. Mechanisms of Resistance

Despite the remarkable clinical success of targeted therapies, therapeutic resistance remains the principal limitation to durable cancer control. Most patients who initially respond to targeted treatment eventually experience disease progression. Resistance may occur either before treatment initiation (primary resistance) or after an initial period of response (acquired resistance).

The development of resistance reflects the dynamic and adaptive nature of tumor biology, where selective drug pressure promotes survival of resistant cellular clones (19).

5.1 Primary Resistance

Primary resistance refers to the failure of tumors to respond to therapy despite the presence of an apparently actionable molecular target. This phenomenon highlights the complexity of oncogenic signaling networks and the presence of multiple redundant survival pathways within cancer cells.

One major cause of intrinsic resistance is activation of alternative signaling pathways that compensate for inhibition of the intended molecular target. Even when a receptor such as EGFR is successfully inhibited, parallel pathways such as MET or PI3K signaling may continue to drive tumor proliferation. Additionally, co-existing genetic alterations (co-mutations) can modify drug sensitivity and prevent effective pathway suppression. For instance, concurrent mutations in downstream signaling proteins may render receptor inhibition ineffective.

The tumor microenvironment also contributes to primary resistance. Stromal cells, inflammatory mediators, hypoxia, and growth factors secreted by surrounding tissues can maintain cancer cell survival despite pharmacological blockade of the primary oncogenic driver (20). Consequently, target expression alone does not always predict therapeutic response.

5.2 Acquired Resistance

Acquired resistance develops after an initial period of clinical response and represents the most common cause of treatment failure in targeted oncology. Continuous drug exposure creates selective pressure, allowing resistant clones to expand and dominate the tumor population.

a) Target Mutation

Secondary mutations within the drug-binding domain of the target protein can reduce drug affinity and restore signaling activity. For example, point mutations in kinase domains alter receptor conformation and prevent effective inhibitor binding (21).

b) Bypass Signaling Activation

Cancer cells may activate alternative proliferative pathways that circumvent the inhibited receptor. Activation of parallel receptors or downstream signaling molecules restores cell growth and survival despite continued therapy (22).

c) Tumor Heterogeneity

Tumors consist of genetically diverse subclones. Targeted therapy eliminates sensitive clones but allows pre-existing resistant clones to expand, a process known as clonal selection and evolution (23).

d) Histological Transformation

In some cancers, particularly lung cancer, tumor cells undergo phenotypic transformation under therapeutic pressure. For instance, adenocarcinoma may transform into a more aggressive small-cell phenotype that is no longer dependent on the original oncogenic driver (21).

5.3 Cellular Mechanisms

In addition to genetic alterations, cellular adaptive mechanisms also contribute to resistance. Cancer cells may increase expression of drug efflux transporters that actively remove the drug from the intracellular environment, reducing effective drug concentration. Metabolic reprogramming can alter cellular dependence on targeted pathways, enabling survival under pharmacological inhibition. Epigenetic modifications may also change gene expression patterns and promote a resistant phenotype without altering the DNA sequence (20).

Resistance mechanisms are often multifactorial and evolve over time, making single-agent therapy insufficient for long-term disease control. Understanding these mechanisms is essential for designing combination treatments and next-generation inhibitors aimed at achieving durable therapeutic responses.

6. Toxicity and Clinical Challenges

Although targeted therapies are generally more selective than conventional chemotherapy, they are not free from adverse effects. Because most molecular targets are also expressed in normal tissues, inhibition of these pathways can disrupt physiological cellular functions and produce characteristic toxicity profiles. Unlike cytotoxic chemotherapy, which mainly causes bone marrow suppression and gastrointestinal toxicity, targeted therapies produce mechanism-specific adverse

reactions related to the biological role of the inhibited pathway.

Cutaneous toxicity is among the most common adverse effects, particularly with epidermal growth factor receptor inhibitors. Patients frequently develop acneiform rash, xerosis, and paronychia due to inhibition of epidermal growth signaling required for normal skin integrity. While often manageable, severe reactions may necessitate dose modification. Vascular endothelial growth factor inhibitors commonly cause hypertension as a result of reduced nitric oxide production and increased peripheral vascular resistance. Endocrine disturbances such as hypothyroidism are observed with several kinase inhibitors because of thyroid vascular and cellular dysfunction. Cardiotoxicity, particularly reduced left ventricular ejection fraction, is associated with HER2-directed therapies due to interference with cardiomyocyte survival pathways (24).

Multikinase inhibitors pose an additional challenge because they target multiple signaling pathways simultaneously. Although this broad activity can improve antitumor efficacy, it also increases the likelihood of off-target toxicity including hepatotoxicity, fatigue, mucositis, and metabolic disturbances (25). Consequently, treatment requires careful monitoring and individualized dose adjustment to balance efficacy and safety.

Biomarker Limitations

The effectiveness of targeted therapy depends heavily on accurate identification of predictive biomarkers. However, not all patients harboring a target mutation respond to therapy, and some patients without detectable mutations may still benefit. Variability in testing techniques, tumor heterogeneity, and temporal evolution of mutations can lead to false-negative or misleading results. Additionally, a single biomarker often fails to capture the complexity of tumor signaling networks, reducing predictive reliability (24). These limitations emphasize the need for dynamic and multi-parameter molecular profiling.

Cost and Accessibility

Targeted therapies are significantly more expensive than conventional chemotherapy due to complex drug development, manufacturing, and companion diagnostic testing. The high cost of treatment creates a substantial economic burden for healthcare systems and limits patient access, particularly in low- and middle-income countries. Long-term administration further increases financial toxicity for patients and families, making affordability a major barrier to widespread adoption of precision oncology.Beyond survival outcomes, assessment of patient-reported quality of life has become an essential component of modern oncology care, as targeted therapies often require prolonged administration and may significantly influence functional status and daily living (30).

Variable Response Rates

Despite appropriate molecular targeting, therapeutic responses vary widely among patients. Some tumors exhibit only partial response or rapidly develop resistance even when the oncogenic driver is correctly inhibited. This variability arises from tumor heterogeneity, adaptive signaling mechanisms, and pharmacokinetic differences among individuals. As a result, targeted therapy often produces disease control rather than complete eradication, requiring continuous treatment and careful monitoring (25).

7. Strategies to Overcome Resistance

Because therapeutic resistance is inevitable in many patients receiving targeted therapy, modern oncology increasingly focuses on strategies that delay, prevent, or overcome resistance. These approaches aim to suppress tumor adaptability, target multiple survival pathways, and personalize treatment based on dynamic tumor evolution.

7.1 Combination Targeting

Simultaneous inhibition of multiple oncogenic pathways is one of the most effective approaches to overcoming resistance. Cancer cells frequently activate compensatory signaling cascades when a single pathway is blocked, allowing continued proliferation despite therapy. Combination targeting prevents this escape mechanism by suppressing parallel or downstream pathways at the same time.

For example, dual inhibition of receptor tyrosine kinases and downstream signaling proteins can produce more sustained tumor control than monotherapy. In addition, combining targeted therapy with chemotherapy or immunotherapy enhances tumor cell killing and reduces the likelihood of resistant clone selection. Clinical studies have demonstrated improved progression-free survival and delayed disease relapse using combination regimens compared with single-agent therapy (26).

7.2 Next-Generation Inhibitors

Development of next-generation inhibitors specifically designed to bind mutated targets has significantly improved management of resistant cancers. Structural modification of drug molecules allows effective inhibition of receptors that have undergone conformational changes due to resistance mutations.

These agents demonstrate higher binding affinity, improved selectivity, and better tissue penetration, particularly within the central nervous system. By targeting resistance mutations directly, they restore pathway inhibition and prolong clinical response (16). Sequential use of first-, second-, and third-generation inhibitors has therefore become a standard strategy in precision oncology.

7.3 Adaptive Therapy

Adaptive therapy is an emerging treatment strategy that recognizes cancer as an evolving biological system. Instead of continuous maximum-dose therapy, treatment is dynamically adjusted based on tumor response and molecular monitoring. Drug holidays, dose modulation, and treatment switching are used to maintain a population of drug-sensitive cells that suppress resistant clones.

This evolutionary-based approach aims to delay selection of fully resistant tumor populations and extend disease control. Continuous monitoring through imaging and molecular diagnostics allows clinicians to modify therapy before clinical progression occurs (27).

7.4 Nanomedicine Delivery

Nanotechnology-based drug delivery systems improve the therapeutic index of targeted agents by enhancing tumor-specific drug accumulation. Nanocarriers exploit the abnormal tumor vasculature and enhanced permeability retention effect to deliver drugs preferentially into malignant tissue.

Improved tumor penetration increases intracellular drug concentration, which can overcome certain pharmacokinetic resistance mechanisms. In addition, controlled release systems maintain therapeutic drug levels for longer durations while reducing systemic toxicity (28). This approach is particularly promising for highly potent targeted therapies.

7.5 AI-Guided Personalized Therapy

Artificial intelligence is increasingly used to predict therapeutic resistance before clinical failure occurs. Machine learning algorithms integrate genomic, proteomic, and clinical data to identify patterns associated with drug response and resistance.

AI-guided models can recommend optimal treatment selection, predict adverse drug reactions, and determine the best time to switch therapy. Early detection of emerging resistant clones allows proactive therapeutic modification, improving long-term outcomes and minimizing ineffective treatment exposure (19).

8. Future Perspectives

The future of oncology is increasingly centered on comprehensive molecular characterization and dynamic treatment adaptation. As cancer is recognized as a heterogeneous and evolving disease, therapeutic strategies are shifting from static, single-target approaches toward integrated, systems-based precision medicine.

One of the most promising developments is multi-omics tumor profiling. By integrating genomic, transcriptomic, proteomic, metabolomic, and epigenomic data, clinicians can obtain a holistic understanding of tumor biology. This comprehensive molecular landscape allows identification of multiple actionable targets, resistance mechanisms, and pathway interactions that cannot be captured by single-gene testing alone. Multi-omics approaches may improve patient stratification and guide rational combination therapy selection (26).

Real-time molecular monitoring through circulating tumor DNA analysis and liquid biopsy technologies is also transforming cancer management. Unlike traditional tissue biopsy, which provides a static snapshot of tumor genetics, liquid biopsy enables continuous assessment of tumor evolution. Emerging resistance mutations can be detected months before radiographic progression, allowing early therapeutic modification and improved disease control.

Personalized drug combinations represent another critical direction for future oncology. Rather than applying standardized regimens, treatment algorithms may soon be tailored according to each patient's unique molecular profile. Rational design of combination therapies targeting parallel and downstream pathways can prevent compensatory signaling and delay

resistance. Such individualized regimens require robust biomarker validation and advanced computational modeling (29).

Computational modeling of tumor evolution is gaining increasing attention. Cancer behaves as an adaptive ecosystem, where selective pressure from therapy drives clonal expansion of resistant cells. Mathematical modeling and artificial intelligence can simulate tumor dynamics and predict optimal dosing schedules to minimize resistance development. Integration of genomic data with pharmacological modeling will enable more precise dose optimization, improved therapeutic sequencing, and reduced toxicity (23).

Ultimately, the convergence of molecular biology, bioinformatics, pharmacology, and artificial intelligence is expected to move oncology toward fully individualized therapy, where treatment decisions are continuously refined based on real-time biological data.

9. Conclusion

Targeted therapy has fundamentally transformed cancer treatment by shifting oncology from non-specific cytotoxic chemotherapy toward molecular precision medicine. The development of monoclonal antibodies, small-molecule kinase inhibitors, antibody-drug conjugates, and synthetic lethality-based agents has significantly improved response rates and survival outcomes across multiple solid tumors and hematologic malignancies.

Despite these advances, major clinical challenges remain. Drug resistance—both primary and acquired—continues to limit long-term efficacy. Tumor heterogeneity, adaptive signaling mechanisms, toxicity profiles, and biomarker limitations complicate therapeutic decision-making. In addition, economic constraints and disparities in access restrict the global implementation of precision oncology (27).

Future therapeutic success will depend on rational combination strategies, next-generation inhibitors targeting resistance mutations, validated predictive biomarkers, and integration of computational approaches to anticipate tumor evolution. As multi-omics profiling and artificial intelligence become increasingly embedded in clinical practice, oncology is expected to evolve toward dynamic, data-driven, and individualized cancer care. Achieving durable cancer control will require continued collaboration between molecular scientists, pharmacologists, clinicians, and data scientists to translate biological insights into effective and accessible therapies (29).

References

1. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell*. 2011;144(5):646-674.
2. Garraway LA, Lander ES. Lessons from the cancer genome. *Cell*. 2013;153(1):17-37.
3. Sawyers C. Targeted cancer therapy. *Nature*. 2004;432(7015):294-297.
4. Malone ER, Oliva M, Sabatini PJB, Stockley TL, Siu LL. Molecular profiling for precision cancer therapies. *Genome Med*. 2020;12:8.
5. Herbst RS, Morgensztern D, Boshoff C. The biology and management of non-small cell lung cancer. *Nature*. 2018;553(7689):446-454.
6. Lemmon MA, Schlessinger J. Cell signaling by receptor tyrosine kinases. *Cell*. 2010;141(7):1117-1134.
7. Zhang J, Yang PL, Gray NS. Targeting cancer with small molecule kinase inhibitors. *Nat Rev Cancer*. 2009;9(1):28-39.
8. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of chemotherapy plus trastuzumab for HER2-positive breast cancer. *N Engl J Med*. 2001;344:783-792.
9. Scott AM, Wolchok JD, Old LJ. Antibody therapy of cancer. *Nat Rev Cancer*. 2012;12(4):278-287.
10. Roskoski R Jr. Properties of FDA-approved small molecule protein kinase inhibitors. *Pharmacol Res*. 2019;144:19-50.
11. Dy GK, Adjei AA. Understanding, recognizing, and managing toxicities of targeted anticancer therapies. *CA Cancer J Clin*. 2013;63(4):249-279.
12. Lord CJ, Ashworth A. PARP inhibitors: synthetic lethality in the clinic. *Science*. 2017;355(6330):1152-1158.
13. Robson M, Im SA, Senkus E, et al. Olaparib for metastatic breast cancer in patients with BRCA mutation. *N Engl J Med*. 2017;377:523-533.
14. Beck A, Goetsch L, Dumontet C, Corvaïa N. Strategies and challenges for antibody-drug conjugates. *Nat Rev Drug Discov*. 2017;16(5):315-337.
15. Lambert JM, Morris CQ. Antibody-drug conjugates (ADCs) for personalized treatment of solid tumors. *Adv Ther*. 2017;34(5):1015-1035.

16. Camidge DR, Kim HR, Ahn MJ, et al. Brigatinib versus crizotinib in ALK-positive NSCLC. *N Engl J Med*. 2018;379:2027-2039.
17. Mok TSK, Wu YL, Kudaba I, et al. Pembrolizumab plus chemotherapy in advanced lung cancer. *N Engl J Med*. 2019;381:2020-2031.
18. Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress and challenges. *Nat Rev Cancer*. 2017;17(1):20-37.
19. Kourou K, Exarchos TP, Exarchos KP, Karamouzis MV, Fotiadis DI. Machine learning applications in cancer prognosis and prediction. *Comput Struct Biotechnol J*. 2015;13:8-17.
20. Holohan C, Van Schaeybroeck S, Longley DB, Johnston PG. Cancer drug resistance: mechanisms and approaches. *Nat Rev Cancer*. 2013;13:714-726.
21. Gainor JF, Shaw AT. Emerging paradigms in resistance to targeted therapy in lung cancer. *J Clin Oncol*. 2013;31:3987-3996.
22. Engelman JA, Settleman J. Acquired resistance to tyrosine kinase inhibitors during cancer therapy. *Curr Opin Genet Dev*. 2008;18(1):73-79.
23. Dagogo-Jack I, Shaw AT. Tumour heterogeneity and resistance to cancer therapies. *Nat Rev Clin Oncol*. 2018;15(2):81-94.
24. Swanton C. Intratumor heterogeneity: evolution through space and time. *Cancer Res*. 2012;72(19):4875-4882.
25. Burrell RA, McGranahan N, Bartek J, Swanton C. The causes and consequences of genetic heterogeneity in cancer evolution. *Nature*. 2013;501:338-345.
26. Dancey JE, Bedard PL, Onetto N, Hudson TJ. The genetic basis for cancer treatment decisions. *Cell*. 2012;148(3):409-420.
27. Dienstmann R, Rodon J, Barretina J, Tabernero J. Genomic medicine frontier in cancer therapy. *Nat Rev Clin Oncol*. 2013;10:307-317.
28. Turner NC, Reis-Filho JS. Genetic heterogeneity and cancer drug resistance. *Lancet Oncol*. 2012;13(4):e178-e185.
29. Vogelstein B, Papadopoulos N, Velculescu VE, Zhou S, Diaz LA Jr, Kinzler KW. Cancer genome landscapes. *Science*. 2013;339(6127):1546-1558.
30. Archana S, Penchala N, Kumar AD, Anusha M. Assessing quality of life in oncology: a review of current measurement tools and gaps across the cancer care continuum. Int J Pharm Health Care Res. 2025;13(2):196-200.