International Journal of Web of Multidisciplinary Studies
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
website: https://ijwos.com
Volume 3 Issue 4 , April 2026
E-ISSN : 3049-2424
DOI: https://doi.org/10.71366/ijwos

Advancing Cancer Care Through Diversity: A Comprehensive Review of Conventional, Targeted, and Emerging Therapies

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Article Info

Article History:

Published:9 April 2026

Publication Issue:
Volume 3, Issue 4
April-2026

Page Number:
104-111

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Abstract:

Cancer remains one of the leading causes of morbidity and mortality worldwide, with projections indicating approximately 2,114,850 new cases and 626,140 deaths in the United States alone in 2026. Traditional modalities such as surgery, chemotherapy, and radiotherapy have been foundational but are often limited by toxicity, resistance, and incomplete efficacy against advanced or metastatic disease. Over the past two decades, a diverse array of therapies has emerged, including targeted small-molecule inhibitors, peptide drugs, monoclonal antibodies and antibody-drug conjugates (ADCs), immunotherapies (e.g., checkpoint inhibitors), cell-based therapies (CAR-T, CAR-NK, TIL), gene therapies (including CRISPR-based editing), oncolytic viruses, nanotechnology-enhanced delivery systems, and photodynamic approaches. These modalities emphasize precision, personalization, and multimodal combinations to improve outcomes while reducing side effects. This review synthesizes current knowledge on these diverse therapies, their mechanisms, clinical applications, advantages, limitations, and future directions, drawing from recent advances up to 2025–2026. While promising, challenges such as resistance, cost, accessibility, and toxicity persist, underscoring the need for continued innovation and equitable implementation.

Keywords: cancer therapy, targeted therapy, immunotherapy, checkpoint inhibitors, CAR-T cell therapy, antibody-drug conjugates (ADCs)

1. Introduction

Cancer is a heterogeneous group of diseases characterized by uncontrolled cell proliferation, driven by genetic and epigenetic alterations. Globally, the burden is immense[1]. Estimates from GLOBOCAN and related projections forecast continued growth, with older populations (aged 60+) accounting for a disproportionate share of cases and deaths[2,3]. In the US, 2026 projections include ~2,114,850 new diagnoses (~5,800 daily) and ~626,140 deaths (~1,720 daily)[4,5]. Mortality rates have declined ~34% since 1991 due to prevention, early detection, and therapeutic advances, averting millions of deaths—yet disparities remain stark, particularly among racial and ethnic minorities[6,7].

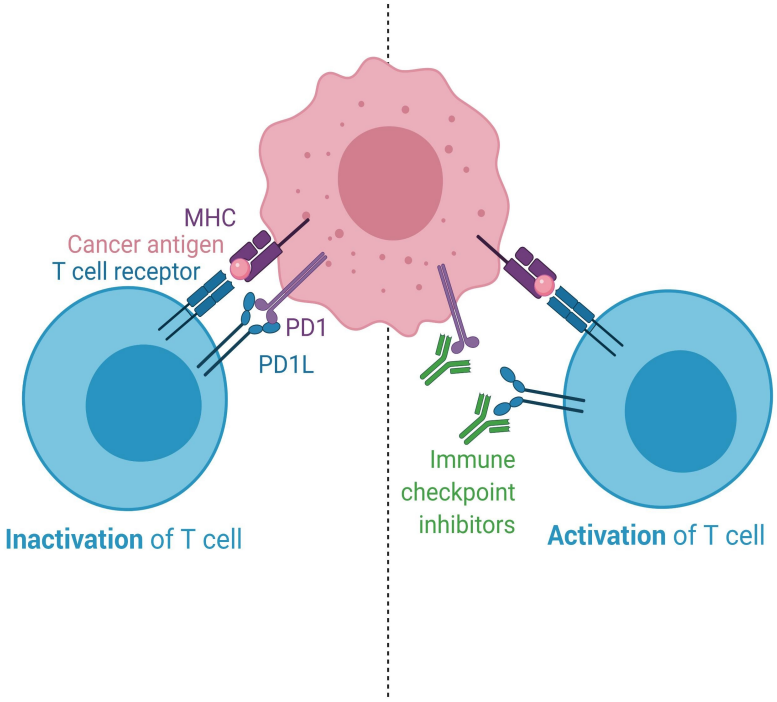

FIGURE-1 Cance Immunotherapy (Checkpoint Inhibition Mechanism)

Historical milestones trace from surgical resection under anesthesia (mid-1800s), radiation (late 1800s), chemotherapy (WWII era), to modern targeted agents (e.g., imatinib in 2001) and immunotherapies (e.g., checkpoint inhibitors in 2014)[8,9]. Today, the field has shifted toward precision oncology, integrating molecular profiling for individualized care[10,11]. Market growth reflects this: the global anti-tumor drug market is projected to expand significantly. Diverse therapies now span small molecules to biologics, cells, genes, and viruses, often combined in multimodal regimens to address tumor heterogeneity, microenvironment immunosuppression, and resistance[12].

Conventional Therapies

Surgery remains the cornerstone for localized solid tumors, offering curative potential when combined with neoadjuvant (pre-operative) or adjuvant (post-operative) therapies to shrink tumors or eliminate residual disease[13]. Success is evident in breast, lung, colorectal, and pancreatic cancers, though it is limited for metastatic or inoperable cases[14].

Chemotherapy uses cytotoxic agents to target rapidly dividing cells systemically, addressing micrometastases[15]. It is frequently paired with radiotherapy (chemoradiotherapy) in head/neck, cervical, and esophageal cancers for enhanced local control and organ preservation. Limitations include systemic toxicity, resistance, and off-target effects on healthy tissues.

Radiation Therapy (including proton/carbon ion) delivers high-energy beams to induce DNA damage in tumors. Advances in precision delivery minimize damage to surrounding tissues. It excels in palliative care and combinations but faces challenges like radioresistance in hypoxic tumors[16].

These form the backbone of multimodal approaches, where integration with newer agents optimizes outcomes.

Targeted Therapies

i. Small-Molecule Targeted Drugs inhibit specific oncogenic proteins (e.g., kinases). Examples include imatinib (BCR-ABL in CML/GIST), EGFR inhibitors (osimertinib), and KRAS G12C inhibitors (sotorasib). PROTACs (proteolysis-targeting chimeras) and molecular glues degrade "undruggable" targets like transcription factors. Advantages: oral administration, lower cost, fewer side effects than traditional chemo[17]. Limitations resistance (e.g., EGFR mutations), off-target effects, and metabolic instability. Recent advances focus on covalent/allosteric inhibitors and AI-driven design.

ii. Peptide Drugs (10–50 amino acids) offer high specificity and low immunogenicity. Radiolabeled peptides (e.g., 177Lu-DOTATATE for neuroendocrine tumors) enable peptide receptor radionuclide therapy (PRRT) and imaging. Modifications improve stability and oral bioavailability. They target receptors like SSTR or integrins for angiogenesis inhibition. Advantages: tissue penetration, cost-effectiveness. Limitations: short half-life, protease degradation[18].

iii. Antibody Drugs and ADCs include monoclonal antibodies (mAbs) like trastuzumab (HER2+ breast cancer), rituximab (CD20+ lymphoma), and checkpoint inhibitors (pembrolizumab, nivolumab for PD-1/PD-L1). ADCs (e.g., trastuzumab deruxtecan) conjugate antibodies to cytotoxins for targeted payload delivery. Mechanisms: receptor blockade, ADCC, or immune activation. As of 2023, ~79 mAbs were FDA-approved, many for cancer. Advantages: high specificity, synergy in combinations. Limitations: high cost, infusion reactions, resistance[19].

iv. Anti-angiogenic agents (e.g., bevacizumab targeting VEGF) restrict tumor blood supply and are widely combined with chemo or immunotherapy.

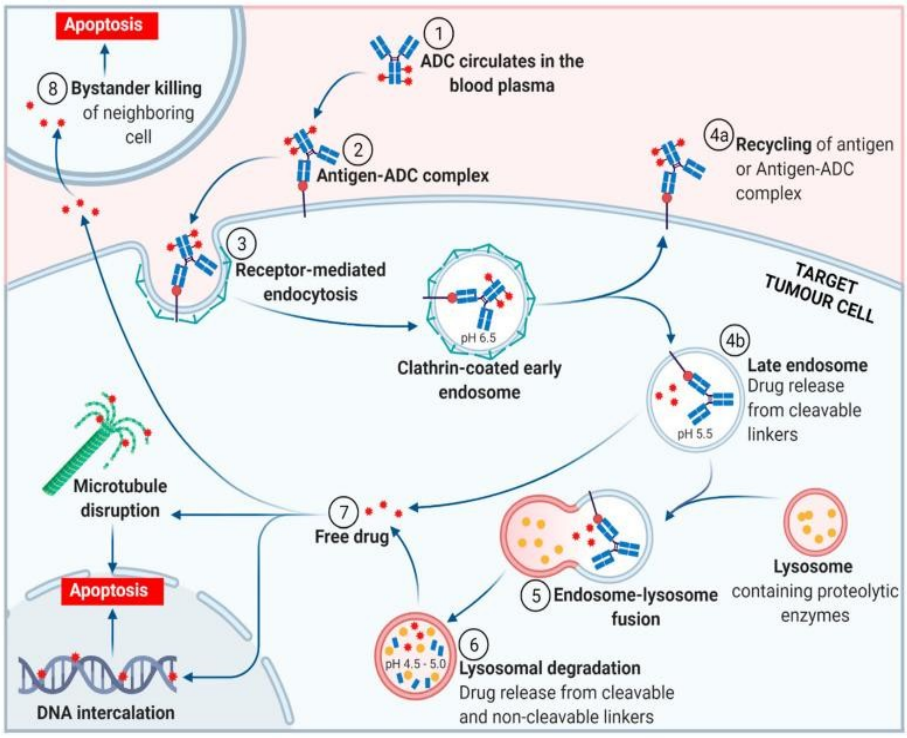

FIGURE 2- Targeted Therapy & Antibody-Drug Conjugate (ADC) Mechanism

2. Immunotherapy and Cell-Based Therapies

Immunotherapy harnesses the immune system. Checkpoint inhibitors (anti-PD-1/PD-L1, anti-CTLA-4) reinvigorate T cells, revolutionizing melanoma, NSCLC, and other cancers. Combinations with targeted agents improve survival[20].

Cell Therapies include:

a. CAR-T cells: Engineered T cells targeting antigens (e.g., CD19 in hematologic malignancies). Highly effective but limited in solid tumors due to antigen heterogeneity and microenvironment barriers; associated with cytokine release syndrome (CRS).

b. CAR-NK and CAR-M: Lower toxicity alternatives with innate killing; early-stage promise.

c. TIL (tumor-infiltrating lymphocytes): Patient-derived, high specificity but complex manufacturing.

d. TCR-T: Targets intracellular antigens.

CRISPR editing enhances these (e.g., PD-1 knockout for reduced exhaustion). Allogeneic "off-the-shelf" versions aim to reduce costs. Challenges: solid-tumor infiltration, manufacturing complexity, toxicity[21].

Gene Therapy and Emerging Modalities

Gene Therapy introduces, edits, or silences genes. Tools include ZFNs, TALENs, and CRISPR/Cas9 (with base/prime editing for precision without double-strand breaks)[22]. Applications: correcting mutations (e.g., TP53, KRAS), engineering CAR-T, or delivering mRNA for neoantigen vaccines. mRNA platforms enable rapid, personalized vaccines. Advantages: precision, potential for durable responses. Limitations: delivery (viral vectors risk immunogenicity/off-targets), safety, cost.

Oncolytic Viruses (OVs) selectively replicate in and lyse tumor cells while stimulating immunity via immunogenic cell death and antigen release. Examples: T-VEC (HSV-1 for melanoma, approved 2015), G47Δ (glioblastoma). Combinations with checkpoint inhibitors or chemo/radio enhance efficacy. Recent 2025 advances focus on armored viruses (expressing cytokines/immune modulators) and better delivery. Advantages: dual direct/immune effects. Limitations: antiviral immunity, delivery to solid tumors[23].

Nanotechnology and Other Emerging Approaches: Nanoparticles improve drug delivery, crossing barriers with reduced toxicity. Photodynamic therapy (PDT), photothermal therapy, and sonodynamic approaches use light/sound-activated agents. Ferroptosis inducers and mitochondria-targeted therapies address metabolic vulnerabilities[24].

3. Multimodal and Combination Therapies

Optimal outcomes often require integration: surgery + neoadjuvant targeted/immunotherapy; chemoradiotherapy + checkpoint blockade; or gene/cell therapy with OVs. Personalized medicine via genomic profiling tailors combinations, minimizing toxicity[25]. Examples include bevacizumab + atezolizumab in HCC or CAR-T + ICIs. Synergy overcomes resistance but increases adverse events and costs. Ongoing trials refine sequencing and biomarkers[26,27].

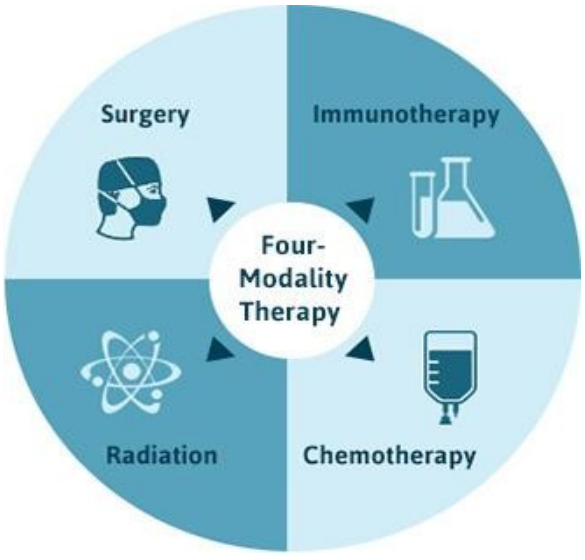

FIGURE 3- Multimodal Cancer Therapy Approach

Challenges and Future Directions

Key hurdles include therapy resistance, tumor heterogeneity, high costs/accessibility (especially in low-resource settings), toxicity management, and equitable global implementation[28,29]. Safety concerns (e.g., CRS in cell therapy, off-target editing) persist. Future directions[30,31]. AI/multi-omics for prediction; advanced delivery (nanoparticles, LNPs); "off-the-shelf" allogeneic cells; combination of OVs with CRISPR/mRNA; and focus on prevention/early detection. Global collaboration and policy reforms are essential[32,33].

4. Conclusion

Diverse cancer therapies have transformed the treatment landscape from blunt cytotoxic approaches to precise, immune-engaging, and genetically targeted strategies. While conventional modalities remain vital, integration with targeted, immuno-, cell-, gene-, and viral therapies offers unprecedented hope for improved survival and quality of life. Continued research, clinical trials, and multidisciplinary efforts will be critical to overcoming remaining barriers and realizing the full potential of precision oncology for all patients.

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