Advanced Targeted Therapies in Cancer

Shrawasti Jadhav[1], Swati Pirdhankar[2], Disha Koli[3], Dr. Babita More[4]

[1,3] *Final year B.Pharm Students, Yadavrao Tasgaonkar Institute of Pharmacy, Bhivpuri Road, Maharashtra, India*

[2] *Associate Professor, Yadavrao Tasgaonkar Institute of Pharmacy, Bhivpuri Road, Maharashtra, India*

[4] *Vice Principle & Professor, Yadavrao Tasgaonkar Institute of Pharmacy, Bhivpuri Road, Maharashtra, India.*

Abstract:

Advanced targeted therapies have transformed the landscape of cancer treatment by concentrating on the specific genetic and molecular abnormalities that drive tumor development and progression. Unlike traditional treatments such as chemotherapy and radiotherapy, which often affect both healthy and cancerous cells, targeted therapies act selectively on critical signaling pathways, oncogenes, and tumor-specific biomarkers. This category of treatment includes small-molecule inhibitors, monoclonal antibodies, antibody–drug conjugates, gene therapy approaches, and CAR-T cell therapy, all designed to directly attack cancer cells while minimizing damage to normal tissues. The incorporation of biomarkers and precision medicine has further refined cancer care by enabling treatment strategies tailored to each patient's unique tumor characteristics. Recent advancements, including liquid biopsy technologies, improved targeted agents, and artificial intelligence–assisted treatment planning, have strengthened the impact of these therapies. However, issues such as drug resistance, tumor heterogeneity, high cost, limited accessibility, and the need for specialized infrastructure continue to pose significant challenges. Despite these limitations, advanced targeted therapies represent a major milestone in oncology, offering improved treatment effectiveness, enhanced quality of life, and a promising future for personalized cancer management.

Keywords: Advanced targeted therapies, cancer, precision medicine, tyrosine kinase inhibitors, monoclonal antibodies, antibody–drug conjugates, PROTACs, biomarker-guided therapy, mechanism of action, clinical applications

1. Introduction

Over the last few decades, there has been great advancement in cancer treatment, particularly with the development of therapies designed to target specific molecular changes within tumors. These approaches, is known as targeted therapies, have transformed how certain cancers are managed. In diseases such as lung cancer, brain cancer, blood cancer they have significantly changed the treatment by offering more precise and effective options. The integration of these advanced technologies with new drug development has greatly speed up the progress of personalized medicine. This approach focuses on understanding both the genetic makeup and environmental influences behind a disease, allowing healthcare providers to tailor prevention strategies, diagnostic methods, and treatments to each individual patient. (1, 2)

Cancer been a major global health concern, harming millions of people around the world. Although significant advances have been made in cancer care over the years, leading to better survival and improved quality of life, traditional treatments such as chemotherapy and radiation still come with challenges, including limited

effectiveness in some cases and notable side effects. Recently, targeted therapies have emerged as an exciting and innovative approach, reshaping cancer treatment by offering more precise and promising ways to combat the disease. (3) Targeted therapies works in cancer treatment by targeting specific affected cell. This works by effective attack on cancer cell and reducing side effect. These treatments function by targeting specific molecules and biological pathways that are essential for cancer cells to grow and survive. By disrupting these processes, targeted therapies work to stop or slow the advancement of the disease, which may result in improved treatment success. In addition, these therapies can be customized based on the unique genetic profile of a patient's tumor, making them a vital element of precision medicine. (4)

2. Concept of Targeted Therapies

The main concept behind targeted therapy is precision treatment. Before starting treatment, doctors analyze the patient's tumor using tests such as genetic profiling or biomarker analysis. Based on these results, a targeted drug is selected that can effectively block the specific abnormality found in the cancer cells. This approach is often called personalized or precision medicine, as the treatment is tailored to the individual patient rather than using the same drug for everyone (5, 6) Targeted therapy works by interfering with key processes that cancer cells need to grow and survive. These therapies may block growth signals, stop cell division, trigger cancer cell death, or prevent the tumor from developing its own blood supply. Some targeted drugs also help the immune system to better recognize and destroy cancer cells. (7, 8) Overall, the concept of targeted therapy is to improve treatment effectiveness while reducing side effects. Because these drugs mainly affect cancer cells and spare normal cells, patients usually experience fewer adverse effects compared to chemotherapy. This makes targeted therapy an important and promising strategy in modern cancer treatment (9, 10)

Molecular Basis of Targeted Therapies:-

Targeted cancer therapies are developed based on a thorough understanding of the molecular mechanisms that drive cancer development. These treatments are specifically designed to act on genetic and molecular abnormalities that promote the growth and survival of cancer cells. By concentrating on the distinct features of cancer cells, targeted therapies interfere with their signaling pathways, helping to control disease progression while reducing harm to normal, healthy cells. (11)

Key Genetic and Molecular Alterations in Cancer; - A wide range of genetic and molecular abnormalities have been discovered across different types of cancer. These changes help cancer cells grow uncontrollably, escape normal death signals, and spread to other parts of the body. Some of the most important alterations include:

1. Oncogene activation:
Oncogenes are genes that, when mutated or produced in excess, stimulate continuous cell growth and survival. Well-known examples include **HER2** in breast cancer and **EGFR** in lung cancer. (12)

2. Inactivation of tumor suppressor genes:
Tumor suppressor genes normally act as the body's natural defense system by controlling cell division and preventing tumor formation. When these genes are damaged or mutated, cells can multiply without control. Common examples include **TP53 (p53)** found in many cancers and **BRCA1/BRCA2** in breast and ovarian cancers. (12)

3. Disruption of cell signaling pathways:
Errors in major signaling pathways, such as the **MAPK** and **PI3K/AKT** pathways, can promote continuous cell growth, survival, and cancer progression. (12)

3. Types of Targeted Therapies

1. **Small-Molecule Inhibitors: -** Small-molecule inhibitors are a type of targeted cancer therapy designed to block specific molecules that play an important role in cancer cell growth and survival. These drugs are usually taken orally and are small enough to enter cancer cells, where they act on key intracellular signaling pathways. By attaching to their target molecules, they interrupt essential signaling processes, which helps stop tumor growth and can lead to cancer cell death. Common examples include imatinib, which targets the BCR-ABL fusion protein in chronic myeloid leukemia (CML), and vemurafenib, which targets the BRAF V600E mutation in melanoma. (13)

2. **Monoclonal Antibodies:-** Monoclonal antibodies (mAbs) are specially designed antibodies that recognize and attach to particular proteins found on the surface of cancer cells. Once bound, they can either block important signals that cancer cells need to grow or flag these cells so that the immune system can identify and destroy them. By harnessing the body's natural immune defenses, monoclonal antibodies help generate a targeted attack against cancer cells. Well-known examples include trastuzumab, which targets the HER2 protein in breast cancer, and rituximab, which targets the CD20 antigen in B-cell lymphomas. (14)

3. **Gene Therapies and Viral Vectors: -** Gene therapies use specially engineered viruses or vectors to deliver therapeutic genes into cancer cells. Once inside, these vectors can integrate with the cancer cell's DNA, helping to modify its behavior, slow tumor growth, or stop it entirely. Some gene therapies are also designed to trigger programmed cell death (apoptosis) in cancer cells. A well-known example is CAR-T cell therapy, in which a patient's T-cells are genetically modified to express chimeric antigen receptors (CARs). These receptors enable the T-cells to specifically recognize and attack cancer cells, such as CD19-**expressing cells in B-cell leukemia and lymphomas**. (15, 16)

Mechanism of Action of Advanced Targeted Therapies:-

Advanced targeted therapies act by selectively targeting specific molecular abnormalities present in cancer cells. Tyrosine kinase inhibitors inhibit overactive tyrosine kinases involved in abnormal signal transduction and uncontrolled cancer cell proliferation. Monoclonal antibodies bind to specific antigens expressed on the surface of cancer cells and block growth-promoting signaling pathways, while antibody–drug conjugates deliver cytotoxic agents directly into cancer cells to induce selective cell death. Targeted protein degraders such as PROTACs promote degradation of oncogenic proteins through the ubiquitin–proteasome pathway. Biomarker-guided precision therapy uses molecular profiling to select the most appropriate targeted therapy for individual patients, thereby improving treatment efficacy and reducing toxicity (17, 18)

Role of Biomarkers and Precision Medicine in Advanced Targeted Cancer Therapies:-

1. Personalized treatment selection: - Biomarkers play a key role in identifying tumor-specific genetic mutations, molecular pathways, and abnormal protein expressions. Techniques such as genomic sequencing and molecular profiling help detect actionable targets within cancer cells. Based on these findings, targeted therapies are selected that are specifically tailored to an individual patient's tumor biology. This personalized approach improves treatment precision and therapeutic effectiveness. It also avoids the use of non-specific treatments that may not benefit the patient. Thus, biomarkers form the cornerstone of precision medicine in oncology. (19)

2. Prediction of treatment response: - Biomarkers are widely used to predict how a patient will respond to a specific targeted therapy. Genetic, proteomic, and molecular biomarkers help differentiate responders from non-responders before treatment initiation. This enables clinicians to choose the most effective drug at an early stage. Predictive biomarkers reduce trial-and-error therapy and unnecessary delays in treatment. As a result, patient outcomes and survival rates are significantly improved. (20)

3. Minimization of toxicity: - Precision medicine helps minimize treatment-related toxicity by ensuring that targeted therapies are given only to patients who are likely to benefit. Since these therapies act on specific molecular targets, damage to normal cells is reduced. This leads to fewer adverse effects compared to conventional chemotherapy. Reduced toxicity improves patient tolerance, compliance, and overall quality of life. Thus, biomarker-based treatment selection enhances both safety and effectiveness. (21)

4. Real-time disease monitoring: - Advanced biomarkers such as circulating tumor DNA obtained through liquid biopsy allow continuous and real-time monitoring of cancer progression. These biomarkers help assess treatment response, detect minimal residual disease, and identify early development of drug resistance. Real-time monitoring enables timely modification of treatment strategies. This dynamic approach improves long-term disease control and personalized patient management. (22)

5. Support for advanced targeted modalities: - Biomarker identification is essential for the successful application of advanced targeted therapies such as antibody–drug conjugates, small-molecule inhibitors, and immunotherapies. These therapies require specific molecular targets to function effectively. Biomarkers ensure selective targeting of cancer cells while sparing normal tissues. This increases therapeutic precision and reduces off-target toxicity. Consequently, biomarkers play a critical role in the development and clinical use of modern targeted cancer therapies. (23)

6. Improved clinical decision-making:- Integration of biomarker data with clinical, pathological, and imaging information supports evidence-based and individualized clinical decision-making. Precision medicine enables oncologists to design optimal treatment strategies tailored to each patient's disease profile. It also assists in monitoring disease progression and adjusting therapy as needed. This comprehensive approach improves treatment outcomes and represents a major advancement in modern cancer care. (18)

Recent Advances in Targeted Cancer Therapies:-

1. Targeting "undruggable" cancer proteins:-Recent advances have made it possible to target cancer proteins that were earlier considered "undruggable." Novel strategies such as targeted protein degradation (e.g., PROTACs) allow selective elimination of disease-causing proteins rather than simple inhibition. This has significantly expanded treatment options, particularly in cancers that have developed resistance to conventional therapies. (23)

2. Next-generation antibody-based therapies:-Next-generation antibody-based therapies, especially antibody–drug conjugates (ADCs), have shown major improvements in design. The use of stable linkers and highly potent cytotoxic payloads allows precise delivery of drugs to cancer cells. This leads to selective killing of tumor cells while reducing damage to normal tissues and minimizing systemic toxicity. (23)

3. Refined small-molecule inhibitors: - Refined small-molecule inhibitors exhibit higher specificity and improved activity against resistant cancer mutations. These inhibitors are designed to overcome acquired resistance mechanisms seen with earlier drugs. As a result, they provide enhanced long-term treatment effectiveness and improved patient outcomes. (18)

4. Precision-guided treatment combinations:-Targeted therapies are increasingly combined with immunotherapy or other targeted agents based on molecular and genomic profiling. Such precision-guided treatment combinations allow synergistic effects and improved clinical responses. This approach leads to better disease control and personalized cancer management. (18)

5. Liquid biopsy-guided therapy monitoring: - Liquid biopsy-based analysis, particularly circulating tumor DNA (ctDNA), enables real-time monitoring of treatment response. It allows early detection of disease progression and identification of resistance mechanisms. This helps clinicians modify treatment strategies promptly and improves overall disease management. (18)

6. Expansion beyond single-gene targets: - Modern approaches now move beyond single-gene targeting by using multi-omics strategies. These approaches target complex signaling networks rather than individual mutations. This helps address tumor heterogeneity more effectively and improves treatment success in diverse cancer populations. (18)

7. Improved tumor-specific drug delivery: - Innovative drug delivery systems enhance selective accumulation of therapeutic agents at tumor sites. These systems improve drug efficacy while minimizing exposure of normal tissues. As a result, therapeutic outcomes are improved with reduced systemic toxicity. (23)

Clinical Applications:-

1. Biomarker-guided therapy selection:-Targeted drugs are clinically used based on specific genetic or molecular alterations in tumors, improving treatment precision. (24)

2. Use of targeted inhibitors in solid tumors:-Tyrosine kinase inhibitors are routinely applied in cancers such as lung and melanoma to block cancer-driving pathways. (24)

3. Antibody–drug conjugates in advanced cancers:-ADCs deliver cytotoxic agents directly to cancer cells, enhancing efficacy with reduced systemic toxicity. (18)

4. Liquid biopsy in clinical monitoring:-Circulating tumor DNA analysis supports real-time monitoring of treatment response and resistance development. (18)

5. Combination targeted strategies:-Targeted therapies are increasingly combined with immunotherapy or other agents to improve clinical outcomes. (24)

6. Expansion to cell-based targeted therapies:-Targeted cell therapies are being clinically explored beyond blood cancers, showing promise in solid tumors. (18)

Advantages of Advanced Targeted Therapies in Cancer:-

1. High treatment specificity:-Targeted therapies act on specific molecular abnormalities in cancer cells, reducing damage to normal tissues. (24)

2. Improved therapeutic efficacy:-By directly blocking cancer-driving pathways, targeted therapies often show better response rates compared to conventional chemotherapy. (24)

3. Reduced systemic toxicity:-Selective targeting minimizes adverse effects, leading to improved patient tolerance and quality of life. (18)

4. Personalized treatment approach:-Therapy selection is guided by tumor biomarkers, allowing individualized treatment plans. (18)

5. Lower risk of overtreatment:-Patients unlikely to benefit can be spared ineffective therapies through molecular profiling. (24)

6. Better disease monitoring:-Integration with biomarkers and liquid biopsy enables real-time assessment of treatment response. (18)

7. Compatibility with combination therapy: - Targeted therapies can be effectively combined with immunotherapy or other agents to enhance outcomes. (24)

Limitations and Challenges of Advanced Targeted Therapies:-

1. Development of drug resistance: - Although targeted therapies initially show good clinical responses, many cancers eventually develop drug resistance. Genetic mutations, pathway reactivation, or activation of alternative signaling routes reduce long-term efficacy, limiting sustained clinical benefit. (24)

2. Tumor heterogeneity: - Tumors often consist of multiple genetically distinct cell populations. This heterogeneity leads to variable responses to targeted agents, as not all tumor cells depend on the same molecular target, resulting in incomplete tumor control. (18)

3. Restricted benefit to selected patients: - The effectiveness of targeted therapies is limited to patients who possess actionable biomarkers. Patients lacking these molecular alterations do not benefit, thereby restricting the overall applicability of targeted treatments. (24)

4. High cost and limited accessibility: - Targeted drugs and associated molecular diagnostic testing are expensive. High treatment costs and limited availability of advanced testing facilities reduce accessibility, especially in resource-limited healthcare settings. (18)

5. Limitations of single-target approaches:-Single-target therapies may fail due to complex and interconnected cancer signaling networks. Inhibition of one pathway can be bypassed by compensatory mechanisms, leading to reduced therapeutic effectiveness. (24)

6. Off-target toxicity:-Despite improved selectivity, targeted therapies can still affect normal tissues expressing similar molecular targets. This may result in off-target toxicities, highlighting that targeted therapies are not completely free from adverse effects. (18)

7. Need for advanced infrastructure and expertise:-Successful clinical implementation of targeted therapies requires advanced molecular diagnostics, specialized infrastructure, and trained personnel. Lack of such resources can limit widespread clinical adoption. (24)

Future Perspectives of Advanced Targeted Therapies:-

The future of advanced targeted therapies in cancer appears highly promising due to continuous advancements in molecular biology, genomics, and biotechnology. In the coming years, cancer treatment is expected to move strongly toward personalized medicine. The use of next-generation sequencing, molecular profiling, and advanced biomarker testing will allow better understanding of tumor-specific genetic and molecular changes. This will help clinicians select targeted drugs that are most effective for individual patients, improving treatment response and reducing unnecessary toxicity. Personalized approaches are also expected to improve early diagnosis, treatment monitoring, and prediction of therapeutic outcomes.(23)(24)

Another major future direction involves the development of combination treatment strategies and innovative drug delivery systems. Targeted therapies will increasingly be used in combination with immunotherapy, chemotherapy, or radiotherapy to overcome drug resistance and enhance long-term patient survival. Novel drug

delivery technologies, such as nanoparticle-based systems and antibody–drug conjugates, will further increase treatment precision by delivering drugs directly to cancer cells while sparing healthy tissues. In addition, artificial intelligence and bioinformatics tools will support the identification of new molecular targets and accelerate drug discovery. Although challenges such as high treatment cost, tumor heterogeneity, and acquired resistance remain, ongoing research and clinical trials are expected to address these limitations. Overall, advanced targeted therapies are likely to transform cancer management by making treatment more precise, effective, and patient-centered in the future. (23)(24)

4. Conclusion

Advanced targeted therapies have brought a major improvement in the treatment of cancer by acting on specific molecular and genetic changes found in cancer cells. Unlike conventional chemotherapy, these therapies mainly affect cancer cells and cause less harm to normal healthy tissues, which helps in reducing side effects and improving patient comfort. The use of biomarkers, molecular profiling, and genetic testing has made it possible to design personalized treatment plans for individual patients, leading to better treatment response and disease control. Even though challenges such as drug resistance, tumor heterogeneity, limited availability of suitable targets, and high treatment cost still remain, continuous research and ongoing clinical trials are helping to find effective solutions. In addition, the future use of combination therapies, improved drug delivery systems, and advanced technologies such as artificial intelligence and bioinformatics is expected to further enhance the accuracy and effectiveness of targeted cancer treatments. Overall, advanced targeted therapies represent an important step toward precision oncology and are expected to improve survival rates as well as quality of life for cancer patients. (24)(25)

References

1. Tsimberidou AM, Iskander NG, Hong DS, Wheler JJ, Fal chook GS, Fu S, Piha-Paul S, Naing A, Janku F, Luthra R, Ye Y, Wen S, Berry D, Kurzrock R (2012) Personalized medicine in a phase I clinical trials program: the MD Anderson Cancer Center initiative. Clin Cancer Res Off J Am Assoc Cancer Res 18(22):6373–6383. doi:10.1158/1078-0432.CCR-12-1627
2. Von Hoff DD, Stephenson JJ Jr, Rosen P, Loesch DM, Borad MJ, Anthony S, Jameson G, Brown S, Cantafio N, Richards DA, Fitch TR, Wasserman E, Fernandez C, Green S, Suther land W, Bittner M, Alarcon A, Mallery D, Penny R (2010) Pilot study using molecular profiling of patients' tumors to find potential targets and select treatments for their refractory can cers. J Clin Oncol Off J Am Soc Clin Oncol 28(33):4877–4883. doi:10.1200/JCO.2009.26.5983
3. Yarden, Y., & Pines, G. (2012). The ERBB network: a convergence point of signaling pathways in cancer. Nature Reviews Cancer, 12(8), 623-631.
4. Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of cancer: the next generation. Cell, 144(5), 646-674.
5. Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med. 2015;372(9):793–795.
6. Dienstmann R, Rodon J, Barretina J, Tabernero J. Precision oncology: a reality or a promise? Nat Rev Clin Oncol. 2017;14(6):337–348.
7. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell. 2011;144(5):646–674.
8. Cohen P. Protein kinases as drug targets. Nat Rev Drug Discov. 2002;1(4):309–315.
9. Scott AM, Wolchok JD, Old LJ. Antibody therapy of cancer. Nat Rev Cancer. 2012;12(4):278–287.

10. DeVita VT, Lawrence TS, Rosenberg SA. Cancer: Principles & Practice of Oncology. 11th ed. Wolters Kluwer; 2019.

11. Schwaederle, M., Zhao, M., Lee, J. J., Eggermont, A. M., Schilsky, R. L., Mendelsohn, J., ... & Kurzrock, R. (2015). Impact of precision medicine in diverse cancers: a meta-analysis of phase II clinical trials. Journal of Clinical Oncology, 33(32), 3817-3825.

12. Drilon, A., & Li, G. (2013). Mechanisms of resistance and sensitivity to anti-HER2 therapies in HER2+ breast cancer. Oncogene, 34(28), 3999-4008.

13. Druker, B. J., Talpaz, M., Resta, D. J., Peng, B., Buchdunger, E., Ford, J. M., ... & Sawyers, C. L. (2001). Efficacy and safety of a specific inhibitor of the BCR ABL tyrosine kinase in chronic myeloid leukemia. New England Journal of Medicine, 344(14), 1031-1037.

14. Hodi, F. S., O'Day, S. J., McDermott, D. F., Weber, R. W., Sosman, J. A., Haanen, J. B., ... & Urba, W. J. (2010). Improved survival with ipilimumab in patients with metastatic melanoma. New England Journal of Medicine, 363(8), 711-723.

15. Slamon, D. J., Leyland-Jones, B., Shak, S., Fuchs, H., Paton, V., Bajamonde, A., ... & Norton, L. (2001). Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2. New England Journal of Medicine, 344(11), 783 792.

16. Naldini, L. (2015). Gene therapy returns to centre stage. Nature, 526(7573), 351-360.

17. Roskoski, R. Properties of FDA-approved small-molecule protein kinase inhibitors. Pharmacological Research, 2019.

18. Garraway, L. A., & Verweij, J. Precision oncology. Journal of Clinical Oncology, 2013

19. Jain, K. K. Precision medicine for cancer: Role of biomarkers. Current Opinion in Pharmacology, 2020, 54: 1–6.

20. Henry, N. L., & Hayes, D. F. Cancer biomarkers. Molecular Oncology, 2012, 6(2): 140–146.

21. Collins, F. S., & Varmus, H. A new initiative on precision medicine. New England Journal of Medicine, 2015, 372(9): 793–795.

22. Wan, J. C. M., et al. Liquid biopsies come of age. Nature Reviews Cancer, 2017, 17(4): 223–238.

23. Drago, J. Z., Modi, S., & Chandarlapaty, S. Unlocking the potential of antibody–drug conjugates. Nature Reviews Clinical Oncology, 2021, 18(6): 327–344.

24. Sawyers, C. L. Targeted cancer therapy. Nature, 2004; 432: 294-297

25. Dienstmann R, et al.Precision oncology: from molecular profiling to clinical practice.Nature Reviews Clinical Oncology, 2017; 14: 113–130.