Personalized Drug Therapy in Oncology: Clinical Insights and Future Perspectives

Changxuan Liang
Zhuhai College of Science and Technology, Zhuhai, Guangdong, China

Abstract: Cancer treatment has made progress through personalized medical therapies that tailor strategies based on patient characteristics. This article explores the application of personalized therapies in oncology, including biomarker-guided therapies, liquid biopsies, next-generation sequencing, personalized immunotherapy, and nanotechnology-based drug delivery. Focusing on personalized drug therapy in oncology, this article delves into its clinical application. It elaborates on the use of biomarkers to guide medication, liquid biopsy for auxiliary diagnosis, and personalized immunotherapy, showcasing their role in advancing precision medicine. At the same time, it discusses the challenges faced in this field, such as high costs and complex data processing, and looks forward to the future prospects of personalized drug therapy in oncology. Despite advancements, challenges such as high costs and complex data analysis issues still persist.
***Keywords*:** oncology; personalized drug therapy; genetic factors; physiological state; biomarker-guided therapy

1. Introduction

Cancer, a complex disease with patient variability, has limitations in traditional treatments. Personalized medicine focuses on tailoring treatments to individual patient characteristics, including genetic and physiological factors, to optimize results and reduce side effects. This review covers the implementation of personalized drug therapy in oncology, current successes, and future prospects.

2. Patient-Specific Factors in Personalized Drug Therapy

2.1 Genetic Factors

2.1.1 Somatic Mutations

Somatic mutations are key to cancer progression and are treated with personalized drugs. In NSCLC, EGFR mutations occur in 10-30% of patients, particularly Asians, non-smokers, and women. Drugs like gefitinib, erlotinib, and osimertinib target these mutations. Clinical trials show these drugs improve progression-free survival (PFS) in patients with EGFR-activating mutations over standard chemotherapy. The IPASS study found that EGFR-mutant NSCLC patients treated with gefitinib had a PFS of 9.5 months, compared to 6.3 months for those on chemotherapy.

Another well-studied example is the anaplastic lymphoma kinase (ALK) rearrangement in NSCLC. Approximately 3-7% of NSCLC patients harbor ALK rearrangements. Crizotinib, a first-generation ALK inhibitor, has demonstrated remarkable efficacy in these patients. In the PROFILE 1005 study, the overall response rate (ORR) to crizotinib in ALK-positive NSCLC patients was 60.8%, and the median PFS was 9.7 months. Second-and third-generation ALK inhibitors, such as ceritinib, alectinib, and brigatinib, have further improved outcomes, with alectinib showing a median PFS of up to 34.8 months in the ALEX study.

2.1.2 Germline Mutations

Germline mutations also play a crucial role in personalized cancer treatment. Inherited mutations in genes like BRCA1 and BRCA2 are associated with an increased risk of breast, ovarian, and other cancers. PARP (poly ADP-ribose polymerase) inhibitors, such as olaparib, have been developed to target tumors with BRCA mutations. In patients with germline BRCA-mutated ovarian cancer, olaparib maintenance therapy after platinum-based chemotherapy significantly improved PFS. In the SOLO1 trial, patients treated with olaparib had a median PFS of 41.2 months, compared to 13.8 months in the placebo group.

2.2 Physiological State

2.2.1 Age

Age affects cancer treatment. Elderly patients have decreased organ function and may be refractory to standard

chemotherapy. FOLFOX The protocol is suitable for young patients, but elderly patients need adjustment. For some elderly patients, dose reduction or selection of capecitabine monotherapy may be more appropriate to balance efficacy and toxicity. [1]Studies show that although survival in elderly patients may decrease slightly, the quality of life can be maintained and the risk of serious adverse events is reduced.

2.2.2 Renal and Hepatic Function

Kidney and liver function significantly affects the pharmacokinetics of anticancer drugs. For example, cisplatin is excreted primarily through the kidney, and patients with impaired renal function have reduced cisplatin clearance, leading to drug accumulation and increased risk of toxicity, including nephrotoxicity and ototoxicity. Therefore, it is essential to adjust the doses based on the estimated glomerular filtration rate (eGFR). For drugs metabolized by the liver, such as doxorubicin, liver function indicators, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin levels, should be considered. In patients with cirrhosis or other liver dysfunction, the potentially altered metabolism of doxorubicin may require appropriate dose reduction or use of alternative drugs to avoid excessive toxicity.

3. Current Clinical Practice of Personalized Drug Therapy in Oncology

3.1 Biomarker-Guided Therapy

Biomarker-guided therapy has become the cornerstone of personalized drug therapy in oncology. Biomarkers can be used to predict a patient's response to a particular treatment, identify patients who are likely to benefit from a specific drug, and monitor treatment response. For example, in breast cancer, the presence of human epidermal growth factor receptor 2 (HER2) overexpression or amplification is a well-established biomarker. Trastuzumab, a monoclonal antibody that targets HER2, has significantly improved the prognosis of HER2-positive breast cancer patients. [2]In the HERA trial, patients with HER2-positive breast cancer who received trastuzumab for 1 year after surgery had a 34% reduction in the risk of recurrence compared to those who did not receive trastuzumab.

BRAF mutations in melanoma have resulted in the creation of BRAF inhibitors like vemurafenib and dabrafenib. Roughly half of melanoma patients have these mutations. BRAF inhibitors have demonstrated high response rates in treating BRAF-mutant melanoma patients. The BRIM-3 trial showed vemurafenib extended median overall survival to 13.6 months for BRAF V600E-mutant patients, compared to 9.7 months with dacarbazine.

3.2 Liquid Biopsy

Liquid biopsy, analyzing CTCs, ctDNA, and exosomes in blood, is key for personalized cancer treatment. CTCs offer insights into genetic mutations and real-time tumor status. For instance, in metastatic breast cancer, CTCs can predict treatment response, with higher counts indicating a poorer prognosis and changes during treatment showing its efficacy.

CtDNA analysis is crucial for its high sensitivity in detecting somatic mutations in cancer cells. In NSCLC, it helps identify EGFR mutations and monitor resistance mutations during TKI treatment. Detecting the T790M mutation in ctDNA can guide the switch to osimertinib for treating T790M-positive NSCLC.

4. Future Perspectives

4.1 Next-Generation Sequencing (NGS) and Multi-Omics Approaches

Next-generation sequencing technologies are becoming more advanced and cost-effective. In the future, comprehensive genomic profiling using NGS will be more widely adopted in clinical practice. Instead of just testing for a few known mutations, NGS can analyze the entire cancer genome, epigenome, and transcriptome. This will enable the identification of rare and novel mutations that may be potential therapeutic targets. Multi-omics approaches, which integrate genomic, proteomic, and metabolomic data, will provide a more comprehensive understanding of the tumor's molecular landscape. For example, combining genomic data with proteomic data can help clarify how genetic mutations translate into changes in protein expression and function, leading to more precise drug development and treatment selection.

4.2 Immunotherapy and Personalization

Immunotherapy has revolutionized cancer treatment and personalization of this approach is imminent. Currently, drugs like pembrolizumab and nivolumab are used for various cancers, but not all patients respond. Future research aims to find biomarkers that can predict patient responses to immunotherapy. TMB, MSI, and specific immune cell populations in the tumor microenvironment are being studied as potential biomarkers. Personalized cancer vaccines, targeting unique tumor antigens for each patient, are also promising. [3]These vaccines could enable the immune system to specifically target and

destroy cancer cells, offering a more precise and effective treatment.

4.3 Nanotechnology-Enabled Personalized Drug Delivery

Nanotechnology has significant potential for personalized drug delivery in oncology. Nanoparticles can be designed to carry anti-cancer drugs and target specific cells or tissues. For instance, they can be modified with ligands that attach to receptors on cancer cells, like the folate receptor in ovarian cancers. This targeted approach enhances drug concentration at the tumor and decreases side effects. Future drug delivery systems could be tailored to individual tumor and patient characteristics to improve treatment results.

5. Conclusion

Significant progress has been made in personalized cancer drug treatment by combining patient genetic and physiological characteristics for therapy. Clinical practices such as biomarker-guided treatment and liquid biopsy have improved treatment outcomes. In the future, the development of technologies such as Next-Generation Sequencing (NGS), multi-omics, personalized immunotherapy, and nanotechnology-based drug delivery is expected to further enhance the precision and effectiveness of cancer treatment. However, challenges remain, including the high cost of personalized therapy, the need for widespread adoption of advanced diagnostic technologies, and the complexity of interpreting multidimensional data. Overcoming these challenges is crucial for realizing the full potential of personalized cancer drug treatment and improving the lives of cancer patients worldwide.

References

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