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PHARMACOGENOMICS IN CANCER THERAPY: PERSONALIZED MEDICINE FOR BETTER OUTCOMES

Anannya Mathew¹ *, Kummari Ganesh² , Bhargav Raj M. S. 3 , Dhanya P. V. 4 , Immadi Madhan Mohan⁵ , Habeeb Rahman Khan⁶ , Mohammadakil Shaikh⁷ , Shaikh Mohmed Adnan Mohmed Javid⁸ , Divy H. Bhimani⁹ , Morziul Haque¹⁰ and Santosh S. 11

¹Pharm.D, anannyamathew199928@gmail.com

²Pharm.D (Fellowship in Critical Care Pharmacotherapy), MNR College of Pharmacy Sangareddy, Telangana. Ganeshkummari8@gmail.Com

 3 Clinical Pharmacologist, Sri Shankara Cancer Hospital and Research Centre. drbhargavraj@gmail.com

⁴Clinical Pharmacologist, Healius Cancer Centre and Hematology Clinic. dhanyapv48@gmail.com 5 PharmD, Santhiram College of Pharmacy, Nerwada, Panyam, Nandyal Andhra Pradesh.

madhanmohanimmadi13@gmail.com

⁶Pharm.D, Shadan College of Pharmacy, Hyderabad Telangana. habeebrk7@gmail.com ⁷Pharm.D, School of Pharmacy, RK University, Rajkot, Gujarat. **akilshaikh25786@gmail.com** ⁸ Pharm.D, Shree Dhanvantary Pharmacy College, Kim, Surat, Gujarat. **adnanshaikh2807200@gmail.com** ⁹ Pharm.D, School of Pharmacy, RK University, Rajkot, Gujarat. divybhimani12@gmail.com ¹⁰Doctor of Pharmacy, University Institute of Pharma Sciences, Chandigarh University, Mohali, Punjab, India. haquemorziul69@gmail.com

¹¹Pharm.D, Saradavilas College of Pharmacy, Krishnamurthy Puram, Mysore, Karnataka. santhoshupamanyu@gmail.com

***Corresponding Author: Anannya Mathew**

Pharm. D, MNR College of Pharmacy Sangareddy, Telangana. **Email ID:** anannyamathew199928@gmail.com

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ABSTRACT

Pharmacogenomics, the study of how genetic differences impact drug reactions, is essential to cancer therapy because it makes customized treatment plans possible. The integration of pharmacogenomics in cancer care is examined in this review, which emphasizes how genetic profiling enables personalized therapy that improve efficacy and minimize side effects. Based on the patient's genetic composition, personalized medicine enables targeted cancer treatments that improve therapeutic outcomes and increase survival rates. Discussed are significant developments in pharmacogenomic applications for cancer treatment, including the utilization of immunotherapies and targeted treatments. Furthermore, the difficulties and potential paths for pharmacogenomic-based cancer therapy implementation in clinical settings are analyzed. In general, this review emphasizes how crucial it is to use pharmacogenomics in cancer treatment in order to provide tailored, precision medicine for the best possible outcomes for patients.

KEYWORDS: Pharmacogenomics, Cancer therapy, Personalized medicine, Targeted therapy, Genetic profiling, precision medicine.

Overview of cancer therapy

Cancer therapy therefore ranges widely, from a variety of therapeutic approaches all aimed at reducing or eliminating the cancerous cells in the body. The major goals of treatment in cancer are to cure the disease, halt disease progression, alleviate symptoms, and ultimately improve quality of life of those affected. The type and stage of malignancy and the individual patient's preferences and overall state of health, taken together, influence the therapeutic decision. The major tumor treatments include:

- **1. Surgery:** In the vast majority of instances, and with few exceptions for localized tumors, the first modality for treating a tumor involves the physical removal of the tumor. If the cancer is localized, surgery is the only treatment. It can also be combined in the management of advanced malignancies and for whatever microscopic disease may remain.
- **2. Radiation therapy:** This involves the destruction or shrinkage of tumors and cancer cells by high-energy radiation. Apart from being used singly, radiation

therapy can also be used with the mentioned methods. Improvements with techniques like proton therapy, brachytherapy, and external beam radiation nowadays allow treating cancers more effectively by saving healthy tissues.

- **3. Chemotherapy:** Chemotherapy uses drugs that are toxic to any cells that are active and dividing, such as cancer cells. Chemotherapy can be local or systemic to eliminate the cancer barrier that surrounds the possible metastatic cancer cells that may have spread throughout the body. It works very well against certain blood cancers like leukemia and lymphomas and so chemotherapy is frequently used in combination with other treatments.
- **4. Immunotherapy:** This therapeutics goes a mile further to increase the chances of the immune system finding and killing off tumor cells that have been altered or otherwise don't belong in the body. This involves the use of adoption therapy using CAR-T cells, checkpoint immune therapy, and cancer vaccinations. it can be clearly seen that with this ratio, astonishing outcomes were accomplished in diseases that at that time were considered refractive to treatment such as melanoma and some lung cancers.
- **5. Targeted therapy:** It is such a type of treatment whereby medicines or other materials developed against cancer act selectively on the cancerous cells with little effect on the healthy ones. In disrupting the activity of some molecules that take part in development and growth of the tumor, these medicines impede growth and spread of cancer. Examples include Tyrosine kinase inhibitors and Monoclonal antibodies.
- **6. Hormone therapy:** Cancers that are hormonesensitive, like breast and prostate cancer, can be treated with hormone therapy. It functions by preventing the body from producing hormones or by altering the way hormones function within the body.
- **7. Stem cell transplantation:** Cancers of the blood, such as multiple myeloma, lymphoma, and leukemia, are treated with this therapy. In order to replace the stem cells that were damaged by heavy doses of chemotherapy or radiation therapy, healthy stem cells are transplanted.
- **8. Combination therapy:** To increase efficacy, cancer treatment frequently combines the aforementioned techniques. The kind, stage, and unique patient characteristics dictate the combination that is selected.^[4,5]

Importance of personalized medicine in oncology

Precision medicine, another name for personalized medicine, is a revolutionary approach to oncology that customizes treatment to the unique needs of each patient and their malignancy. The potential of personalized medicine to enhance patient outcomes by tailoring treatment plans to the distinct genetic, biochemical, and environmental characteristics of the patient and the tumor underscores its significance in the field of

oncology. Important elements of oncology-specific customized medication include:

- **1. Genomic profiling:** New developments in genomic technologies enable the sequencing of cancer genomes, which enables the discovery of certain gene expressions, mutations, and molecular markers that propel the growth of cancer. The choice of targeted treatments that are most likely to be successful for the particular type of cancer is guided by this information.
- **2. Biomarker identification:** Biomarkers are quantifiable markers of physiological processes or therapeutic response. Biomarkers in oncology help doctors select the best course of action by forecasting a patient's reaction to a certain drug. For example, patients with breast cancer who have overexpressed HER2 may benefit from trastuzumab or other HER2-targeted treatments.
- **3. Reduced toxicity:** In keeping patients away from superfluous treatments that are unlikely to benefit them, personalized medicine lessens toxic events and otherwise increases the overall safety profile of cancer therapy.
- **4. Improved efficacy:** Personalized medicine raises hopes of better outcomes, like an increased survival rate and quality of life, through matching the patient with the therapies that are likely to be of benefit according to genetic makeup of tumor.
- **5. Adaptive treatment strategies:** The use of personalized medicine enables the continuance of real-time modifications that monitor a patient's reaction to treatment. This adaptive strategy will mean treatments can be altered or adjusted in response to how the cancer is progressing and changing, as well as the patient's response.
- **6. Patient-Centric care:** Personalized medicine is patient-centric and considers individual needs and conditions of each individual while adopting and designing a treatment approach. This not only maximizes the effect of the therapy but also respects the patient's values and preferences.
- **7. Innovation and Research:** Thus, the trend for personalized medicine has encouraged much innovation in oncology research-to create new diagnostic tools, targeted treatments, and less toxic and more successful combination approaches.

Personalized medicine in oncology has great promise for improved, safer, and patient-focused therapy, making it a key step in the fight against cancer. Personalized medicine improves the accuracy and effectiveness of cancer therapy by customizing care for each patient, which eventually results in better patient outcomes.^[6,7,8,9]

Pharmacogenomics

The study of pharmacogenomics focuses on how a person's genetic composition affects how they react to medications. It combines the fields of genomics, which studies genomes, and pharmacology, which studies drugs, to comprehend how genetic variations impact the

safety and efficacy of pharmaceuticals. Personalized medicine will result from optimizing pharmacological therapy based on each person's unique genetic profile.

Historical Perspective and Evolution Early beginnings

- **Ancient observations:** The idea of customized medicine originated from early studies in which different people responded differently to herbal remedies, suggesting hereditary implications.
- 19th and Early 20th century: The foundation for pharmacogenomics was laid by developments in biochemistry and the identification of enzymes such as cytochrome P450, which demonstrated the importance of metabolism in drug response.

Mid-20th century

 1960s: The study of how individual gene variants affect drug response led to the coining of the term "pharmacogenetics." An analysis of drug metabolism in the past revealed genetic variations (such as polymorphisms in the enzyme pseudocholinesterase that alter the metabolism of succinylcholine).

Late 20th Century

- **1970s-1980s:** The field grew as additional genetic variations influencing drug response and metabolism were found. With the development of methods like gene sequencing, more in-depth genetic analysis became possible.
- **1990s:** By more precisely connecting genetic differences to medication reactions, the Human Genome Project's draft sequence, completed in 2000, offered a comprehensive map of human genes and revolutionized pharmacogenomics.

21st century

- **2000s:** The 2000s saw the widespread adoption of the term "pharmacogenomics," which reflected the incorporation of genomics with pharmacology. Large-scale investigations relating genetic variations to drug response have been made possible by developments in high-throughput genotyping and bioinformatics.
- **2010s:** The 2010s saw a rise in the use of pharmacogenomics in clinical practice, along with the development of guidelines and recommendations for genetic testing across a range of treatment domains (psychiatric, cardiology, oncology, etc.).
- **2020s and Beyond:** Creating individualized treatment regimens, enhancing patient outcomes, and incorporating pharmacogenomics into standard clinical practice are now the main priorities. Wholegenome sequencing and precision medicine are two examples of genomics advancements that are propelling the industry ahead.

From early genetic observations, pharmacogenomics has developed into a sophisticated field that combines pharmacology and genomics to enhance and tailor medication therapy.^[9,10,11,12]

Role of pharmacogenomics in cancer treatment

By customizing treatments to each patient's genetic profile, pharmacogenomics plays a critical role in the treatment of cancer by increasing efficacy and minimizing side effects

- **1. Personalized treatment:** Pharmacogenomics makes it possible to tailor cancer therapies to a patient's genetic composition. This method can assist in determining which medications are most likely to be beneficial and which might have negative side effects.
- **2. Drug metabolism:** Genetic differences may have an impact on a patient's drug metabolism. For instance, changes in the CYP450 enzyme family can impact the toxicity and effectiveness of chemotherapy drugs by altering how they re metabolized. Comprehending these variances aids in modifying dosages to reduce adverse effects and optimize therapeutic advantages.
- **3. Targeted therapies:** Pharmacogenomics encourages the development and application of targeted medicines. It means that therapies could be made to directly attack only the genetic abnormalities peculiar to the cancer cells and thus protect normal cells and reduce accidental damage.
- **4. Predicting drug response:** The genetic test was able to predict the response of an individual to certain drugs. Patients with HER2-positive breast cancer may also be responsive to certain treatments that target the HER2 protein, such as trastuzumab or Herceptin.
- **5. Reducing adverse effects:** Genetic predisposition information on toxic effects that some drugs induce helps health professionals avoid medications that are most likely to cause harm. For example, variations in the TPMT gene render the risk a patient has for developing thiopurine medication toxicity during the treatment of cancer.
- **6. Optimizing dosing:** Genetic information is useful in the identification of the optimal dose of a particular drug. For instance, individuals of certain genetic backgrounds may require higher or even lower dosages of particular drugs, such as warfarin, which is sometimes prescribed to cancer patients against blood clotting conditions.
- **7. Developing new drugs:** Pharmacogenomics also helps in the development of new drugs by identifying new genetic targets for therapy. This can lead to the development of entirely new drugs that are less toxic and more potent.
- **8. Guiding combination therapies:** Several drugs that are used together in combination therapy may be prescribed in order to affect pathways or mechanisms related to cancer growth, guided by knowledge of the genetic profile of a patient's tumor. [13,14,15,16]

Tools and Technologies

A range of instruments and technologies are used in pharmacogenomics research to comprehend and utilize the connection between drug response and heredity. The main instruments and technologies employed in this discipline are outlined below

1. Genotyping technologies

- **Polymerase Chain Reaction (PCR):** A basic method used in genotyping to detect genetic differences, PCR amplifies particular DNA sequences.
- **SNP Genotyping arrays:** Arrays that identify single nucleotide polymorphisms throughout the genome are called SNP genotyping arrays. These highthroughput technologies may analyze from thousands to millions of SNPs in one experiment.
- **Next-Generation Sequencing (NGS):** NGS includes target sequencing, whole-exome sequencing, and whole-genome sequencing, techniques that give very valuable genetic information for the identification of less common variants and have comprehensively investigated the genetic basis of drug response.

2. Bioinformatics tools

- **Genome-Wide Association Studies (GWAS):** Techniques that allow the screening of gigantic databases across populations in order to pick up genetic variants that could associate with specific drug responses or adverse drug reactions.
- **Variant Annotation and Interpretation Software:** Programs such as ANNOVAR and SnpEff interpret the functional consequence and clinical relevance of the detected genetic variants.
- **Genomic Databases:** DbSNP, ClinVar, the 1000 Genomes Project. This database gives information about genetic variants and their disease and drug response associations.

3. Pharmacogenomics databases

- **PharmGKB:** An extensive database offering guidance for clinical practice as well as details on how genetic variations impact drug responses.
- **Clinical Pharmacogenetics Implementation Consortium (CPIC):** Guidelines and suggestions for incorporating pharmacogenetic information into clinical practice are provided by the Clinical Pharmacogenetics Implementation Consortium (CPIC).
- **DrugBank:** Provides comprehensive details on drug metabolism, interactions, and the effects of genetic variants on the safety and efficacy of pharmaceuticals.

4. Functional genomics

 Gene expression profiling: Profiling of gene expression involves the application of methods such as RNA-sequencing in the measurement of gene expression levels and the impacts genetic variation has on such levels. This helps in understanding the pharmacological mechanisms and resistance pathways.

- **Proteomics:** The proteome studies the discovery of how genetic differences influence protein expression and functionality that might have an effect on drug reaction to an individual.
- **5. Pharmacogenomic assays**
- **Metabolite profiling:** Methods (such as liquid chromatography-mass spectrometry, or LC-MS) for analyzing drug metabolism and identifying biomarkers of drug response and toxicity.
- **In vitro functional assays:** Laboratory procedures (such as enzyme activity assays) used to evaluate the functional impact of genetic variations on medication metabolism and efficacy.

6. Clinical decision support systems

- **Electronic Health Records (EHRs):** Systems that integrate pharmacogenomic data to guide personalized treatment decisions and track patient outcomes.
- **Clinical Decision Support Tools:** Software that uses pharmacogenomic data to provide recommendations for drug selection and dosing based on genetic profiles.

7. Ethical and Regulatory tools

- **Genetic counseling services:** Assist patients and medical professionals in comprehending the significance of the findings from pharmacogenomic testing.
- **Regulatory guidelines:** Organizations such as the FDA offer guidelines about the application of pharmacogenomic data in clinical practice and drug development.

8. Machine Learning and AI

- **Predictive modeling:** Based on genetic information and clinical characteristics, machine learning algorithms and artificial intelligence (AI) are utilized to anticipate drug reactions and side effects.
- **Integration of Multi-Omics Data:** To improve knowledge of medication responses and illness causes, genomics is combined with other omics data (proteomics, metabolomics). [17,18,19,20]

Pharmacogenomics in cancer: Mechanisms and Pathways

1. Drug metabolism pathways

- **Cytochrome P450 Enzymes (CYP450):** Chemotherapeutic treatment drugs may alter their way of metabolism due to some variations in genes encoding cytochrome P450 enzymes. As an example, CYP2D6 polymorphisms may give changes in the efficiency of tamoxifen, a major drug given to patients with breast cancer, in its metabolism.
- **UDP-Glucuronosyltransferases (UGTs):** The enzymes known as UDP-Glucuronosyltransferases

(UGTs) play a role in the phase II metabolism of medications. Changes in UGT1A1 can impact the way the chemotherapeutic medication irinotecan is metabolized, potentially causing toxicity and uneven treatment results.

2. Drug transporters

- **ATP-Binding Cassette (ABC) transporters:** Drug absorption, distribution, and excretion are impacted by transporters such as P-glycoprotein (P-gp, encoded by ABCB1) and Multidrug Resistance-Associated Proteins (MRPs). Medication resistance may be influenced by genetic differences in these transporters. For instance, by lowering the intracellular concentrations of several chemotherapeutic drugs, greater expression of P-gp can result in resistance to those medicines.
- **Solute Carrier (SLC) transporters:** Methotrexate absorption and effectiveness may be impacted by transporters such SLC22A4.

3. Drug targets

- **Oncogenes and Tumor suppressor genes:** Treatment effectiveness may be impacted by variations in genes encoding therapeutic targets. For instance, some inhibitors can specifically target BRAF gene alterations in malignancies such as melanoma. Similarly, in non-small cell lung cancer (NSCLC), EGFR gene alterations can affect how the cancer cell responds to EGFR inhibitors.
- **HER2/ERBB2:** Trastuzumab (Herceptin), a HER2 specific medication, targets the overexpression or amplification of the HER2 gene in breast cancer. Making informed judgments about treatment requires genetic testing to determine HER2 status.

4. DNA Repair Pathways

- **BRCA1/BRCA2:** These genes' mutations affect DNA repair processes and raise the risk of developing ovarian and breast cancers. BRCAmutant tumors can be effectively treated with PARP inhibitors like olaparib, which work by taking advantage of the damaged DNA repair pathway.
- **Mismatch Repair (MMR) Genes:** Microsatellite instability (MSI) is caused by mutations in MMR genes (e.g., MLH1, MSH2). In malignancies such as colorectal cancer, the MSI status can predict the response to immune checkpoint drugs.

5. Immune system modulation

- **Immune checkpoint inhibitors:** These drugs are used to treat a variety of cancers. Differences in genes linked to immune checkpoint pathways, such as PD-1 and PD-L1, can impact how the body reacts to them. Patients who are more likely to benefit from these medications can be identified with the use of genetic testing.
- **Tumor Mutational Burden (TMB):** A high TMB may suggest that immune checkpoint inhibitors will

be responded to more likely. The TMB test aids in the patient selection process for these treatments.

- **6. Pharmacogenomic biomarkers**
- **Pharmacogenomic biomarkers:** Certain biomarkers are employed in the prediction of medication toxicity and response. For example, variations in the TPMT gene may have an impact on thiopurine metabolism, which may change how leukemias and lymphomas are treated.
- **Response predictors:** In colorectal cancer, genetic markers such as KRAS mutations can indicate a patient's likelihood of developing resistance to specific targeted therapy, like EGFR inhibitors.

7. Epigenetic modifications

 DNA Methylation and Histone modification: Epigenetic modifications can affect how a medicine affects a gene's expression and reaction to it. Comprehending these alterations facilitates the creation of novel therapeutic approaches and the anticipation of responses to epigenetic medications.

8. Cancer genomics

 Whole-Genome and Whole-Exome Sequencing: These methods offer thorough genetic profiles of cancers, pointing out modifiable alterations and guiding therapeutic choices. For instance, sequencing can identify mutations that may be the target of particular treatments or that suggest a patient's vulnerability to particular medications. Pharmacogenomics in cancer seeks to integrate these pathways and mechanisms to optimize treatment regimens, increase efficacy, reduce side effects, and eventually provide more individualized and efficient cancer care.^[21,22,23,24]

Personalized medicine in cancer therapy

In cancer therapy, personalized medicine refers to developing treatment plans that are specific to each patient's genetic, molecular, and environmental attributes. Optimizing pharmaceutical efficacy, reducing adverse effects, and enhancing overall patient outcomes are the objectives

1. Genomic profiling

 Genomic Sequencing and Profiling of Tumors Finding certain therapeutic targets is made easier by examining the genetic abnormalities and changes present in a patient's tumor. Comprehensive information regarding genetic changes is provided by methods such as whole-exome sequencing (WES) and whole-genome sequencing (WGS). For instance, genetic profiling in non-small cell lung cancer (NSCLC) can identify mutations like those in EGFR, ALK, or ROS1, which can then be treated with particular tyrosine kinase inhibitors (TKIs).

2. Targeted therapies

 These medications are intended to specifically target certain molecular anomalies present in cancer cells.

Finding pertinent biomarkers aids in choosing the right treatments. Trastuzumab (Herceptin) targets the HER2 receptor in HER2-positive breast cancer, improving prognoses for patients with HER2 overexpression or amplification. Drugs such as vemurafenib and dabrafenib particularly target the mutant BRAF protein in melanoma with BRAF V600E mutations.

3. Immunotherapy

 Using biomarkers like tumor mutational burden (TMB) or PD-L1 expression, personalized medicine in immunotherapy identifies individuals who are likely to benefit from checkpoint inhibitors. By blocking PD-1 or PD-L1 interactions, medications such as pembrolizumab and nivolumab improve the immune system's capacity to target cancer cells.

4. Predictive and Prognostic biomarkers

- Determine which patients are most likely to benefit from a certain treatment. As an illustration, colorectal cancer KRAS mutations can forecast EGFR inhibitor resistance.
- Prognostic biomarkers aid in the decision-making process regarding treatment by offering insight into the probable trajectory and result of the illness. As an illustration, PSA (prostate-specific antigen) levels in prostate cancer can reveal information about the course of the illness and how well a treatment is working.

5. Tumor microenvironment analysis

 The extracellular matrix, stromal cells, and immune system can all affect how well a treatment works. Personalized strategies may include altering the microenvironment to improve the efficacy of therapy. As an illustration, comprehending the immunological environment surrounding tumors can aid in the development of combination treatments that boost immune system activity.

6. Integrative approaches

 Depending on the patient's particular tumor profile and genetic make-up, personalized medicine frequently combines immunotherapies, targeted therapies, and conventional treatments. As an illustration, combining checkpoint inhibitors with chemotherapy or targeted therapies may enhance results by tackling many facets of tumor biology.

7. **Patient-Centric strategies**

 Treatment modalities are therefore designed in such a way that efficacy can be maximized with minimum toxicity, taking into consideration specific patient-related factors, which include genetics and biomarkers. Ongoing observation of genetic alterations and response by a patient could culminate in adaptive therapies, which would alter medications as required and in response to changes in the characteristics of the cancer. [25,26,27,28]

Pharmacogenomics in specific cancer treatments

Challenges and Limitations in pharmacogenomics Where pharmacogenomics studies how genes affect the working of drugs and promisingly assures personalized

treatment, a number of obstacles and restrictions intervene against its wide usage in clinical settings.

Complexity of genetic variants: The complexity of the genetic variant is one of the major challenges in pharmacogenomics. Most genes, with variable contribution, often influence drug response. This, as a result of a polygenic effect, makes it difficult to predict results accurately. Further, less common genetic variations make the prediction difficult and may give unexpected responses of the treatments. These variants may not be well known or documented. It is hard to develop comprehensive pharmacogenomic profiles, as the interactions of several genes and environmental factors are very complex.

Limited clinical Utility and Evidence: Although recent research into genetics has increased, pharmacogenomics still has, in general, limited therapeutic usefulness for most drugs. A lack of evidence, which will consistently link certain genetic variations to clinical outcomes, may also slow the integration of pharmacogenomic data into ordinary medical practice. Also, there is a general lack of knowledge about the potential impact that genetic variation may have on the efficacy and safety of medications because many clinical trials are not designed to stratify participants based on genetic information. For example, because of these sorts of limitations, medical professionals might be unwilling to use pharmacogenomic testing if compelling clinical evidence is not demonstrated.

Cost and Accessibility: Due to the high cost of pharmacogenomics, not everybody up to date can gain access to this technique because it involves genetic testing and further analysis. Even though the cost of genetic sequencing has reduced with time, interpretation, validation, and translation into clinical practice are really costly. The cost barrier prevents adoption from being widely accepted, especially for underfunded healthcare systems. Moreover, it may widen health disparities as such personalized modes of treatment may not be conducted on people in deprived areas.

Ethical, Legal and Social implications: Pharmacogenomics raises several important ethical, legal, and social issues. Since genetic information is sensitive and personal in nature, privacy and security of data become very critical. Though protective legislation exists in many countries, for example, the Genetic Information Nondiscrimination Act (GINA) of the US, the possibility of discrimination on the basis of genetics by agencies providing insurance or employment cannot be ruled out. Secondly, there is also an ethical issue of informed consent since the patients cannot fully understand what the genetic testing will imply. The issues pinpointed herein raise critical consideration in order for pharmacogenomics to realize its benefits without costing human rights and communal values.

Integration into clinical practice: Another major challenge is the translation of pharmacogenomics into clinical practice. It may be that medical practitioners lack

the necessary skills to interpret and apply genetic information with the aim of determining treatment options. The second point is that the amount of genetic information set to be generated will definitely surpass what the healthcare systems could handle and therefore requires an improvement in the decision-support software and EHRs. This is an interdisciplinary collaboration between geneticists, pharmacists, and physicians themselves. Lacking adequate training, resources, and support, the promise of pharmacogenomics may be somewhat inconceivable in the context of ordinary medical practice.

Regulatory and Standardization issues: The licensing and standardization of pharmacogenomic tests are complicated by the constantly changing regulatory environment in the field of pharmacogenomics. There is frequently disagreement over which genetic testing should be done and how the results should be interpreted, and different nations have different legal frameworks. This discrepancy may cause patients and healthcare professionals to get confused, which could damage the reputation and practicality of pharmacogenomics. Furthermore, because genetic science is dynamic, rules and policies must constantly change to accommodate new findings, which can be a laborious and timeconsuming process.[29,30,31,32]

Future directions in pharmacogenomics

1. Integration into clinical practice

It is expected that pharmacogenomics, when incorporated into standard clinical practice, would emerge as a key component of personalized medicine. Healthcare professionals will be able to customize pharmacological therapy based on patient genetic profiles as more genetic data becomes available, which will enhance treatment outcomes and reduce adverse drug responses. Standardized clinical guidelines and practices that integrate pharmacogenomic testing into routine medical decision-making will become more important to facilitate this change.

2. Expansion of pharmacogenomic testing

In the future, more diverse genes involving medication metabolism, efficacy, and toxicity will be covered by pharmacogenomics. This will be achieved through the development of extended genetic panels capable of predicting drug responses to a wide array of agents for better treatment decisions. With advancement in technology and reduction of costs in genetic testing, pharmacogenomic testing shall be made more available to more and larger populations, especially underserved ones.

3. Data Integration and Big data analytics

Pharmacogenomic data will be increasingly combined with other sources of health care data, such as lifestyle, electronic health records, and environmental ones. AI and big data analytics will be used to decode complex data sets, develop trends, and thus provide more accurate

predictions about drug response. Such technologies will help devise predictive models that can guide personalized treatment.

4. Ethical, Legal and Social Implications (ELSI)

This increased use of pharmacogenomics will, in the future, ensure that ELSI associated with genetic testing receives greater priority. Issues such as informed consent, genetic discrimination, and patient privacy have to be managed with caution. All future efforts are very likely to develop strict policies and regulations so that patients' rights are protected and appropriate ethics in the use of pharmacogenomic information in medical treatment are fostered.

5. Global Implementation and Access

In the future, pharmacogenomics will also involve efforts to support access and implementation at the global level; this includes making sure that diverse populations all over the world benefit from pharmacogenomic advances. For the wide dissemination of pharmacogenomics, especially in low- and middle-income countries, overcoming obstacles on strategies such as cost, infrastructure, and education is key. It will require a collaboration on the part of governments, health care providers, and the pharmaceutical industry to achieve equity in access to pharmacogenomic-driven healthcare.

6. Development of New Drug Therapies

Pharmacogenomics will persist in propelling the creation of novel pharmacological treatments that exhibit reduced adverse effects and increased efficacy. Pharmaceutical companies can create more accurate and tailored therapies by designing drugs that target certain genetic variants by knowing the genetic basis of drug reactions. This strategy is anticipated to completely change how complicated diseases like cancer, heart disease, and neurological problems are treated, as genetics greatly influence how these conditions advance and respond to treatment.[33,34,35]

CONCLUSION

By creating individualized medicine and providing safer and more effective treatments based on each patient's unique genetic profile, pharmacogenomics has completely changed the field of cancer therapy. Oncologists can choose the best therapy and minimize side effects by having a thorough grasp of the genetic differences that affect drug response. Precision medications and immunotherapies are two examples of focused medicines made possible by the incorporation of pharmacogenomics into clinical practice, which greatly improves patient survival and quality of life. Pharmacogenomic techniques will continue to be the forefront of cancer treatment, even though there are still obstacles to overcome, such as the need for more widespread access to genetic testing and the need to overcome implementation inequities. Personalized medicine will become the cornerstone of cancer care as research and clinical application expand, guaranteeing

improved therapeutic outcomes for patients with a variety of cancer types.

REFERENCES

- 1. Debela DT, Muzazu SG, Heraro KD, Ndalama MT, Mesele BW, Haile DC, Kitui SK, Manyazewal T. New approaches and procedures for cancer treatment: Current perspectives. SAGE Open Med, 2021; 12, 9: 20503121211034366.
- 2. Tohme S, Simmons RL, Tsung A. Surgery for Cancer: A Trigger for Metastases. Cancer Res, 2017; 1, 77(7): 1548-1552.
- 3. Anand U, Dey A, Chandel AKS, Sanyal R, Mishra A, Pandey DK, De Falco V, Upadhyay A, Kandimalla R, Chaudhary A, Dhanjal JK, Dewanjee S, Vallamkondu J, Pérez de la Lastra JM. Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. Genes Dis, 2022; 18, 10(4): 1367-1401. doi: 10.1016/j.gendis.2022.02.007. Erratum in: Genes Dis, 2024; 20, 11(4): 101211.
- 4. Gupta SL, Basu S, Soni V, Jaiswal RK. Immunotherapy: an alternative promising therapeutic approach against cancers. Mol Biol Rep, 2022; 49(10): 9903-9913.
- 5. Chu DT, Nguyen TT, Tien NLB, Tran DK, Jeong JH, Anh PG, Thanh VV, Truong DT, Dinh TC. Recent Progress of Stem Cell Therapy in Cancer Treatment: Molecular Mechanisms and Potential Applications. Cells, 2020; 28, 9(3): 563.
- 6. Krzyszczyk P, Acevedo A, Davidoff EJ, Timmins LM, Marrero-Berrios I, Patel M, White C, Lowe C, Sherba JJ, Hartmanshenn C, O'Neill KM, Balter ML, Fritz ZR, Androulakis IP, Schloss RS, Yarmush ML. The growing role of precision and personalized medicine for cancer treatment. Technology (Singap World Sci), 2018; 6(3-4): 79-100.
- 7. Sarhadi VK, Armengol G. Molecular Biomarkers in Cancer. Biomolecules, 2022; 23, 12(8): 1021.
- 8. Verma M Personalized medicine and cancer. *J. Pers. Med*, 2012; 2: 1–14.
- 9. Personalized Medicine Coalition. *The personalized medicine report. Opportunity, challenges, and the future*, 2017.
- 10. Oates JT, Lopez D. Pharmacogenetics: An Important Part of Drug Development with A Focus on Its Application. Int J Biomed Investig, 2018; 1(2): 111.
- 11. Chang MT, McCarthy JJ, Shin J. Clinical application of pharmacogenetics: focusing on practical issues. *Pharmacogenomics*, 2015; 16: 1733–1741.
- 12. Belle DJ, Singh H. Genetic factors in drug metabolism. *Am Fam Physician*, 2008; 77: 1553–1560.
- 13. Novelli G, Ciccacci C, Borgiani P, et al. Genetic tests and genomic biomarkers: regulation, qualification and validation. *Clin Cases Miner Bone Metab*, 2008; 5: 149–154.
- 14. Visvikis-Siest S, Theodoridou D, Kontoe MS, Kumar S, Marschler M. Milestones in Personalized

Medicine: From the Ancient Time to Nowadays-the Provocation of COVID-19. Front Genet, 2020; 30, 11: 569175.

- 15. Franczyk B, Rysz J, Gluba-Brzózka A. Pharmacogenetics of Drugs Used in the Treatment of Cancers. Genes (Basel), 2022; 7, 13(2): 311.
- 16. Relling MV, Klein TE. CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. *Clin Pharmacol Ther*, 2011; 89: 464–467.
- 17. van der Lee M, Kriek M, Guchelaar HJ, Swen JJ. Technologies for Pharmacogenomics: A Review. Genes (Basel), 2020; 4, 11(12): 1456.
- 18. Krebs K., Milani L. Translating pharmacogenomics into clinical decisions: Do not let the perfect be the enemy of the good. *Hum. Genom,* 2019; 13: 39.
- 19. Gong L, Whirl-Carrillo M, Klein TE. PharmGKB, an Integrated Resource of Pharmacogenomic Knowledge. Curr Protoc, 2021; 1(8): e226.
- 20. Singh S, Kumar R, Payra S, Singh SK. Artificial Intelligence and Machine Learning in Pharmacological Research: Bridging the Gap Between Data and Drug Discovery. Cureus, 2023; 30, 15(8): e44359.
- 21. Lu DY, Lu TR, Xu B, Ding J. Pharmacogenetics of cancer therapy: breakthroughs from beyond? Future Sci OA, 2015; 1, 1(4): FSO80.
- 22. Choi YH, Yu AM. ABC transporters in multidrug resistance and pharmacokinetics, and strategies for drug development. Curr Pharm Des, 2014; 20(5): 793-807.
- 23. Morris LG, Chan TA. Therapeutic targeting of tumor suppressor genes. Cancer, 2015; 1, 121(9): 1357-68.
- 24. Handy DE, Castro R, Loscalzo J. Epigenetic modifications: basic mechanisms and role in cardiovascular disease. Circulation, 2011; 17, 123(19): 2145-56.
- 25. Zhou Y, Peng S, Wang H, Cai X, Wang Q. Review of Personalized Medicine and Pharmacogenomics of Anti-Cancer Compounds and Natural Products. *Genes*, 2024; 15(4): 468.
- 26. Mercogliano MF, Bruni S, Mauro FL, Schillaci R. Emerging Targeted Therapies for HER2-Positive Breast Cancer. Cancers (Basel), 2023; 26, 15(7): 1987.
- 27. Lo Nigro C, Ricci V, Vivenza D, Granetto C, Fabozzi T, Miraglio E, Merlano MC. Prognostic and predictive biomarkers in metastatic colorectal cancer anti-EGFR therapy. World J Gastroenterol, 2016; 14, 22(30): 6944-54.
- 28. Vanneman M, Dranoff G. Combining immunotherapy and targeted therapies in cancer treatment. Nat Rev Cancer, 2012; 22, 12(4): 237-51.
- 29. Roden DM, Altman RB, Benowitz NL, Flockhart DA, Giacomini KM, Johnson JA, Krauss RM, McLeod HL, Ratain MJ, Relling MV, Ring HZ, Shuldiner AR, Weinshilboum RM, Weiss ST; Pharmacogenetics Research Network.

Pharmacogenomics: challenges and opportunities. Ann Intern Med, 2006; 21, 145(10): 749-57.

- 30. Ventola CL. Pharmacogenomics in clinical practice: reality and expectations. P T, 2011; 36(7): 412-50.
- 31. Stratton TP, Olson AW. Personalizing Personalized Medicine: The Confluence of Pharmacogenomics, a Person's Medication Experience and Ethics. *Pharmacy*, 2023; 11(3): 101.
- 32. McKinnon RA, Ward MB, Sorich MJ. A critical analysis of barriers to the clinical implementation of pharmacogenomics. Ther Clin Risk Manag, 2007; 3(5): 751-9.
- 33. Hicks JK, Dunnenberger HM, Gumpper KF, Haidar CE, Hoffman JM. Integrating pharmacogenomics into electronic health records with clinical decision support. Am J Health Syst Pharm, 2016; 1, 73(23): 1967-1976.
- 34. Johnson KB, Wei WQ, Weeraratne D, Frisse ME, Misulis K, Rhee K, Zhao J, Snowdon JL. Precision Medicine, AI, and the Future of Personalized Health Care. Clin Transl Sci, 2021; 14(1): 86-93.
- 35. Qahwaji R, Ashankyty I, Sannan NS, Hazzazi MS, Basabrain AA, Mobashir M. Pharmacogenomics: A Genetic Approach to Drug Development and Therapy. *Pharmaceuticals*, 2024; 17(7): 940.