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Review Article

Specificity and Personalized medicine: a novel approach to Cancer management

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Abstract

With the advent of precision and personalized medicine (PPM), medical care can now be tailored to the unique needs of each patient. Cancer is one of the leading causes of death in India. Despite the lack of long-term effectiveness and significant side effects, maximal chemotherapy regimens are used in cancer patients. A new tool called PPM was developed to improve the success of therapy. Insights into pharmacogenomics have contributed to the development and possibility of individualized cancer treatment. In modern PPM, genetic or other information about a particular patient is systematically used to select or optimize preventive and therapeutic therapies for that patient. Knowing a patient's protein, genetic, and metabolic profiles can help physicians provide them with the best possible care. The development of companion diagnostics that use molecular assays to measure proteins, genes, or specific mutations to stratify disease status, select the appropriate drug, and adjust dosage accordingly is a central feature of this medical strategy. As a result, recent breakthroughs in oncology have sparked interest in the field as a whole and prompted calls for greater emphasis on the role of the oncology department or healthcare system in the pursuit of greater accuracy and individualization. In this article, we will review the state of the art and discuss possible future developments that could help accelerate the development of PPM drugs to treat cancer that has become resistant to standard therapies in individual patients. The focus is on the phenotypic (activity-based) rather than genotypic (mechanism-based) approach to PPM development and how it can benefit cancer patients. The article's perspective, which focuses on the specific changes in the tumor, opened the way for precise and individualized treatment.

KEYWORDS: *Cancer, personalized medicine, therapeutic outcome, tumor*

Introduction

Precision medicine means that the medical treatment of each patient is tailored to their individual needs. The idea of personalized medicine takes this diversity into account and treats each patient's tumor as if it were unique. Most often, the term personalized medicine refers to a medical approach that aims to tailor the healthcare system to each individual patient. This means that medical decisions, practices and/or products are made based on what is best for each patient. So precision medicine is often the same as personalized medicine. Precision medicine is based on a thorough understanding of each person's molecular profile. It does this by looking for early signs of markers such as genomic, proteomic and metabolomic changes, and using bioinformatics to get a clear picture of how gene regulation (functional protein) and disease status are related. Microarrays and next-generation sequencing (NGS) are widely used to obtain genetic information [1-4]. The precision and personalized

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medicine (PPM) strategy is defined by treatments tailored to specific tissues, gene mutations and personal factors important to each individual case of cancer. The use of immunotherapy has propelled the field of cancer treatment towards the idea of precision and personalized medicine (PPM), where each person's therapy is selected based on their needs. PPM is a more effective model intended to replace the one-size-fits-all approach. It is a way to encourage the development of specialized treatments for each cancer type, based on the measurement and manipulation of key patient characteristics and omics data (transcriptomics, metabolomics, proteomics, etc.). Soda, et al. found a mutation in anaplastic lymphoma kinase (ALK) that causes tumors in about 5% of non-small cell lung cancers. Other chemotherapy drugs and modern chemotherapy drugs have failed because they have bad side effects or stop working. And the main reason chemotherapy does not work that well is because cancer cells become resistant to it [5, 6]. There is also a growing group of PPM products called Companion Diagnostics (CDx). These are molecular tests that measure levels of proteins, genes, or specific mutations in order to find a specific, effective therapy for a person's condition. Some examples are Dako Denmark's HERCEPTEST and HER2 FISH PharmDx Kit finding over-expression of HER2 protein and genes in adenocarcinoma tissues from fixed breast, metastatic stomach or gastroesophageal junction adenocarcinoma. These CDx allow people to choose a treatment that is more likely to work for them, based on what their cancer looks like. Since the drug trastuzumab was approved for the treatment of HER2 receptor-positive breast cancer in 1998, the FDA has shown its support for the PPM method by approving this and other technologies.

When Precision Medicine was approved in 2015, it advanced the PPM field by asking the FDA to create new platforms to evaluate PPM diagnostics and treatments [7-11]. Personalized medicine gives doctors new, more precise tools to examine not only what they can see, what a tumor looks like on a mammogram or what cells look like under a microscope, but also the molecules that make up each patient. A profile of a patient's genetic variation can help doctors select drugs or treatment plans with fewer harmful side effects or better outcomes. It can also show a tendency to get certain diseases before they appear, giving the doctor and patient the opportunity to work out a plan for monitoring and prevention. The ability to profile the activity of genes, proteins and metabolites is changing the way we classify diseases and select treatments [12-14]. In this way, physicians can go beyond the one-size-fits-all model of medicine and make the best clinical decisions for each patient. So, PPM is a better tool to help cancer patients manage their disease. Cancer is one of the most common reasons people die in India. In 2020 alone, there will be an estimated 1,324,413 new cancer cases and 851,678 cancer-related deaths. Much work is being done to learn more about and treat this group of diseases. Cancer is characterized by an accumulation of cellular mutations, which manifest themselves as tumors that grow out of control. But cancer is a very complicated and diverse disease. There are more than 100 different types of cancer, each starting in a different organ or sub-tissue and growing from a different cell type. In the population there are 646,030 new cancer cases in men and 678,383 in women. Each year, 438,297 male cancer patients and 413,381 female cancer patients die. Developing a new drug costs a lot of money and takes a long time. In theory, using pharmacogenomic data, or information about how genes affect how patients respond to drugs, could reduce the time and cost of medication. Researchers could select patients for studies based on their genetics and use those who are most likely to respond or have the fewest side effects. This method, known as enriching the running pool, could reduce the size, length, and cost of clinical trials. So, it is very expensive and takes much more time [5, 15, 16]. Also, the use of pharmacogenomics early in the drug development process could reduce failed products by focusing resources on drug candidates and is therefore likely a safe and effective way to treat cancer. The goal of personalized medicine is to get the right drug to the right patient, at the right time, in the right dose, and with little or no side effects. Using the example of cancer, this article talks about the current status of this very ineffective treatment strategy [17-19].

Methodology

A thorough literature search was performed using multiple search terms related to PPM and cancer management to search PubMed, MEDLINE, Google Scholar and the Cochrane Library databases. We looked at systematic

reviews, meta-analyses, and population-based studies. All research articles and reviews that used the word PPM were included. During the screening process, the abstracts that dealt with the topic and were written in English were selected. Full-text articles have been carefully and thoroughly screened. During the literature review, all articles dealing with PPM and cancer therapy were screened and a short list was created. The articles have been read carefully and this review article has been written based on what has been read.

History of PPM

No one seems to know exactly where precision medicine came from. This makes it clearer what precision medicine and personalized medicine are. In the coming year to know what PPM means. What does this have to do with personalized medicine? What advances are there in evidence-based medicine? Has not it always been the job of healthcare professionals to provide flawless advice? The phrase has come to mean how personal information and biomarkers, even genetic biomarkers, can be used to make cancer treatments more effective for each patient. Understanding how genetic information and other patient data has long been used has taken some time to figure out what is new about the age-old goal of moving from individual and seemingly unique patient outcomes to generalizable knowledge about management and disease, and the important Role played by statisticians in this process [20, 21]. While the term precision medicine may seem broad, its trendy followers actually have two goals in mind. The first is basically an advance in pharmacogenetics, the science of making medicines based on genetic information. Pharmacogenetics is not a new field, and neither is the desire to use genetic information to improve health in general. Karl Pearson and Francis Galton, who were among the leading figures in biometrics and statistics in the 19th century, were very interested in the connection between genetics and disease. They were particularly interested in promoting eugenic reforms to prevent degeneration in diseases ranging from insanity to cataracts. Eugenics focuses on individual differences to find out and measure how constitutional and environmental factors influence disease distribution [22-24]. Pharmacogenetics had already begun to study how the biochemistry of drug compounds and the role of genetics and evolution in human diversity affect their response to drugs. After the Human Genome Project was successfully completed around the turn of the century, proponents of precision medicine effectively took over pharmacogenetics. The National Institutes of Health (NIH), led by Francis S Collins, then made investments to try to use this new information to transform genetic medicine in ways that went far beyond studying known mutations and chromosomal abnormalities. Some of the new discoveries were very important. For example, Herceptin (trastuzumab) and Erbitux are two very successful drugs based on the genes of cancer cells (cetuximab) that give us hope that our knowledge of other diseases will change over time. Robert Koch's idea that all diseases have an organic cause fitted perfectly with diseases like tuberculosis, but did not work at all for other diseases. Similarly, genetic approaches will likely work for some diseases but not for most. Proponents of precision medicine also want to be able to leverage and combine more new sources of information about how diseases occur and how they can be treated [25-27]. The idea is that if researchers can find specific genes, biomarkers, or other factors that alter the likelihood of a disease developing or causing it to disappear, they can make more precise interventions. This idea of PPM is also based on a long history of using biomedical data to tailor treatments to each patient, numerically comparing the results of different treatments, and creating statistical tools. Physicians have long said that it is their job to make treatment suggestions that meet each patient's individual needs and disease management. This was true in most of India before modern medicine, where traditional medicine said that every human being has a natural balance of humors or cardinal substances. With diseases that appear when things get out of balance. Although ideas about what causes a disease and how to treat it can be based on theories. Instead, modern advocates of precision medicine often compare it to empirical studies of therapeutics, trying to determine which treatments produce better measurable outcomes. The idea of testing therapies on patient groups and comparing the results is also very old [26, 28, 29].

Why do we need it?

But even though the DNA is the same in every cell, genes that code for proteins in one organ work differently than genes that code for proteins in other organs. In cancer, different tumors may have the same DNA, but the patterns of organic

events are different in each tumor type. Gene-Expression microarray is a technology that allows us to look at the gene expression profile of hundreds of genes simultaneously and to see the difference between a gene expression profile associated with cancer and a normal one. Standard treatment has been based on cohort-based epidemiological studies for many years. These studies do not take into account how different people's genes are, and most conclusions are based on the entire population. Before creating a treatment plan, precision and personalized medicine look at a person's genes and past health problems. In traditional personalized medicine, care is based on a person's medical history, social situation, environment and lifestyle. This is the parameter PPM should use [30-34].

Reduce the Duration, Cost, and Rate of Failure of Clinical Trials

Creating a new drug can be a long and expensive process. In theory, using pharmacogenomic data, or information about how genes affect how a patient responds to a drug, could reduce the time and cost of creating new drugs. Researchers could select people for studies based on their genes and use those who are most likely to respond or have the fewest side effects. This method, called study pool enrichment, could reduce the size, length and cost of clinical trials. Also, the early use of pharmacogenomics in the drug development process could reduce product failures by focusing resources on drug candidates most likely to be safe and effective [23, 35].

Decrease the Price of Health Care

When integrated into the healthcare system, precision and personalized medicine can help solve many problems that have existed for a long time, such as, and treatment that is not planned in advance. Economists believe using a genetic test to determine the right amount of the blood thinner warfarin could prevent 17,000 strokes, 85,000 major bleeds and up to 43,000 hospitalizations. The healthcare system as a whole would save billions of dollars each year [36, 37]. An economic analysis of the Oncotype Dx gene expression test examined how much it really costs to treat breast cancer in women in a health plan with more than one member that was only given to people with metastatic colorectal cancer whose KRAS gene had not been altered since they are the only people who would benefit from the drugs. Personalized medicine is when the right treatment is given to the right person at the right time to increase effectiveness and reduce side effects. This can lead to both better clinical outcomes and lower costs. These should be the goals of smart healthcare reform, along with facilitating people's care [38-40].

Improve Drug Safety

A large number of hospital admissions are associated with adverse drug reactions (ADRs). Many ADRs are caused by changes in genes that code for cytochrome P450 family enzymes. Because of these differences, a drug can be digested faster or slower than in the general population. As a result, some people may have difficulty inactivating and eliminating a drug from their body, essentially leading to overdose as it builds up, while others may eliminate the drug before it can take effect [2, 41]. The consequences of not accounting for the variation in these genes when dosing can range from uncomfortable to fatal. Warfarin administration does not prevent blood clots due to genetic differences in a drug metabolizing enzyme (CYP2C9) and a vitamin K metabolizing enzyme (VKORC1). During the first year of treatment, the dosage is usually adjusted to the individual patient through numerous rounds of trial and error, which may also put the patient at risk of severe bleeding or new blood clots. The need to get warfarin medications right the first time to avoid side effects prompted the Food and Drug Administration to propose genotyping for all warfarin patients. Therefore, approaching a PPM provides a thorough insight [41, 42].

Improve Patient Adherence to Treatment

When a patient does not follow their treatment plan, it damages their health and costs more. When personalized therapies work better or have fewer side effects, patients are more likely to stick with their treatments. The effects may be most noticeable in treating conditions like asthma, diabetes and cancer, where not following the rules often makes the condition worse. This point is supported by at least one study. Hypercholesterolemia, or high cholesterol, can be passed from parent to child [43-45]. This can increase the odds of having a heart attack before the age of 40 by 50 times in men and 125 times in women. Standard cholesterol monitoring can detect the disease early,

but genetic testing offers even more benefits. Knowing that there is a genetic predisposition to hypercholesterolemia gives patients a strong reason to make lifestyle changes and take their condition seriously. This is because the condition can be found before there are any visible signs of illness. At 2 years, more than 86% of patients who received a genetic diagnosis adhered to their treatment plan, compared to only 38% before the test [46-48].

Choosing the PPM model above traditional treatment methods

Before a PPM treatment can be developed and administered to patients, it is necessary to correlate a particular gene or mutation with a clinical outcome. It can take years of research conducted by numerous experts to discover a phenotype or polymorphism that has therapeutic significance. In addition, more research is needed to determine which polymorphism leads to a good or negative response to therapy in individuals. The Human Genome Project is used to sequence the DNA of large numbers of people as a first step in understanding the genetic code (HGP). This procedure becomes less difficult as sequencing tools expand. Bioinformatics plays a crucial role in understanding these vast datasets, which poses the greatest problems [49, 50]. Immunotherapy, which uses a patient's immune system to fight cancer, is another type of cancer treatment that has paved the way for more specific and successful therapies. Immunotherapy treatments include monoclonal antibodies (mAbs), checkpoint inhibitors, cytokines, vaccination, and adoptive cell transfer, particularly as hematopoietic somatic cell transplants (HSCTs) and chimeric antigen receptor T-cell (CAR-T) cell therapies. The advent of immunotherapy has shifted the field of cancer treatment towards precision and personalized medicine (PPM), where therapeutic choices are individualized for each patient. Over the past decade, it has become increasingly clear that no two malignancies are identical and therefore may respond differently to standard therapies such as chemotherapy and radiation. This traditional approach to cancer therapy is extremely simple; it leads to inefficient, expensive therapies and undesirable side effects for patients [48, 50, 51]. PPM is the foundation of a more effective paradigm poised to replace this unified approach. The PPM domain is built on data that captures current and historical environmental exposure and physical health. Based on these statistics, patients are categorized into several clinically useful goals. PPM can be used to determine genetic susceptibility to a disease, identify patient populations for clinical trials, and identify individuals who are more likely to respond favorably to a particular therapy. The completion of the Human Genome Project (HGP) gave scientists the ability to read and analyze a person's genetic makeup and identify genetic predispositions to certain diseases. This significant event prompted a shift from a reactive to a preventive approach to health. Scientists are currently attempting to gain a comprehensive understanding of body function at different omics levels and how genetic predispositions are affected by environmental stress. All of this information will eventually allow scientists and physicians to more accurately predict how patients will respond to a particular drug [52, 53]. An invaluable tool facilitating individualized therapy, CDx tests patients for genetic traits that indicate whether the patient would respond to a particular treatment. This strategy can have a significant impact on patient care. The revolution lies in the transition from a clinician choosing a more or less experimental generic drug for the patient to a doctor successfully treating the disease with PPM. This article covers the areas of personalized medicine and precision medicine, collectively referred to as PPM. Although the terms are now frequently interchanged, they both refer to the use of unique patient characteristics to determine optimal treatment. Originally, the discipline was known as tailor-made medicine. However, as it grew in popularity and use in science, media, and society, it became associated with a misperception. Many people mistakenly believed that because of personalization, unique treatments would be created for each individual. To clarify the exact objective of the field, the scientific community, particularly the National Research Council, has advocated the use of precision and personalized medicine. Nevertheless, PPM continues to gain popularity in the general population [54-56]. In this overview, the current state of the cancer-related PPM sector is divided into three categories. We start by explaining how

•Get PPM data. - This section discusses the many omics approaches (genomics, transcriptomics, proteomics, and metabolomics) used to define an individual's disease status. The article discusses the understanding and implementation of these data as tools

for clinical study design and therapy selection [55, 57].

•Development of a PPM therapy. - New cancer treatments such as organoids, monoclonal antibodies (mAbs), cancer vaccines and CAR-T cells are considered from a PPM perspective. There is also talk of changing federal regulations for PPM products to ensure they are safe and effective [58].

•More general effects of PPM. - The economic and moral issues of PPM are taken into account. From an economic point of view, PPM is difficult to set up and the current payer system may need to be changed [58].

From an ethical point of view, the nature of the sector can be scary, so it is important to put in place enough safeguards for the privacy and health of the targeted patients. This report states that PPM is good for the patient and, in turn, for the scientific community because it strengthens collaboration and helps people learn more about the biological complexities of cancer and its treatment. However, this does not mean that there are not major problems and changes that come with new fields, especially from the perspective of biotech companies and society at large [59-61]. Cancer has typically been treated with broad, unified methods such as chemotherapy, radiation, and surgery to remove tumors. The effectiveness of these treatments varies greatly from person to person, and they often injure healthy organs and tissues that do not have cancer. The PPM approach is characterized by treatments tailored to each cancer patient's specific tissues, gene mutations and private factors. Companion Diagnostics (CDx) help identify what treatments are easiest for a patient's tumor, and new cell therapies are used to attack the cancer while causing as little damage as possible to healthy tissue. This makes the PP M model in Figure A more effective and safer [60, 62].

Precision and personalized medicine and the role of the clinical pharmacist

Pharmacy professionals are well trained in how to take medication, how to adjust dosage, and how to encourage the right way of using medication. The idea of personalized medicine also suits them well, allowing a clinical pharmacist (CP) with a PharmD or MPharm pharmacy practice or clinical pharmacy to use personalized medicines more effectively in cancer treatment. Still, more people need to know about this topic and more research needs to be done, but based on what we now know; we can say that clinical pharmacists or pharmacologists will receive most of the personalized medicines that will be used to treat cancer in the future [4, 64-67].

Conclusion

Since the sequencing of the entire human genome in 2003, which was a major step forward, the PPM field has grown and developed greatly. Over the past decade, PPM has led to a number of improvements for people with solid tumors. To make a real and useful change that could help all clinical outcomes, we need to know more about biology. To get better, you need a multi-omic approach that can account for changes in DNA and RNA, proteomics, and metabolomics.

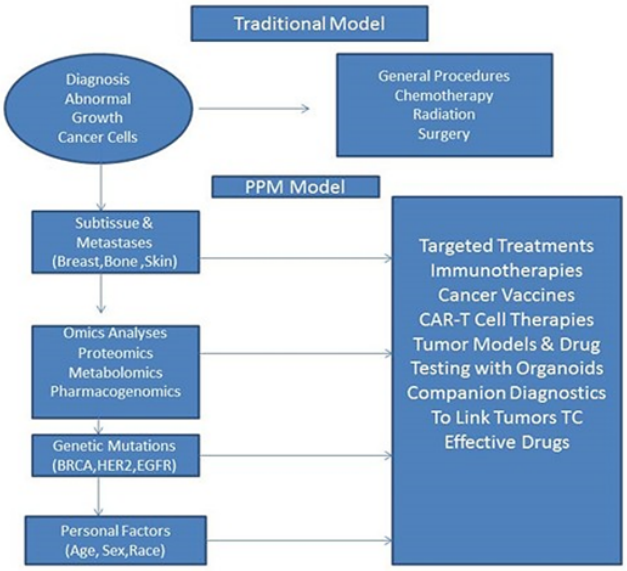

Figure 1. Traditional model vs. PPM model for treating cancer [62-64]

Personalized medicine means ensuring that the right treatment or drug is given to the right person. It also means finding out if a person is likely to get sick, sometimes years before the disease has fully developed. It is important and timely to ask: have we reached the point where we can treat each patient's cancer based on their entire DNA structure? We are not there yet, so the answer is no. But the field is changing, and personalized medicine has much to offer to improve cancer care now and in the future. This article goes beyond just putting things in order by linking this information to individual patient outcomes and responses to treatment. PPM therapies could be very helpful in the treatment of cancer because tumors can be very different and each patient needs to be treated individually. Recent research has focused on making more accurate tumor models (organoids) and using the specificity of the system to make effective cancer vaccines or monoclonal antibodies (mAbs). In phase I clinical trials where patients were selected based on a specific biomarker, response rates and progression-free survival were better for those who received precise, individualized treatment. The manufacture of PPM therapies must also be done carefully and with an eye on changing regulations. As researchers learn more about PPM and companies manufacture PPM treatments, regulators, clinicians, patients, and the general public need to consider the larger impact of PPM. Scientists, biopharmaceutical companies, insurers, clinicians, regulators, and patients all need to collaborate at scale to advance PPM and make it a viable area that benefits everyone.

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