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A Review on Pharmacogenomics Implications for Drug Development and Clinical Practice

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ABSTRACT: ***Pharmacogenomics is expected to be one of the earliest clinical uses of the Human Genome Project, and it will undoubtedly have a significant effect on medical practice. The impact of pharmacogenomics on the drug discovery process, especially drug safety, production, market segmentation, market growth, differentiation, and customized health care, is discussed in this paper. We also go through three obstacles to pharmacogenomics' translation towards clinical practice: reliance on information systems, limited health-care funding, and scientific ambiguity around particular uses of the technology's validation. There is presently no institutional agenda in place to encourage and nurture innovation, create progressive information technology, or secure the funding needed to improve the application of pharmacogenomic techniques in patient care, to our knowledge. Although the promise of these technologies is pushing change in clinical sciences, it is unclear which requirements at the health-care system level will be addressed.***

KEYWORDS: ***Drug, Genotype, Pharmaceuticals, Pharmacogenetics, Pharmacogenomics.***

1. INTRODUCTION

Pharmacogenomics seems to be the study on the impact of large inter individual genetic variability on medication response, effectiveness, and metabolism, so it is expected to be one of the Human Genome Project's earliest clinical applications. In both the biomedical and lay press, pharmacogenomics has been greeted with excitement. In the late 1950s, the subject was known as pharmacogenetics, but more recent advances broadened and deepened the scope of the field, leading to the introduction of the name pharmacogenomics. Genetic variation on drug metabolic enzymes and drug transporters is a determinant of pharmacokinetics and therapeutic index, while genetic variation on pharmacodynamic factors, such as a drug's target and route components, is a determinant of pharmacokinetics and therapeutic index. Pharmacogenomics is concerned with the impact of many genes and perhaps the whole genome on a medication's effectiveness and safety, as well as the impact of a medicine on the expressed genome as well as its derivatives. The possible consequences of pharmacogenomics on medication development and clinical practice are discussed in this article[1].

- *Pharmacogenomics and Medication Development:*

Pharmacogenomics has the potential to have a significant effect on drug development. The FDA has identified pharmacogenomics as "one of the technologies that will lead to innovation in the pharmaceutical sector," and guidelines was recently published that officially incorporates pharmacogenomics into the medication development process. Pharmacogenetic methods are now included in over a dozen new drug applications and more than 70 investigational new drug applications, and it is probable that this optional component of the Food and Drug Administration's

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drug review and approval process will become obligatory. Although the effect of pharmacogenomics in the laboratory and in the field is still being established, we will look at some of the possible uses of pharmacogenomics in the drug development process. Drug safety, productivity, market segmentation, market growth, and distinctiveness are five areas where pharmacogenomics is expected to have an impact on the drug development process. Each of these topics is looked at in turn[2].

1.1.Drug Security:

Several medicines have been removed from the market due to a low-frequency incidence of adverse drug events (e.g., forecoxa, troglitazone, and cerivastatin). Although many of these adverse responses are likely to be idiosyncratic, they may be linked to hereditary variables that could be discovered using pharmacogenomic methods. Pharmacogenomics may have two potentially significant consequences for medication development : identifying subgroups at risk for adverse outcomes and avoiding or restricting drug exposure to genetically determined subgroups. To begin with, it may enable a company to “save” a medication that has been discovered to have adverse responses before to introduction, especially if dose-related toxicity is connected to a genetic variation in a drug-metabolizing enzyme. The company might create a diagnostic screening test to identify individuals who are at risk for adverse responses and either stop using the medication or change the dosage in such patients, enabling the drug to remain a viable treatment choice in low-risk populations. Second, after a medication is authorized, pharmacogenomic analysis may be utilized to address any safety concerns that emerge during post-marketing monitoring[3].

1.2.Productivity:

Target, compound, as well as patient selection will all benefit from the use of genetic technology. Genomic signatures may be utilized in animal models during preclinical development to assess a drug's potential to regulate a pathway or disease mechanism, and therefore serve as a tool for compound or series selection. These signatures may be used in phase 2 or 3 clinical studies as potential indicators for response in people. Testing medicines in normal volunteers who have genetic variations in key enzymes involved in a drug's metabolism in phase 1 studies will lead to an early assessment of whether dosage modifications need be made in subsequent stages of testing. The use of genetic response signatures or particular patient groups in phase 2 trials may decrease variability in response and speed up the route to "proof of concept[4].

1.3.Segmentation of the Market:

Medical treatment has always been focused on recognizing a disease process as a collection of clinical symptoms and indicators, which is a very subjective and inaccurate approach. As our knowledge of disease processes improves, there will be a growing trend toward categorizing syndromes according to their underlying biologic mechanisms. Hypertension, for example, may be the result of a variety of underlying pathophysiologic processes (eg, sodium reabsorption, as well as endothelial nitric oxide synthase). As a result, it may be more suitable for manufacturers to segment the market and create treatments that target underlying mechanisms rather than clinical phenotype[5].

1.4.Expansion of the Market:

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Pharmacogenomic methods may enable market growth by establishing connections to common pathways underlying the biology of various disease states, much as better patient selection allows for market segmentation. Imatinib, a tyrosine kinase inhibitor initially designed for patients with chronic myeloid leukemia, has been shown to be successful in the treatment of gastrointestinal stromal tumors47 and may have potential for additional applications. 48 Patients with prostate cancer may benefit from trastuzumab, a breast cancer treatment[6].

1.5.Distinctiveness:

There may be a chance for manufactures to distinguish their goods from others in a clinical research industry guided by pharmacogenomics. It is now simple for other manufacturers to reanalyze their own clinical data to evaluate the effectiveness of their goods in the same subgroups if a company offers a product to a high-risk population or another clinical subgroup. A pharmacogenomic approach that includes acquiring a label for patients with particular genotypes may provide a company with a long-term competitive advantage. This potential, however, may only arise during the shift from a clinical to a genomic approach. Also, until pharmacogenomics enables businesses to clearly distinguish their medicines from all others, "fast followers" and "me too" goods are unlikely to be a viable approach for premium pricing. A fast follower, on the other hand, may have an edge over others in the class if it is supported by a pharmacogenomics-informed development approach[7].

- *Customized and Genomic Medicine:*

The use of pharmacogenomics or functional biologic principles to personalized medicine is referred to as personalized medicine. It may be feasible to increase the productivity of drug research and development by using pharmacogenomics concepts. Pharmacogenomics will also aid in the creation of the appropriate medication for the right patient by enabling for improved identification of genes, pathways, and drug targets. Hundreds, if not thousands, of genes will be examined for their involvement in medication response in genomic medicine. This approach is being used in the “real world” to stratify warfarin dosage based on polymorphisms in the gene encoding the vitamin K epoxide reductase complex. There are many obstacles to implementing a pharmacogenomic approach, including (1) information technology, (2) funding, and (3) scientific uncertainty[8].

1.6.Personalized Health Care Funding:

Personalized health care has the potential to broaden the use of risk-stratification methods and preventive health measures, such as pharmacogenomic testing, to reduce clinical events. However, it is unclear if this technology will help the health-care system save money. The cost of pharmacological treatment is expected to rise as more medicines are brought to market for smaller subgroups of patients. It is probable that customized medicine will result in the customization of current treatments, which will save money. When pharmacogenomics is included into clinical development processes, however, the outcome is more effectiveness or safety at a higher cost. In general, the funding of preventative treatments is an important element of the business model for individualized health care; however, the present third-party payment structure in the United States makes this difficult[9].

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Although the aim of preventive is to optimize resource usage and lower long-term costs, the present employee-based health insurance paradigm makes this economically unappealing. First, the time between identifying a risk and experiencing a clinical event may be lengthy. Second, there is no indication that using preventative measures lowers overall spending. Third, because of the present degree of worker mobility and turnover, employers and insurers have an economic incentive to postpone the adoption of preventative services. Precision medicine, like other preventative health efforts, may need an alternate funding structure that includes a mix of personal accountability and insurance. Prevention should be viewed as an investing in human capital on a precision medicine scale, similar to other human capital accumulation (e.g., higher education), and could be addressed in the same way through government investment, support for private funding of technology, and the possibility of public subsidies based on need.

1.7.Uncertainty in Science:

Pharmacogenomics offers a unique potential to quickly transfer fundamental research into clinical treatment. However, it presents a problem for health professionals to verify that the research and its application are mature and legitimate before they are disseminated in the marketplace. The creation of new and perhaps unfamiliar diagnostic tests that might offer risk stratification or predictions for the future is one of the initial components of genomic medicine. Although some techniques (e.g., single nucleotide polymorphism [SNP] genotyping) have been standardized and are highly reproducible, there is no universal "gold standard" for point procedure under the Clinical Laboratory Increase in performance Amendments framework for other techniques, including such RNA-based microarray analysis, which have been used to predict chemotherapy. Furthermore, economic constraints guarantee that the period between laboratory and commercial use for this amazing breakthrough in technology is extremely short. Clinicians and patients will have access to a wide range of risk-stratification data with varying clinical value in such an environment. This problem has previously been met in the development of genetic testing for BRCA1/BRCA2, where early clinical usage was fraught with clinical ambiguity. 58,60 The inability to teach patients and doctors not just about risk-fundamental stratification's ideas, but also about the validation of suggested risk-stratification techniques, is a shortcoming of our medical education process and poses a significant intellectual challenge.

1.8.Pharmacogenomics and drug response variability:

There are many variables that influence a disease's medication response. They may be classified as unpredictable (environmental impact, compliance, and the patient's genetic profile) or predictable (environmental influence, compliance, and the patient's genetic profile) (age, sex, race, body weight, disease state, nutritional status etc.) With the development of pharmacogenetic testing and the discovery of the human genome, the patient's genetic composition may now be considered a predictor of medication response. However, since there are other uncontrollable variables, the prediction based on pharmacogenomic testing may not be 100%. However, by using pharmacogenomic testing, the medication may be modified to be more effective and safer. In comparison to pharmacogenomics, the breadth of pharmacogenetic testing for assessing medication response variability is extremely restricted. A study of polymorphisms in the promoter or coding areas of 2 adrenoceptors found a link between haplotypes as well as bronchodilator responsiveness to salbutamol, but no link between individual b2 adrenoceptor genotypes and

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bronchodilator response. Another example is the variability in ACE inhibitor medication reaction[10].

2. DISCUSSION

Pharmacogenomics is a potential instrument in the pharmaceutical business that is only waiting to be used to its full potential. Pharmacogenetic techniques are now in use all around the globe, especially for evaluating medication safety profiles. Only a tiny percentage of the overall number of pharmacogenetic research has been able to be translated into clinical practice. Haplotype analysis and genome wide scan techniques were developed in response to the requirement to analyze numerous genes. Haplotype analysis and genome wide scans, on the other hand, will not be used in clinical practice for patient testing due to the present expense of analysis for a single SNP. However, the pharmaceutical sector may use these techniques in their drug development process. Gradual integration of pharmacogenomic research into drug discovery and development will result in significant cost savings, as well as a safer clinical trial and fewer failures. As a result, when pharmacogenomic studies are utilized in the future, many prospective medicines that may be lost owing to the impact on outliers in a research may be preserved.

3. CONCLUSION

Pharmacogenomics is the study of the impact of interindividual genetic variability on drug response, effectiveness, and metabolism, and it is anticipated to be one of the Human Genome Project's first clinical applications. In both the biomedical and lay press, pharmacogenomics has been met with enthusiasm. In the late 1950s, the field of study was known as pharmacogenetics, but with recent advancements in the subject's depth and breadth, the name pharmacogenomics has gained popularity. Many of the ideas presented in this article will put our current paradigm of drug development or clinical practice to the test. To be honest, certain elements of the pharmacogenomic enterprise may be impossible to execute inside current corporate frameworks, while others pose a danger to existing businesses. There is currently no institutional agenda in place to encourage and nurture innovation, create advanced information technology, or get the necessary funding to utilize pharmacogenomic technologies for patient care. The clinical sciences are changing as a result of the potential of these technologies. It's unclear if the bigger system-level requirements will be handled in the same way.

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