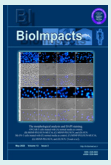
Latimer, ***BioImpacts,*** 2023, 13(3), 181-182
doi: 10.34172/bi.2023.27686
http://bi.tbzmed.ac.ir/

Article Info



Article Type:
Perspective

The implications of pharmacogenomics in oncology

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Received 17 Nov. 2022, **Accepted** 4 Dec. 2022, **ePublished** 1 May 2023

Although the use of pharmacogenomics in medicine is growing, the field of oncology is distinguished from other specialties in its use of tumor cell DNA sequencing for identifying appropriate tailored treatment. The reason for this is clear; oncology has perhaps the greatest need for finding an appropriate drug regimen when cancer is advanced or recurrent, and time is of the essence. Pharmacogenomics offers the best hope for a targeted therapy to be applied in the recurrent or advanced cancer setting by identifying a druggable mutation in a specific gene. In addition, pharmacogenomics in cancer treatment offers the potential to better predict differences in drug response, drug resistance, treatment efficacy, or toxicity among chemotherapy and targeted-therapy patients.[1,2]

Another facet of oncologic pharmacogenomics involves DNA sequencing of the non-diseased DNA of the same patient in order to predict whether a specific patient can actually metabolize the drugs that are most likely to impact the tumor of this patient. This represents an approach to chemotherapy that was not previously utilized. With evaluation of the cytochrome p450 subtypes in the liver for example, prodrugs will then be converted to drugs in the case of a drug like capecitabine, and less active forms of drugs will be metabolized into active forms in the case of a drug like tamoxifen.

Using the example of childhood ALL, the number of survivors treated with chemotherapy alone increased from 18% (1970-1979) to 54% (1990-1999) and the life expectancy increased over those 3 decades.[3] These data underscore the need to use the right chemotherapy and the right amount of chemotherapy to prevent secondary cancers and cardiac issues in patients who are cured and live for decades after their treatment. Pharmacogenomics will improve this process.

Because of the use of standard of care regimens for newly diagnosed cancers, insurance companies and Medicare do not cover the cost of tumor or cancer cell sequencing. Instead, standard of care regimens based on clinical trial evidence and existing biomarkers are used as the front line for treating newly diagnosed cancer. However, if the cancer recurs or is discovered at a late stage, tumor sequencing is often covered by health insurance companies and Medicare.[4] As the cost of sequencing decreases, one wonders how many patients will choose to perform tumor sequencing at initial diagnosis at their own expense (currently $10 000). When this happens the oncology team must be flexible about the possibility of adding targeted therapies. It is increasingly desirable to augment the oncology team with an oncology pharmacist who can offer insights into the particular combinations of drugs, which may be proposed with additional pharmacogenomic information.

A person with a known germline mutation that predisposes him/her to cancer, seeking tumor sequencing will generally not be covered for this sequencing by insurance. In addition, if a genetic mutation that predisposes the patient to cancer is discovered during tumor sequencing, an insurance company may refuse to cover costs of subsequent chemotherapy because of a "pre-existing condition" in spite of the Genetic Information Nondiscrimination Act (GINA) (Medline plus, NLM). The Affordable Care Act based insurance has been known to cover the cost of cancer treatment, if a cancer predisposing gene mutation is found.

Pharmacogenomics in oncology has deep implications for clinical trials. The unresponsive patient groups in clinical trials are now frequently subjected to tumor DNA sequencing to attempt to explain why they did not respond to treatment. Because of this additional layer of information, clinical trials may not need to be as large as they have been historically.

Pharmacogenomics in oncology when it identifies a druggable mutation saves money for the insurance

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company and reduces morbidity and potentially mortality in the patient.

As tumor sequencing becomes an established norm in the practice of oncology, and as pharmacogenomics becomes intrinsic in medical and pharmacy school curricula, we can expect that cancer therapy will continue to lengthen life but also successfully cure more cancers.

Competing Interests
None.

Ethical Statement
Not applicable.

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