Implementing Pharmacogenomic and Genetic Testing into Prostate Cancer Clinics: a Literature Review of Current Trends and Applications

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Abstract:
Prostate cancer (PC) is the second leading cause of death amongst American men, with most patients receiving androgen deprivation therapy (ADT) and eventually developing resistance to treatment. The 5-year survival rate from 2015-2020 for men with distant disease was 33%, demonstrating the need for more optimal treatment regimens for patients with distant or metastatic prostate cancer.

Pharmacogenomic (PGx) testing, a component of precision medicine, focuses on the way a patient’s genome affects drug metabolism. Combining PGx testing with current genetic testing provides an innovative and personalized approach to treating PC while both reducing adverse events and optimizing treatment dosages to fit the patient’s genetic make-up. This review paper describes how clinicians can use PGx testing in combination with genetic testing for PC patients.

**Keywords:** Pharmacogenetics, Genetics, Prostate Cancer, Precision Medicine, PGx testing

**Introduction:**

Prostate cancer (PC) is the second leading cause of death amongst American men, and about 1 in 8 men will be diagnosed with PC in their lifetime. Prostate cancer can be divided into four categories. Localized PC is confined to the prostate. It includes a broad spectrum of disease severity, covering indolent disease not requiring treatment to aggressive disease requiring intense treatment, typically including the use of androgen deprivation therapy (ADT). ADT targets the hypothalamic-pituitary-gonadal axis in efforts to reduce the level of serum testosterone equivalent to chemical castration (serum testosterone levels of <50 ng/mL). Most patients on ADT eventually develop resistance to treatment and are classified as castration-resistant. The second and third categories differ based on the state of metastases while castration resistant. These patients are classified as having either Non-Metastatic Castration-Resistant Prostate Cancer (nmCRPC) or Metastatic Castration-Resistant Prostate Cancer (mCRPC). Patients may initially be diagnosed with metastatic disease, or they may develop metastatic disease without the long-term use of ADT. These patients fall into the last category, metastatic castration-sensitive prostate cancer (mCSPC) and may still be effectively treated with ADT.
From 2015-2020, the 5-year survival rate of PC patients diagnosed with localized disease was >99%, however, when diagnosed with distant disease the 5-year survival rate declines to 33.3%. This drastic difference shows the need to further optimize treatments for patients with metastatic PC. Treatment plans can be personalized for patients through precision medicine, which considers information regarding a patient’s genome, home environment, and general lifestyle choices in addition to the clinical knowledge regarding patient disease. Since the completion of the Human Genome project in 2003, there have been rapid advancements in applying genetic information to the care of oncology patients. The ability to genetically characterize PC has opened the doorway to use precision medicine to optimize treatment decisions for men with PC based on their genetic profile.

The current literature does a poor job differentiating between genetics, genomics, pharmacogenetics, and pharmacogenomics. Genetics is the study of genes with a focus on hereditary traits passed down from parents to offspring. Genomics is the study of how all DNA in a person interacts with itself and the environment. The National Cancer Institute (NCI) considers the terms pharmacogenetics and pharmacogenomics to be interchangeable, defining them as the study of how a person’s genes affect their response to drugs. Germany and Kueber (2022) define pharmacogenomics as a broader term used to describe acquired and inherited variants across the entire genome. This paper will primarily focus on genetics, pharmacogenetics, and pharmacogenomics, using pharmacogenetics and pharmacogenomics interchangeably under the abbreviation (PGx), as reflected throughout the literature. This paper will also focus on testing performed on normal cells, known as germline testing.

PGx testing can be performed on healthy body cells (germline testing). Benefits of combining genetic and PGx testing for treating PC patients include the possibility to personalize cancer therapies, optimize prescribed medication and dose administered, and avoid potential adverse events. The amount of genetic testing in clinics greatly outweighs PGx testing, with >75% of oncology clinicians ordering somatic next-generation sequencing for their patients and PGx testing lagging far behind. While
reasons for this gap vary clinic to clinic, some may be due to a general lack of knowledge regarding PGx testing, how and when to order tests, and how to interpret test results.  

In 2019, Weitzel et al. published a four-step approach to implementing PGx testing into a primary care setting. The four steps are as follows: patient identification, PGx test ordering, application of PGx test results, and patient education. This paper applies this four-step approach to PC clinics, shows how PGx testing intersects with genetic testing, and describes the effects of known germline variants have on current treatments for PC.

**Step 1: Patient identification**

There is little data in the literature specifically addressing what percentage or population of PC patients should receive PGx testing. Alternatively, there are several guidelines for general genetic testing. Tuffaha et al. published a scoping review in 2023 on the current guidelines for genetic testing in PC. Out of the 23 guidelines and consensus statements reviewed, most recommended genetic testing in men with metastatic PC. The recommendations, however, varied regarding who to test, testing methods and implementation. The decision of which PC patients should receive genetic and/or PGx testing falls heavily on the clinicians, so clinicians need to be properly informed of the benefits and barriers to testing. Germline genetic testing in prostate cancer typically involves risk screening for the potential of developing PC in the future. It may seem unnecessary to screen patients who present to the clinic already diagnosed with PC, however, the test results could still prove beneficial to the patient’s family, in particular blood relatives. Genetic testing can provide information on homologous repair defects which might predict sensitivity to poly(ADP-ribose) polymerase (PARP) inhibitors, immune checkpoint inhibitors, and other biomarkers recently shown to be integral in PC treatment decisions.
PGx testing can provide information leading to dose optimization while avoiding potential adverse events. Therapies used to treat metastatic PC such as Taxotere (docetaxel), have been found to cause adverse events including neutropenia and anemia. PGx test results could show a patient is at higher risk of these adverse events, therefore leading to a dose modification to prevent the adverse event. In similarity to the guidelines and consensus statements on genetic testing for PC, men with metastatic PC, especially those on docetaxel treatment, could potentially benefit from PGx testing.

When choosing which patients to test, clinicians also need to be aware of testing barriers including cost of testing, turnaround time for results, race and ethnicity differences, and ethical considerations. New technological advancements with next-generation sequencing have lowered testing costs, lowered turnaround time, and increased test availability. In 2022, Morris et al. published a systematic review finding 77/108 (71%) studies about PGx guided treatment to be either cost saving or cost effective. However, the cost of PGx testing and insurance coverage should still be considered per individual case.

Test turnaround time, the time it takes for results once samples are sent, varies from days to weeks. Timing is especially important for clinicians choosing treatment plans for PC patients due to the need for some patients to begin treatment soon after their initial diagnosis. For patients not requiring immediate treatment, early testing should still be considered. When a patient gets tested early in their treatment plan, such as right after initial diagnosis regardless of staging, clinicians will have the test result data to use in the future if ever needed. This reduces the affect turnaround time could have if patients only be tested once needing to start advanced treatment options.

Another consideration for clinicians when choosing a patient for PGx testing is race and ethnicity. Some PC studies in the United States have shown a lack of data in African-American men compared to patients of European and Asian descent. While most data on PC associated loci show similarities between both men of European and men of African descent, some loci in men of European descent have
lower effects, no effects, or even the opposite effect compared to the loci in men of African descent. One study reported that Asian men with mCRPC on docetaxel had higher incidences of hematological complications compared to Western populations. Asian populations have been found to be more prone than other populations to myelosuppression with docetaxel and other taxanes. 18

There are ethical considerations that need to be addressed with patients before testing. Patients need to be fully informed on the possible implications of PGx testing including unfavored test results and violation of privacy. Some patients may not desire to know if they or their children have a variant putting them at a higher risk for developing disease in the future. Other patients may worry about life insurance issues arising from test results. 15

**Step 2: Pharmacogenomic test ordering**

Testing requires collecting DNA samples from patients. DNA information can be collected via various methods including collecting blood samples, saliva samples, and buccal swabs. 6 Blood samples serve as an excellent source of genetic material and have been successful in detecting both prostate specific antigen and circulating tumor cells which can give a more detailed view of tumor heterogeneity than conventional biopsy as well as characterizing differentially expressed miRNAs or miRNA panels involved in tumor progression. 19 Buccal swabs are also able to collect genomic data for germline testing, but despite being a rapid collection technique, buccal swabs may be unreliable and not collect enough material for genomic testing if the patient had something to eat or drink prior to sample collection. 20

When choosing a PGx test, it is important to make sure the test will provide information on the actionable genes of interest. Some PC specific actionable genes as discussed below include: *HSD3B1, SLCO2B1, SULT1E1, CYP3A5, CYP17A1, and CYP1B1*. Other general cancer specific genes are *UGT1A1, DPYD, ACYP2, WSF1, HLA, NUDT15, TPMT, ARHGEF10, EPHA5, FGD4, and CEP72*. 11
Step 3: Application of pharmacogenomic test results

Nomenclature

With the rapid increase in the availability of genetic information across cancer care, it is crucial that clinicians understand foundational genetic terminology and information. In literature, the term “mutation” is now more commonly referred to as a genetic “variant” and “single nucleotide polymorphism (SNP)” is also called a “single nucleotide variant (SNV).” Genetic variants and SNV nomenclature can be difficult to interpret in literature, and the nomenclature can be broken down into various components. The first component describes the location of the gene on the chromosome. The chromosome containing the gene of interest is numbered 1-22 or named “X” or “Y” if a sex chromosome. Each chromosome has two arms: the short arm and the long arm referred to as “p” and “q” respectively. The targeted gene is given a number based on how many positions away from the centromere it is located. Variants in the BRCA1 gene have been associated with PC. The full name to describe the location of BRCA1 is 17q12.1, meaning BRCA1 can be found on chromosome 17, long (q) arm, at position 12.1.

The next component describes variants in genes. While there is currently not a standard in naming genetic variants found across literature, the Human Genome Variation Society provides guidelines and recommendations that help understand the names found in the literature. It is recommended to use a letter prefix to indicate the type of sequence used. Common letter prefixes are “c” for a coding DNA reference, “g” for a linear genomic reference, and “p” for a protein reference sequence. Amino acid changes are typically described using the three-letter abbreviations and nucleotide changes are typically described using the single letter abbreviation. Specific abbreviations describe the variant type, such as “>” to describe a substitution and “del” to describe a deletion. For example, the variant description “g.123.A>G” would describe a substitution of the nucleotide Adenosine to Guanine at position “123” in the reference sequence “g.” Another example is EGFR L858R c.2573T>G (p.Leu858Arg). Nucleotide 2573 in the EGFR
gene has undergone a substitution from thymine to glutamine, which changed the amino acid sequence from leucine to arginine at codon 858.  

Another common way to label an SNP is using the “rs” number (also called the “rsID and RefSNP) found in the Single Nucleotide Polymorphism Database (dbSNP). Each SNP has a non-redundant designated rs number given by the dbSNP in efforts to further standardize nomenclature when discussing variants and SNPs.  

**PGx genes and variants in Prostate Cancer**

Genes that encode various proteins involved in drug metabolism can be used to predict how a patient with PC will respond to systemic therapy. Some of these genes and their corresponding germline variants are described in Table 1.

**HSD3B1**

The HSD3B1 gene (OMIM 109715) encodes 3β-hydroxysteroid dehydrogenase-1 (3βHSD1), an enzyme responsible for catalyzing adrenal androgen precursors into dihydrotestosterone (DHT). 3βHSD1 can become resistant to ubiquitination and degradation if there is an amino acid change (p.367T>N) in addition to a single nucleotide variant (SNV) (rs1047303, NM 000862.3: c.1100 C>A) in exon 4 of the HSD3B1 gene. This resistance to degradation results in an increased concentration of the enzyme and an increase in DHT production which has been linked to developing CRPC. The variant 3βHSD1 enzyme with a HSD3B1(1245C) allele and 367T variant has been associated with higher levels of protein accumulation, which results in increased levels of DHT.

A 2016 study by Hearn et al. compared the association between inheriting the HSD3B1(1245C) allele and progression-free survival (PFS), distant metastasis-free survival (DMFS), and overall survival (OS) of patients with PC. PFS was significantly associated with HSD3B1 and decreased as the number of inherited HSD3B1 alleles increased with a median 6.6 years in homozygous wild-type men (95% CI, 3.8
to not reached); 4.1 years in heterozygotes (95% CI, 3.0 to 5.5); and 2.5 years in homozygous variant men (95% CI, 0.7 to not reached); P=0.011. DMFS was also found to decrease as the number of variant alleles inherited increased with a median 9.1 years in homozygous wild-type men (95% CI, 7.4 to not reached); 6.8 years in heterozygotes (95% CI, 4.3 to 7.4); and 3.6 years in homozygous variant men (95% CI, 1.0 to 7.3; P=0.014). Additionally, OS diminished according to the number of variant \textit{HSD3B1} alleles inherited with a median, 9.7 years (95% CI 6.7 to 12.1) in homozygous wild-type men; 6.8 years (95% CI 5.2 to 8.0) in heterozygotes; and 4.6 years (95% CI 1.6 to 7.5) in homozygous variant men; P=0.0042.

\textit{SLCO2B1}

Solute carrier organic anion transporter family member 2B1 (\textit{SLCO2B1}) transports testosterone, DHEAS, and drugs like abiraterone. Several studies have found correlations with SNVs in the \textit{SCLO2B1} gene and resistance to ADT targeting the androgen axis. For example, variant rs12422149 has been associated with increased sensitivity to abiraterone.

Terakawa et al. studied the association between the level of expression of \textit{SLCO2B1} and PC recurrence after radical prostatectomy. There was a significantly higher level of \textit{SLCO2B1} expression in multiple tested categories including Gleason Score (GS \leq 6 vs GS = 7; p = 0.047, GS = 7 vs GS \geq 8; p = 0.002), pathological primary tumor (pT2 vs pT3/4; p < 0.001), and surgical margin status (positive vs negative; p = 0.013), respectively. It was concluded that PC patients with a high level of \textit{SLCO2B1} expression demonstrated worse disease-free survival than PC patients with lower levels of \textit{SLCO2B1} expression.

\textit{SULT1E1}

Estrogen is important for the pathogenesis and progression of PC. One member of the cytosolic sulfotransferases superfamily, estrogen sulfotransferase (\textit{SULT1E1}), catalyzes reactions involving the sulfonation of estrogenic compounds. Agarwal et al. evaluated 832 single nucleotide polymorphisms from 61 genes involved in the androgen metabolic pathway. The purpose of this study was to search for any
trends between the SNPs and time treatment failure in men with mCRPC on abiraterone acetate therapy. 
*SULT1E1* was found to have six single nucleotide polymorphisms (rs3775777, rs4149534, rs10019305, rs3775770, rs4149527, and rs3775768) associated with time to treatment failure and therefore could serve as potential biomarkers for patients on abiraterone acetate therapy. 

**Cytochrome P450**

Cytochrome P450 (CYP) is a superfamily of membrane proteins that catalyze phase 1 oxidation or demethylation reactions in drug metabolism and other substances. *CYP3A5* promotes luminal cell growth and metabolizes intra-prostatic androgens. *CYP3A5* is expressed primarily in normal prostate cells but is less expressed in prostate tumor cells. This suggests that polymorphisms in *CYP3A5* can increase the risk of PC. CYP 17α-hydroxylase/17,20-lyase (*CYP17A1*) is essential in the production of both androgen and glucocorticoid. *CYP17A1* catalyzes two reactions in the process of converting precursor steroids to testosterone. Abiraterone in combination with prednisone is used to treat both mCRPC and mCSPC. Abiraterone is a *CYP17A1* inhibitor, however, variants found in the CYP17A1 gene have been associated with resistance to abiraterone. 

Crucitta et al (2020) investigated the relationship between the SNV *CYP17A1* rs2486758 (c.-362T>C) and the use of abiraterone to treat patients with mCRPC. 60 patients with mCRPC treated with abiraterone underwent PGx testing DNA extracted from blood samples. Patients with the SNV *CYP17A1* rs2486758 (c.-362T>C) demonstrated a shorter median progression-free survival (PFS) and prostate-specific antigen-PFS (PSA-PFS) compared to patients carrying the TT genotype. This suggests as association between the SNV *CYP17A1* rs2486758 (c.-362T>C) and poorer clinical outcomes for patients with mCRPC on abiraterone therapy.

**Step 4: Patient education**
After analyzing test results and using them to plan future treatment plans, clinicians must be able to communicate the results and decisions to patients. Being properly educated on their test results allows a patient to make more informed decisions on their health. As with other lab and test results, clinicians must communicate the significance of the test results to the patients, as this understanding can increase patient confidence in their treatment plan. For example, if PGx testing results in a dose modification of an ongoing treatment, the patient might feel more comfortable with the change if they understand the reasoning behind it.

Patient health literacy needs to be considered when discussing results. PGx testing can provide a large depth of results, with an average of 14 pages of information in multigene panel results. When discussing with patients it is important for clinicians to focus on the clinically actionable results, so patients do not feel overwhelmed or lost. Printed or electronic documentation summarizing the testing and results could potentially facilitate communicating results with patients. These summaries should be concise, simple, and easy to interpret. Additionally, clinicians need to note genetic and PGx information in patient charts for other medical providers to use.

Clinicians should also be able to supply the patient with external resources to learn more about the test results. There are several online websites and databases that can educate both clinicians and patients on genetic and PGx testing. The National Cancer Institute has pages designated for the genetics of cancer as well as a dictionary of genetic terms. The U.S. Food and Drug Administration also provides an updated list of the biomarkers and genes related to for PC therapies. FDA approved medications for PC are listed in Table 2. Another resource for clinicians to utilize is genetic counselors. Genetic counselors are trained to educate patients on personal and family concerns regarding a hereditary trait found in PGx testing, cancer surveillance and prevention, additional testing for the patient and their high-risk family members, and more. A genetic counselor may be more equipped to discuss PGx test
results and future applications. Clinicians may consider referral to a genetic counselor when patient test results have clinical actionability.

**Applications in Clinic / Current Treatment**

**Docetaxel:**

Since its FDA approval in 2004, docetaxel (Taxotere) has been used as a chemotherapy treatment of mCRPC. Docetaxel is metabolized by *CYP3A4* and *CYP3A5* and is transported by the influx transporter *SLCO1B3*. The SNVs *CYP3A4* (rs2740574) or *CYP3A5* (rs776746) have been correlated with enhanced docetaxel clearance, and docetaxel dose for these patients should be adjusted accordingly. Variants in *SLCO1B3* (rs11045585) have been associated with increased leukopenia/neutropenia in patients on docetaxel treatment. Therefore, knowing a patient has the *SLCO1B3* (rs11045585) variant before starting docetaxel treatment could allow for dose modification to prevent or reduce leukopenia/neutropenia in the patient.

Variants in *CYP1B1* have also been associated with changes in treatment response of docetaxel-based combination therapies. Patients with one copy of the *CYP1B1*/*1* ancestral allele had a better prognosis than patients with two copies of the *CYP1B1*/*3* (rs1056836) variant when treated with docetaxel combined with estramustin, thalidomide, and prednisone. The *CYP1B1* 4326GG polymorphism has been linked to docetaxel clinical response, possibly acting as a new biomarker for mCRPC treatment.

Hertz et al. (2016) studied SNVs associated with docetaxel-induced neuropathy, finding that a *VAC14* (rs875858) SNV could serve as a predictor of docetaxel-induced neuropathy. Patil et al. (2021) studied the pharmacokinetic variability of docetaxel based on genetic variations. The study analyzed the polymorphic loci on the absorption, distribution, metabolism, and elimination genes from blood samples of 50 patients with head and neck or PC on docetaxel treatment. The target variants included *CYP3A4* (A392G), *CYP3A5* (A6986G), *SLCO1B1* (G1187A) and *ABCB1* (C1236T, G2677T, C3435T). The
authors concluded that none of the genetic variants explained the inter-individual variability in metabolizing docetaxel, and there was no basis for individual dosing based on variants in these genes. 37

**Immunotherapy**

Immunotherapy is another type of PC treatment. Some PC immunotherapies are ipilimumab, nivolumab, tremelimunab, pembrolizumab, and durvalumab. 37,38 Genes associated with a greater likelihood of response to these can be found in TABLE 2. A low percentage of mCRPC patients are responsive to immunotherapy, for example, only around 5-17% of mCRPC patients are estimated to respond to pembrolizumab monotherapy. It is thought that the low responsiveness is due to a low infiltration of T-cells, low tumor mutation burden, low PD-L1 expression, and immunosuppressive tumor microenvironment. 39

Genetic testing could help avoid and overcome immunotherapy resistance by targeting specific PC genetic aberrations. Aberrant gene-due resistance to therapy include overexpression of human epidermal growth receptor type 2 of tyrosine kinase (HER2), phosphatidylinositol 3-kinase (PI3K)-Akt/mammalian target of rapamycin (mTOR) pathway, suppression of apoptosis machinery by overexpression of antiapoptotic Bcl-2 gene, and suppression of proteolytic cleavage of poly(ADP-ribose) polymerase-1 (PARP-1) preventing apoptosis-proper DNA fragmentation. 39 Further research directly linking PGx testing with immunotherapy for PC should be conducted to allow clinicians to make better decisions when applying PGx testing with immunotherapy to patient care.

**Radiotheranostics**

Radiotheranostic therapies use radiation emitting molecules to damage target cell DNA and trigger cell death. Radiotheranostic molecules are typically composed of a radionuclide, a chelator, and a ligand/probe to bind to the target cells. 40 In PC, two molecular targets for radiotheranostic therapies are prostate-specific membrane antigen (PSMA) and gastrin releasing peptide receptor (GRPR). PSMA-11,
PSMA-I&T, PSMA-617, and $^{68}$Ga-RM2 are examples of radiotheranostic therapies with PSMA-11, PSMA-I&T, PSMA-617 inhibiting PSMA and $^{68}$Ga-RM2 targeting GRPR.  

Applying PGx testing to radiotheranostic therapy has potential to further personalize treatment options by increasing the efficiency of therapy and reducing toxicity. Germline mutations in the CHEK2 gene have been associated with response to Lutetium-177-PSMA-617. Somatic mutations in TP53, CHEK2, and ATM were found to be associated with a lack of response to treatment with Actinium-225-PSMA therapy.

Privé et al. investigated variations in DNA damage repair genes and the corresponding tumor response to PSMA-RLT. The study found no association between the DNA damage repair genes and responsiveness to PSMA-RLT. Van der Doelen et al. studied the quality of life in 13 patients with mCRPC on Actinium-225-PSMA radiotheranostic therapy, searching for possible biomarkers present in tissue biopsies. The group concluded that patients with DNA damage repair alterations tended to have longer overall survival.

**Conclusion:**

In conclusion, genetic and PGx testing is a growing field of research, particularly in patients with PC. The first step of testing begins with selecting a patient. There is little data regarding which patient populations amongst patients with PC benefit the most from genetic PGx testing. The treating clinician should make a well-informed decision for their patient considering the possible application of test results and the barriers to testing. Therefore, clinicians must stay up to date with current trends to be able to properly interpret test results correctly. Numerous genes, such as *HSD3B1*, *SLCO2B1*, *SULT1E1*, *CYP3A5*, *CYP17A1*, and *CYP1B1*, have been associated with PC, and variants to these genes can affect patient treatment. Genetic and PGx testing can be used to determine the patient’s expression of these genes and their potential effect on treatment to personalize the treatment based on the patient’s genes.
Clinicians should consider patient health literacy when communicating test results to patients, and referrals to a genetic counselor should be made as needed.

PGx testing can be applied to various treatment options for PC including chemotherapy, immunotherapy, and radiotheranostics. Genetic and PGx testing is a key aspect of precision medicine. It is an up-and-coming field of study and is already being used in some PC clinics. As more research is released, clinicians will be able to better combine genetic and PGx testing in their clinics and further improve overall patient care.

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Conflict of Interest:

The authors have no conflict of interest to declare.

Author Contributions:

JG designed the paper and wrote the manuscript. JM critically reviewed and completed the manuscript. All authors made a significant contribution to this study and approved the final manuscript.
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Tables:

Table 1. Genes and their corresponding variants with their associated effects on therapy.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Germline Variant</th>
<th>Effect on Therapy</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>HSD3B1</td>
<td>rs1047303 and (1245C) 367T</td>
<td>Increased DHT production</td>
<td>24,25</td>
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<tr>
<td>SLCO2B1</td>
<td>rs12422149</td>
<td>Resistance to ADT</td>
<td>24</td>
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<tr>
<td>SULT1E1</td>
<td>rs3775777, rs4149534, rs10019305, rs3775770, rs4149527, and rs3775768</td>
<td>Increased time to treatment failure and increased sensitivity to abiraterone</td>
<td>28</td>
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<tr>
<td>CYP17A1</td>
<td>rs2486758</td>
<td>Lowered PFS and resistance to abiraterone acetate</td>
<td>24,31</td>
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<tr>
<td>CYP3A4</td>
<td>rs2740574</td>
<td>Enhanced Docetaxel clearance</td>
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<tr>
<td>CYP3A5</td>
<td>rs776746</td>
<td>Enhanced Docetaxel clearance</td>
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Table 2. FDA approved biomarkers and genes of various prostate cancer treatments found in recent literature.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>FDA Biomarker/Gene (SOURCE 75)</th>
<th>Reference</th>
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<tr>
<td>Atezolizumab*</td>
<td>BRAF, ALK, EGFR, CD274 (PD-L1)</td>
<td>38,39</td>
</tr>
<tr>
<td>Avelumab*</td>
<td>CD274 (PD-L1)</td>
<td>39</td>
</tr>
<tr>
<td>Docetaxel</td>
<td>ESR, PGR (Hormone Receptor)</td>
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<tr>
<td>Durvalumab*</td>
<td>ALK, EGFR, CD274 (PD-L1)</td>
<td>38,39</td>
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<td>Flutamide</td>
<td>G6PD</td>
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<tr>
<td>Goserelin Acetate</td>
<td>ESR, PGR (Hormone Receptor)</td>
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<td>Ipilimumab*</td>
<td>HLA-A, ALK, EGFR, CD274 (PD-L1)</td>
<td>28,39</td>
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<td>Lutetium Lu 177</td>
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<td>Vipivotide</td>
<td>FOLH1 (PSMA)</td>
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<td>Tetaxetan</td>
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<tr>
<td>Nivolumab*</td>
<td>BRAF, CD274 (PD-L1), ALK, EGFR, CD274 (PD-L1)</td>
<td>38,39</td>
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<tr>
<td>Drug</td>
<td>Targets</td>
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<tr>
<td>Olaparib</td>
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<td>Tremelimunab*</td>
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*Immunotherapy drugs