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Pharmacogenomics – Gastrointestinal Medication Fact Sheet

Pharmacogenomics (PGx) is the study of genetic variations that influence medication response. PGx enables doctors to test for specific genetic changes to predict whether a patient may have a normal response, a poor response, or a higher risk of side effects before prescribing a specific medication.

The PGx Multi test analyses variations in 9 genes that have been shown to influence drug response and metabolism for over 120 medications used in clinical practice. The report provides medication-specific prescribing considerations which may help to improve the safety and efficacy of medications and reduce the risk of unwanted side effects.

Each gene is allocated a phenotype which defines how well an individual can metabolise medication. These categories are:

- Normal Metaboliser - Fully functional enzyme activity
- Poor Metaboliser – Little to no enzyme activity
- Intermediate Metaboliser - Decreased enzyme activity (activity between normal and poor metabolisers)
- Rapid Metabolisers and Ultrarapid Metabolisers - Increased enzyme activity compared to normal metabolisers

How can PGx be used in Gastrointestinal medicine

Pharmacogenomics is useful in guiding the correct use of some gastrointestinal related medications. The results can lead to a more tailored approach to dosing which can eventuate in a better and safer outcome for the patient. The individual DNA results can be used in conjunction with other clinical information to allow for a more informed decision on the best drug and dose for the patient.

Gastrointestinal medications covered by PGx Multi panel

Drug Class	Drug	Gene
Proton Pump Inhibitors	Esomeprazole Omeprazole Pantoprazole Rabeprazole Lansoprazole	CYP2C19 CYP2C19 CYP2C19 CYP2C19 CYP2C19
Antiemetics	Metoclopramide Ondansetron Tropisetron	CYP2D6 CYP2D6 CYP2D6

Proton Pump Inhibitors

Proton pump inhibitors (PPIs) are used for the treatment and prevention of various conditions including GORD, peptic ulcer disease, dyspepsia, eradication of Helicobacter pylori and prevention of NSAID induced ulcers. PPIs are predominantly metabolised by the enzyme CYP2C19. The CYP2C19 gene encoding the CYP2C19 enzyme is highly polymorphic, resulting in various levels of activity in the general population (ranging from poor metabolisers to ultra rapid metabolisers). The metaboliser status of the patient can be used to predict the rate of PPI drug metabolism and consequently predict the patient's likely drug response.

Example: A patient returning a poor metaboliser result for CYP2C19 predicts significantly reduced drug metabolism and increased drug exposure compared to a normal metaboliser. Current Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines recommend initiating the standard starting daily dose. For chronic therapy (>12 weeks), once efficacy is achieved, consider 50% reduction in daily dose and monitor for continued efficacy.

Conversely, a patient who returns an ultrarapid metaboliser result will have faster drug metabolism and decreased drug exposure compared to a normal metaboliser. CPIC guidelines recommend increasing the starting daily dose by 100% and monitoring for efficacy.

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Antiemetics

Antiemetics are used for the treatment of nausea and vomiting including postoperative and chemotherapy induced nausea and vomiting. Metoclopramide, ondansetron and tropisetron all have different mechanisms of action but they are all predominantly metabolised by the enzyme CYP2D6. The CYP2D6 gene encodes the CYP2D6 enzyme which is involved in metabolism of a large number of medications. It can alter an individual's response to a medication and alter drug activity which can lead to treatment failure or increased adverse effects. The results can determine the level of metabolising activity ranging from poor to ultrarapid metaboliser.

Example: A patient returning a poor metaboliser result will have a slower rate of drug metabolism, increased exposure and therefore increased risk of adverse effects compared to a normal metaboliser. Based on the recent CPIC guidelines, the usual starting dose is recommended for ondansetron and tropisetron but it is advisable to monitor for adverse effects especially at higher doses. In the case of metoclopramide, the FDA suggest a dose reduction and to monitor for adverse effects.

In contrast, an ultrarapid metaboliser will have faster drug metabolism and reduced drug exposure compared to a normal metaboliser. This can result in decreased response to ondansetron and tropisetron and therefore current CPIC guidelines recommend selecting an alternative drug not predominantly metabolised by CYP2D6 for these patients.

Results backed by Scientific Evidence

Our report recommendations are supported by the guidelines of the Royal Dutch Pharmacists Association Pharmacogenetics Working Group & the Clinical Pharmacogenetics Implementation Consortium (CPIC).

- CYP2D6, ondansetron and tropisetron guidelines: https://cpicpgx.org/guidelines/guideline-for-ondansetron-and-tropisetron-and-cyp2d6-genotype/
- CYP2C19 and PPI guidelines: https://cpicpgx.org/guidelines/cpic-guideline-for-proton-pump-inhibitors-and-cyp2c19/

References

https://www.pharmgkb.org/page/cpicFuncPhen

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