syzygy
March 2021

Sullivan Nicolaides PATHOLOGY
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What to expect from your Sonic PGx report

Using genomic information through pharmacogenomics (PGx) to predict drug response is improving treatment outcomes across many areas of medicine. However, while evidence of the clinical benefits of PGx is strong, using it in daily practice can be daunting for many clinicians unfamiliar with genomics and PGx data.

The form of the Sonic PGx report was developed in collaboration with an internationally recognised interpretive service. It incorporates recommendations from expert pharmacogenomic groups and is designed to be easy to read and clinically useful.

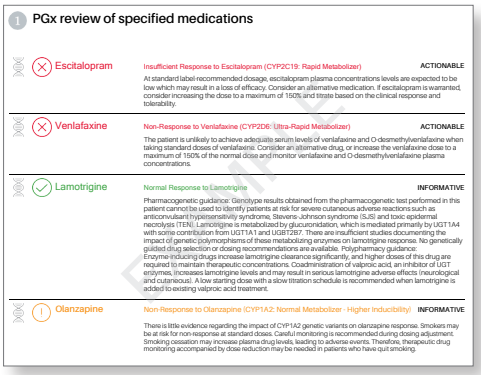
The Sonic PGx panel

This is a 10-gene pharmacogenomic test that checks for 60 significant variations in 10 genes involved in the metabolism of, or response to more than 80 common medications. It provides guidance on medication and dosage across common therapeutic areas, including cardiology, gastroenterology, pain management, psychiatry and addiction medicine. Here's what you can expect to learn from the report.

The report

Section 1. Answering the immediate question

When the request form specifies the medications the patient is taking, or are being considered, the first section of the report provides explicit prescribing advice for these medications.


1 PGx review of specified medications

Escitalopram — Insufficient Response to Escitalopram (CYP2C19: Rapid Metabolizer) — ACTIONABLE

At standard label-recommended dosage, escitalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If escitalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.

Venlafaxine — Non-Response to Venlafaxine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is unlikely to achieve adequate serum levels of venlafaxine and O-desmethylvenlafaxine when taking standard doses of venlafaxine. Consider an alternative drug, or increase the venlafaxine dose to a maximum of 150% of the normal dose and monitor venlafaxine and O-desmethylvenlafaxine plasma concentrations.

Lamotrigine — Normal Response to Lamotrigine — INFORMATIVE

Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Lamotrigine is metabolized by glucuronidation, which is mediated primarily by UGT1A4 with some contribution from UGT1A1 and UGBT2B7. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on lamotrigine response. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Enzyme-inducing drugs increase lamotrigine clearance significantly, and higher doses of this drug are required to maintain therapeutic concentrations. Coadministration of valproic acid, an inhibitor of UGT enzymes, increases lamotrigine levels and may result in serious lamotrigine adverse effects (neurological and cutaneous). A low starting dose with a slow titration schedule is recommended when lamotrigine is added to existing valproic acid treatment.

Olanzapine — Non-Response to Olanzapine (CYP1A2: Normal Metabolizer - Higher Inducibility) — INFORMATIVE

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Figure 1 Example report

The term ACTIONABLE indicates there is strong clinical evidence for this advice, while INFORMATIVE means the clinical evidence is less strong. In our experience, one in five patients with medications specified on the request form has a ⊗ DO NOT USE caution, and one in three patients has a ! USE WITH CAUTION warning.

Section 2. Advice regarding other medications

This section lists more than 80 common medications, together with a simple summary of the prescribing advice. It provides advice for multiple medications that have the same indication.

In our experience, two in three patients will have at least one ⊗ DO NOT USE caution in this section of the report, and three in four patients will have at least one ! USE WITH CAUTION warning.

Section 3. Detailed advice about other medications

The third section of the report provides detailed advice on medications that have a ⊗ DO NOT USE or ! USE WITH CAUTION warning in section 2.

Section 4. Genetic details

The final section of the report summarises the genetic results, including the genes tested, the variants identified in each gene (genotype), the predicted effect on enzyme or receptor activity (phenotype), and the variants included in the analysis.

What to order

Sonic PGx (Genetic test) Pharmacogenomic panel (Collections are performed at all collection centres).

Request form

An interactive PGx request form is available at www.snp.com.au/links/pharmacogenetic-request.

Cost

The Sonic PGx panel does not attract a Medicare rebate and is privately billed. For current pricing please refer to www.snp.com.au/links/pharmacogenomics.

Technical bulletins

Technical bulletins providing a detailed description of the Sonic PGx report and PGx psychotropic therapy testing are available to download from the Sonic Genetics website www.snp.com.au/links/pharmacogenomic-screen or from your Medical Liaison Manager on 1300 767 284.

Study confirms clinical utility of PGx in psychotropic therapy

The Sonic PGx panel examines 10 genes that regulate the absorption, distribution, metabolism and excretion (ADME) of medications. The ADME processes determine what level of 'exposure' to a medication that a patient will have. The panel looks for variants that can cause extreme medication exposures in patients – either low levels leading to treatment failure or high levels leading to toxicity. A recent review of the Sonic PGx test reports of more than 2000 patients who were being prescribed psychotropic medications showed that more than one third were advised to revise their medication or dosage. Figure 2 shows the proportions of patients taking a specified medication who received the PGx advice.

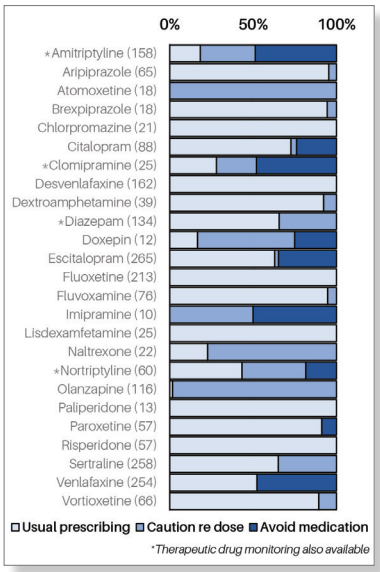


Figure 2 PGx prescribing guidance

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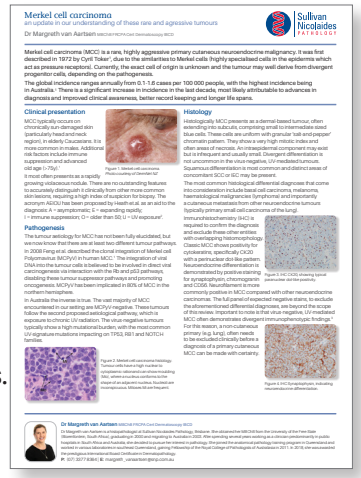
New SNP bulletin: Merkel Cell Carcinoma

Merkel cell carcinoma (MCC) is a relatively rare, highly aggressive, primary cutaneous neuroendocrine malignancy. It occurs globally, with the highest incidence being in Australia.

The vast majority of MCCs usually occur in chronically sun damaged skin, especially around the head and neck. The typical patient is elderly and often immunosuppressed. About 30% of cases present with advanced disease.

MCC has no outstanding clinical features to differentiate it from more common skin lesions. Histologically the tumour has a basaloid appearance, and immunohistochemistry (IHC) is often needed to confirm a diagnosis and differentiate it from other mimickers, such as basal cell carcinoma, melanoma, haematological malignancies, and metastasis from other neuroendocrine tumours – typically primary small cell carcinoma of the lung.

SNP dermatopathologist, Dr Margreth van Aartsen, has authored a bulletin to help clinicians in their understanding of MCC.


Merkel cell carcinoma
an update in our understanding of these rare and aggressive tumours
Dr Margreth van Aartsen

The bulletin covers the possible clinical presentation that can be encountered; the pathogenesis and the histology of MCC, including a list of conditions that must be excluded. It also covers tumour staging and prognosis, the treatment and management of MCC, including new therapies. This bulletin will be a highly useful resource for all clinicians.

Copies can be downloaded from the SNP website snp.com.au/links/merkel or by contacting your Medical Liaison Manager on 1300 767 284.

Pathologist Profile

Dr Peter Hutson MBBS BMedSci(Hons) FRCPA

We welcome anatomical pathologist Dr Peter Hutson to our Brisbane laboratory where he is reporting gynaecological pathology, dermatopathology, cytology and medical renal pathology cases.

He has a particular interest in ovarian neoplasms and placental pathology. Dr Hutson was previously at The Royal Brisbane and Women's Hospital where he attended regular gynaecologic oncology multidisciplinary team meetings. He continues to attend these meetings at the RBWH in a visiting capacity.

Dr Hutson graduated in Medicine from Griffith University, Queensland in 2008 having first gained First Class Honours in Medical Science from Flinders University, Adelaide. He completed his internship and residency at Nambour Hospital, then went on to advanced training in anatomical pathology, rotating through several institutions, including SNP, throughout southeast Queensland.

Dr Hutson is available for consultation.

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E: peter_hutson@snp.com.au

Be prepared for Easter

Warfarin Care enrolments

To ensure the safe and complete enrolment of patients into our Warfarin Care program, enrolments will be closed from 5 pm Thursday March 18 2021 and will reopen at 9 am Tuesday April 6 2021.

Cardiology services

The Cardiology Department will be closed from 4:30 pm Thursday April 1 2021 and re-open at 9 am Tuesday April 6 2021.

Collection centres

Please see www.snp.com.au for addresses and hours of operation of collection centres during the Easter period.

Patient test collection notes

Updated and new instructions

SNP provides collection notes to assist patients to prepare for pathology collections. These notes can be supplied to your clinic as a full set and re-ordered using the pathology stores request form. Collection notes can also be downloaded from the patient section of our website https://www.snp.com.au/patients/collection-information/collection-notes/

Updates have been made to these notes:

- Therapeutic drug tests – item 34177
- Urea breath test – item 34181
- Urine collection (MCS) – item 34160.

For more information, or a list of the latest notes and versions, please contact your Medical Liaison Manager (P: 1300 767 284 E: education@snp.com.au).

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