PharmGKB Training Exercise – Oncology

How to use this exercise

This exercise is intended to help new users familiarize themselves with the PharmGKB website and some of the different types of information available. **This exercise is not for use in a classroom setting for credit**, including professional development such as CME, as the answer sheet is freely available on the PharmGKB website.

We recommend that the trainer first provide an introduction to the PharmGKB website and its key features, including the genotype pickers available for the CPIC dosing guidelines. This exercise can then be used to reinforce areas covered in the introduction.

The 'What is PharmGKB?' page at www.pharmgkb.org/whatIsPharmgkb has helpful explanations of the different types of information that can be accessed on the PharmGKB website. This page will be useful for any trainers who are themselves unfamiliar with the PharmGKB website.

This exercise should take about 20-30 minutes to complete following an introduction to the website.

During the training session, each person will require access to an internet-connected computer where they can access the PharmGKB website.

This exercise is split into two parts; Part 1 and Part 2. Participants work through Part 1 to determine which genes they require genotype information for. Once they have completed Part 1, they should be given Part 2, which provides the genotype information. An answer sheet is provided at the end of this document.

PharmGKB is for research purposes only and does not provide medical advice or recommend when to order a pharmacogenetic test. All questions are written under the assumption that a patient's genetic information is already available.

If you have any questions or comments regarding this training exercise, please contact the PharmGKB team at feedback@pharmgkb.org

PharmGKB Training Exercise – Oncology

Part 1

A patient has been recently diagnosed with colorectal cancer and is about to begin chemotherapy treatment. You are considering prescribing capecitabine as the chemotherapy agent.

The patient has had their genome sequenced as part of your department's clinical pharmacogenetics program and you wonder if their genetic information could help you make a more informed decision about the patient's treatment.

1) Look up the Clinical Guideline Annotations and Drug Label Annotations for capecitabine on PharmGKB. Which gene should you check for variants?

2) Look up the Fluoropyrimidine Pharmacokinetic Pathway on the PharmGKB website. How do variants in this gene affect a patient's response to capecitabine?

3) The sequencing results for the patient show that they carry the c.2846A>T variant. No other variants were detected. What is the patient's metabolizer status?

4) What is the CPIC recommendation for capecitabine in patients with this diplotype?

After two weeks of chemotherapy, the patient develops nausea and vomiting as a side-effect of treatment. They are prescribed ondansetron to manage these symptoms. After two days, there is no improvement in the patient's nausea or vomiting.

Because you've already had to change the patient's treatment based on their genetics, you go back to the sequencing data to see the lack of response to ondansetron might also be caused by a genetic variant.

5) Which gene would you check for variants?

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Part 2

The test results for the patient show that they have a gene duplication and, as a result, carry three CYP2D6 alleles; two *1 (also known as *1xN) and a *2.

6) What is the patient's CYP2D6 metabolizer status?

7) How does this metabolizer status affect the patient's response to ondansetron?

8) What is the CPIC recommendation for ondansetron treatment in CYP2D6 ultrarapid metabolizers?

PharmGKB Training Exercise – Oncology Answers

A patient has been recently diagnosed with colorectal cancer and is about to begin chemotherapy treatment. You are considering prescribing capecitabine as the chemotherapy agent.

The patient has had their genome sequenced as part of your department's clinical pharmacogenetics program and you wonder if their genetic information could help you make a more informed decision about the patient's treatment.

1) Look up the Clinical Guideline Annotations and Drug Label Annotations for capecitabine on PharmGKB. Which gene should you check for variants? DPYD

2) Look up the Fluoropyrimidine Pharmacokinetic Pathway on the PharmGKB website. How do variants in this gene affect a patient's response to capecitabine? Capecitabine is a prodrug of fluorouracil. DYPD metabolizes fluorouracil to inactivate it. Reduced function DYPD variants mean that inactivation of fluorouracil is greatly reduced. This increases the number of active molecules present and puts the patient at an increased risk of toxicity.

3) The sequencing results for the patient show that they carry the c.2846A>T variant. No other variants were detected. What is the patient's metabolizer status? Intermediate metabolizer

4) What is the CPIC recommendation for capecitabine in patients with this diplotype? Reduce the starting dose by 50%, then titrate the dose based on toxicity.

After two weeks of chemotherapy, the patient develops nausea and vomiting as a side-effect of treatment. They are prescribed ondansetron to manage these symptoms. After two days, there is no improvement in the patient's nausea or vomiting.

Because you've already had to change the patient's treatment based on their genetics, you go back to the sequencing data to see the lack of response to ondansetron might also be caused by a genetic variant.

5) Which gene would you check for variants? CYP2D6

The test results for the patient show that they have a gene duplication and, as a result, carry three CYP2D6 alleles; two *1 (also known as *1xN) and a *2.

6) What is the patient's CYP2D6 metabolizer status? Ultrarapid metabolizer

7) How does this metabolizer status affect the patient's response to ondansetron? Increased metabolism of ondansetron by CYP2D6 so fewer active compounds are present in the body.

8) What is the CPIC recommendation for ondansetron treatment in CYP2D6 ultrarapid metabolizers? Use an alternative drug which isn't metabolized by CYP2D6 e.g. granisetron