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

An adult female patient is receiving chemotherapy for non-Hodgkin lymphoma. To help determine the best course of treatment, they had their genome sequenced before starting chemotherapy.

Three weeks after beginning chemotherapy, the patient develops an *Aspergillus* infection, which you want to treat with either voriconazole or posaconazole. They are also starting to have symptoms of tumor lysis syndrome, which you can treat with either allopurinol or rasburicase.

You check the patient's genetic test results to see if they have any variants which would affect their response to any of these drugs.

1) Are there any Level 1 Clinical Annotations, FDA Drug Label Annotations or Clinical Guideline Annotations that genetic variants affect response to posaconazole? If so, which gene are these variants located in?

2) Are there any Level 1 Clinical Annotations, FDA Drug Label Annotations or Clinical Guideline Annotations that genetic variants affect response to voriconazole? If so, which gene are these variants located in?

3) Are there any Level 1 Clinical Annotations, FDA Drug Label Annotations or Clinical Guideline Annotations that genetic variants affect response to allopurinol? If so, which gene are these variants located in?

4) Are there any Level 1 Clinical Annotations, FDA Drug Label Annotations or Clinical Guideline Annotations that genetic variants affect response to rasburicase? If so, which gene are these variants located in?

Part 2

These are the patient's genotypes at the relevant genes:

Gene	Genotype/Diplotype
CYP2C19	*1/*17
HLA-B	*18:08/*35:10
G6PD	Bangkok/Chatham

5) What is their CYP2C19 metabolizer status?

6) What is the CPIC recommendation for voriconazole in patients with this metabolizer phenotype?

7) Which drug will you prescribe to treat the fungal infection?

8) Do you prescribe allopurinol or rasburicase to this patient to treat the tumor lysis syndrome? Why?

PharmGKB Training Exercise – Oncology Answers

An adult female patient is receiving chemotherapy for non-Hodgkin lymphoma. To help determine the best course of treatment, they had their genome sequenced before starting chemotherapy.

Three weeks after beginning chemotherapy, the patient develops an *Aspergillus* infection, which you want to treat with either voriconazole or posaconazole. They are also starting to have symptoms of tumor lysis syndrome, which you can treat with either allopurinol or rasburicase.

You check the patient's genetic test results to see if they have any variants which would affect their response to any of these drugs.

1) Are there any Level 1 Clinical Annotations, FDA Drug Label Annotations or Clinical Guideline Annotations that genetic variants affect response to posaconazole? If so, which gene are these variants located in? No

2) Are there any Level 1 Clinical Annotations, FDA Drug Label Annotations or Clinical Guideline Annotations that genetic variants affect response to voriconazole? If so, which gene are these variants located in? Yes, a Level 1A clinical annotation, an FDA drug label, a DPWG guideline and a CPIC guideline for voriconazole and CYP2C19.

3) Are there any Level 1 Clinical Annotations, FDA Drug Label Annotations or Clinical Guideline Annotations that genetic variants affect response to allopurinol? If so, which gene are these variants located in? Yes, a Level 1A Clinical Annotation, an FDA label, a PRO guideline and a CPIC guideline for allopurinol and HLA-B.

4) Are there any Level 1 Clinical Annotations, FDA Drug Label Annotations or Clinical Guideline Annotations that genetic variants affect response to rasburicase? If so, which gene are these variants located in? Yes, a Level 1A Clinical Annotation, an FDA label and a CPIC guideline for rasburicase and G6PD.
Note – G6PD is located on the X chromosome, hence why the patient is female in this exercise

These are the patient's genotypes at the relevant genes:

Gene	Genotype/Diplotype
CYP2C19	*1/*17
HLA-B	*18:08/*35:10
G6PD	Bangkok/Chatham

5) What is their CYP2C19 metabolizer status, as determined by CPIC? Rapid metabolizer

6) What is the CPIC recommendation for voriconazole in patients with this metabolizer phenotype? Choose an alternative drug that is not dependent on CYP2C19 metabolism.

PharmGKB Training Exercise – Oncology Answers

7) Which drug will you prescribe to treat the fungal infection? Posaconazole

8) Do you prescribe allopurinol or rasburicase to this patient to treat the tumor lysis syndrome? Why? Prescribe allopurinol. Patient carries two deficient G6PD alleles and is at risk of developing acute hemolytic anemia if treated with rasburicase.