PharmGKB Training Exercise – Infectious Disease

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 – Infectious Disease

Part 1

The patient is co-infected with HIV and hepatitis C genotype I and needs to begin treatment to manage both infections.

You want to prescribe peginterferon alfa and ribavirin to treat the hepatitis C infection and atazanavir, abacavir or raltegravir to control the HIV infection.

You see in their medical records that the patient has had their genome sequenced and decide to check the data to see if the patient is carrying any variants which may affect their reaction to antiviral treatment.

1) Are there any FDA Drug Label Annotations or Clinical Guideline Annotations available for peginterferon alfa and ribavirin treatment?

2) Are there any FDA Drug Label Annotations or Clinical Guideline Annotations available for abacavir, atazanavir or raltegravir?

3) Which genes should be checked for variants?

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Part 2

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

Gene	Genotype/Diplotype
IFNL3	CC
HLA-B	*08:73/*57:01
UGT1A1	*28/*37

4) What does the IFNL3 genotype indicate about the patient's possible response to peginterferon alfa and ribavirin treatment?

5) Does the patient's HLA-B diplotype influence your selection of antiretroviral drug? How? Why?

6) Does the patient's UGT1A1 diplotype influence your selection of antiretroviral drug? How? Why?

7) Which antiretroviral drug would you prescribe to the patient?

PharmGKB Training Exercise – Infectious Disease Answers

The patient is co-infected with HIV and hepatitis C genotype I and needs to begin treatment to manage both infections.

You want to prescribe peginterferon alfa and ribavirin to treat the hepatitis C infection and atazanavir, abacavir or raltegravir to control the HIV infection.

You see in their medical records that the patient has had their genome sequenced and decide to check the data to see if the patient is carrying any variants which may affect their reaction to antiviral treatment.

1) Are there any FDA Drug Label Annotations or Clinical Guideline Annotations available for peginterferon alfa and ribavirin treatment? Yes, there is a CPIC guideline for peginterferon alfa, ribavirin and IFNL3 as well as an FDA label for peginterferon alfa-2b and IFNL3.

2) Are there any FDA Drug Label Annotations or Clinical Guideline Annotations available for abacavir, atazanavir or raltegravir? FDA label, CPIC guideline and DPWG guideline for abacavir and HLA-B, CPIC guideline for atazanavir and UGT1A1, FDA label for raltegravir and UGT1A1. **Note that the FDA drug label for raltegravir and UGT1A1 states that there is no evidence that UGT1A1 variants have a clinically meaningful effect on raltegravir pharmacokinetics.**

3) Which genes should be checked for variants? IFNL3, HLA-B, UGT1A1

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

Gene	Genotype/Diplotype
IFNL3	CC
HLA-B	*08:73/*57:01
UGT1A1	*28/*37

4) What does the IFNL3 genotype indicate about the patient's possible response to peginterferon alfa and ribavirin treatment? Patient is likely to respond favorably to treatment

5) Does the patient's HLA-B diplotype influence your selection of antiretroviral drug? How? Why? Abacavir shouldn't be used because the presence of the *57:01 allele means that the patient has a significantly increased risk of experiencing hypersensitivity to abacavir.

6) Does the patient's UGT1A1 diplotype influence your selection of antiretroviral drug? How? Why? Patient is highly likely to develop jaundice as a result of atazanavir treatment, which can result in discontinuation of treatment. Atazanavir can still be prescribed but the patient should be advised about the likelihood of developing jaundice.

7) Which antiretroviral drug would you prescribe to the patient? Either atazanavir or raltegravir. Raltegravir is the preferred option.