



PharmGKB Training Exercise – Cardiology

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

Part 1

A patient with cerebral ischemia is prescribed clopidogrel and simvastatin. After a few days of treatment, they only show a low level of platelet reduction and are starting to show symptoms of myopathy.

You remember seeing in the patient's medical notes that they had their genome sequenced some time ago and decide to check the sequencing data and find out if the patient has a genetic variant affecting their response to clopidogrel or simvastatin.

1) Are there any Clinical Guideline Annotations, FDA Drug Label Annotations or Level 1 Clinical Annotations on the PharmGKB website for clopidogrel?

2) Are there any Clinical Guideline Annotations, FDA Drug Label Annotations or Level 1 Clinical Annotations on the PharmGKB website for simvastatin?

3) Which genes should you check for variants?

Part 2

4) Briefly explain the relationship between CYP2C19 and clopidogrel. (Hint: look at the clopidogrel pathway on the PharmGKB website).

5) Briefly explain the relationship between SLCO1B1 and simvastatin. (Hint: look at the simvastatin pathway on the PharmGKB website).

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

Gene	Genotype/Diplotype
CYP2C19	*3/*3
SLCO1B1	*1b/*5

6) What is the patient's CYP2C19 metabolizer status?

7) Based on the CYP2C19 results, would you change the choice or dosage of clopidogrel? Why?

8) What is the patient's SLCO1B1 phenotype?

9) Based on the SLCO1B1 results, would you change the choice or dosage of simvastatin? Why?

PharmGKB Training Exercise – Cardiology Answers

A patient with cerebral ischemia is prescribed clopidogrel and simvastatin. After a few days of treatment, they only show a low level of platelet reduction and are starting to show symptoms of myopathy.

You remember seeing in the patient's medical notes that they had their genome sequenced some time ago and decide to check the sequencing data and find out if the patient has a genetic variant affecting their response to clopidogrel or simvastatin.

1) Are there any Clinical Guideline Annotations, FDA Drug Label Annotations or Level 1 Clinical Annotations on the PharmGKB website for clopidogrel? **Yes, a CPIC guideline, a DWPB guideline, a RNPGB guideline, an FDA drug label and three Level 1A clinical annotations for clopidogrel and CYP2C19.**

2) Are there any Clinical Guideline Annotations, FDA Drug Label Annotations or Level 1 Clinical Annotations on the PharmGKB website for simvastatin? **Yes, a CPIC guideline, a DWPB guideline, a RNPGB guideline, an FDA label and two Level 1A clinical annotations for simvastatin and SLCO1B1.**

3) Which genes should you check for variants?
CYP2C19 (clopidogrel) and SLCO1B1 (simvastatin)

4) Briefly explain the relationship between CYP2C19 and clopidogrel. Hint: look at the clopidogrel pathway on the PharmGKB website
CYP2C19 metabolizes clopidogrel to its active metabolite.

5) Briefly explain the relationship between SLCO1B1 and simvastatin. Hint: look at the simvastatin pathway on the PharmGKB website
SLCO1B1 transports simvastatin into liver cells for metabolism into active and inactive metabolites.

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

Gene	Genotype/Diplotype
CYP2C19	*3/*3
SLCO1B1	*1b/*5

6) What is the patient's CYP2C19 metabolizer status? **Poor metabolizer**

7) Based on the CYP2C19 results, would you change the choice or dosage of clopidogrel? Why? **Use a different anti-platelet therapy e.g. prasugrel or ticagrelor.**

8) What is the patient's SLCO1B1 phenotype? **Decreased function**

9) Based on the SLCO1B1 results, would you change the choice or dosage of simvastatin? Why? **Either prescribe a lower dose of simvastatin or consider an alternative statin.**