PharmGKB Training Exercise – Transplant Surgery

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 – Transplant Surgery

Part 1

You have prescribed tacrolimus to a patient who has just had a kidney transplant. Prior to the operation, the patient told you that they have been genotyped by a direct-to-consumer genetic testing company and gave you access to the data.

You decide to check the data to see if you can find any results that could be used to inform the starting dose of tacrolimus.

1) 1) Are there any Clinical Guideline Annotations or relevant Level 1 Clinical Annotations associated with tacrolimus?

2) Which gene is supported by the most evidence?

3) Is the protein encoded by this gene involved in the pharmacokinetics or pharmacodynamics of tacrolimus? (Hint: look at the PharmGKB pathways for tacrolimus) Briefly explain the role of this protein.

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Part 2

The genotyping results show that the patient has the *1/*7 diplotype.

4) What is the patient's CYP3A5 metabolizer status, according to CPIC?

5) What are the CPIC recommendations for this diplotype?

6) What are the DPWG recommendations for this diplotype?

A week later, the patient develops an *Aspergillus* infection, which you want to treat with either voriconazole or posaconazole. You go back to the genotype data to see if they have any variants which would affect their response to either drug.

7) Are there any Clinical Guideline annotations for posaconazole? If so, which gene do the guidelines cover?

8) Are there any Clinical Guideline annotations for voriconazole? If so, which gene do the guidelines cover?

9) The patient's genetic data show that they have the *17/*17 diplotype at the gene of interest. What is their metabolizer status?

10) What are the CPIC recommendations for this diplotype?

11) What are the DPWG recommendations for this diplotype?

PharmGKB Training Exercise – Transplant Surgery Answers

You have prescribed tacrolimus to an adult patient who has just had a kidney transplant. Prior to the operation, the patient told you that they had been genotyped by a direct-to-consumer genetic testing company and gave you access to the data.

You decide to check the data to see if you can find out if any results should be used to inform tacrolimus starting dose.

1) Are there any Clinical Guideline Annotations or relevant Level 1 Clinical Annotations associated with tacrolimus? Yes, a CPIC guideline and a DWPG guideline for tacrolimus and CYP3A5. There is also a RNPGx guideline for tacrolimus and CYP3A4 and CYP3A5. Two Level 1 clinical annotations for tacrolimus and CYP3A5 and one clinical annotation for tacrolimus and CYP3A4.

Be sure to check the Phenotype tags on the clinical annotations as some of the Level 1 clinical annotations are specific to liver transplant patients.

2) Which gene is supported by the most evidence? CYP3A5

3) Is the protein encoded by this gene involved in the pharmacokinetics or pharmacodynamics of tacrolimus? (Hint: look at the PharmGKB pathways for tacrolimus) Briefly explain the role of this protein.
CYP3A5 is involved in tacrolimus pharmacokinetics. It metabolizes tacrolimus to 13-O-demethyl-tacrolimus, 31-O-dimethyl-tacrlimus and other metabolites

The genotyping results show that the patient has the *1/*7 diplotype.

4) What is the patient's CYP3A5 metabolizer status, according to CPIC? Intermediate metabolizer

5) What are the CPIC recommendations for this diplotype?
Increase the starting dose 1.5 to 2 times more than the recommended starting dose (do not exceed 0.3mg/kg/day) then carry out therapeutic drug monitoring.

6) What are the DPWG recommendations for this diplotype?
Use 1.5 times the initial dose that would yield the desired result in non-expressers then use therapeutic drug monitoring.

A week later, the patient develops an *Aspergillus* infection, which you want to treat with either voriconazole or posaconazole. You go back to the genotype data to see if they have any variants which would affect their response to either drug.

7) Are there any Clinical Guideline annotations for posaconazole? If so, which gene do the guidelines cover? No

8) Are there any Clinical Guideline annotations for voriconazole? If so, which gene do the guidelines cover? Yes, CYP2C19

9) The patient's genetic data show that they have the *17/*17 diplotype at the gene of interest. What is their metabolizer status? Ultrarapid metabolizer

10) What are the CPIC recommendations for this diplotype?
Choose an alternative agent.

11) What are the DPWG recommendations for this diplotype?
Use 1.5 times the initial dose and monitor plasma concentrations.