The efficacy of a didactic and case-based pharmacogenomics education program on improving the knowledge and confidence of Alberta pharmacists

Supplementary Materials

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Supplementary Materials 1

Survey

Education of Pharmacists in Pharmacogenomics: Pre- and Post- Education Evaluation

Survey Information/Implied Consent

Study Title: Evaluation of the Effectiveness of a Didactic and Case-Based Education Program on Pharmacist Knowledge and Comfort in Pharmacogenomics

Principle Investigator (PI):

Dalia A. Hamdy, RPh (ACP), PhD, MBA

Clinical Assistant Professor, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, Canada

(780) 604-0481

dhamdi@ualberta.ca

Co-PI:

Dr. Sherif Hanafy Mahmoud

Clinical Associate Professor, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, Canada

(780) 492-5364

smahmoud@ualberta.ca

Co-Investigators:

Mrs. Meagan Hayashi

MSc. Student, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB, Canada

mrshield@ualberta.ca

Invitation to Participate: You are invited to participate in a web-based online survey regarding your knowledge in pharmacogenomics and its application in community practice. You will be asked to complete 2 surveys: one before and one after the educational program.

Pharmacogenomics is defined as the utilization of individual genetic variation in DNA to predict drug safety and response. Pharmacists are medication experts who routinely examine patient medication profiles for drug interactions, therapeutic duplications, dose adjustments, appropriateness of therapy management. Personalization of therapy based on the patient's genetic profile utilizing pharmacogenetic testing is a future mechanism that may help increase medication effectiveness, and reduce time and money wasted for patients and the health care system. Despite how the idea of the pharmacogenomics sound applicable and feasible, there remains few challenges that healthcare system needs to tackle in order to be able to implement such practice into action. They include: a. knowledge barriers such as healthcare professionals' education and patient education, b. insurance and payer coverage and c. access to testing. Community pharmacists are in a position to facilitate access to testing and patient education as well as assist other health care professionals.

Purpose of the study: Our proposed research aims to educate pharmacists on the principles of pharmacogenomics, and evaluate the effectiveness of this education program on pharmacist knowledge and comfort in pharmacogenomic principles

Participation: Your participation in this survey is voluntary, however, it is going to help us assess the learning outcomes of the educational course you are attending. You may refuse to take part in the research or exit the survey at any time without penalty. You are free to decline to answer any question you do not wish to answer for any reason. If you want to participate in the study, please complete the survey. It should take approximately 15 minutes to complete the survey.

Once you have completed the survey, please click the “submit” button

Benefits: You will receive no direct benefits from participating in this research study other than the exposure to new PGX knowledge and practice in addition to increasing your confidence during PGX patient counselling. However, the results from this study will be shared with you following data analysis, via the platform from which you were recruited.

Risks: There are no foreseeable risks involved in participating in this study other than those encountered in day-to-day life.

Confidentiality and Anonymity: Your survey answers data will be stored in REDCap, a secure password protected database hosted at the University of Alberta. The survey will not collect identifying information such as your name, email address, or IP address. Therefore, your responses will remain anonymous. No one will be able to identify you or your answers, and no one will know if you participated in the study. The information that you will share will remain strictly confidential and will be used solely for the purposes of this research. The only people who will have access to the research data are the research team members mentioned above. Additionally, the Research Ethics Board (REB) and The University of Alberta Auditors may also have access to the data. In order to minimize the risk of security breaches and to help ensure your confidentiality we recommend that you use standard safety measures such as signing out of your account, closing your browser and locking your screen or device when you are no longer using them / when you have completed the study. Results will be published in pooled (aggregate) format. Anonymity is guaranteed since you are not being asked to provide your name or any personal information.

In order to link the pre- and post- survey data, we kindly ask you to provide a unique code at the start of the survey (by utilizing the last three letters of the participant's mother's maiden names and the two digits of your birth day e.g. ITH23) which by no means will identify you as a participant.

Data Storage: Your survey answers data will be stored in REDCap, a secure password-protected database hosted at the University of Alberta. The data will be stored for a minimum of 5 years.

Voluntary Participation: You are under no obligation to participate and if you choose to participate, you may refuse to answer questions that you do not want to answer. Should you choose to withdraw midway through the electronic survey simply close the link. This will not remove your results from the database: to do so you must email the Principal Investigator at the contact information provided in this consent page, and provide your identifying code to remove your results. Once the identifiers are removed it will no longer be possible to withdraw the data from the study.

Information about the Study Results: Given the anonymous nature of the survey, research findings will not available to the participants. However, we intend to publish the research findings in a peer reviewed journal

CONTACT Information:If you have questions at any time about the study or the procedures, you may contact the research team members: Dr. Dalia A. Hamdy at dhamdi@ualberta.ca or Dr. Sherif Mahmoud at smahmoud@ualberta.ca .

The plan for this study has been reviewed by a Research Ethics Board at the University of Alberta. If you have any questions regarding your rights as a research participant or how the research is being conducted, you may contact the Research Ethics Office at 780-492-2615.

Please print a copy of this form for your records.

ELECTRONIC CONSENT:

By proceeding with the survey, you are providing consent to the researchers and allowing your results to be used in the study as described above.

Please proceed to the next page to begin the survey.

Please provide us with some information about yourself.

Please provide the last three letters of your mother's maiden name, and the day of the month you were born, for anonymized coding purposes. (i.e. if these answers Smith & January 24th you would enter ITH24)	_____
Please indicate if you are completing this survey prior to or after the education program portion of this study:	◯ Pre-education survey ◯ Post-education survey
What gender do you identify as?	◯ Male ◯ Female ◯ Other ◯ Prefer not to say
What year were you born?	_____
What year did you graduate with your first pharmacy degree?	_____
In which country did you obtain your first pharmacy degree?	◯ Canada ◯ United States ◯ Other
Please specify:	_____
What degrees or certifications do you currently hold? (check all that apply)	☐ Diploma ☐ Bachelor of Science ☐ Pharm D ☐ Residency ☐ MBA ☐ MSc ☐ PhD
How many years have you been practicing pharmacy?	◯ less than 2 years ◯ 2-5 years ◯ 6-10 years ◯ more than 10 years

What pharmacy or healthcare settings have you worked in throughout your career? (check all that apply)	☐ Community pharmacy ☐ Hospital ☐ Primary Care Network ☐ Research ☐ Industry ☐ Other
Please specify:	_____
What authorizations or credentials do you currently have? (Check all that apply)	☐ Additional Prescribing Authorization ☐ Certification to Administer Injections ☐ Certified Diabetes Educator ☐ Board Certified Ambulatory Care Pharmacist ☐ Other
Please specify:	_____

Pharmacogenomics is the utilization of individual genetic variation in DNA to predict drug safety and response. The genetic variants could be on the drug metabolizing enzyme, transporter and/or receptor levels. The aim of pharmacogenomic testing is to provide tailored medication therapy, such as drug choice and dose, based on the individual's genetic variants to provide optimal therapy outcomes.

Please respond to the following statements with Yes or No.

I received education on the topic of pharmacogenomics during my pharmacy degree program.	◯ Yes ◯ No
I received education on the topic of pharmacogenomics during post-graduate studies and/or while completing continuing education activities.	◯ Yes ◯ No
I have experience with pharmacogenomic testing.	◯ Yes ◯ No

Please respond to the following statements with Strongly Agree, Agree, Neutral, Disagree, Strongly Disagree.

Pharmacogenomics can enhance the provision of medication-related services (e.g. dispensing, care-planning).	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree
Pharmacogenomics testing is cost-effective.	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree
I am comfortable identifying patients who may benefit from pharmacogenomic testing.	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree
I am comfortable answering patient questions regarding pharmacogenomics testing.	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree
I am comfortable educating patients on the risks and benefits of pharmacogenomics testing.	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree
I am comfortable explaining ethical and legal considerations to patients in the process of informed consent for pharmacogenomics testing.	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree

I am comfortable interpreting a genotype in a pharmacogenetic test result into a phenotype.	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree
I am familiar with the evidence-based resources and websites available for pharmacogenomics.	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree
I am comfortable educating patients on their pharmacogenetic test results.	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree
I am comfortable explaining pharmacogenetic test results to other healthcare providers.	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree
I am comfortable applying the results from pharmacogenomic testing when making drug therapy decisions (e.g., selecting medication, dosing, monitoring).	◯ Strongly agree ◯ Agree ◯ Neutral ◯ Disagree ◯ Strongly disagree

The following skill testing questions are designed to assess your knowledge of pharmacogenomics prior to and after receiving pharmacogenomics education as part of this study.

Please answer the following questions to the best of your current knowledge. If you do not know the answer to any of the questions, please use the response “I don’t know”. Please try to avoid guessing.

Which pharmacogene is most relevant to antiplatelet selection?	◯ CYP1A2 ◯ CYP2C9 ◯ CYP2C19 ◯ CYP2D6 ◯ COMT ◯ I don't know
If a patient provides you with a result for a CYP2D6 test, and is asking you to provide their physician with a recommendation for treatment of depression, which online resource would you find most useful in interpreting their phenotype (metabolism status)?	◯ Lexicomp ◯ eCPS ◯ PharmGKB.org ◯ PharmacyGenes.org ◯ I don't know

Which of the following would be considered the MOST correct definition of incidental findings in the context of pharmacogenomic testing?	◯ Coincidental identification of a drug-gene interaction that was not the focus of the test ordered (e.g. CYP2C19 testing for antiplatelet selection that also shows patient is at higher risk of side effects from their current antidepressant) ◯ Identification of polymorphisms that indicate a different risk of an inheritable disease (e.g. CACNA1S testing to determine the risk of malignant hyperthermia with volatile anesthetics and succinylcholine that also reveals genetic risk for the development of hypokalemic periodic paralysis, an inheritable and sometimes debilitating disease) ◯ Identification of polymorphisms that indicate a different risk of an inheritable disease (e.g. CACNA1S testing to determine the risk of malignant hyperthermia with volatile anesthetics and succinylcholine that also reveals genetic risk for the development of hypokalemic periodic paralysis, an inheritable and sometimes debilitating disease) ◯ Finding a drug-gene interaction for which there is no current drug-related problem (e.g. panel testing shows ultrarapid metabolism of PPIs via CYP2C19, however the patient feels GERD is well controlled at current low dosage) ◯ A pharmacogenomic test ordered and completed in error with identified drug-gene interactions found ◯ I don't know
Pharmacogenetic testing for VKORC1 looks at a change in drug effect at the level of:	◯ Pharmacokinetics ◯ Pharmacodynamics ◯ Off-target effect ◯ I don't know
HLA-B genotyping in patients with Chinese ancestry is suggested in the FDA guidelines for which antiepileptic drugs? (check all that apply)	☐ Phenytoin ☐ Valproic acid ☐ Lamotrigine ☐ Carbamazepine ☐ I don't know
Which medications have known drug-gene interactions, with therapy modification recommendations available through a clinical guideline? (check all that apply)	☐ Sertraline ☐ Bupropion ☐ Hydromorphone ☐ Metoprolol ☐ Pravastatin ☐ I don't know
Which of the following cannot be done without the patient's consent regarding the sharing of pharmacogenetic test results? i) Sharing results with a patient's physician ii) Sharing results with an insurance company iii) Sharing results with a related patient who may carry the same gene iv) Documenting results on the patients' pharmacy care record	◯ i, ii, and iv ◯ i, and iv ◯ only i ◯ only iv ◯ i, ii, iii, and iv ◯ I don't know

Supplementary Materials 2

Pharmacogenomics for Alberta Pharmacists – Course Outline

Table S2.1. Outline of Pharmacogenomics for Alberta Pharmacists, Didactic Component. Within the live course, cases were introduced, discussed, and unfolded between almost every session.

Session Number	Session Title
1	Genetics 101
2	Introduction to Pharmacogenomics
3	Applications of Pharmacogenomics in Cardiovascular Medicine
4	Pharmacogenomics and the Patient Care Process
5	Essential Resources in Pharmacogenomics
6	Applications of Pharmacogenomics in Psychiatry
7	Applications of Pharmacogenomics in Pain Management
8	Ethical, Legal, and Social Considerations within Pharmacogenomic Testing
9	Practical Implementation of Pharmacogenomics in the Pharmacy
10	Applications of Pharmacogenomics in Oncology
11	Pharmacogenomics Expanded

Table S2.2. Outline of Pharmacogenomics for Alberta Pharmacists, Case Study Component. Full class in the live session consisted of 10-15 pharmacists, and small groups 3-5 pharmacists. Asynchronous participants received cases as a word document with all questions presented in live sessions (including each question presented to all small groups) and space to provide a response, with answer keys to each question on the following page. In all cases and methods of participation, pharmacists were encouraged to utilize resources and knowledge gained through the course to answer the questions to the best of their ability prior to reviewing answers.

Case Number	**Case Focus**	**Description of Live Course Activity**
1	Cardiovascular PGx	Full class discussion in introduction prior to session 1, in application of pharmacogenomics to this case after session 2, and in formulating care-plan after session 3.
2	Psychiatric PGx	Full class discussion in introduction prior to session 4, small group breakout room simulation with facilitator after session 5 to practice using resources, and full class discussion to discuss findings of each group after session 6.
3	Pain PGx	Full class discussion in introduction prior to session 7, small group breakout room simulation with facilitator after session 7 to discuss therapeutic alternatives, followed by full class discussion to review findings of each group.
4	ELSI of PGx	Full class discussion in introduction prior to session 8, small group breakout room discussion with facilitator after session 9 to discuss specific ELSI question assigned, followed by full group discussion to review responses of each group.
5	Oncology PGx	Full class discussion in introduction prior to session 10, and full class discussion in case unfolding after session 10.
6	Polypharmacy PGx	Full class discussion throughout case presentation as each new problem developed.

Supplementary Materials 3

Pharmacogenomics for Alberta Pharmacists – Case Study Example

Pharmacogenomics for Alberta Pharmacists

Case Study #1 – Art Terry (Cardiovascular PGx)

Instructions:

Use resources and knowledge gained throughout the course, in addition to standard pharmacy resources, to answer the questions in the space provided. Once satisfied with your response, you may proceed to the next page in the case study to compare your response to answers provided by the course facilitators and gain additional information to help you with the case as it progresses.

We welcome any questions or comments about these cases. Please forward these to mrshield@ualberta.ca.

Thank You!

The Research Team

Case 1 -Art Terry: Introduction

Meet Art:

- 52-year-old married male truck driver
- Previous history of poorly controlled hypertension
  - Last pharmacy visit BP 168/92 mmHg
  - Was taking Losartan 100mg po daily, started amlodipine 5mg daily after BP reading above
- No other previously diagnosed medical conditions or medications

Case 1 – Art Terry: Introduction

One day, Art develops chest pain on a hike. After descending it is not resolved and he goes to the emergency department.

Art is diagnosed with an NSTEMI, and transferred to cardiology for percutaneous intervention with stent placement.

Art has an uncomplicated short-stay in the cardiology unit and is discharged from hospital the next day.

Case 1 – Art Terry: Introduction

Art's discharge Rx:

- Losartan 100mg po daily
- Amlodipine 10mg po daily
- Metoprolol 25mg po BID
- ASA 81mg po daily
- Clopidogrel 75mg po daily
- Atorvastatin 80mg po daily

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AbEx Health Services

You are the pharmacist assessing Art's medications prior to or after discharge. What other information do you need in your assessment of Art's medications?

(Proceed to next page for answers)

You are the pharmacist assessing Art's medications prior to or after discharge. What other information do you need in your assessment of Art's medications?

KEY

- Family history – Art's father had a fatal myocardial infarction at age 47. No other relevant history.
- Other medication history – originally had tried ramipril for hypertension but switched to losartan due to cough (resolved with switch)
- Lifestyle – Art smokes a ½ pack per day for the last 20 years, and is a casual social drinker
- Weight - 5'11", 210lbs, BMI 29.3kg/m^2
- Vital signs – BP 138/88mmHg, HR 53bpm
- Goals of treatments – wife wants to do a big multi-day hike and he wants to make her happy. Also, he wants to be around for his now adult children and future grandchildren, as he is sad he did not have his dad around
- Laboratory tests – Creatinine 87umol/L, liver function tests all within normal limits, lipids HDL 0.8 mmol/L, LDL 4.62 mmol/L, TC 6.20 mmol/L, TG: 1.6mmol/L, electrolytes all within normal limits
- Adherence – excellent, uses dosette even prior to this hospitalization. That is why he was frustrated about his poor blood pressure control
- Over-the-counter use: none
- Stent type: drug eluting stent (paclitaxel)

Case 1 – Art Terry: Follow-Up

Art returns to the pharmacy 1 month after his NSTEMI.

He says his legs hurt so bad he can hardly walk. He is worried it will affect his cardiac rehab and ability to do hikes with his wife, including a dream trip on the Camino de Santiago.

In desperation to find out if it could be due to his medications, he found a pharmacogenetic test to take, and is hoping you can help him understand and utilize it.

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Case 1 – Art Terry: Follow-Up

Consider…

What proteins (metabolizing enzymes, transporters, receptors/drug targets) are involved in Art's response to his current medications?

Art's discharge Rx:

- Losartan 100mg po daily
- Amlodipine 10mg po daily
- Metoprolol 25mg po BID
- ASA 81mg po daily
- Clopidogrel 75mg po daily
- Atorvastatin 80mg po daily

What proteins (metabolizing enzymes, transporters, receptors/drug targets) are involved in Art's response to his current medications?

(Proceed to next page for answers)

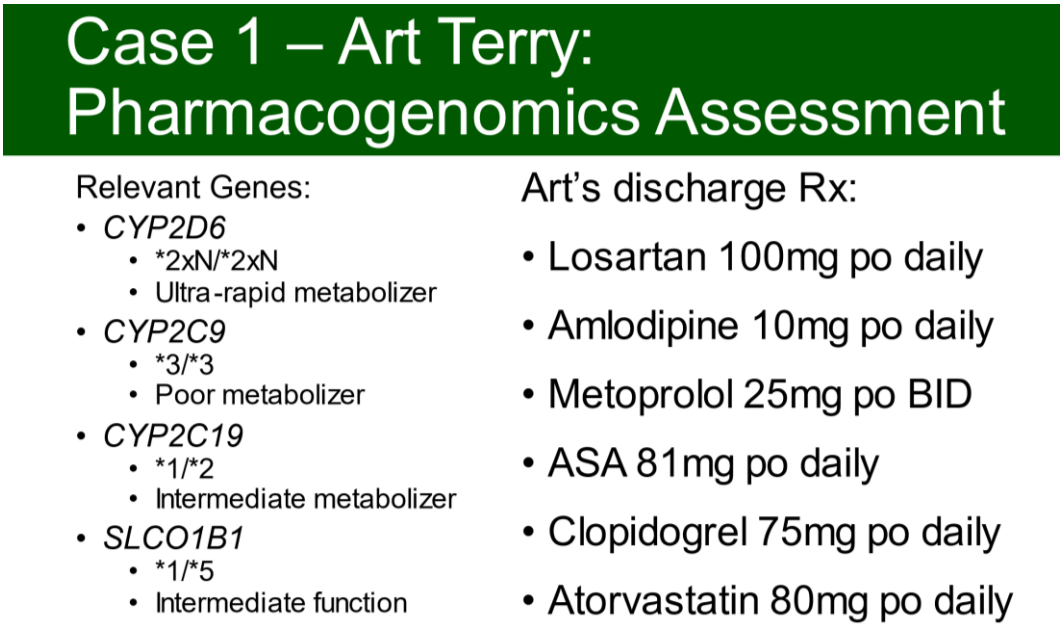
What proteins (metabolizing enzymes, transporters, receptors/drug targets) are involved in Art's response to his current medications?

KEY

- Losartan is metabolized by CYP3A4 and 2C9 into a more potent metabolite
- Losartan acts on the AT_1 receptor to enact its effect
- Amlodipine is metabolized by CYP3A4
- Amlodipine acts on calcium channels in vascular smooth muscle
- Metoprolol is metabolized by CYP2D6 for clearance
- Metoprolol acts on beta-1 receptors in the heart
- ASA covalently binds to COX-1 and COX-2 enzymes
- ASA's metabolite, salicylate (active), is conjugated by saturable UGT enzymes
- Clopidogrel's absorption from the intestine is facilitated by p-glycoprotein
- Clopidogrel is a prodrug activated mainly by CYP2C19
- Clopidogrel acts on $P2Y_{12}$ receptor on platelets
- Atorvastatin is transported by OATP 1B1 (encoded by SLCO1B1)
- Atorvastatin is metabolized by CYP3A4
- Atorvastatin inhibits HMG-CoA reductase enzyme

While Art's medications interact with all of these different proteins, we do not necessarily have the capacity to test all of these genes, or the evidence to provide therapy recommendations based on those results we can obtain.

Additionally, it is important to consider non-drug differential in the cause of Art's symptoms. For this case, the patient's physician has ruled out non-drug causes to his myopathy.

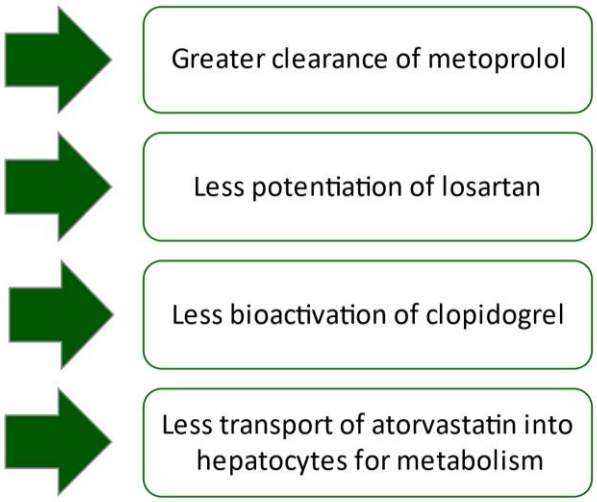


What do these test results (and phenotypes) mean for Art's current medications?

(Proceed to next page for answers)

Relevant Genes:

- *CYP2D6*
  - *2xN/*2xN
  - Ultra-rapid metabolizer
- *CYP2C9*
  - *3/*3
  - Poor metabolizer
- *CYP2C19*
  - *1/*2
  - Intermediate metabolizer
- *SLCO1B1*
  - *1/*5
  - Intermediate function



Knowing the drug-gene interactions present, list some drug and nondrug alternatives for management of hypertension and coronary artery disease.

Metoprolol	
Losartan	
Clopidogrel	
Atorvastatin	

(Proceed to next page for answers)

Knowing the drug-gene interactions present, list some drug and nondrug alternatives for management of hypertension and coronary artery disease.

KEY

Metoprolol: The Royal Dutch Pharmacists Association November 2018 guidelines: “For CYP2D6 ultra metabolizers, use the maximum dose for the relevant indication as a target dose, and if the effectiveness is still insufficient: increase the dose based on effectiveness and side effects to 2.5 times the standard dose or select an alternative drug.” Considering current heart rate (53 BPM) however, no medication changes are recommended at this time. Suggest home BP/HR monitoring, target HR <110bpm. See BP management below.

Losartan: As blood pressure is currently adequately controlled, could consider maintaining current therapy. If the patient is concerned about pill burden (i.e. is amlodipine necessary if a more potent ARB can be used for this patient?) could consider transitioning to another ARB not affected by known genetics; there are no current dosing guidelines for losartan with pharmacogenomic test results on PharmGKB. If changes in medications, create a monitoring plan with positive and negative parameters with the patient. Blood pressure monitoring as noted above is advisable, to a target <140/<90mmHg and an avoidance of side-effects such as symptomatic hypotension. Encourage lifestyle changes (patient already physically active, advise DASH diet, smoking cessation).

Clopidogrel: The Clinical Pharmacogenetics Implementation Consortium 2013 guidelines advise use of alternative antiplatelet therapy (prasugrel or ticagrelor) due to the increased risk of adverse cardiovascular outcomes (moderate level of evidence). Consider other factors such as drug coverage and cost in this decision, especially given intermediate-metabolism status (evidence is stronger for poor-metabolizers). (Scott SA, et al. Clin Pharmacol Ther. 2013 Sep;94(3):317-23.) General cardiovascular risk reduction measures also advisable as noted above.

Atorvastatin: First, it would be reasonable to consider if the patient is consuming grapefruit juice, which can increase the risk of myopathies. He did in fact start drinking grapefruit juice in the last month, forgetting the education to avoid. The Royal Dutch Pharmacists Association August 2020 Guidelines: “The risk of myopathy can be elevated. The gene variation may lead to reduced atorvastatin transport to the liver, which may increase atorvastatin plasma concentrations.” This may explain this patient’s current adverse drug reaction. Also from these guidelines: “Rosuvastatin and pravastatin are influenced to a similar extent by the SLCO1B1 gene variation but are not influenced by CYP3A4 inhibitors such as amiodarone, verapamil and diltiazem. Fluvastatin is not influenced significantly by the SLCO1B1 gene variation or CYP3A4 inhibitors.” Therefore, some options to consider would be changing to Fluvastatin, dose reduction in atorvastatin with avoidance of grapefruit, or changing therapy to rosuvastatin moderate intensity dose, with follow-up for resolution of myopathy. Other non-drug considerations would be adequate hydration on hikes, avoidance of alcohol (especially in excess) warning and counselling of the signs and symptoms of rhabdomyolysis, and cardiovascular risk reduction as above.