Personalized Prescribing Inc.

Dear Dr,

According to Stephanie's pharmacogenetic test results:

She is at increased risk of muscle pain on statins due to her genes (**SLCO1B1 rs4149056 TC also known as *1/*5**). For patients with the T/C or C/C genes, healthcare providers can consider:

1. **Using lower doses of water-soluble statins (*Rosuvastatin* or *Pravastatin*).** However, Stephanie experienced muscle pain and an elevation in muscle enzymes on Rosuvastatin 5 mg once daily, and this medication was subsequently discontinued. For patients with statin-induced myopathy, discontinuation is warranted if myalgia is intolerable OR CK levels are >4 ULN. *If considering a re-challenge, try alternate-day dosing of statins, as this has been shown to have equal LDL lowering efficacy.*

2. ***Ezetimibe* or *Colesevelam* can be used as an alternative to statins for LDL lowering**. The maximal expected reduction in LDL using these alternative agents is 15-20%, though the combination of Ezitimibe and Colesevelam can result in an LDL reduction of 40-45%. Of all these agents, only Ezetimibe has shown some promise for CV risk reduction and only in combination with Simvastatin, according to the IMPROVE-IT trial.

3. **If further LDL –lowering is needed due to high CV risk, *a PCSK9-inhibitor* can be considered in patients who experience statin intolerance**, as these agents can reduce LDL by 50-70%.

This patient has no problems metabolizing Esomeprazole and Celecoxib via the following genes **CYP2C19***1/*1 and **CYP2C9***1/*1. However, there is a need to prevent B12 deficiency and bone loss with chronic use of Esomeprazole. Thus, we would recommend supplementation with:

- **Vitamin B12** 1000 mcg/day
- **Calcium *citrate*** 400 mg/day
- **Vitamin D** 2000 IU/day

*Note: Only the *citrate* form of Calcium can be used, given that proton pump inhibitors, such as esomeprazole, can prevent the absorption of other forms of Calcium.

Future Considerations:

This patient is a **CYP2D6 *1/*4 intermediate metabolizer**. Exercise caution with the use of **strong CYP2D6 inhibitors** (i.e. Bupropion, Fluoxetine, Paroxetine, Fluvoxamine, and Quinidine) in the presence of *CYP2D6 substrates* (i.e. Tamoxifen, Codeine and its derivatives, and Metoprolol), given that this patient already has reduced CYP2D6 activity.

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For muscle pain treatment, this patient is less likely to respond to codeine and its derivatives (i.e. hydrocodone and oxycodone); higher doses may be needed. This patient is more likely to respond to **morphine, hydromorphone, NSAIDs and Tylenol** at regular starting doses (as these medications do not require metabolism by CYP2D6 for activation).

References:

- Smith, HS. (2009). Opioid Metabolism. *Mayo Clinic Proceedings*. *84,* 7, 613-624.
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- Mancini, G. B. J, et al. (2016). Diagnosis, Prevention, and Management of Statin Adverse Effects and Intolerance: Canadian Consensus Working Group Update. *Canadian Journal of Cardiology, 32,* 7.
- Orringer, CE, et al. (2017). Update on the Use of PCSK9 Inhibitors in Adults: Recommendations from an Expert Panel of the National Lipid Association. *Journal of Clinical Lipidology*.
- Waters, DD et al. (2016). PCSK9 Inhibitors for Statin Intolerance? *JAMA*. *315*, 15, 1571-1571.

Other untested clinical and genetic factors can also affect medication response. This patient has been informed to follow-up with her physician prior to making any changes to her medications.

Please feel free to contact me, if you have any questions.

Regards,

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