savings/. Accessed June 28, 2018.
9. GoodRx. Linzess Prices and Linzess Coupons. Available from: https://www.goodrx.com/linzess. Accessed June 28, 2018.
10. GoodRx. Amitiza Prices and Amitiza Coupons. Available from: https://www.goodrx.com/ https://www.goodrx.com/amitiza. Accessed June 28, 2018.
11. Trulance® (plecanatide) patient assistance program. Accessed June 28, 2018. Available from: https://www.trulance.com/savings/

Personalized Medicine Corner

Genotype-Guided Opioid Prescribing

Chronic pain affects approximately 100 million American adults, with an estimated total cost of $560 to $635 billion annually. This alarming cost and the negative impact on patients' quality of life of poor pain control highlight the need for better methods to improve chronic pain management.[1]

Providers need to prescribe the optimal opioid regimen that allows adequate pain control with minimal adverse effects. However, due to the subjective nature of pain tolerance and variability of opioid response, selection of the right drug, right dose, and right frequency can be challenging. These challenges can be overcome with clinical pharmacogenetics by helping providers predict the expected responses to certain opioids and provide a personalized pain regimen based on the patient's genetics. As genetic testing costs and regulation restrictions decrease, we expect more institutions to apply pharmacogenetics clinically with increasing evidence and access to testing.[2]

Codeine, tramadol, and, to a lesser extent, oxycodone and hydrocodone are biotransformed by CYP2D6 to metabolites with greater affinity for the opioid *mu* receptor. One to two percent of individuals have the *CYP2D6* genotype associated with ultra-rapid metabolism. Ultra-rapid metabolizers are at risk for toxic concentrations of the active metabolites of codeine and tramadol and serious adverse effects, including respiratory depression and even death. In contrast, five to ten percent of individuals are CYP2D6 poor metabolizers with no enzyme activity. Another 2 to 11% are intermediate metabolizers with significant reductions in CYP2D6 activity. Poor and intermediate metabolizers have impaired ability to biotransform codeine and tramadol to their active metabolites and may attain little to no analgesic effect from these drugs. In addition to genotype, a number of medications inhibit the CYP2D6 enzyme, which can lead patient conversion to a poor or intermediate metabolizer CYP2D6 phenotype. The Clinical Pharmacogenetics Implementation Consortium recommends use of opioids that are not primarily metabolized by CYP2D6 or non-opioids in ultra-rapid and poor metabolizers because of the risk for toxicity and non-response, respectively.[3]

A pilot study from the UF Health Personalized Medicine Program compared a *CYP2D6* genotype-guided approach to pain management versus usual care in adult patients with chronic pain. For patients in the genotype-guided arm with the poor, intermediate, or ultra-rapid metabolizer phenotype based on *CYP2D6* genotype and concomitant use of any CYP2D6 inhibitors, recommendations were made to avoid codeine, tramadol, and to a lesser extent, hydrocodone and oxycodone. Among poor and intermediate metabolizers treated with codeine or tramadol at baseline, a significant reduction in pain intensity was observed in the genotype-guided arm compared to the usual care arm. These data suggest that a genotype-guided approach to opioid prescribing may lead to better pain control.[4]

Personalizing pain management based on patient genetics and other patient-specific factors can move the healthcare system closer achieving optimal pain regimens that provide patients with adequate pain relief and limited adverse effects on a larger scale.

For questions about this guideline contact the UF Health Personalized Medicine Program. Please send an email to PMP-HELP@ctsi.ufl.edu.

References:

1. Gaskin DJ, Richard P. The Economic Costs of Pain in the United States. J Pain. 2012;13(8):715-724.
2. Smith DM, Weitzel KW, Cavallari LH, et al. Clinical Application of pharmacogenetics in pain management. Per Med. 2018;(Epub ahead of print)
3. Crews KR, Gaedigk A, Dunnenberger DM, et al. CPIC guidelines for cytochrome P450 2D6 genotype and codeine therapy: 2014 update. Clin Pharmacol Ther. 2014;95:376-82.
4. Smith DM, Weitzel KW, Elsey AR, et al. Outpatient CYP2D6 Genotype-Supported Opioid Therapy: A Prospective Trial. Poster presented at: American Society for Clinical Pharmacology and Therapeutics; 2018 Mar 21-24; Orlando, FL.

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