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30th Anniversary of PharmaNote®

We are excited to be starting our 30th year of publishing the PharmaNote® newsletter. We sincerely appreciate all our readers and thank all our contributors. We look forward to providing you new and updated treatment information to assist in patient care.

Vorapaxar (Zontivity®) for Secondary Prevention of Thrombotic Cardiovascular Events

Sheena Mathew, PharmD Candidate

Ischemic heart disease (IHD) is the leading cause of death worldwide.[1] In 2010, IHD and stroke collectively killed 12.9 million people, accounting for nearly 25% of all deaths worldwide.[2] The burden of IHD, which consists of years of life lost from death or years of disability living with nonfatal acute myocardial infarction (MI), angina pectoris, and ischemic heart failure, has increased by 29 million disability-adjusted life-years (a 29% relative increase) from 1990 to 2010.[3] Over $75 billion dollars are spent annually on direct medical costs associated with acute coronary syndromes (ACS) in the United States, with the majority used for drug therapy and associated costs.[4] Additionally, patients with either peripheral artery disease (PAD) and previous MI are at an increased risk of death and cardiovascular complications, including recurrent MI, heart failure, angina and stroke.[5] However, effective use of drug therapy, including anti-platelet agents, can lead to significant reductions in morbidity, mortality, and costs associated with this disease.[5]

Stroke and MI are typically triggered by the rupture or erosion of "vulnerable" atherosclerotic plaque, a phenomenon termed atherothrombosis.[5] Atherothrombosis is largely attributed to the activation of platelets which is believed to occur primarily via: (1) cyclooxygenase (COX)-1-mediated thromboxane A_2 (TXA_2) synthesis and activation via the TXA_2 receptor; (2) adenosine diphosphate via the $P2Y_{12}$ receptor; and, (3) thrombin via the protease activated receptor (PAR)-1.[5]

Aspirin, an irreversible COX-1 inhibitor, has been used for secondary prevention of atherothrombotic events for decades. Recently, new agents have been introduced to the market, including thienopyridines (i.e., clopidogrel and prasugrel), which irreversibly inhibit $P2Y_{12}$ receptors, and cyclopentyl-traizolo-pyrimidines (i.e., ticagrelor), which reversibly inhibit $P2Y_{12}$ receptors. Yet, over 10% of patients treated with these agents experience a major cardiovascular ischemic event within 1 year,[6] suggesting that treatment of these conditions have not been optimized. Additionally, the introduction of these more potent antiplatelet agents has been associated with an increased risk of bleeding.[6,7] Despite the use of combined aspirin and $P2Y_{12}$ receptor inhibitors, patients continue to suffer from major cardiovascular and cerebrovascular disease.[5] Thus, there still remains room for improvement in the prevention of ischemic heart disease.

Vorapaxar (Zontivity®) acts via a novel mechanism to reduce thrombotic cardiovascular events. In May 2014, vorapaxar was granted an FDA-approved indication for the secondary prevention of thrombotic cardiovascular events.

INSIDE THIS ISSUE:

Vorapaxar is the only agent available in the U.S. from a new class of drugs called protease-activated receptor-1 (PAR-1) antagonists, also known as thrombin receptor antagonists.[8] This article will review the pharmacology, pharmacokinetics, pertinent clinical trials, safety and dosing of vorapaxar for secondary prevention of thrombotic cardiovascular events in patients with previous MI or PAD.

Pharmacology

Pharmacodynamics

Vorapaxar inhibits PAR-1, which is expressed on platelets, smooth muscle cells, endothelial cells and fibroblasts.[5] Thrombin mediates its cellular effects through various PARs, but has the greatest affinity for PAR-1; these PARs play critical roles in coagulation, inflammation and vascular homeostasis. By targeting PAR-1, vorapaxar inhibits platelet aggregation and regulates vascular activity.[9,10] Although binding is reversible, vorapaxar dissociates slowly from PAR-1, resulting in a long elimination half-life of nearly 8 days, and making the binding effectively irreversible.[11]

Vorapaxar achieves ≥80% inhibition of thrombin receptor activating peptide (TRAP)-induced platelet aggregation within one week of treatment initiation. Four weeks after vorapaxar is discontinued, a 50% inhibition of thrombin-induced platelet aggregation can still be expected.[11] The extent of platelet inhibition is dependent on both dose and concentration; a 40-mg loading dose of vorapaxar produces a potent and predictable degree of platelet inhibition, whereas a 20-mg dose achieves lower platelet inhibition.[12]

Pharmacokinetics

The pharmacokinetic properties of vorapaxar are summarized in **Table 1**. Ingestion of vorapaxar with a high-fat meal results in only a small delay and decrease in peak concentrations.[11] Vorapaxar and its major circulating active metabolite, M20, are both extensively bound (≥99%) to human plasma proteins. The systemic exposure of the active metabolite M20 is ~20% of the exposure to the parent drug. Vorapaxar is highly bound to serum albumin and does not preferentially distribute into red blood cells. The effective half-life of vorapaxar is 3-4 days and the terminal elimination half-life is nearly 8 days. Steady state following once-daily dosing is achieved by 21 days.[11]

Table 1 | Pharmacokinetic properties of vorapaxar.[11]

Property	Vorapaxar
T_{max}	1-2 hours
Protein Binding	≥99%
Metabolism	CYP3A4 (major) and CYP2J2 (minor)
Elimination	95% feces; 5% urine
Half-Life	8 days (range, 5-13 days)
Bioavailability	100%
Volume of Distribution	424 L

T_{max} = time to peak concentration; **CYP =** Cytochrome P450.

Drug-Drug Interactions

Table 2 summarizes potential drug-drug interactions with vorapaxar that have been studied to date. In vitro metabolism studies show that vorapaxar and its active metabolite, M20, are unlikely to cause clinically significant inhibition or induction of major CYP isoforms or inhibition of OATP1B1, OATP1B3, BCRP, OAT1, OAT3, and OCT2 transporters.[11] Vorapaxar is a weak inhibitor of the P-glycoprotein transporter. Clinical trials suggest that co-administration of a weak or moderate CYP3A inhibitor with vorapaxar does not increase bleeding risk or alter the efficacy of vorapaxar.[14,15] Consequently, no dose adjustment of vorapaxar is recommended in patients taking weak-to-moderate CYP3A4 inhibitors.[11] However, strong inhibitors and strong inducers of CYP3A4 should be avoided when using vorapaxar.[11]

Finally, an increased risk of bleeding may be present with the concurrent use of certain medications that also increase bleeding risk (e.g., anticoagulants, fibrinolytic therapy, chronic NSAIDs, SSRIs, and SNRIs). Concomitant use of warfarin or other anticoagulants with vorapaxar should be avoided.[11]

Special Populations

According to the FDA-approved labeling, no dose adjustments are recommended based on age, race, sex, weight, or the presence of mild-to-moderate renal insufficiency.[11] However, elderly patients are at an increased risk of bleeding, thus patient age should be considered before initiating vorapaxar altogether.

Vorapaxar is classified as FDA Pregnancy Category B. Nursing mothers should avoid vorapaxar since data on excretion of vorapaxar and its metabolites into human milk are unavailable. No dose adjustment is required in patients with mild or moderate hepatic impairment. However, vorapaxar should be avoided in patients with severe hepatic impairment.[11]

Clinical Trials

Two phase 3 trials, TRA 2°P-TIMI 50 and TRACER, have assessed the safety and efficacy of vorapaxar when used concomitantly with standard care, including antiplatelet drugs. **Table 3** shows the baseline characteristics of patients enrolled in each study. Study design, endpoints, and results of the TRA 2°P-TIMI 50 and TRACER trials are summarized in **Table 4**. No studies have evaluated the use of vorapaxar as monotherapy for secondary prevention of thrombotic events.

TRA 2°P-TIMI 50 was a multicenter, randomized, double-blind, placebo-controlled study that enrolled 26,449 patients who had evidence or a history of atherosclerosis involving the coronary, cerebral, or peripheral vascular systems.[14] Eligible patients had a history of atherosclerosis, defined as a spontaneous MI or ischemic stroke within the previous 2 weeks to 12 months, PAD associated with a history of intermittent claudication in conjunction with either an ankle-brachia index of <0.85, or previous revasculariza-

Table 2 | Potential drug-drug interactions with vorapaxar.[11,13]

Interacting Drugs	Examples	Effect
Potent CYP3A4 Inducers	Rifampin, carbamazepine, St. John's wort, phenytoin	↓ plasma vorapaxar concentrations
Potent CYP3A4 Inhibitors	Ketoconazole, clarithromycin, ritonavir, amiodarone	↑ plasma vorapaxar concentrations
Drugs that ↑ bleeding risk	NSAIDs, anticoagulants, antiplatelets, SSRIs/SNRIs	↑ risk of bleeding

tion for limb ischemia. Patients were ineligible if they were planning to undergo a revascularization procedure, had a history of bleeding diathesis, had recent active abnormal bleeding, were receiving ongoing treatment with warfarin, or had active hepatobiliary disease.

Patients were randomly assigned to receive either vorapaxar 2.5 mg daily or placebo in addition to standard care, which could include aspirin, a thienopyridine, or both, or dipyridamole. The primary efficacy endpoint of the study was the composite of cardiovascular death, MI or stroke. The composite of cardiovascular death, MI, stroke, or urgent coronary revascularization (UCR) was assessed as the secondary efficacy endpoint. Bleeding was assessed using the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) and Thrombolysis in Myocardial Infarction (TIMI) classification systems, with GUSTO moderate or severe bleeding defined as the safety end point of primary interest.

The primary composite efficacy endpoint of cardiovascular-related death, MI or stroke occurred in 9.3% of the vorapaxar-treated persons compared to 10.5% of placebo-treated persons (hazard ratio [HR] 0.87; 95% CI 0.80 to 0.94). In January 2011, after 24 months follow-up, the data and safety monitoring board recommended vorapaxar discontinuation in all patients with previous stroke after an interim review identified an excess of intracranial hemorrhage in patients taking vorapaxar who had a history of stroke. Among patients with previous stroke, the 3-year event rate of GUSTO moderate or severe bleeding was 4.7% in the vorapaxar group and 2.8% in the placebo group (HR 1.74; 95% CI 1.26 to 2.39). Furthermore, among those with a history of stroke, the rate of intracranial hemorrhage in the vorapaxar group was 2.4%, as compared with 0.9% in the placebo group (HR 2.55; 95% CI 1.52 to 4.28), with corresponding rates of fatal bleeding of 0.5% and 0.3%, respectively (HR 1.48; 95% CI 0.53 to 4.16). The rates of intracranial hemorrhage and fatal bleeding were lower in patients without a history of stroke, regardless of treatment assignment.

Overall, the TRA 2°P-TIMI 50 study showed that the addition of vorapaxar significantly reduced the rate of cardiovascular death, MI, or stroke in patients with a history of atherothrombosis who were receiving standard therapy. However, patients receiving vorapaxar also experienced a significantly increased risk of moderate or severe bleeding,

Table 3 | Baseline characteristics of patients in the TRA 2°P-TIMI 50 and TRACER trials.[14,15]

	TRA 2°P-TIMI 50		TRACER	
Characteristic	**Placebo** (N=13,224)	**Vorapaxar** (N=13,225)	**Placebo** (N=6,471)	**Vorapaxar** (N=6,473)
Median (IQR) Age, years	61 (53-69)	61 (53-69)	64 (58-72)	64 (58-71)
Female sex (%)	24.0	23.8	28.2	28.0
White race (%)	87.2	87.5	85.4	28.0
Cardiovascular risk factors (%)				
Hypertension	69.0	68.4	71.0	70.1
Hyperlipidemia	83.3	83.1	62.2	62.4
Diabetes mellitus	25.4	25.5	31.4	31.5
Current tobacco use	20.8	20.8	27.6	27.0
Cardiovascular disease history (%)				
MI	67.2	67.3	29.2	29.4
PCI	*NR*	*NR*	23.7	24.1
CABG	*NR*	*NR*	11.8	12.0
Stroke	18.5	18.4	4.1	4.5
PAD	14.3	14.3	7.1	7.2
Use of antiplatelet drugs (%)				
Thienopyridine	62.3	62.0	87.1	87.6
ASA	93.5	93.5	96.9	96.4
≤100 mg	*NR*	*NR*	60.2	60.0
>100 mg	*NR*	*NR*	39.8	40.0
Dipyridamole	3.6	3.6	*NR*	*NR*

IQR = interquartile range; **MI** = myocardial infarction; **PCI** = percutaneous coronary intervention; **CABG** = coronary artery bypass graft; **PAD** = peripheral artery disease; **ASA** = aspirin; **NR** = not reported.

including intracranial hemorrhage; this increased risk of bleeding was particularly high in patients with a history of stroke.[14]

TRACER was a multinational, double-blind, placebo-controlled randomized trial that enrolled 12,944 patients who had ACS without ST-segment elevation.[15] Patients were eligible if they had acute symptoms of coronary ischemia within 24 hours before hospital presentation and at least one of the following: a cardiac troponin (I or T) or creatinine kinase MB (CK-MB) level that was higher than the upper limit of the normal range, a new ST-segment depression of more than 0.1 mV, or a transient ST-segment elevation (<30 minutes) of more than 0.1 mV in at least two contiguous leads. Patients were also required to have one or more of the following: age ≥55 years, previous MI, Percutaneous Coronary Intervention (PCI), Coronary Artery Bypass Graft (CABG) surgery, diabetes mellitus, or PAD.

Patients were randomly assigned to receive either a 40-mg loading dose of vorapaxar followed by vorapaxar 2.5 mg once daily or matching placebo. The primary efficacy end point was a composite of cardiovascular-related death, MI, stroke, recurrent ischemia with re-hospitalization, or UCR. The key secondary end point was a composite of cardiovascular-related death, MI, or stroke. The main safety end points were a composite of moderate or severe bleeding according to the GUSTO classification and clinically significant bleeding according to the TIMI classification, defined as TIMI major or minor bleeding or bleeding that required unplanned medical or surgical treatment or laboratory evaluation.

A safety review led to early termination of the study (by approximately 5 months) since the protocol-defined target number of efficacy endpoints had been reached. Additionally, vorapaxar treatment was discontinued early in patients with a history of stroke after evidence of harm was seen in a similar population in the TRA 2°P-TIMI 50 study. After a median follow-up of 502 days, the primary end point occurred in 16% of patients receiving vorapaxar and 17% patients receiving placebo, corresponding to a 2-year Kaplan-Meier rate of 18.5% in the vorapaxar group and 19.9% in the placebo group (HR 0.92; 95% CI 0.85 to 1.01).

The rate of GUSTO-rated moderate or severe bleeding was greater in vorapaxar-treated patients (6.1%) compared with placebo-treated patients (4.5%; HR 1.35; 95% CI 1.16 to 1.58). Additionally, an increased the rate of clinically significant TIMI bleeding was observed in vorapaxar-treated patients (20.2%) compared with placebo-treated patients (14.6%; HR 1.43; 95% CI 1.31 to 1.57). The vorapaxar group also had a higher prevalence of GUSTO-rated severe bleeding, TIMI major bleeding, and intracranial hemorrhage.

In summary, the results of the TRACER trial suggest that, in patients with ACS, the addition of vorapaxar to standard therapy did not significantly reduce the primary composite end point of composite of cardiovascular-related death, MI, stroke, recurrent ischemia with re-hospitalization, or UCR, but did significantly increase the risk of major bleeding, including intracranial hemorrhage.[15]

Adverse Events

Bleeding, including life-threatening and fatal bleeding, is the most commonly reported side effect associated with vorapaxar.[11] General risk factors for increased bleeding include older age, low body weight, reduced renal or hepatic function, history of bleeding disorders, and use of certain concomitant medications (e.g., anticoagulants, fibrinolytic therapy, chronic NSAIDs, SSRIs, SNRIs).[11] Rates of bleeding in patients without a history of stroke or TIA are shown in **Table 5**.

Bleeding should be suspected in patients who are hypotensive and have recently undergone coronary angiography, PCI, CABG, or other surgical procedures.[11] No known treat-

Table 4 | Summary of vorapaxar phase 3 clinical trials.[14,15]

Study	Treatment Arms	Primary Endpoints	Event Rates & HR[a] (95% CI)	Conclusions
TRA 2°P-TIMI 50[14]	• 2.5 mg vorapaxar once daily (n=13,225) • Placebo once daily (n=13,224)	Efficacy: Composite CV death, MI, and stroke at 3 years Safety: GUSTO moderate or severe bleeding at 3 years	Efficacy: • 9.3% (V) vs. 10.5% (P) • HR 0.87 (0.80 to 0.94) Safety: • 4.2% (V) vs. 2.5% (P) • HR 1.66 (1.43 to 1.93)	Vorapaxar reduced CV death, MI and stroke, but also increased bleeding
TRACER[15]	• 40-mg LD followed by vorapaxar 2.5 mg once daily (n=6471) • Placebo once daily (n=6473)	Efficacy: Composite of CV death, MI, stroke, recurrent ischemia with re-hospitalization, or UCR at 2 years Safety: GUSTO moderate or severe bleeding at 2 years	Efficacy: • 18.5% (V) vs. 19.9% (P) • HR 0.92 (0.85 to 1.01) Safety: • 6.1% (V) vs. 4.5% (P) • HR 1.35 (1.16 to 1.58)	Vorapaxar did not reduce CV death, MI, stroke, recurrent ischemia with re-hospitalization or UCR, but increased bleeding

GUSTO = Global Use of Strategies to Open Occluded Coronary Arteries; **CV =** cardiovascular; **MI** = myocardial infarction; **UCR** = urgent coronary revascularization; **LD =** loading dose; **V =** vorapaxar; **P =** placebo.
[a]Hazard Ratio comparing vorapaxar group vs. placebo group.

ment exists to reverse the antiplatelet effects of vorapaxar. Due to its long half-life, brief discontinuation of vorapaxar is ineffective for managing an acute bleeding event, as are dialysis and platelet transfusion. Further, no standard test is available to assess bleeding risk in an overdose situation.[11]

Other adverse reactions associated with the use of vorapaxar included anemia (5.0%), depression (2.4%), and rashes/eruptions/exanthemas (2.2%).[14,15]

Dosing

Vorapaxar is administered at a dose of 2.08 mg orally once daily with aspirin, clopidogrel, or both and may be taken with or without food.[11]

Cost

Vorapaxar is supplied as a yellow, oval-shaped 2.08 mg tablet. Pricing data for Zontivity® was obtained for a one month prescription from three community pharmacies located in Gainesville, FL, where the average monthly cost for 30 tablets was $328 (range, $318 to $334).

Summary

Vorapaxar is the first agent approved for secondary prevention of thrombotic cardiovascular events in patients with a history of MI or PAD that targets thrombin- dependent PAR-1. The recommended dosing of vorapaxar is 2.08 mg orally once daily, with or without food. No specific dose adjustments are needed based on age, race, gender, weight and the presence of mild or moderate renal insufficiency. Vorapaxar has not been studied for monotherapy, and thus should be used with concomitant aspirin, clopidogrel, or both, as appropriate.

Vorapaxar has been associated with a decreased rate of cardiovascular-related deaths, MI and stroke in patients with a history of IHD, taking background antiplatelet therapy. The benefits however, do not come without risks. Vorapaxar can significantly increase the risk of fatal bleeding, including intracranial hemorrhage, and its use is contraindicated in patients with active pathological bleeding or a history of stroke, TIA, or ICH. Vorapaxar is a viable option for the secondary prevention of atherothrombotic events, but must be used cautiously to avoid serious bleeding.

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Table 5 | Bleeding rates in the TRACER and TRA 2°P-TIMI 50 studies.[14,15]

	Endpoint	Vorapaxar (N=13,225)	Placebo (N=13,224)	Hazard Ratio (95% CI)
TRA 2°P-TIMI50[14]	GUSTO Moderate or Severe Bleeding	438 (4.2%)	267 (2.5%)	1.66 (1.43-1.93)
	Fatal Bleeding	29 (0.3%)	20 (0.2%)	1.46 (0.82-2.58)
	Intracranial Hemorrhage	102 (1.05)	53 (0.5%)	1.94 (1.39-2.70)
	TIMI Clinically Significant Bleeding	1,759 (15.8%)	1,241 (11.1%)	1.46 (1.36-1.57)
	Endpoint	**Vorapaxar (N=6,446)**	**Placebo (N=6,441)**	**Hazard Ratio (95% CI)**
TRACER[15]	GUSTO Moderate or Severe Bleeding	391 (6.1%)	290 (4.5%)	1.35 (1.16-1.58)
	Fatal Bleeding	15 (0.2)	8 (0.1%)	1.89 (0.80-4.45)
	Intracranial Hemorrhage	40 (0.6%)	12 (0.2%)	3.39 (1.78-6.45)
	TIMI Clinically Significant Bleeding	1065 (16.5%)	755 (11.7%)	1.43 (1.31-1.57)

IQR = interquartile range; **MI =** myocardial infarction; **PCI =** percutaneous coronary intervention; **CABG =** coronary artery bypass graft; **PAD =** peripheral artery disease; **ASA =** aspirin; **NR =** not reported.
Data represent n (%) or hazard ratio (95% CI).

PharmaNote® Throwback

Vol. 1, Issue 1, October 1, 1985

Oral Acyclovir (Zovirax®)

Mike Sever – 5th Year Pharmacy Student

Class: Antiviral agent.

Description: Oral Capsules containing 200 mg of acyclovir each.

Chemistry: 9-[(2-Hydroxyethoxy) methyl] guanine.

Mechanism of Action: Acyclovir is activated by viral enzymes to the acyclovirtriphosphate, which interferes with herpes-simplex virus "DNA-Polymerase". This Action inhibits viral DNA replication through DNA chain termination.[5]

Indications: Acyclovir is indicated for the treatment of initial episodes of herpes virus infection, and the management of recurrent episodes of genital herpes.[2] Acyclovir has also been shown to be effective verses Herpes zoster,[3,4] and is being studied in patients with Herpes encephalitis and other Herpes infections.

Pharmacokinetics: The bioavailability of oral acyclovir has been shown to be between 15 and 20%. Steady-state plasma levels are achieved in approximately two days. Acyclovir doses of 200 mg every 4 hours produced plasma levels of between 0.3 and 0.55 mcg/ml; and doses of 400 mg every 4 hours produced levels of 0.62 to 1.2 mcg/ml. Plasma half-life and total body clearance are dependent upon the status of the patient' renal function.

Efficacy: Oral acyclovir has been shown to be as effective as I.V. administered acyclovir in treating initial and recurrent genital herpes. Both formulations were effective in decreasing duration, healing time, and pain associated with initial and recurrent herpes infections. Oral acyclovir was also shown to be effective in reducing the number and duration of recurrent herpes episodes when used as prophylaxis.[1,3,4]

Dosage: For the initial, primary lesion, acyclovir is given at a rate of 200 mg every 4 hours. For prophylactic therapy, 400 mg every 12 hours or 200 mg every 8 hours is given for up to 6 months of therapy. For recurrent lesions that occur infrequently, (i.e. every two months), patient initiated therapy of 200 mg five times a day for 5 days is indicated. This therapy should be initiated at the onset of the infection, during the first symptoms of "prodrine".[5]

Pregnancy: Acyclovir is considered to be in pregnancy category C, not to be used in pregnant patients. Use of acyclovir in lactation and in children is not indicated at this time.

Cost: The cost of oral acyclovir (Zovirax®), is $63.80 per #100.

Interactions: Probenecid increased the half-life of acyclovir, decreasing its renal excretion.

Contraindications: Hypersensitivity or intolerance to acyclovir.

Adverse Drug Reactions: Short-term: Nausea/vomiting (2.7%); headache (0.6%); less common…diarrhea, dizziness, anorexia, edema, fatigue, rash, and leg pain. Long-term: (6 months of therapy): headache (13.1%); diarrhea (8.8%); nausea/vomiting (8.0%); vertigo (3.6%); less common…fatigue, fever, arthralgia.

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Personalized Medicine Corner

What is personalized medicine? How does it fit into my practice?

Personalized medicine uses an individual's genetic information to guide decisions about preventing, diagnosing, and treating disease. There are significant inter-individual variations in drug response and disease progression that affect the likelihood for therapeutic effect and the risk for adverse drug effects. Clinicians often need to take a "trial-and-error" approach to treatment, which may contribute to poor outcomes, adverse drug events, drug interactions, and poor medication adherence.[1]

Pharmacogenomics is one component of a personalized medicine approach that can help clinicians individualize drug therapy based on genetic variations to identify the most appropriate drug and dose for each patient. Prescribing information for 150 medications contains pharmacogenomic data, including drug exposure and response variability, risk for adverse events, genotype-specific dosing, and polymorphic drug targets.[2] Nearly 25% of outpatients are taking at least one of these drugs for the treatment of chronic conditions including depression, venous thromboembolism prophylaxis, pain management, and others.[3] Research and scientific advancements have reached a point where personalized treatment strategies based on genomic information and other factors are used clinically to guide drug selection and dosing. For example, many UF Health clinicians are using pharmacogenomic testing to identify polymorphisms in drug metabolizing enzymes that guide antiplatelet selection after coronary interventions or dosing of thiopurines for oncology and gastrointestinal disorders.

However, fitting pharmacogenomics into the everyday practice of medicine remains a challenge for most clinicians. Questions about what test to order, how to interpret test results, and insurance reimbursement often prevent clinicians from ordering a test.[4] Evidence is mounting, though, for the clinical benefits and utility of pharmacogenomic testing. These developments, along with efforts of patients, clinicians, and researchers alike, are breaking down the barriers that health care providers face in using

Want to know more about what clinicians are doing at UF Health? See our patient and clinician resources at www.personalizedmedicine.ufhealth.org.

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