Overview of Azole Metabolism and Drug Interactions

	Fluc	Itra	Posa	Vori	Isa
Inhibitor					
2C19	+++			++*	(+)
2C9	++	+		++	(+)
3A4	++	+++	+++	+++	++
Other	UGT +	p-gp +			UGT + p-gp +
Substrate					
2C19				+++*	
2C9				+++	
3A4		+++		+	+++
Other			UGT1A4 +		

**CYP 2C19 polymorphisms: 15-20% Asians, 3-5% of Caucasians, Blacks are poor metabolizers*

Select substrates of shared CYP pathways

- 34A substrates: amiodarone, tacrolimus, cyclosporine, prednisolone (the active metabolite of prednisone), sirolimus, many statins (e.g. atorvastatin, lovastatin, simvastatin), rifampin, rifabutin
- 3A4 inducer: rifampin, rifabutin
- 2C9 substrate: warfarin
- UGT substrate: mycophenolate
- UGT inducer: rifampin, rifabutin
- p-gp substrate: digoxin, rifampin

References:

1. Brüggemann, Roger JM, et al. "Clinical relevance of the pharmacokinetic interactions of azole antifungal drugs with other coadministered agents." Clinical Infectious Diseases 48.10 (2009): 1441-1458.
2. Groll, Andreas H., et al. "Pharmacokinetic assessment of drug-drug interactions of isavuconazole with the immunosuppressants cyclosporine, mycophenolic acid, prednisolone, sirolimus, and tacrolimus in healthy adults." Clinical pharmacology in drug development 6.1 (2017): 76-85.
3. Miceli, Marisa H., and Carol A. Kauffman. "Isavuconazole: a new broad-spectrum triazole antifungal agent." Clinical Infectious Diseases 61.10 (2015): 1558-1565.
4. Rybak, Jeffrey M., et al. "Isavuconazole: pharmacology, pharmacodynamics, and current clinical experience with a new triazole antifungal agent." Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy 35.11 (2015): 1037-1051.