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The Importance of Gene-Drug-Drug-Interactions in Pharmacogenomics Decision Support



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Pharmacogenomics (PGx) Decision Support



The intake of other prescription drugs can alter the activity of enzymes and transporters whose function PGx tests aim to predict!



Example: Prescription of Tramadol



PGx result: **CYP2D6 Ultrarapid metabolizer** PGx recommendation: **Reduce dose by 30%** Also receiving Fluoxetine: a **strong CYP2D6 inhibitor**

 \rightarrow **Dosage**??

Pharmacogenomic dosing guidelines consider only SINGLE gene-drug interactions!

How frequent are such problematic coprescriptions?

PGx drugs (= drugs for which dosing can be optimized based on PGx guidelines)



Drugs that **inhibit** or **induce** the activity of the respective enzymes or transporters

We screened Austrian claims data for concomitant prescriptions of 4,440 distinct interaction pairs.

55 PGx drugs across 7 genes

193 inhibitor / inducer drugs

GAP-DRG database operated by the Main Association of Austrian Social Security Institutions

1,587,829 Austrian insurance holders

393,476,104 prescriptions (years 2006 and 2007)



58.8% of our study population received at least one PGx drug

On average, **every 4th** patient who was treated with a PGx drug concomitantly received an inhibitor or inducer of the respective enzyme or transporter!

In half of the cases, co-prescriptions of *moderate* (47.3%) or *strong* (7.3%) inhibitors or inducers

How can gene-drug-drug interactions be addressed in PGx decision support?

Future perspective:

 Development and incoporation of more sophisticated dosing algorithms based on pharmacometric data

Interim solution:

 Use a minimum-set of highrelevance gene-drug-drug interaction to alert healthcare providers of potential interactions

	Required Patient Information
	Age: Sex: -Select- V Ethnicity: -Select- V
farin Dosing	Race: -Select-
ical Trial	Height: (feet andinches) or (cms)
<u>comes</u>	Smokes: -Select- ▼ Liver Disease: -Select- ▼
orrhage Risk	Indication: -Select- V Baseline INR: Target INR: Randomize & Blind
ient Education	Amiodarone/Cordarone® Dose: mg/day
tact Us	Statin/HMG CoA Reductase Inhibitor: Pravastatin/Pravachol® Any azole (eg. Fluconazole): Yes
erences	Sulfamethoxazole/Septra/Bactrim/Cotrim/Sulfatrim: No •
sarv	Genetic Information
ut lle	VKORC1-1639/3673: Not available/pending
ut Us	VKORC1-1639/3673: Not available/pending CYP4F2 V433M: Not available/pending
<u>ut Us</u>	VKORC1-1639/3673: Not available/pending CYP4F2 V433M: Not available/pending GGCX rs11676382: Not available/pending
ut Us nt: on 3.0	VKORC1-1639/3673: Not available/pending CYP4F2 V433M: Not available/pending GGCX rs11676382: Not available/pending CYP2C9*2: Not available/pending
ut Us nt: 	VKORC1-1639/3673: Not available/pending CYP4F2 V433M: Not available/pending GGCX rs11676382: Not available/pending CYP2C9*2: Not available/pending CYP2C9*3: Not available/pending
nt: on 3.0 ; May 14, 2016	VKORC1-1639/3673: Not available/pending CYP4F2 V433M: Not available/pending GGCX rs11676382: Not available/pending CYP2C9*2: Not available/pending CYP2C9*3: Not available/pending CYP2C9*5: Not available/pending
tt US n 3.0 : May 14, 2016	VKORC1-1639/3673: Not available/pending CYP4F2 V433M: Not available/pending GGCX rs11676382: Not available/pending CYP2C9*2: Not available/pending CYP2C9*3: Not available/pending CYP2C9*5: Not available/pending CYP2C9*5: Not available/pending CYP2C9*6: Not available/pending
ut US it: 1 May 14, 2016	VKORC1-1639/3673: Not available/pending CYP4F2 V433M: Not available/pending GGCX rs11676382: Not available/pending CYP2C9*2: Not available/pending CYP2C9*3: Not available/pending CYP2C9*5: Not available/pending CYP2C9*5: Not available/pending CYP2C9*5: Not available/pending CYP2C9*6: Not available/pending

www.WarfarinDosing.org

WARFARINDOSING

Gene-drug-drug interactions are not uncommon.

Addressing them in PGx decision support helps to increase medication safety!



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